



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled, 2-Part Phase 2 Study to Evaluate the Safety and Efficacy of LY3337641 in Adult Subjects with Rheumatoid Arthritis: The RAjuvenate Study

Summary

EudraCT number	2015-003289-97
Trial protocol	SK AT PL DE ES
Global end of trial date	20 August 2018

Results information

Result version number	v1
This version publication date	25 August 2019
First version publication date	25 August 2019

Trial information

Trial identification

Sponsor protocol code	I8K-MC-JPDA
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02628028
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16173

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 8772854559,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 August 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	20 August 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the safety and effectiveness of LY3337641 in adults with rheumatoid arthritis (RA).

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	22 August 2016
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	Puerto Rico: 14
Country: Number of subjects enrolled	Argentina: 57
Country: Number of subjects enrolled	United States: 71
Country: Number of subjects enrolled	Japan: 25
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Poland: 32
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Mexico: 35
Country: Number of subjects enrolled	South Africa: 13
Country: Number of subjects enrolled	Slovakia: 4
Country: Number of subjects enrolled	Australia: 3
Worldwide total number of subjects	286
EEA total number of subjects	60

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)	278
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study consist of 2-parts. Part A included participants with at least mildly active rheumatoid arthritis (RA) and Part B included participants with moderately to severely active RA. Long-term extension (LTE) period allowed eligible participants who completed Part B of study to receive LY3337641 up to an additional 52 weeks.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Placebo

Arm description:

Participants received oral dose of placebo once daily (QD) for 4 weeks.

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

Dosage and administration details:

Participants received oral dose of placebo once daily (QD) for 4 weeks.

Arm title	Part A: 5 mg LY3337641
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Arm description:

Participants received oral dose of 5 mg LY3337641 QD for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	5 mg LY3337641
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received oral dose of 5 mg LY3337641 QD for 4 weeks.

Arm title	Part A: 10 mg LY3337641
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Arm description:

Participants received oral dose of 10 mg LY3337641 QD for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	10 mg LY3337641
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received oral dose of 10 mg LY3337641 QD for 4 weeks.

Arm title	Part A: 30 mg LY3337641
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Arm description:

Participants received oral dose of 30 mg LY3337641 QD for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	30 mg LY3337641
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received oral dose of 30 mg LY3337641 QD for 4 weeks.

Arm title	Part B: Placebo
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Arm description:

Participants received oral dose of placebo QD for 12 weeks.

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

Dosage and administration details:

Participants received oral dose of placebo QD for 12 weeks.

Arm title	Part B: 5 mg LY3337641
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Arm description:

Participants received oral dose of 5 mg LY3337641 QD for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	5 mg LY3337641
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received oral dose of 5 mg LY3337641 QD for 12 weeks.

Arm title	Part B: 10 mg LY3337641
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Arm description:

Participants received oral dose of 10 mg LY3337641 QD for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	10 mg LY3337641
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received oral dose of 10 mg LY3337641 QD for 12 weeks.

Arm title	Part B: 30 mg LY3337641
Arm description: Participants received oral dose of 30 mg LY3337641 QD for 12 weeks.	
Arm type	Experimental
Investigational medicinal product name	30 mg LY3337641
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received oral dose of 30 mg LY3337641 QD for 12 weeks.

Number of subjects in period 1	Part A: Placebo	Part A: 5 mg LY3337641	Part A: 10 mg LY3337641
Started	9	9	10
Received at Least 1dose of Study Drug	9	9	10
Completed	9	9	9
Not completed	0	0	1
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	-	1
Physician decision	-	-	-
Missing information	-	-	-
Adverse event, non-fatal	-	-	-
Site Terminated by Sponsor	-	-	-
Study Terminated by Sponsor	-	-	-
Lost to follow-up	-	-	-
Lack of efficacy	-	-	-

Number of subjects in period 1	Part A: 30 mg LY3337641	Part B: Placebo	Part B: 5 mg LY3337641
Started	8	62	63
Received at Least 1dose of Study Drug	8	62	63
Completed	8	46	49
Not completed	0	16	14
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	2	4
Physician decision	-	-	1
Missing information	-	2	1
Adverse event, non-fatal	-	2	1
Site Terminated by Sponsor	-	-	1
Study Terminated by Sponsor	-	7	6
Lost to follow-up	-	-	-

Lack of efficacy	-	3	-
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Number of subjects in period 1	Part B: 10 mg LY3337641	Part B: 30 mg LY3337641
Started	62	63
Received at Least 1dose of Study Drug	62	63
Completed	46	48
Not completed	16	15
Adverse event, serious fatal	-	1
Consent withdrawn by subject	1	1
Physician decision	-	-
Missing information	2	4
Adverse event, non-fatal	3	2
Site Terminated by Sponsor	1	-
Study Terminated by Sponsor	7	7
Lost to follow-up	1	-
Lack of efficacy	1	-

Period 2

Period 2 title	Long-term extension (LTE) period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Long Term Extension: LY3337641-5 mg

Arm description:

Participants who completed Part B of study received oral dose of 5 mg LY3337641 QD for an additional 52 weeks.

Arm type	Experimental
Investigational medicinal product name	5 mg LY3337641
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants who completed Part B of study received oral dose of 5 mg LY3337641 QD for an additional 52 weeks.

Arm title	Long Term Extension: LY3337641-10 mg
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Arm description:

Participants who completed Part B of study received oral dose of 10 mg LY3337641 QD for an additional 52 weeks.

Arm type	Experimental
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Investigational medicinal product name	10 mg LY3337641
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants who completed Part B of study received oral dose of 10 mg LY3337641 QD for an additional 52 weeks.

Arm title	Long Term Extension: LY3337641-30 mg
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Arm description:

Participants who completed Part B of study received oral dose of 30 mg LY3337641 QD for an additional 52 weeks.

Arm type	Experimental
Investigational medicinal product name	30 mg LY3337641
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants who completed Part B of study received oral dose of 30 mg LY3337641 QD for an additional 52 weeks.

Number of subjects in period 2^[1]	Long Term Extension: LY3337641-5 mg	Long Term Extension: LY3337641-10 mg	Long Term Extension: LY3337641-30 mg
Started	61	58	61
Placebo Re-randomized in LTE	14	13	14
Completed	1	0	0
Not completed	60	58	61
Consent withdrawn by subject	2	3	3
Missing information	3	4	3
Adverse event, non-fatal	1	-	3
Study Terminated by Sponsor	52	51	51
Lack of efficacy	2	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 14 participants on part B placebo arm completed part B treatment period, re-randomized to Part B: 5 mg LY3337641- LTE period.

13 participants on part B placebo arm completed part B treatment period, re-randomized to Part B: 10 mg LY3337641- LTE period and

14 participants on part B placebo arm completed part B treatment period, re-randomized to Part B: 30 mg LY3337641- LTE period.

Baseline characteristics

Reporting groups

Reporting group title	Part A: Placebo
Reporting group description: Participants received oral dose of placebo once daily (QD) for 4 weeks.	
Reporting group title	Part A: 5 mg LY3337641
Reporting group description: Participants received oral dose of 5 mg LY3337641 QD for 4 weeks.	
Reporting group title	Part A: 10 mg LY3337641
Reporting group description: Participants received oral dose of 10 mg LY3337641 QD for 4 weeks.	
Reporting group title	Part A: 30 mg LY3337641
Reporting group description: Participants received oral dose of 30 mg LY3337641 QD for 4 weeks.	
Reporting group title	Part B: Placebo
Reporting group description: Participants received oral dose of placebo QD for 12 weeks.	
Reporting group title	Part B: 5 mg LY3337641
Reporting group description: Participants received oral dose of 5 mg LY3337641 QD for 12 weeks.	
Reporting group title	Part B: 10 mg LY3337641
Reporting group description: Participants received oral dose of 10 mg LY3337641 QD for 12 weeks.	
Reporting group title	Part B: 30 mg LY3337641
Reporting group description: Participants received oral dose of 30 mg LY3337641 QD for 12 weeks.	

Reporting group values	Part A: Placebo	Part A: 5 mg LY3337641	Part A: 10 mg LY3337641
Number of subjects	9	9	10
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	9	7	9
From 65-84 years	0	2	1
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	54.3	54.0	56.9
standard deviation	± 11.43	± 11.75	± 6.44

Gender categorical Units: Subjects			
Female	8	8	9
Male	1	1	1
Race Units: Subjects			
American Indian or Alaska Native	2	1	1
Asian	0	0	0
Black or African American	1	1	0
White	6	7	9
More than one race	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	4	3	3
Not Hispanic or Latino	5	6	7
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Puerto Rico	0	0	0
Argentina	0	0	0
United States	6	6	6
Japan	0	0	0
Spain	0	0	0
South Korea	0	0	0
Austria	0	0	0
Poland	0	0	2
Italy	0	0	0
Mexico	3	3	2
South Africa	0	0	0
Slovakia	0	0	0
Australia	0	0	0

Reporting group values	Part A: 30 mg LY3337641	Part B: Placebo	Part B: 5 mg LY3337641
Number of subjects	8	62	63
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	62	63
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	51.9	50.47	50.06
standard deviation	± 5.72	± 8.75	± 9.20

Gender categorical Units: Subjects			
Female	5	54	53
Male	3	8	10
Race Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	0	7	14
Black or African American	1	1	2
White	7	53	46
More than one race	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	2	34	26
Not Hispanic or Latino	6	24	29
Unknown or Not Reported	0	4	8
Region of Enrollment Units: Subjects			
Puerto Rico	0	4	2
Argentina	0	15	13
United States	7	12	13
Japan	0	6	6
Spain	0	1	3
South Korea	0	0	5
Austria	0	1	0
Poland	1	9	9
Italy	0	1	2
Mexico	0	10	6
South Africa	0	2	3
Slovakia	0	0	0
Australia	0	1	1

Reporting group values	Part B: 10 mg LY3337641	Part B: 30 mg LY3337641	Total
Number of subjects	62	63	286
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	59	61	278
From 65-84 years	3	2	8
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	51.74	51.86	-
standard deviation	± 9.36	± 8.91	-

Gender categorical			
Units: Subjects			
Female	56	53	246
Male	6	10	40
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	6
Asian	9	10	40
Black or African American	2	2	10
White	50	51	229
More than one race	1	0	1
Ethnicity			
Units: Subjects			
Hispanic or Latino	23	21	116
Not Hispanic or Latino	26	23	126
Unknown or Not Reported	13	19	44
Region of Enrollment			
Units: Subjects			
Puerto Rico	3	5	14
Argentina	15	14	57
United States	15	6	71
Japan	6	7	25
Spain	3	6	13
South Korea	0	3	8
Austria	0	0	1
Poland	4	7	32
Italy	2	5	10
Mexico	7	4	35
South Africa	5	3	13
Slovakia	2	2	4
Australia	0	1	3

End points

End points reporting groups

Reporting group title	Part A: Placebo
Reporting group description: Participants received oral dose of placebo once daily (QD) for 4 weeks.	
Reporting group title	Part A: 5 mg LY3337641
Reporting group description: Participants received oral dose of 5 mg LY3337641 QD for 4 weeks.	
Reporting group title	Part A: 10 mg LY3337641
Reporting group description: Participants received oral dose of 10 mg LY3337641 QD for 4 weeks.	
Reporting group title	Part A: 30 mg LY3337641
Reporting group description: Participants received oral dose of 30 mg LY3337641 QD for 4 weeks.	
Reporting group title	Part B: Placebo
Reporting group description: Participants received oral dose of placebo QD for 12 weeks.	
Reporting group title	Part B: 5 mg LY3337641
Reporting group description: Participants received oral dose of 5 mg LY3337641 QD for 12 weeks.	
Reporting group title	Part B: 10 mg LY3337641
Reporting group description: Participants received oral dose of 10 mg LY3337641 QD for 12 weeks.	
Reporting group title	Part B: 30 mg LY3337641
Reporting group description: Participants received oral dose of 30 mg LY3337641 QD for 12 weeks.	
Reporting group title	Long Term Extension: LY3337641-5 mg
Reporting group description: Participants who completed Part B of study received oral dose of 5 mg LY3337641 QD for an additional 52 weeks.	
Reporting group title	Long Term Extension: LY3337641-10 mg
Reporting group description: Participants who completed Part B of study received oral dose of 10 mg LY3337641 QD for an additional 52 weeks.	
Reporting group title	Long Term Extension: LY3337641-30 mg
Reporting group description: Participants who completed Part B of study received oral dose of 30 mg LY3337641 QD for an additional 52 weeks.	
Subject analysis set title	LY3337641
Subject analysis set type	Full analysis
Subject analysis set description: Participants received single oral dose of 5 mg, 10 mg and 30 mg LY3337641 tablet QD for 4 weeks in Part A and 12 weeks in Part B.	

Primary: Number of Participants With One or More Treatment-Emergent Adverse Events (TEAEs) or Adverse Events of Special Interest (AESIs) or Any Serious AEs (SAEs) in Part A

End point title	Number of Participants With One or More Treatment-Emergent Adverse Events (TEAEs) or Adverse Events of Special Interest (AESIs) or Any Serious AEs (SAEs) in Part A ^{[1][2]}
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End point description:

TEAEs are any untoward medical occurrence that either occurs or worsens at any time after treatment baseline, and in the opinion of the investigators is possibly related to study drug. Skin Rash was the only event that was considered an AESI. A serious AE is defined as an event that results in death, initial or prolonged hospitalization, is life-threatening, leads to persistent or significant disability/incapacity, is associated with congenital anomaly/birth defect, or is considered significant by the investigator for any other reason. A summary of SAEs and other non-serious AEs, regardless of whether or not they were possibly related to study drug, is located in the Reported Adverse Event section. Analysis population description (APD) included all randomized participants who received at least 1 dose of the study drug in Part A.

End point type	Primary
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End point timeframe:

Up to 6 Weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No inferential statistics were planned or conducted for this endpoint.

[2] - 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: This end point is planned only for Part A.

End point values	Part A: Placebo	Part A: 5 mg LY3337641	Part A: 10 mg LY3337641	Part A: 30 mg LY3337641
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	9	10	8
Units: subjects				
TEAEs	3	1	6	2
AESIs	0	0	0	0
SAEs	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Achieving American College of Rheumatology 20% (ACR20) Response in Part B

End point title	Percentage of Participants Achieving American College of Rheumatology 20% (ACR20) Response in Part B ^[3]
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End point description:

ACR20 Responder Index is composite of clinical, laboratory, and functional measures in rheumatoid arthritis (RA). "ACR20 Responder" is a participant who has at least 20% improvement in both tender and swollen joint counts and in at least 3 of the following 5 criteria: Physician's Global Assessment of Disease Activity, Patient's Global Assessment of Disease Activity, Patient's Global Assessment of Arthritis Pain using visual analog scale (VAS), Health Assessment Questionnaire-Disability Index (HAQ-DI) and high-sensitivity C-reactive protein (hsCRP). Participants with missing responses and/or participants who discontinue study or drug before analysis timepoint are deemed non-responders. APD included all randomized participants who received at least 1 dose of the study drug, for participants who completed or early discontinued dosing treatment period before the study was terminated in Part B. Missing values due to discontinuation of study or drug, or missing data were imputed using NRI.

End point type	Primary
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End point timeframe:

Week 12

Notes:

[3] - 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: This end point is planned only for Part B.

End point values	Part B: Placebo	Part B: 5 mg LY3337641	Part B: 10 mg LY3337641	Part B: 30 mg LY3337641
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	56	52	55
Units: Percentage of Participants				
number (confidence interval 95%)	48.1 (34.8 to 61.5)	55.4 (42.3 to 68.4)	44.2 (30.7 to 57.7)	50.9 (37.7 to 64.1)

Statistical analyses

Statistical analysis title	ACR20 Response
Comparison groups	Part B: Placebo v Part B: 5 mg LY3337641
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.473
Method	Regression, Logistic

Statistical analysis title	ACR20 Response
Comparison groups	Part B: Placebo v Part B: 10 mg LY3337641
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.67
Method	Regression, Logistic

Statistical analysis title	ACR20 Response
Comparison groups	Part B: Placebo v Part B: 30 mg LY3337641
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.823
Method	Regression, Logistic

Secondary: Percentage of Participants Achieving American College of Rheumatology 50% (ACR50) Response in Part B

End point title	Percentage of Participants Achieving American College of Rheumatology 50% (ACR50) Response in Part B ^[4]
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End point description:

ACR50 Responder Index is composite of clinical, laboratory, and functional measures in RA. "ACR50 Responder" is a participant who has at least 50% improvement in both tender and swollen joint counts and in at least 3 of the following 5 criteria:

Physician's Global Assessment of Disease Activity, Patient's Global Assessment of Disease Activity, Patient's Global Assessment of Arthritis Pain using VAS, HAQ-DI and hsCRP. Participants with missing

responses and/or participants who discontinue study or drug before analysis timepoint are deemed non-responders. Analysis population description included all randomized participants who received at least 1 dose of the study drug, for participants who completed or early discontinued dosing treatment period before the study was terminated in Part B. Missing values due to discontinuation of study or drug, or missing data were imputed using non-responder imputation (NRI).

End point type	Secondary
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End point timeframe:

Week 12

Notes:

[4] - 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: This end point is planned only for Part B.

End point values	Part B: Placebo	Part B: 5 mg LY3337641	Part B: 10 mg LY3337641	Part B: 30 mg LY3337641
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	56	52	55
Units: Percentage of Participants				
number (confidence interval 95%)	27.8 (15.8 to 39.7)	25.0 (13.7 to 36.3)	15.4 (5.6 to 25.2)	29.1 (17.1 to 41.1)

Statistical analyses

Statistical analysis title	ACR50 Response
Comparison groups	Part B: Placebo v Part B: 5 mg LY3337641
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.743
Method	Regression, Logistic

Statistical analysis title	ACR50 Response
Comparison groups	Part B: Placebo v Part B: 10 mg LY3337641
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.124
Method	Regression, Logistic

Statistical analysis title	ACR50 Response
Comparison groups	Part B: Placebo v Part B: 30 mg LY3337641

Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.858
Method	Regression, Logistic

Secondary: Percentage of Participants Achieving American College of Rheumatology 70% (ACR70) Response in Part B

End point title	Percentage of Participants Achieving American College of Rheumatology 70% (ACR70) Response in Part B ^[5]
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End point description:

ACR70 Responder Index is composite of clinical, laboratory, and functional measures in RA. "ACR70 Responder" is a participant who has at least 70% improvement in both tender and swollen joint counts and in at least 3 of the following 5 criteria:

Physician's Global Assessment of Disease Activity, Patient's Global Assessment of Disease Activity, Patient's Global Assessment of Arthritis Pain using VAS, HAQ-DI and hsCRP. Participants with missing responses and/or participants who discontinue study or drug before analysis timepoint are deemed non-responders.

Analysis population description included all randomized participants who received at least 1 dose of the study drug, for participants who completed or early discontinued dosing treatment period before the study was terminated in Part B. Missing values due to discontinuation of study or drug, or missing data were imputed using non-responder imputation (NRI).

End point type	Secondary
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End point timeframe:

Week 12

Notes:

[5] - 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: This end point is planned only for Part B.

End point values	Part B: Placebo	Part B: 5 mg LY3337641	Part B: 10 mg LY3337641	Part B: 30 mg LY3337641
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	56	52	55
Units: Percentage of Participants				
number (confidence interval 95%)	16.7 (6.7 to 26.6)	8.9 (1.5 to 16.4)	1.9 (0.0 to 5.7)	16.4 (6.6 to 26.1)

Statistical analyses

Statistical analysis title	ACR70 Response
Comparison groups	Part B: Placebo v Part B: 5 mg LY3337641
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.199
Method	Regression, Logistic

Statistical analysis title	ACR70 Response
Comparison groups	Part B: Placebo v Part B: 10 mg LY3337641
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.028
Method	Regression, Logistic
Parameter estimate	Hazard ratio (HR)

Statistical analysis title	ACR70 Response
Comparison groups	Part B: Placebo v Part B: 30 mg LY3337641
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.863
Method	Regression, Logistic

Secondary: Change From Baseline in the Disease Activity Score (DAS) 28-high-sensitivity C-reactive Protein (hsCRP) in Part B

End point title	Change From Baseline in the Disease Activity Score (DAS) 28-high-sensitivity C-reactive Protein (hsCRP) in Part B ^[6]
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End point description:

Disease Activity Score (DAS) modified to include 28 joint count (DAS28) consisted of composite score of following variables: tender joint count (TJC28), swollen joint count (SJC28), C-reactive protein (CRP) (milligrams per liter), and Patient's Global Assessment of Disease Activity using VAS. DAS28 was calculated using following formula: $DAS28-CRP = 0.56 * \text{square root}(\text{sqrt}(TJC28) + 0.28 * \text{sqrt}(SJC28) + 0.36 * \text{natural log}(CRP + 1) + 0.014 * \text{Patient's Global VAS} + 0.96$. Scores ranged 1.0-9.4, where lower scores indicated less disease activity. Analysis population description included all randomized participants who received at least 1 dose of the study drug, for participants who completed or early discontinued dosing treatment period before the study was terminated in Part B. Missing values due to discontinuation of study or drug, or missing data were imputed using non-

End point type	Secondary
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End point timeframe:

Baseline, Week 12

Notes:

[6] - 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: This end point is planned only for Part B.

End point values	Part B: Placebo	Part B: 5 mg LY3337641	Part B: 10 mg LY3337641	Part B: 30 mg LY3337641
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	63	62	63
Units: units on a scale				
arithmetic mean (standard deviation)	-1.62 (± 1.447)	-1.55 (± 1.182)	-1.24 (± 1.146)	-1.80 (± 1.453)

Statistical analyses

Statistical analysis title	DAS28-hsCRP
Comparison groups	Part B: Placebo v Part B: 5 mg LY3337641
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.863
Method	Mixed-effects Model for Repeated Measure
Parameter estimate	Mean difference (final values)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.44
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	DAS28-hsCRP
Comparison groups	Part B: Placebo v Part B: 10 mg LY3337641
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.503
Method	Mixed-effects Model for Repeated Measure
Parameter estimate	Mean difference (final values)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.65
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	DAS28-hsCRP
Comparison groups	Part B: Placebo v Part B: 30 mg LY3337641
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.289
Method	Mixed-effects Model for Repeated Measure
Parameter estimate	Mean difference (final values)
Point estimate	-0.27

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	0.23

Secondary: Percentage of Participants Who Achieve Low Disease Activity Using DAS28-hsCRP in Part B

End point title	Percentage of Participants Who Achieve Low Disease Activity Using DAS28-hsCRP in Part B ^[7]
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End point description:

Disease Activity Score (DAS) modified to include 28 joint count (DAS28) consisted of composite score of following variables: tender joint count (TJC28), swollen joint count (SJC28), C-reactive protein (CRP) (milligrams per liter), and Patient's Global Assessment of Disease Activity using VAS. DAS28 was calculated using following formula: $DAS28-CRP = 0.56 * \text{square root}(\text{sqrt}(TJC28) + 0.28 * \text{sqrt}(SJC28) + 0.36 * \text{natural log}(CRP + 1) + 0.014 * \text{Patient's Global VAS} + 0.96$. Scores ranged 1.0-9.4, where lower scores indicated less disease activity. Analysis population description included all randomized participants who received at least 1 dose of the study drug, for participants who completed or early discontinued dosing treatment period before the study was terminated in Part B. Missing values due to discontinuation of study or drug, or missing data were imputed using non-

End point type	Secondary
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End point timeframe:

Week 12

Notes:

[7] - 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: This end point is planned only for Part B.

End point values	Part B: Placebo	Part B: 5 mg LY3337641	Part B: 10 mg LY3337641	Part B: 30 mg LY3337641
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	49	47	46
Units: Percentage of Participants				
number (confidence interval 95%)	24.2 (13.5 to 34.9)	28.6 (17.4 to 39.7)	17.7 (8.2 to 27.3)	25.4 (14.6 to 36.1)

Statistical analyses

Statistical analysis title	Low Disease Activity Using DAS28-hsCRP
Comparison groups	Part B: Placebo v Part B: 5 mg LY3337641
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.626
Method	Regression, Logistic

Statistical analysis title	Low Disease Activity Using DAS28-hsCRP
Comparison groups	Part B: Placebo v Part B: 10 mg LY3337641

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.418
Method	Regression, Logistic

Statistical analysis title	Low Disease Activity Using DAS28-hsCRP
Comparison groups	Part B: Placebo v Part B: 30 mg LY3337641
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.951
Method	Regression, Logistic

Secondary: Percentage of Participants Who Achieve Clinical Remission Using DAS28-hsCRP in Part B

End point title	Percentage of Participants Who Achieve Clinical Remission Using DAS28-hsCRP in Part B ^[8]
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End point description:

Disease Activity Score (DAS) modified to include 28 joint count (DAS28) consisted of composite score of following variables: tender joint count (TJC28), swollen joint count (SJC28), C-reactive protein (CRP) (milligrams per liter), and Patient's Global Assessment of Disease Activity using visual analog scale (VAS) (participant global VAS). DAS28 was calculated using following formula: $\text{DAS28-CRP} = 0.56 \times \sqrt{\text{TJC28}} + 0.28 \times \sqrt{\text{SJC28}} + 0.36 \times \ln(\text{CRP} + 1) + 0.014 \times \text{Patient's Global VAS} + 0.96$. Clinical remission is defined as DAS28-hsCRP <2.6. Analysis population description included all randomized participants who received at least 1 dose of the study drug, for participants who completed or early discontinued dosing treatment period before the study was terminated in Part B. Missing values due to discontinuation of study or drug, or missing data were imputed using non-responder imputation (NRI).

End point type	Secondary
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End point timeframe:

Week 12

Notes:

[8] - 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: This end point is planned only for Part B.

End point values	Part B: Placebo	Part B: 5 mg LY3337641	Part B: 10 mg LY3337641	Part B: 30 mg LY3337641
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	49	47	46
Units: Percentage of Participants				
number (confidence interval 95%)	17.7 (8.2 to 27.3)	17.5 (8.1 to 26.8)	6.5 (0.3 to 12.6)	22.2 (12.0 to 32.5)

Statistical analyses

Statistical analysis title	Clinical Remission Using DAS28-hsCRP
Comparison groups	Part B: Placebo v Part B: 5 mg LY3337641
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.905
Method	Regression, Logistic

Statistical analysis title	Clinical Remission Using DAS28-hsCRP
Comparison groups	Part B: Placebo v Part B: 10 mg LY3337641
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.069
Method	Regression, Logistic

Statistical analysis title	Clinical Remission Using DAS28-hsCRP
Comparison groups	Part B: Placebo v Part B: 30 mg LY3337641
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.547
Method	Regression, Logistic

Secondary: Pharmacokinetics (PK): Clearance Parameter of LY3337641

End point title	Pharmacokinetics (PK): Clearance Parameter of LY3337641
End point description: Apparent total body clearance of drug was evaluated. Analysis population description included all randomized participants who received at least 1 dose of the study drug and have evaluable PK data in in Part A and Part B.	
End point type	Secondary
End point timeframe: Part A: Weeks 1, 2, and 4, Day 1 (0.5 to 2 hours postdose); Part B: Weeks 2, 4, 8, and 12, Day 1 (0.5 to 2 hours postdose)	

End point values	LY3337641			
Subject group type	Subject analysis set			
Number of subjects analysed	209			
Units: Liter per hour (L/hr)				
arithmetic mean (standard error)	29.1 (± 5.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 88 Weeks

Adverse event reporting additional description:

All randomized participants who received at least 1 dose of the study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Part A: Placebo
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Reporting group description:

Participants received oral dose of placebo once daily (QD) for 4 weeks.

Reporting group title	Part A: LY3337641-5mg
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Reporting group description:

Participants received oral dose of 5 mg LY3337641 QD for 4 weeks.

Reporting group title	Part A: LY3337641-10mg
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Reporting group description:

Participants received oral dose of 10 mg LY3337641 QD for 4 weeks.

Reporting group title	Part A: LY3337641-30mg
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Reporting group description:

Participants received oral dose of 30 mg LY3337641 QD for 4 weeks.

Reporting group title	Part B: Placebo
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Reporting group description:

Participants received oral dose of placebo QD for 12 weeks.

Reporting group title	Part B: LY3337641-5mg
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Reporting group description:

Participants received oral dose of 5 mg LY3337641 QD for 12 weeks.

Reporting group title	Part B: LY3337641-10mg
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Reporting group description:

Participants received oral dose of 10 mg LY3337641 QD for 12 weeks.

Reporting group title	Part B: LY3337641-30mg
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Reporting group description:

Participants received oral dose of 30 mg LY3337641 QD for 12 weeks.

Reporting group title	Long Term Extension: LY3337641-5 mg
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Reporting group description:

Participants who completed Part B of study received oral dose of 5 mg LY3337641 QD for an additional 52 weeks.

Reporting group title	Long Term Extension: LY3337641-10 mg
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Reporting group description:

Participants who completed Part B of study received oral dose of 10 mg LY3337641 QD for an additional 52 weeks.

Reporting group title	Long Term Extension: LY3337641-30 mg
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Reporting group description:

Participants who completed Part B of study received oral dose of 30 mg LY3337641 QD for an additional 52 weeks.

Serious adverse events	Part A: Placebo	Part A: LY3337641-5mg	Part A: LY3337641-10mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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			
ankle fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
foot fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
hand fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
joint dislocation			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
multiple injuries			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
patella fracture alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
pubis fracture alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
wrist fracture alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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 venous thrombosis alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Hepatobiliary disorders cholecystitis acute alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders nephrolithiasis alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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			
pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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	Part A: LY3337641-30mg	Part B: Placebo	Part B: LY3337641-5mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	2 / 62 (3.23%)	0 / 63 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (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			
ankle fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (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
foot fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (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
hand fracture			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (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
joint dislocation			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	0 / 63 (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
multiple injuries			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (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
patella fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (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
pubis fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (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
wrist fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (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			
venous thrombosis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (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
Hepatobiliary disorders			
cholecystitis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
nephrolithiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (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			
pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (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	Part B: LY3337641-10mg	Part B: LY3337641-30mg	Long Term Extension: LY3337641-5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 62 (0.00%)	3 / 63 (4.76%)	1 / 61 (1.64%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

ankle fracture				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	0 / 61 (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	
foot fracture				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	0 / 62 (0.00%)	1 / 63 (1.59%)	0 / 61 (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	
hand fracture				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	0 / 61 (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	
joint dislocation				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	0 / 61 (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	
multiple injuries				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	0 / 62 (0.00%)	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0	
patella fracture				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	0 / 61 (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	
pubis fracture				
alternative dictionary used: MedDRA 21.1				

subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	0 / 61 (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
wrist fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	0 / 61 (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			
venous thrombosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 62 (0.00%)	1 / 63 (1.59%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
cholecystitis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
nephrolithiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	0 / 61 (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			
pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	0 / 61 (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	Long Term Extension: LY3337641-10 mg	Long Term Extension: LY3337641-30 mg	
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Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 58 (5.17%)	1 / 61 (1.64%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
foot fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hand fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
joint dislocation			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
multiple injuries			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
patella fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pubis fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
wrist fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
venous thrombosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
cholecystitis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
nephrolithiasis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part A: Placebo	Part A: LY3337641-5mg	Part A: LY3337641-10mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)	1 / 9 (11.11%)	6 / 10 (60.00%)
Nervous system disorders			
carotid artery aneurysm			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
dizziness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
headache			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
non-cardiac chest pain			
alternative dictionary used:			

MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
benign prostatic hyperplasia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed ^[1]	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
erectile dysfunction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed ^[2]	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
diarrhoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
dry mouth			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
nausea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue			

disorders			
osteopenia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
rheumatoid arthritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
laryngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
pharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
sinusitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
urinary tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			

hypertriglyceridaemia alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
hypokalaemia alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0

Non-serious adverse events	Part A: LY3337641-30mg	Part B: Placebo	Part B: LY3337641-5mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	7 / 62 (11.29%)	10 / 63 (15.87%)
Nervous system disorders			
carotid artery aneurysm alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 62 (0.00%) 0	0 / 63 (0.00%) 0
dizziness alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 62 (0.00%) 0	0 / 63 (0.00%) 0
headache alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 62 (0.00%) 0	1 / 63 (1.59%) 1
General disorders and administration site conditions			
fatigue alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 62 (0.00%) 0	0 / 63 (0.00%) 0
non-cardiac chest pain alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 62 (0.00%) 0	1 / 63 (1.59%) 1
Reproductive system and breast disorders			

benign prostatic hyperplasia alternative dictionary used: MedDRA 21.1 subjects affected / exposed ^[1] occurrences (all)	0 / 3 (0.00%) 0	1 / 8 (12.50%) 1	0 / 10 (0.00%) 0
erectile dysfunction alternative dictionary used: MedDRA 21.1 subjects affected / exposed ^[2] occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 10 (0.00%) 0
Gastrointestinal disorders constipation alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 62 (0.00%) 0	0 / 63 (0.00%) 0
diarrhoea alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 62 (0.00%) 0	1 / 63 (1.59%) 1
dry mouth alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 62 (0.00%) 0	0 / 63 (0.00%) 0
nausea alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 62 (0.00%) 0	0 / 63 (0.00%) 0
Respiratory, thoracic and mediastinal disorders cough alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 62 (1.61%) 1	0 / 63 (0.00%) 0
Musculoskeletal and connective tissue disorders osteopenia alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
rheumatoid arthritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	3 / 63 (4.76%)
occurrences (all)	0	1	4
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
laryngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	2 / 62 (3.23%)	3 / 63 (4.76%)
occurrences (all)	0	2	3
pharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	2 / 62 (3.23%)	0 / 63 (0.00%)
occurrences (all)	0	3	0
sinusitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
urinary tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
hypertriglyceridaemia			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
hypokalaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 62 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part B: LY3337641- 10mg	Part B: LY3337641- 30mg	Long Term Extension: LY3337641-5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 62 (19.35%)	19 / 63 (30.16%)	11 / 61 (18.03%)
Nervous system disorders			
carotid artery aneurysm			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
dizziness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 63 (0.00%)	1 / 61 (1.64%)
occurrences (all)	1	0	1
headache			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 62 (1.61%)	1 / 63 (1.59%)	0 / 61 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 62 (0.00%)	4 / 63 (6.35%)	0 / 61 (0.00%)
occurrences (all)	0	4	0
non-cardiac chest pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

benign prostatic hyperplasia alternative dictionary used: MedDRA 21.1 subjects affected / exposed ^[1] occurrences (all)	0 / 6 (0.00%) 0	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0
erectile dysfunction alternative dictionary used: MedDRA 21.1 subjects affected / exposed ^[2] occurrences (all)	0 / 6 (0.00%) 0	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0
Gastrointestinal disorders constipation alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 1	0 / 63 (0.00%) 0	0 / 61 (0.00%) 0
diarrhoea alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0	2 / 63 (3.17%) 3	0 / 61 (0.00%) 0
dry mouth alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0	0 / 63 (0.00%) 0	0 / 61 (0.00%) 0
nausea alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 2	1 / 63 (1.59%) 1	1 / 61 (1.64%) 1
Respiratory, thoracic and mediastinal disorders cough alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 1	1 / 63 (1.59%) 1	2 / 61 (3.28%) 2
Musculoskeletal and connective tissue disorders osteopenia alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
rheumatoid arthritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	4 / 62 (6.45%)	2 / 63 (3.17%)	1 / 61 (1.64%)
occurrences (all)	4	2	1
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 62 (0.00%)	2 / 63 (3.17%)	1 / 61 (1.64%)
occurrences (all)	0	2	1
laryngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 62 (1.61%)	5 / 63 (7.94%)	1 / 61 (1.64%)
occurrences (all)	2	5	1
pharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 62 (1.61%)	3 / 63 (4.76%)	0 / 61 (0.00%)
occurrences (all)	1	4	0
sinusitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 62 (1.61%)	1 / 63 (1.59%)	0 / 61 (0.00%)
occurrences (all)	1	1	0
urinary tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 62 (1.61%)	1 / 63 (1.59%)	2 / 61 (3.28%)
occurrences (all)	1	1	2
Metabolism and nutrition disorders			
hypertriglyceridaemia			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 62 (1.61%)	0 / 63 (0.00%)	1 / 61 (1.64%)
occurrences (all)	1	0	1
hypokalaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 62 (0.00%)	2 / 63 (3.17%)	0 / 61 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Long Term Extension: LY3337641-10 mg	Long Term Extension: LY3337641-30 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 58 (20.69%)	10 / 61 (16.39%)	
Nervous system disorders			
carotid artery aneurysm			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences (all)	0	0	
dizziness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences (all)	0	0	
headache			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences (all)	0	0	
non-cardiac chest pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			

benign prostatic hyperplasia alternative dictionary used: MedDRA 21.1 subjects affected / exposed ^[1] occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	
erectile dysfunction alternative dictionary used: MedDRA 21.1 subjects affected / exposed ^[2] occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	
Gastrointestinal disorders constipation alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 58 (0.00%) 0	0 / 61 (0.00%) 0	
diarrhoea alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 58 (0.00%) 0	0 / 61 (0.00%) 0	
dry mouth alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 58 (0.00%) 0	0 / 61 (0.00%) 0	
nausea alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	1 / 58 (1.72%) 1	0 / 61 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders cough alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	1 / 58 (1.72%) 1	2 / 61 (3.28%) 2	
Musculoskeletal and connective tissue disorders osteopenia alternative dictionary used: MedDRA 21.1			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>rheumatoid arthritis</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 58 (0.00%)</p> <p>0</p> <p>1 / 58 (1.72%)</p> <p>2</p>	<p>0 / 61 (0.00%)</p> <p>0</p> <p>2 / 61 (3.28%)</p> <p>2</p>	
<p>Infections and infestations</p> <p>bronchitis</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>laryngitis</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>nasopharyngitis</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>pharyngitis</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>sinusitis</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>urinary tract infection</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 58 (5.17%)</p> <p>4</p> <p>0 / 58 (0.00%)</p> <p>0</p> <p>0 / 58 (0.00%)</p> <p>0</p> <p>2 / 58 (3.45%)</p> <p>2</p> <p>2 / 58 (3.45%)</p> <p>2</p> <p>3 / 58 (5.17%)</p> <p>4</p>	<p>1 / 61 (1.64%)</p> <p>1</p> <p>0 / 61 (0.00%)</p> <p>0</p> <p>2 / 61 (3.28%)</p> <p>2</p> <p>1 / 61 (1.64%)</p> <p>1</p> <p>2 / 61 (3.28%)</p> <p>2</p> <p>4 / 61 (6.56%)</p> <p>4</p>	
<p>Metabolism and nutrition disorders</p> <p>hypertriglyceridaemia</p> <p>alternative dictionary used: MedDRA 21.1</p>			

subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences (all)	0	0	
hypokalaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	
occurrences (all)	2	0	

Notes:

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

Justification: Gender specific events only occurring in male or female subjects have had the number of subjects at risk adjusted accordingly.

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

Justification: Gender specific events only occurring in male or female subjects have had the number of subjects at risk adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 June 2016	The main changes include the addition of a 4 week lead in safety study, and a lowering of the top dose from 40mg to 30mg. In the European Union (EU), the ongoing initial Clinical Trial Application (CTA)s were withdrawn prior to approval. Therefore the submission of the amended JPDA(a) will be the re-submission of the initial CTA for the study, rather than an amendment of an approved protocol in the EU countries.
31 October 2016	The main changes include (1) expanding Part B from 3 arms to 4 arms by addition of a 5-mg QD dose group, (2) the sample size was increased from 150 subjects to 244 subjects in Part B, and (3) for Part B, region (Japan vs non-Japan) was added as a stratification factor due to regulatory requirements in Japan for evaluating the consistency of results between Japanese subjects and the overall population. In addition, region (Japan vs non-Japan) was added as an independent variable in the primary analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Early termination leading to fewer number of subjects included in primary analysis than planned.

Notes: