Clinical trial results:
The Effect of LY2409021 on Blood Pressure and Pulse Rate, as Assessed by Ambulatory Blood Pressure Monitoring, in Subjects with Type 2 Diabetes Mellitus

Summary

EudraCT number	2013-003834-33
Trial protocol	CZ PL
Global end of trial date	20 January 2015

Results information

Result version number	v1 (current)
This version publication date	27 June 2018
First version publication date	27 June 2018

Trial information

Trial identification

Sponsor protocol code	I1R-MC-GLDI

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02091362
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 15261

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 January 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 January 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the trial is to determine the effect of a study drug known as LY2409021 on blood pressure and pulse rate in participants with type 2 diabetes mellitus (T2DM) when compared to placebo. The study has two periods. Each participant will receive LY2409021 or placebo in each period. At least 4 weeks will pass between periods. The study will last about 23 weeks for each participant. Participants may remain on stable dose metformin, as prescribed by their personal physician.

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: -

Evidence for comparator: -

Actual start date of recruitment	24 March 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	Czech Republic: 41
Country: Number of subjects enrolled	United States: 146
Country: Number of subjects enrolled	Poland: 36
Country: Number of subjects enrolled	Mexico: 47
Worldwide total number of subjects	270
EEA total number of subjects	77

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)	207
From 65 to 84 years	63
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	Period 1
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	LY2409021/Placebo

Arm description:

Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks;
Wash-out: 4 weeks;
Period 2: Single daily dose of placebo administered orally for 6 weeks.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single daily dose of placebo administered orally for 6 weeks.

Investigational medicinal product name	LY2409021
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks

Arm title	Placebo/LY2409021

Arm description:

Period 1: Single daily dose of placebo administered orally for 6 weeks;
Wash-out: 4 weeks;
Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

Number of subjects in period 1	LY2409021/Placebo	Placebo/LY2409021
Started	133	137
Completed	128	133
Not completed	5	4
Consent withdrawn by subject	2	3
Adverse event, non-fatal	2	-
Lost to follow-up	-	1
Protocol deviation	1	-

Period 2	
Period 2 title	Wash-out
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	LY2409021/Placebo

Arm description:

Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks;
Wash-out: 4 weeks;
Period 2: Single daily dose of placebo administered orally for 6 weeks.

Arm type	Experimental
Investigational medicinal product name	LY2409021
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

No drug administered during wash out period.

Arm title	Placebo/LY2409021

Arm description:

Period 1: Single daily dose of placebo administered orally for 6 weeks;
Wash-out: 4 weeks;
Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

Arm type	Experimental
Investigational medicinal product name	LY2409021
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single daily dose of placebo administered orally for 6 weeks.

Number of subjects in period 2	LY2409021/Placebo	Placebo/LY2409021
Started	128	133
Completed	127	130
Not completed	1	3
Consent withdrawn by subject	-	2
Lost to follow-up	1	1

Period 3

Period 3 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	LY2409021/Placebo

Arm description:

Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks;
Wash-out: 4 weeks;
Period 2: Single daily dose of placebo administered orally for 6 weeks.

Arm type	Experimental
Investigational medicinal product name	LY2409021
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks

Arm title	Placebo/LY2409021

Arm description:

Period 1: Single daily dose of placebo administered orally for 6 weeks;
Wash-out: 4 weeks;
Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

Investigational medicinal product name	LY2409021
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks

Number of subjects in period 3	LY2409021/Placebo	Placebo/LY2409021
Started	127	130
Completed	125	128
Not completed	2	2
Consent withdrawn by subject	1	1
Adverse event, non-fatal	1	-
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	LY2409021/Placebo
Reporting group description:	
Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks; Wash-out: 4 weeks; Period 2: Single daily dose of placebo administered orally for 6 weeks.	
Reporting group title	Placebo/LY2409021
Reporting group description:	
Period 1: Single daily dose of placebo administered orally for 6 weeks; Wash-out: 4 weeks; Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.	

Reporting group values	LY2409021/Placebo	Placebo/LY2409021	Total
Number of subjects	133	137	270
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	58.3	57.2	
standard deviation	± 8.9	± 8.9	-
Gender, Male/Female Units: Participants			
Female	57	60	117
Male	76	77	153
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	63	62	125
Not Hispanic or Latino	61	69	130
Unknown or Not Reported	9	6	15
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	20	22	42
Asian	2	3	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	12	23	35
White	92	87	179
More than one race	7	2	9

Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Czech Republic	19	22	41
United States	72	74	146
Poland	18	18	36
Mexico	24	23	47
Diagnosis of Hypertension Units: Subjects			
Yes	89	93	182
No	44	44	88
HBA1c Categories Units: Subjects			
≥ 7.5 %	49	51	100
< 7.5%	84	86	170

End points

End points reporting groups

Reporting group title	LY2409021/Placebo

Reporting group description:

Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks;
Wash-out: 4 weeks;
Period 2: Single daily dose of placebo administered orally for 6 weeks.

Reporting group title	Placebo/LY2409021

Reporting group description:

Period 1: Single daily dose of placebo administered orally for 6 weeks;
Wash-out: 4 weeks;
Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

Reporting group title	LY2409021/Placebo

Reporting group description:

Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks;
Wash-out: 4 weeks;
Period 2: Single daily dose of placebo administered orally for 6 weeks.

Reporting group title	Placebo/LY2409021

Reporting group description:

Period 1: Single daily dose of placebo administered orally for 6 weeks;
Wash-out: 4 weeks;
Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

Reporting group title	LY2409021/Placebo

Reporting group description:

Period 1: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks;
Wash-out: 4 weeks;
Period 2: Single daily dose of placebo administered orally for 6 weeks.

Reporting group title	Placebo/LY2409021

Reporting group description:

Period 1: Single daily dose of placebo administered orally for 6 weeks;
Wash-out: 4 weeks;
Period 2: Single daily dose of 20 milligrams (mg) LY2409021 administered orally for 6 weeks.

Subject analysis set title	LY2409021 20 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Single daily dose of 20 milligrams (mg) LY2409021 administered orally in 1 of 2 treatment periods

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Single daily dose of placebo matching LY2409021 administered orally in 1 of 2 treatment periods

Subject analysis set title	Population PK
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Modified intent-to-treat (mITT) population consisting of all randomized subjects who received at least one dose of study drug and had at least one measureable drug concentration..

Primary: Change from Baseline to 6 Weeks in Mean 24-Hour Systolic Blood Pressure

End point title	Change from Baseline to 6 Weeks in Mean 24-Hour Systolic Blood Pressure

End point description:

Systolic blood pressure obtained from Ambulatory Blood Pressure Monitoring (ABPM).

Analysis Population Description: Randomized participants who received at least 1 dose of study drug and had an ABPM reading, only subjects with non-missing baseline value and at least one non-missing post-baseline value of the response variable were included in analysis.

End point type	Primary
End point timeframe:	
Baseline, 6 Weeks	

End point values	LY2409021 20 mg	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	241[1]	239[2]		
Units: mmHg				
least squares mean (confidence interval 95%)	2.79 (1.62 to 3.95)	0.53 (-0.70 to 1.76)		

Notes:

[1] - See Description.

[2] - See description.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	LY2409021 20 mg v Placebo
Number of subjects included in analysis	480
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis

Secondary: Change from Baseline to 6 Weeks in Mean 24-Hour Diastolic Blood Pressure

End point title	Change from Baseline to 6 Weeks in Mean 24-Hour Diastolic Blood Pressure

End point description:

Diastolic blood pressure obtained from Ambulatory Blood Pressure Monitoring (ABPM). LS Mean of treatment differences, adjusted for country, diagnosis of hypertension, sequence, treatment, period, time within period, treatment by time within period interaction, and the baseline measurement as covariate.

Analysis Population Description: Randomized participants who received at least 1 dose of study drug and had an ABPM reading, only subjects with non-missing baseline value and at least one non-missing post-baseline value of the response variable were included in analysis.

End point type	Secondary
End point timeframe:	
Baseline, 6 Weeks	

End point values	LY2409021 20 mg	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	241[3]	239[4]		
Units: mmHg				
least squares mean (confidence interval 95%)	1.37 (0.61 to 2.14)	0.00 (-0.76 to 0.77)		

Notes:

[3] - See description.

[4] - See description.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to 6 Weeks in Mean 24-Hour, Daytime, and Nighttime Peripheral Pulse Rate

End point title	Change from Baseline to 6 Weeks in Mean 24-Hour, Daytime, and Nighttime Peripheral Pulse Rate

End point description:

Pulse rate obtained from Ambulatory Blood Pressure Monitoring (ABPM). LS Mean of treatment differences, adjusted for country, diagnosis of hypertension, sequence, treatment, period, time within period, treatment by time within period interaction, and the baseline measurement as covariate.

End point type	Secondary

End point timeframe:

Baseline, 6 Weeks

End point values	LY2409021 20 mg	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	241[5]	239[6]		
Units: beats/minute				
least squares mean (confidence interval 95%)				
24 Hour Pulse Rate	0.46 (-0.46 to 1.37)	0.43 (-0.53 to 1.40)		
Mean Daytime Pulse Rate	0.74 (-0.26 to 1.75)	0.56 (-0.48 to 1.61)		
Mean Nighttime Pulse Rate	-0.39 (-1.35 to 0.57)	-0.04 (-1.03 to 0.96)		

Notes:

[5] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

[6] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to 6 Weeks in Mean 24-Hour, Daytime, and Nighttime Pulse Pressures

End point title	Change from Baseline to 6 Weeks in Mean 24-Hour, Daytime, and Nighttime Pulse Pressures

End point description:

Pulse Pressures obtained from Ambulatory Blood Pressure Monitoring (ABPM). LS Mean of treatment differences, adjusted for country, diagnosis of hypertension, sequence, treatment, period, time within period, treatment by time within period interaction, and the baseline measurement as covariate.

End point type	Secondary

End point timeframe:

Baseline, 6 Weeks

End point values	LY2409021 20 mg	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	241[7]	239[8]		
Units: mmHg				
least squares mean (confidence interval 95%)				
24-Hour Pulse Pressure	1.51 (0.76 to 2.25)	0.62 (-0.13 to 1.38)		
Daytime Pulse Pressure	1.49 (0.68 to 2.29)	0.54 (-0.29 to 1.38)		
Nighttime Pulse Pressure	1.51 (0.69 to 2.32)	0.80 (0.00 to 1.60)		

Notes:

[7] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

[8] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to 6 Weeks in Mean 24-Hour, Daytime, and Nighttime Mean Arterial Pressures (MAP)

End point title	Change from Baseline to 6 Weeks in Mean 24-Hour, Daytime, and Nighttime Mean Arterial Pressures (MAP)

End point description:

Mean Arterial Pressures obtained from Ambulatory Blood Pressure Monitoring (ABPM). LS Mean of treatment differences, adjusted for country, diagnosis of hypertension, sequence, treatment, period, time within period, treatment by time within period interaction, and the baseline measurement as covariate.

End point type	Secondary

End point timeframe:

Baseline, 6 Weeks

End point values	LY2409021 20 mg	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	241[9]	239[10]		
Units: mmHg				
least squares mean (confidence interval 95%)				
24 Hour MAP	1.83 (0.99 to 2.68)	0.17 (-0.17 to 1.04)		

Daytime MAP	2.04 (1.14 to 2.94)	0.08 (-0.86 to 1.03)		
Nighttime MAP	1.31 (0.33 to 2.29)	0.33 (-0.68 to 1.33)		

Notes:

[9] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

[10] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hemoglobin A1c (HbA1c)

End point title	Change from Baseline in Hemoglobin A1c (HbA1c)

End point description:

LS Mean of treatment differences, adjusted for country, diagnosis of hypertension, sequence, treatment, period, time within period, treatment by time within period interaction, and the baseline measurement as covariate.

End point type	Secondary

End point timeframe:

Baseline, 6 Weeks

End point values	LY2409021 20 mg	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	241[11]	239[12]		
Units: percentage of HbA1c				
least squares mean (confidence interval 95%)	-0.65 (-0.72 to -0.58)	-0.16 (-0.23 to -0.08)		

Notes:

[11] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

[12] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Population Pharmacokinetics: Apparent Clearance of LY2409021

End point title	Population Pharmacokinetics: Apparent Clearance of LY2409021

End point description:

Population pharmacokinetic parameter apparent clearance (CL/F) is the apparent volume of the body fluid cleared of the drug per unit of time and was estimated by modeling of LY2409021 plasma concentration data from all LY2409021 groups.

Analysis Population Description (APD)All randomized participants who received at least 1 one dose of study drug and had at least one measureable drug concentration.

End point type	Secondary

End point timeframe:

Days 7, 21, 42, 70, 77, 91, 112, 140; 15 minute Predose and Days 7 and 77: 1 hour Postdose.

End point values	Population PK			
Subject group type	Subject analysis set			
Number of subjects analysed	249[13]			
Units: Liter per hour (L/hr)				
geometric mean (geometric coefficient of variation)	0.406 (± 30.7)			

Notes:

[13] - See Description.

Statistical analyses

No statistical analyses for this end point

Secondary: Population Pharmacokinetics: Apparent Volume of Distribution of LY2409021

End point title	Population Pharmacokinetics: Apparent Volume of Distribution of LY2409021

End point description:

Population pharmacokinetic parameter, apparent volume of distribution (V/F) is a theoretical volume that a drug would have to occupy (if it were uniformly distributed), to provide the same concentration as it currently is in blood plasma. Apparent volume of distribution (V/F) was estimated by modeling of LY2409021 plasma concentration data from all LY2409021 groups.

Analysis Population Description (APD): All randomized patients who received at least 1 one dose of study drug and had at least one measurable drug concentration.

End point type	Secondary

End point timeframe:

Days 7, 21, 42, 70, 77, 91, 112, 140; Predose and Days 7 and 77: 1 hour Postdose.

End point values	Population PK			
Subject group type	Subject analysis set			
Number of subjects analysed	249[14]			
Units: Liters				
geometric mean (geometric coefficient of variation)	36.7 (± 23.2)			

Notes:

[14] - See Description.

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:	
All randomized participants who received at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	LY2409021 20 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Wash-out
Reporting group description: -	
Reporting group title	Follow-up
Reporting group description: -	

Serious adverse events	LY2409021 20 mg	Placebo	Wash-out
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 258 (1.55%)	2 / 256 (0.78%)	2 / 249 (0.80%)
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)			
breast cancer			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 258 (0.39%)	0 / 256 (0.00%)	0 / 249 (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
plasma cell myeloma			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 258 (0.00%)	0 / 256 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
liver function test abnormal			

alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 258 (0.39%)	0 / 256 (0.00%)	0 / 249 (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
Injury, poisoning and procedural complications			
forearm fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 258 (0.00%)	1 / 256 (0.39%)	0 / 249 (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
lower limb fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 258 (0.00%)	1 / 256 (0.39%)	0 / 249 (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
road traffic accident			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 258 (0.00%)	1 / 256 (0.39%)	0 / 249 (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
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 258 (0.39%)	0 / 256 (0.00%)	0 / 249 (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
Cardiac disorders			
cardiac failure congestive			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 258 (0.00%)	1 / 256 (0.39%)	0 / 249 (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
Nervous system disorders			

cerebrovascular accident			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 258 (0.39%)	0 / 256 (0.00%)	0 / 249 (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
Blood and lymphatic system disorders			
febrile neutropenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 258 (0.00%)	0 / 256 (0.00%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
epistaxis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 258 (0.39%)	0 / 256 (0.00%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary hypertension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 258 (0.00%)	0 / 256 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
pathological fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 258 (0.00%)	0 / 256 (0.00%)	1 / 249 (0.40%)
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			
diverticulitis			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 258 (0.00%)	0 / 256 (0.00%)	0 / 249 (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

Serious adverse events	Follow-up		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 253 (1.58%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
breast cancer			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
plasma cell myeloma			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
liver function test abnormal			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
forearm fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
lower limb fracture			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
road traffic accident			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
cardiac failure congestive			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
cerebrovascular accident			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
febrile neutropenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
epistaxis			

alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
pulmonary hypertension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
pathological fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
diverticulitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	LY2409021 20 mg	Placebo	Wash-out
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 258 (18.99%)	32 / 256 (12.50%)	25 / 249 (10.04%)
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	12 / 258 (4.65%)	1 / 256 (0.39%)	4 / 249 (1.61%)
occurrences (all)	12	1	4
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	6 / 258 (2.33%)	2 / 256 (0.78%)	2 / 249 (0.80%)
occurrences (all)	6	2	2
blood pressure diastolic increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 258 (1.16%)	3 / 256 (1.17%)	2 / 249 (0.80%)
occurrences (all)	3	3	2
heart rate decreased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 258 (1.16%)	2 / 256 (0.78%)	0 / 249 (0.00%)
occurrences (all)	4	3	0
heart rate increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 258 (1.55%)	3 / 256 (1.17%)	1 / 249 (0.40%)
occurrences (all)	6	3	1
hepatic enzyme increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 258 (1.16%)	1 / 256 (0.39%)	2 / 249 (0.80%)
occurrences (all)	3	1	2
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 258 (0.78%)	3 / 256 (1.17%)	2 / 249 (0.80%)
occurrences (all)	2	3	2
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 258 (1.16%)	1 / 256 (0.39%)	1 / 249 (0.40%)
occurrences (all)	4	1	1
headache			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 258 (1.55%)	4 / 256 (1.56%)	2 / 249 (0.80%)
occurrences (all)	5	4	3
General disorders and administration site conditions			

fatigue			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 258 (0.78%)	4 / 256 (1.56%)	2 / 249 (0.80%)
occurrences (all)	2	4	2
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 258 (1.16%)	0 / 256 (0.00%)	0 / 249 (0.00%)
occurrences (all)	4	0	0
diarrhoea			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	6 / 258 (2.33%)	3 / 256 (1.17%)	3 / 249 (1.20%)
occurrences (all)	6	3	3
dyspepsia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 258 (1.16%)	0 / 256 (0.00%)	0 / 249 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal and connective tissue disorders			
muscle spasms			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 258 (1.16%)	1 / 256 (0.39%)	2 / 249 (0.80%)
occurrences (all)	3	1	2
pain in extremity			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	6 / 258 (2.33%)	3 / 256 (1.17%)	3 / 249 (1.20%)
occurrences (all)	6	3	5
Infections and infestations			
influenza			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 258 (1.55%)	1 / 256 (0.39%)	0 / 249 (0.00%)
occurrences (all)	4	1	0
nasopharyngitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 258 (0.78%)	3 / 256 (1.17%)	3 / 249 (1.20%)
occurrences (all)	2	3	3

Non-serious adverse events	Follow-up		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 253 (11.86%)		
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	7 / 253 (2.77%)		
occurrences (all)	7		
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 253 (1.19%)		
occurrences (all)	3		
blood pressure diastolic increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 253 (0.79%)		
occurrences (all)	2		
heart rate decreased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences (all)	0		
heart rate increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences (all)	1		
hepatic enzyme increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences (all)	1		
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	5 / 253 (1.98%)		
occurrences (all)	5		
Nervous system disorders			

dizziness alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	 1 / 253 (0.40%) 1		
headache alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	 3 / 253 (1.19%) 5		
General disorders and administration site conditions fatigue alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	 2 / 253 (0.79%) 2		
Gastrointestinal disorders abdominal discomfort alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	 0 / 253 (0.00%) 0		
diarrhoea alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	 0 / 253 (0.00%) 0		
dyspepsia alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	 1 / 253 (0.40%) 1		
Musculoskeletal and connective tissue disorders muscle spasms alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	 0 / 253 (0.00%) 0		
pain in extremity alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	3 / 253 (1.19%)		
occurrences (all)	3		
Infections and infestations			
influenza			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 253 (0.79%)		
occurrences (all)	2		
nasopharyngitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 253 (1.19%)		
occurrences (all)	3		

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