



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 |
|-----------------------|-------------|

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 | Investigator, Carer, Subject |

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 |
|------------------|------------------------|

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 |
|------------------|-------------------------|

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 |
|------------------|-------------------------|

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 |
|------------------|-----------------|

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 |
|------------------|------------------------|

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 |
|------------------|-------------------------|

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 | - |
|------------------|---|---|---|

| 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 |
|------------------|--------------------------------------|

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 |
|----------|--------------|

| | |
|--|-----------------|
| 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 |
|------------------|--------------------------------------|

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]} |
|-----------------|---|

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 |
|----------------|---------|

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] |
|-----------------|---|

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 |
|----------------|---------|

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] |
|-----------------|---|

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 |
|----------------|-----------|

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] |
|-----------------|---|

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 |
|----------------|-----------|

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] |
|-----------------|--|

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 |
|----------------|-----------|

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] |
|-----------------|--|

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: $DAS28-CRP = 0.56 * \sqrt{\text{score}} + 0.28 * \sqrt{SJC28} + 0.36 * \ln(CRP + 1) + 0.014 * \text{Patient's Global VAS} + 0.96$. 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 |
|----------------|-----------|

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] |
|-----------------|--|

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 |
|----------------|-----------|

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 |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

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: LY3337641-5mg |
|-----------------------|-----------------------|

Reporting group description:

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

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

Reporting group description:

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

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

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: LY3337641-5mg |
|-----------------------|-----------------------|

Reporting group description:

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

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

Reporting group description:

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

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

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.

| 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 | |
|-------------------------------|---|---|--|

| | | | |
|---|----------------|----------------|--|
| 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: