Clinical trial results:
A Phase 2 Efficacy and Safety Dose-Ranging Study of LY3015014 in Patients with Primary Hypercholesterolemia

Summary

EudraCT number	2013-000622-55
Trial protocol	CZ NL PL DK
Global end of trial date	06 June 2014

Results information

Result version number	v1 (current)
This version publication date	10 June 2017
First version publication date	10 June 2017

Trial information

Trial identification

Sponsor protocol code	I5S-MC-EFJE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01890967
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 14853

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	06 June 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study is designed to define the amount and duration of cholesterol lowering and to assess the safety and tolerability of different dose regimens of LY3015014 in participants with high cholesterol. The study will also investigate how the body processes the drug and how the drug affects the body. Participants will remain on a stable diet and will continue taking cholesterol-lowering medications (statins with or without ezetimibe). After signing the informed consent document, the participant will complete a screening/run-in period that will last at most 8 weeks. Then, the treatment period will last approximately 16 weeks. After the treatment period, the participants will complete a follow-up period lasting approximately 8 weeks for a total study duration ranging from approximately 25 to 32 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:

The study enrolled patients on a stable dose of standard of care (SOC) statin therapy (atorvastatin, simvastatin, rosuvastatin, pravastatin, lovastatin, fluvastatin, or pitavastatin, as approved per country regulations). In addition, a subset of patients who were intolerant of any dose of at least 1 statin was enrolled. Study patients could also be on a stable dose of ezetimibe (as approved per country regulations).

Evidence for comparator: -

Actual start date of recruitment	27 June 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 94
Country: Number of subjects enrolled	Netherlands: 88
Country: Number of subjects enrolled	Czech Republic: 23
Country: Number of subjects enrolled	Puerto Rico: 5
Country: Number of subjects enrolled	United States: 143
Country: Number of subjects enrolled	Japan: 106
Country: Number of subjects enrolled	Denmark: 29
Country: Number of subjects enrolled	Poland: 31
Worldwide total number of subjects	519
EEA total number of subjects	171

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)	373
From 65 to 84 years	146
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

No Text Entered

Period 1

Period 1 title	Randomized
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Q4W

Arm description:

Placebo given subcutaneously (SC) once every 4 weeks (Q4W) for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

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 given subcutaneously (SC) once every 4 weeks (Q4W) for 16 weeks.

Arm title	20 mg LY3015014 Q4W

Arm description:

20 milligrams (mg) LY3015014 given SC Q4W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Arm type	Experimental
Investigational medicinal product name	LY3015014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

20 mg LY3015014 given SC Q4W for 16 weeks.

Arm title	120 mg LY3015014 Q4W

Arm description:

120 mg LY3015014 given SC Q4W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Arm type	Experimental

Investigational medicinal product name	LY3015014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

120 mg LY3015014 given SC every Q4W for 16 weeks.

Arm title	300 mg LY3015014 Q4W

Arm description:

300 mg LY3015014 given SC Q4W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Arm type	Experimental
Investigational medicinal product name	LY3015014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg LY3015014 given SC Q4W for 16 weeks.

Arm title	100 mg LY3015014 Q8W

Arm description:

100 mg LY3015014 given SC once every 8 weeks (Q8W) for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Arm type	Experimental
Investigational medicinal product name	LY3015014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

100 mg LY3015014 given SC every 8 weeks (Q8W) for 16 weeks.

Arm title	300 mg LY3015014 Q8W

Arm description:

300 mg LY3015014 given SC Q8W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Arm type	Experimental
Investigational medicinal product name	LY3015014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg LY3015014 given SC Q8W for 16 weeks.

Number of subjects in period 1	Placebo Q4W	20 mg LY3015014 Q4W	120 mg LY3015014 Q4W
Started	88	88	88
Completed	87	87	86
Not completed	1	1	2
Consent withdrawn by subject	1	-	-
Met exclusion criteria	-	1	2

Number of subjects in period 1	300 mg LY3015014 Q4W	100 mg LY3015014 Q8W	300 mg LY3015014 Q8W
Started	88	87	88
Completed	86	86	87
Not completed	2	1	1
Consent withdrawn by subject	-	-	-
Met exclusion criteria	2	1	1

Period 2

Period 2 title	Treated
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Q4W

Arm description:

Placebo given subcutaneously (SC) once every 4 weeks (Q4W) for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

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 given subcutaneously (SC) once every 4 weeks (Q4W) for 16 weeks.

Arm title	20 mg LY3015014 Q4W

Arm description:

20 milligrams (mg) LY3015014 given SC Q4W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Arm type	Experimental

Investigational medicinal product name	LY3015014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

20 mg LY3015014 given SC Q4W for 16 weeks.

Arm title	120 mg LY3015014 Q4W

Arm description:

120 mg LY3015014 given SC Q4W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Arm type	Experimental
Investigational medicinal product name	LY3015014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

120 mg LY3015014 given SC every Q4W for 16 weeks.

Arm title	300 mg LY3015014 Q4W

Arm description:

300 mg LY3015014 given SC Q4W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Arm type	Experimental
Investigational medicinal product name	LY3015014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg LY3015014 given SC Q4W for 16 weeks.

Arm title	100 mg LY3015014 Q8W

Arm description:

100 mg LY3015014 given SC once every 8 weeks (Q8W) for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Arm type	Experimental
Investigational medicinal product name	LY3015014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

100 mg LY3015014 given SC every 8 weeks (Q8W) for 16 weeks.

Arm title	300 mg LY3015014 Q8W

Arm description:

300 mg LY3015014 given SC Q8W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Arm type	Experimental
Investigational medicinal product name	LY3015014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg LY3015014 given SC Q8W for 16 weeks.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Participants in Period 1 (Randomization Phase) were randomly assigned to a dose dependent treatment arm; a total of 527 participants were randomized. Of the 527 randomized participants, 8 participants did not receive study drug. The 519 participants who actually received at least one dose of study drug in Period 2 (Treatment Phase) were included in the safety population, therefore Period 2 was used for the baseline period.

Number of subjects in period 2	Placebo Q4W	20 mg LY3015014 Q4W	120 mg LY3015014 Q4W
Started	87	87	86
Recieved at least one dose of study drug	87	87	86
Completed	79	79	80
Not completed	8	8	6
Consent withdrawn by subject	2	3	-
Adverse event, non-fatal	3	2	4
Not specified	2	1	1
Protocol Violation	1	2	1

Number of subjects in period 2	300 mg LY3015014 Q4W	100 mg LY3015014 Q8W	300 mg LY3015014 Q8W
Started	86	86	87
Recieved at least one dose of study drug	86	86	87
Completed	78	76	75
Not completed	8	10	12
Consent withdrawn by subject	3	2	-
Adverse event, non-fatal	2	1	7
Not specified	1	4	5
Protocol Violation	2	3	-

Baseline characteristics

Reporting groups	
Reporting group title	Treated

Reporting group description: -

Reporting group values	Treated	Total	
Number of subjects	519	519	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	373	373	
From 65-84 years	146	146	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	58.4		
standard deviation	± 10.2	-	
Gender, Male/Female Units:			
Male	241	241	
Female	278	278	
Region of Enrollment Units: Subjects			
Canada	94	94	
Netherlands	88	88	
Czech Republic	23	23	
Puerto Rico	5	5	
United States	143	143	
Japan	106	106	
Denmark	29	29	
Poland	31	31	

End points

End points reporting groups

Reporting group title	Placebo Q4W

Reporting group description:

Placebo given subcutaneously (SC) once every 4 weeks (Q4W) for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Reporting group title	20 mg LY3015014 Q4W

Reporting group description:

20 milligrams (mg) LY3015014 given SC Q4W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Reporting group title	120 mg LY3015014 Q4W

Reporting group description:

120 mg LY3015014 given SC Q4W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Reporting group title	300 mg LY3015014 Q4W

Reporting group description:

300 mg LY3015014 given SC Q4W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Reporting group title	100 mg LY3015014 Q8W

Reporting group description:

100 mg LY3015014 given SC once every 8 weeks (Q8W) for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Reporting group title	300 mg LY3015014 Q8W

Reporting group description:

300 mg LY3015014 given SC Q8W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Reporting group title	Placebo Q4W

Reporting group description:

Placebo given subcutaneously (SC) once every 4 weeks (Q4W) for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Reporting group title	20 mg LY3015014 Q4W

Reporting group description:

20 milligrams (mg) LY3015014 given SC Q4W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Reporting group title	120 mg LY3015014 Q4W

Reporting group description:

120 mg LY3015014 given SC Q4W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Reporting group title	300 mg LY3015014 Q4W

Reporting group description:

300 mg LY3015014 given SC Q4W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Reporting group title	100 mg LY3015014 Q8W

Reporting group description:

100 mg LY3015014 given SC once every 8 weeks (Q8W) for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Reporting group title	300 mg LY3015014 Q8W

Reporting group description:

300 mg LY3015014 given SC Q8W for 16 weeks.

Participants will remain on stable diet and physician-prescribed statin therapy, if tolerated, with or without ezetimibe.

Primary: Percentage Change from Baseline in Low-Density Lipoprotein Cholesterol (LDL-C)

End point title	Percentage Change from Baseline in Low-Density Lipoprotein Cholesterol (LDL-C)

End point description:

Least square (LS) Means was calculated using analysis of covariance (ANCOVA) adjusted for disease classification, statin dose, baseline LDL-C measurement. Percent change from baseline response is the dependent variable.

The Analysis Population Description for the Modified-Intent-To-Treat population (mITT) is defined as all participants in the Intent-To-Treat (ITT) population who had at least one baseline measurement and one post-randomization measurement of the variable that is analyzed.

End point type	Primary

End point timeframe:

Baseline, Week 16

End point values	Placebo Q4W	20 mg LY3015014 Q4W	120 mg LY3015014 Q4W	300 mg LY3015014 Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79[1]	73[2]	78[3]	76[4]
Units: Percentage change				
least squares mean (standard error)	7.6 (± 2.27)	-14.9 (± 2.39)	-40.5 (± 2.31)	-50.5 (± 2.3)

Notes:

[1] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

[2] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

[3] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

[4] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

End point values	100 mg LY3015014 Q8W	300 mg LY3015014 Q8W		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73[5]	73[6]		
Units: Percentage change				
least squares mean (standard error)	-14.9 (± 2.35)	-37.1 (± 2.44)		

Notes:

[5] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[6] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

Statistical analyses

Statistical analysis title	20mg LY3015914 Q4W versus Placebo Q4W
Comparison groups	Placebo Q4W v 20 mg LY3015014 Q4W
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-22.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.5
upper limit	-16.6
Variability estimate	Standard error of the mean
Dispersion value	3.02

Statistical analysis title	120mg LY3015014 Q4W versus Placebo Q4W
Comparison groups	Placebo Q4W v 120 mg LY3015014 Q4W
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-48.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54
upper limit	-42.3
Variability estimate	Standard error of the mean
Dispersion value	2.98

Statistical analysis title	LY3015014 300mg Q4W versus Placebo Q4W
Comparison groups	Placebo Q4W v 300 mg LY3015014 Q4W

Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-58.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-64.1
upper limit	-52.3
Variability estimate	Standard error of the mean
Dispersion value	3

Statistical analysis title	LY3015014 100mg Q8W versus Placebo Q4W
Comparison groups	100 mg LY3015014 Q8W v Placebo Q4W
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-22.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.5
upper limit	-16.5
Variability estimate	Standard error of the mean
Dispersion value	3.03

Statistical analysis title	LY3015014 300mg Q8W versus Placebo Q4W
Comparison groups	Placebo Q4W v 300 mg LY3015014 Q8W
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-44.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.7
upper limit	-38.8

Variability estimate	Standard error of the mean
Dispersion value	3.04

Secondary: Percentage Change from Baseline in Apolipoprotein A1 (Apo A1), Apolipoprotein B (Apo B)

End point title	Percentage Change from Baseline in Apolipoprotein A1 (Apo A1), Apolipoprotein B (Apo B)

End point description:

LS Mean was calculated using MMRM analysis with baseline measurement, disease classification, statin dose, treatment, visit, and treatment by visit interaction included in the model. Percent change from baseline response is the dependent variable.

The mITT is defined as all participants in the ITT population who had at least one baseline measurement and one post-randomization measurement of the variable that is analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo Q4W	20 mg LY3015014 Q4W	120 mg LY3015014 Q4W	300 mg LY3015014 Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78[7]	77[8]	78[9]	78[10]
Units: Percentage change				
least squares mean (standard error)				
Apolipoprotein A1	0.3 (± 1.4)	2.4 (± 1.43)	6.5 (± 1.41)	6.2 (± 1.41)
Apolipoprotein B	4.2 (± 2.23)	-16.6 (± 2.32)	-34.9 (± 2.28)	-46.8 (± 2.25)

Notes:

[7] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement .

[8] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

[9] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

[10] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

End point values	100 mg LY3015014 Q8W	300 mg LY3015014 Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75[11]	73[12]		
Units: Percentage change				
least squares mean (standard error)				
Apolipoprotein A1	3.8 (± 1.43)	5.8 (± 1.44)		
Apolipoprotein B	-16 (± 2.25)	-31.9 (± 2.31)		

Notes:

[11] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

[12] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline in LDL-C, Total Cholesterol (TC), High-Density Lipoprotein Cholesterol (HDL-C), Triglycerides (TG), Non-HDL-C

End point title	Percentage Change from Baseline in LDL-C, Total Cholesterol (TC), High-Density Lipoprotein Cholesterol (HDL-C), Triglycerides (TG), Non-HDL-C

End point description:

LS Mean was calculated using mixed model repeated measures (MMRM) analysis with baseline measurement, disease classification, statin dose, treatment, visit, and treatment by visit interaction included in the model. Percent change from baseline response is the dependent variable.

The mITT population is defined as all participants in the ITT population who had one baseline measurement and one post-randomization measurement of the variable that is analyzed. N for Reporting Groups 1,2,3,4,5,6 are as follows: LDL-C (n=78,77,78,78,77,73), TG (n=78,78,80,79,76,74), TC (n=78,78,80,79,76,74), HDL-C (n=78,78,80,79,76,74), Non-HDL-C (n=78,78,80,79,76,74), respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo Q4W	20 mg LY3015014 Q4W	120 mg LY3015014 Q4W	300 mg LY3015014 Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[13]	86[14]	86[15]	85[16]
Units: Percentage change				
least squares mean (standard error)				
LDL-C	5.9 (± 2.13)	-18 (± 2.18)	-46.4 (± 2.15)	-56.5 (± 2.14)
TG	3.5 (± 3.26)	-6.1 (± 3.35)	-7.2 (± 3.25)	-15.1 (± 3.26)
TC	3.5 (± 1.44)	-10.5 (± 1.47)	-27.8 (± 1.44)	-34.1 (± 1.44)
HDL-C	1.6 (± 1.58)	4.5 (± 1.6)	7.3 (± 1.57)	8.8 (± 1.58)
Non-HDL-C	4.9 (± 1.83)	-16.1 (± 1.86)	-39.3 (± 1.83)	-48.9 (± 1.83)

Notes:

[13] - All randomized participants who took at least 1 dose of double-blind study medication.

[14] - All randomized participants who took at least 1 dose of double-blind study medication.

[15] - All randomized participants who took at least 1 dose of double-blind study medication.

[16] - All randomized participants who took at least 1 dose of double-blind study medication.

End point values	100 mg LY3015014 Q8W	300 mg LY3015014 Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86[17]	87[18]		
Units: Percentage change				
least squares mean (standard error)				
LDL-C	-18.4 (± 2.14)	-42.2 (± 2.21)		
TG	-7.2 (± 3.29)	-10.6 (± 3.35)		
TC	-11 (± 1.45)	-24.6 (± 1.48)		
HDL-C	4.5 (± 1.59)	8.4 (± 1.61)		
Non-HDL-C	-16.1 (± 1.84)	-35.8 (± 1.88)		

Notes:

[17] - All randomized participants who took at least 1 dose of double-blind study medication.

[18] - All randomized participants who took at least 1 dose of double-blind study medication.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Lipoprotein(a) [Lp(a)]

End point title	Percentage Change From Baseline in Lipoprotein(a) [Lp(a)]

End point description:

Data was log-transformed for MMRM analysis, with change from baseline as the dependent variable, and baseline measurement, disease classification, statin dose, treatment, visit, and treatment by visit interaction included as independent variables. Percentage change from baseline in the original scale was then back-calculated from the log-transformed MMRM analysis.

The mITT is defined as all participants in the ITT population who had at least one baseline measurement and one post-randomization measurement of the variable that is analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo Q4W	20 mg LY3015014 Q4W	120 mg LY3015014 Q4W	300 mg LY3015014 Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68[19]	71[20]	73[21]	75[22]
Units: Percentage Change				
least squares mean (standard error)	-0.31 (± 0.0436)	-16.63 (± 0.0442)	-19.02 (± 0.0427)	-37.29 (± 0.042)

Notes:

[19] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

[20] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

[21] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

[22] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

End point values	100 mg LY3015014 Q8W	300 mg LY3015014 Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70[23]	68[24]		
Units: Percentage Change				
least squares mean (standard error)	-7.54 (± 0.0427)	-21.01 (± 0.0437)		

Notes:

[23] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

[24] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in high sensitivity C-Reactive Protein (hsCRP)

End point title	Change from Baseline in high sensitivity C-Reactive Protein (hsCRP)

End point description:

LS Mean was calculated using MMRM analysis with baseline measurement, disease classification, statin dose, treatment, visit, and treatment by visit interaction included in the model. Percent change from baseline response is the dependent variable.

The mITT is defined as all participants in the ITT population who had at least one baseline measurement and one post-randomization measurement of the variable that is analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo Q4W	20 mg LY3015014 Q4W	120 mg LY3015014 Q4W	300 mg LY3015014 Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78[25]	75[26]	80[27]	78[28]
Units: Percentage change				
least squares mean (standard error)	0.5 (± 0.7)	-0.2 (± 0.72)	1.6 (± 0.69)	-0.3 (± 0.7)

Notes:

[25] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[26] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[27] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[28] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

End point values	100 mg LY3015014 Q8W	300 mg LY3015014 Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76[29]	73[30]		
Units: Percentage change				
least squares mean (standard error)	-0.3 (± 0.7)	-0.7 (± 0.72)		

Notes:

[29] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[30] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Develop Treatment Emergent Anti-LY3015014 Antibodies

End point title	Number of Participants Who Develop Treatment Emergent Anti-LY3015014 Antibodies

End point description:

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo Q4W	20 mg LY3015014 Q4W	120 mg LY3015014 Q4W	300 mg LY3015014 Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[31]	86[32]	86	85[33]
Units: Participants				
number (not applicable)	4	6	10	5

Notes:

[31] - All randomized participants who received at least 1 dose of study treatment and had evaluable data.

[32] - All randomized participants who received at least 1 dose of study treatment and had evaluable data.

[33] - All randomized participants who received at least 1 dose of study treatment and had evaluable data.

End point values	100 mg LY3015014 Q8W	300 mg LY3015014 Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	87		
Units: Participants				
number (not applicable)	4	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline in Free Proprotein Convertase Subtilisin/Kexin Type 9 Antibody (PCSK9) Levels

End point title	Percentage Change from Baseline in Free Proprotein Convertase Subtilisin/Kexin Type 9 Antibody (PCSK9) Levels

End point description:

LS Mean was calculated using MMRM analysis with baseline measurement, disease classification, statin dose, treatment, visit, and treatment by visit interaction included in the model. Percent change from baseline response is the dependent variable.

The mITT is defined as all participants in the ITT population who had at least one baseline measurement and one post-randomization measurement of the variable that is analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo Q4W	20 mg LY3015014 Q4W	120 mg LY3015014 Q4W	300 mg LY3015014 Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77[34]	72[35]	76[36]	75[37]
Units: Percentage change				
least squares mean (standard error)	9.9 (± 5.59)	-16.3 (± 5.81)	-36.6 (± 5.67)	-68 (± 5.71)

Notes:

[34] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[35] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[36] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[37] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

End point values	100 mg LY3015014 Q8W	300 mg LY3015014 Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70[38]	72[39]		
Units: Percentage change				
least squares mean (standard error)	-4.4 (± 5.8)	-35.2 (± 5.72)		

Notes:

[38] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[39] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Area Under the Concentration-Time Curve at Steady-State (AUC,ss) for LY3015014

End point title	Pharmacokinetics (PK): Area Under the Concentration-Time Curve at Steady-State (AUC,ss) for LY3015014[40]

End point description:

End point type	Secondary

End point timeframe:

Week 12-16 (Q4W), Week 8-16 (Q8W)

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The treatment arm randomized to placebo will not have pharmacokinetic data available, so summary statistics will not be reported.

End point values	20 mg LY3015014 Q4W	120 mg LY3015014 Q4W	300 mg LY3015014 Q4W	100 mg LY3015014 Q8W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	83[41]	85[42]	82[43]	84[44]
Units: µg·hr/mL				
geometric mean (geometric coefficient of variation)	1590 (± 29.2)	9670 (± 29.9)	27300 (± 26.3)	7800 (± 28.5)

Notes:

[41] - All randomly assigned participants who received at least 1 dose of study drug & had evaluable data.

[42] - All randomly assigned participants who received at least 1 dose of study drug & had evaluable data.

[43] - All randomly assigned participants who received at least 1 dose of study drug & had evaluable data.

[44] - All randomly assigned participants who received at least 1 dose of study drug & had evaluable data.

End point values	300 mg LY3015014 Q8W			
Subject group type	Reporting group			
Number of subjects analysed	86[45]			
Units: µg·hr/mL				
geometric mean (geometric coefficient of variation)	26600 (± 32.2)			

Notes:

[45] - All randomly assigned participants who received at least 1 dose of study drug & had evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline in Total Proprotein Convertase Subtilisin/Kexin Type 9 Antibody (PCSK9) Levels

End point title	Percentage Change from Baseline in Total Proprotein Convertase Subtilisin/Kexin Type 9 Antibody (PCSK9) Levels

End point description:

LS Mean was calculated using MMRM analysis with baseline measurement, disease classification, statin dose, treatment, visit, and treatment by visit interaction included in the model. Percent change from baseline response is the dependent variable.

The mITT is defined as all participants in the ITT population who had at least one baseline measurement and one post-randomization measurement of the variable that is analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo Q4W	20 mg LY3015014 Q4W	120 mg LY3015014 Q4W	300 mg LY3015014 Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77[46]	76[47]	79[48]	79[49]
Units: Percentage change				
least squares mean (standard error)	14.6 (± 13.66)	9.1 (± 14)	86.4 (± 13.65)	130.6 (± 13.63)

Notes:

[46] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[47] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[48] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[49] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

End point values	100 mg LY3015014 Q8W	300 mg LY3015014 Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75[50]	75[51]		
Units: Percentage change				
least squares mean (standard error)	21.8 (± 13.63)	41 (± 13.63)		

Notes:

[50] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.
[51] - mITT population who had at least 1 baseline measurement and 1 post-randomization measurement.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with an Injection Site Reaction

End point title	Number of Participants with an Injection Site Reaction

End point description:

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo Q4W	20 mg LY3015014 Q4W	120 mg LY3015014 Q4W	300 mg LY3015014 Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	87	86	86
Units: Participants				
number (not applicable)	13	21	28	25

End point values	100 mg LY3015014 Q8W	300 mg LY3015014 Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	87		
Units: Participants				
number (not applicable)	18	20		

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:	
I5S-MC-EFJE	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	LY3015014-20mg-Q4W
Reporting group description: -	
Reporting group title	LY3015014-120mg-Q4W
Reporting group description: -	
Reporting group title	LY3015014-300mg-Q4W
Reporting group description: -	
Reporting group title	LY3015014-100mg-Q8W
Reporting group description: -	
Reporting group title	LY3015014-300mg-Q8W
Reporting group description: -	
Reporting group title	PLACEBO-Q4W
Reporting group description: -	

Serious adverse events	LY3015014-20mg-Q4W	LY3015014-120mg-Q4W	LY3015014-300mg-Q4W
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 87 (3.45%)	6 / 86 (6.98%)	2 / 86 (2.33%)
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)			
laryngeal cancer			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	0 / 86 (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
meningeal neoplasm			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
prostate cancer			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed[1]	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 47 (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 cell carcinoma			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 87 (1.15%)	0 / 86 (0.00%)	0 / 86 (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
squamous cell carcinoma			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	1 / 86 (1.16%)	0 / 86 (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
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	0 / 86 (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
femur fracture			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	0 / 86 (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			
deep vein thrombosis			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 87 (0.00%)	1 / 86 (1.16%)	0 / 86 (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
Cardiac disorders			
atrial fibrillation			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	0 / 86 (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
atrial flutter			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 87 (1.15%)	0 / 86 (0.00%)	0 / 86 (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
coronary artery stenosis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 87 (1.15%)	0 / 86 (0.00%)	0 / 86 (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
myocardial infarction			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	0 / 86 (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
Nervous system disorders			
loss of consciousness			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	0 / 86 (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
paraesthesia			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	0 / 86 (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
subarachnoid haemorrhage			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	0 / 86 (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
Pregnancy, puerperium and perinatal conditions			
pregnancy			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed[2]	0 / 42 (0.00%)	1 / 41 (2.44%)	0 / 39 (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
General disorders and administration site conditions			
chest pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	0 / 86 (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			
dysphagia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
mechanical ileus			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	1 / 86 (1.16%)	0 / 86 (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
Renal and urinary disorders			
calculus ureteric			

alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	0 / 86 (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
Musculoskeletal and connective tissue disorders			
intervertebral disc protrusion			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	1 / 86 (1.16%)	0 / 86 (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
osteoarthritis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	0 / 86 (0.00%)	0 / 86 (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			
lobar pneumonia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	1 / 86 (1.16%)	0 / 86 (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
pneumonia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	1 / 86 (1.16%)	0 / 86 (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

Serious adverse events	LY3015014-100mg-Q8W	LY3015014-300mg-Q8W	PLACEBO-Q4W
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 86 (2.33%)	4 / 87 (4.60%)	5 / 87 (5.75%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

laryngeal cancer			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
meningeal neoplasm			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	0 / 87 (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
prostate cancer			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed[1]	0 / 50 (0.00%)	1 / 44 (2.27%)	0 / 47 (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
renal cell carcinoma			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	0 / 87 (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
squamous cell carcinoma			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	0 / 87 (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
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
femur fracture			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	0 / 87 (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			
atrial fibrillation			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrial flutter			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	0 / 87 (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
coronary artery stenosis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	0 / 87 (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
myocardial infarction			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 86 (1.16%)	0 / 87 (0.00%)	0 / 87 (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
Nervous system disorders			
loss of consciousness			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
paraesthesia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
subarachnoid haemorrhage			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	1 / 87 (1.15%)	0 / 87 (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
Pregnancy, puerperium and perinatal conditions			
pregnancy			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed[2]	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 40 (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
General disorders and administration site conditions			
chest pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	1 / 87 (1.15%)	0 / 87 (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			
dysphagia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	0 / 87 (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
mechanical ileus			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	0 / 87 (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			
calculus ureteric			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 86 (1.16%)	0 / 87 (0.00%)	0 / 87 (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
Musculoskeletal and connective tissue disorders			
intervertebral disc protrusion			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	0 / 87 (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
osteoarthritis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	1 / 87 (1.15%)	0 / 87 (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
Infections and infestations			
lobar pneumonia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	0 / 87 (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
pneumonia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (0.00%)	0 / 87 (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

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

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

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

Non-serious adverse events	LY3015014-20mg-Q4W	LY3015014-120mg-Q4W	LY3015014-300mg-Q4W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 87 (79.31%)	64 / 86 (74.42%)	64 / 86 (74.42%)
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 87 (3.45%)	3 / 86 (3.49%)	0 / 86 (0.00%)
occurrences (all)	3	3	0
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	6 / 87 (6.90%)	11 / 86 (12.79%)	8 / 86 (9.30%)
occurrences (all)	7	13	11
General disorders and administration site conditions			
influenza like illness			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 87 (2.30%)	1 / 86 (1.16%)	1 / 86 (1.16%)
occurrences (all)	2	1	1
injection site bruising			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 87 (1.15%)	8 / 86 (9.30%)	2 / 86 (2.33%)
occurrences (all)	1	9	2
injection site erythema			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 87 (1.15%)	9 / 86 (10.47%)	7 / 86 (8.14%)
occurrences (all)	1	10	10
injection site pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	15 / 87 (17.24%)	11 / 86 (12.79%)	8 / 86 (9.30%)
occurrences (all)	20	17	17
injection site pruritus			

alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	4 / 87 (4.60%)	6 / 86 (6.98%)	8 / 86 (9.30%)
occurrences (all)	6	6	13
injection site reaction			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 87 (1.15%)	5 / 86 (5.81%)	6 / 86 (6.98%)
occurrences (all)	1	7	10
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	6 / 87 (6.90%)	6 / 86 (6.98%)	3 / 86 (3.49%)
occurrences (all)	9	6	3
nausea			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	6 / 86 (6.98%)	3 / 86 (3.49%)
occurrences (all)	0	6	3
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 87 (3.45%)	5 / 86 (5.81%)	2 / 86 (2.33%)
occurrences (all)	3	6	2
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 87 (3.45%)	3 / 86 (3.49%)	6 / 86 (6.98%)
occurrences (all)	3	3	6
back pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	4 / 87 (4.60%)	9 / 86 (10.47%)	3 / 86 (3.49%)
occurrences (all)	6	10	3
myalgia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	6 / 87 (6.90%)	6 / 86 (6.98%)	7 / 86 (8.14%)
occurrences (all)	9	8	9

Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 87 (0.00%)	2 / 86 (2.33%)	3 / 86 (3.49%)
occurrences (all)	0	2	3
influenza			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 87 (5.75%)	2 / 86 (2.33%)	3 / 86 (3.49%)
occurrences (all)	5	3	3
nasopharyngitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	20 / 87 (22.99%)	22 / 86 (25.58%)	14 / 86 (16.28%)
occurrences (all)	23	22	18
upper respiratory tract infection			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 87 (1.15%)	5 / 86 (5.81%)	7 / 86 (8.14%)
occurrences (all)	2	5	8

Non-serious adverse events	LY3015014-100mg-Q8W	LY3015014-300mg-Q8W	PLACEBO-Q4W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 86 (74.42%)	58 / 87 (66.67%)	63 / 87 (72.41%)
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 86 (5.81%)	6 / 87 (6.90%)	0 / 87 (0.00%)
occurrences (all)	5	6	0
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	8 / 86 (9.30%)	2 / 87 (2.30%)	6 / 87 (6.90%)
occurrences (all)	8	8	7
General disorders and administration site conditions			
influenza like illness			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 86 (1.16%)	1 / 87 (1.15%)	6 / 87 (6.90%)
occurrences (all)	2	1	8

injection site bruising			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 86 (2.33%)	4 / 87 (4.60%)	4 / 87 (4.60%)
occurrences (all)	3	4	4
injection site erythema			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 86 (2.33%)	3 / 87 (3.45%)	0 / 87 (0.00%)
occurrences (all)	3	3	0
injection site pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	7 / 86 (8.14%)	9 / 87 (10.34%)	3 / 87 (3.45%)
occurrences (all)	13	12	6
injection site pruritus			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 86 (2.33%)	2 / 87 (2.30%)	1 / 87 (1.15%)
occurrences (all)	2	3	1
injection site reaction			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 86 (3.49%)	2 / 87 (2.30%)	0 / 87 (0.00%)
occurrences (all)	4	2	0
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 86 (3.49%)	1 / 87 (1.15%)	2 / 87 (2.30%)
occurrences (all)	4	1	3
nausea			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 86 (3.49%)	1 / 87 (1.15%)	4 / 87 (4.60%)
occurrences (all)	3	1	4
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 86 (1.16%)	1 / 87 (1.15%)	5 / 87 (5.75%)
occurrences (all)	2	1	5
Musculoskeletal and connective tissue			

disorders			
arthralgia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 86 (2.33%)	4 / 87 (4.60%)	5 / 87 (5.75%)
occurrences (all)	2	5	5
back pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 86 (2.33%)	2 / 87 (2.30%)	3 / 87 (3.45%)
occurrences (all)	2	2	3
myalgia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 86 (3.49%)	6 / 87 (6.90%)	3 / 87 (3.45%)
occurrences (all)	5	6	3
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 86 (2.33%)	3 / 87 (3.45%)	5 / 87 (5.75%)
occurrences (all)	3	3	6
influenza			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 86 (2.33%)	1 / 87 (1.15%)	3 / 87 (3.45%)
occurrences (all)	2	2	3
nasopharyngitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	11 / 86 (12.79%)	15 / 87 (17.24%)	15 / 87 (17.24%)
occurrences (all)	13	18	17
upper respiratory tract infection			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	6 / 86 (6.98%)	5 / 87 (5.75%)	4 / 87 (4.60%)
occurrences (all)	7	5	4

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