



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled, Parallel- Group, Phase 2 Study of Baricitinib in Patients with Systemic Lupus Erythematosus (SLE)

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2015-004404-35 |
| Trial protocol | AT PL ES FR RO |
| Global end of trial date | 09 November 2017 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 23 January 2019 |
| First version publication date | 14 October 2018 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Correction of full data set |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | I4V-MC-JAHH |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02708095 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 16270 |

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 | 09 November 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 09 November 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the efficacy and safety of the study drug known as baricitinib in participants with systemic lupus erythematosus.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 24 March 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 | Argentina: 28 |
| Country: Number of subjects enrolled | Puerto Rico: 17 |
| Country: Number of subjects enrolled | Austria: 8 |
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 6 |
| Country: Number of subjects enrolled | Romania: 13 |
| Country: Number of subjects enrolled | United States: 95 |
| Country: Number of subjects enrolled | Japan: 33 |
| Country: Number of subjects enrolled | Taiwan: 18 |
| Country: Number of subjects enrolled | Poland: 32 |
| Country: Number of subjects enrolled | Mexico: 33 |
| Country: Number of subjects enrolled | France: 16 |
| Country: Number of subjects enrolled | Spain: 15 |
| Worldwide total number of subjects | 314 |
| EEA total number of subjects | 84 |

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) | 294 |
| From 65 to 84 years | 20 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Not applicable

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Participants received Placebo orally once daily (QD) for 24 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:

1 placebo tablet matching baricitinib 4-mg and 1 placebo tablet matching baricitinib 2-mg were administered orally once daily (QD) for 24 weeks.

| | |
|------------------|------------------|
| Arm title | 2 mg Baricitinib |
|------------------|------------------|

Arm description:

Participants received 2 mg of Baricitinib orally QD for 24 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Baricitinib |
| Investigational medicinal product code | LY3009104 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

1 baricitinib 2-mg tablet and 1 placebo tablet matching baricitinib 4-mg administered orally QD for 24 weeks.

| | |
|------------------|------------------|
| Arm title | 4 mg Baricitinib |
|------------------|------------------|

Arm description:

Participants received 4 mg of Baricitinib orally QD for 24 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Baricitinib |
| Investigational medicinal product code | LY3009104 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

1 baricitinib 4-mg tablet and 1 placebo tablet matching baricitinib 2-mg administered orally QD for 24 weeks.

| Number of subjects in period 1 | Placebo | 2 mg Baricitinib | 4 mg Baricitinib |
|---------------------------------------|---------|------------------|------------------|
| Started | 105 | 105 | 104 |
| Completed | 83 | 86 | 86 |
| Not completed | 22 | 19 | 18 |
| Physician decision | 2 | 3 | 2 |
| Consent withdrawn by subject | 5 | 3 | 4 |
| Adverse event, non-fatal | 4 | 10 | 11 |
| Lost to follow-up | 2 | - | - |
| Lack of efficacy | 9 | 3 | - |
| Protocol deviation | - | - | 1 |

Baseline characteristics

Reporting groups

| | |
|--|------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received Placebo orally once daily (QD) for 24 weeks. | |
| Reporting group title | 2 mg Baricitinib |
| Reporting group description: | |
| Participants received 2 mg of Baricitinib orally QD for 24 weeks. | |
| Reporting group title | 4 mg Baricitinib |
| Reporting group description: | |
| Participants received 4 mg of Baricitinib orally QD for 24 weeks. | |

| Reporting group values | Placebo | 2 mg Baricitinib | 4 mg Baricitinib |
|--|---------|------------------|------------------|
| Number of subjects | 105 | 105 | 104 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 44.9 | 43.2 | 45.0 |
| standard deviation | ± 12.8 | ± 11.0 | ± 12.4 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 99 | 96 | 99 |
| Male | 6 | 9 | 5 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 38 | 32 | 32 |
| Not Hispanic or Latino | 52 | 62 | 60 |
| Unknown or Not Reported | 15 | 11 | 12 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 9 | 6 | 10 |
| Asian | 20 | 20 | 20 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 5 | 9 | 7 |
| White | 71 | 68 | 65 |
| More than one race | 0 | 1 | 1 |

| Unknown or Not Reported | 0 | 1 | 1 |
|-------------------------|----|----|----|
| Region of Enrollment | | | |
| Units: Subjects | | | |
| Puerto Rico | 6 | 5 | 6 |
| Argentina | 9 | 12 | 7 |
| Austria | 3 | 2 | 3 |
| South Korea | 1 | 2 | 3 |
| Romania | 4 | 2 | 7 |
| United States | 31 | 34 | 30 |
| Japan | 13 | 10 | 10 |
| Taiwan | 6 | 7 | 5 |
| Poland | 13 | 10 | 9 |
| Mexico | 11 | 8 | 14 |
| France | 2 | 7 | 7 |
| Spain | 6 | 6 | 3 |

| Reporting group values | Total | | |
|---|-------|--|--|
| Number of subjects | 314 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 294 | | |
| Male | 20 | | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 102 | | |
| Not Hispanic or Latino | 174 | | |
| Unknown or Not Reported | 38 | | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 25 | | |
| Asian | 60 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 21 | | |
| White | 204 | | |

| | | | |
|-------------------------|----|--|--|
| More than one race | 2 | | |
| Unknown or Not Reported | 2 | | |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| Puerto Rico | 17 | | |
| Argentina | 28 | | |
| Austria | 8 | | |
| South Korea | 6 | | |
| Romania | 13 | | |
| United States | 95 | | |
| Japan | 33 | | |
| Taiwan | 18 | | |
| Poland | 32 | | |
| Mexico | 33 | | |
| France | 16 | | |
| Spain | 15 | | |

End points

End points reporting groups

| | |
|--|------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received Placebo orally once daily (QD) for 24 weeks. | |
| Reporting group title | 2 mg Baricitinib |
| Reporting group description: | |
| Participants received 2 mg of Baricitinib orally QD for 24 weeks. | |
| Reporting group title | 4 mg Baricitinib |
| Reporting group description: | |
| Participants received 4 mg of Baricitinib orally QD for 24 weeks. | |

Primary: Percentage of Participants who Achieve Remission of Arthritis and/or Rash defined by the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K)

| | |
|--|---|
| End point title | Percentage of Participants who Achieve Remission of Arthritis and/or Rash defined by the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) |
| End point description: | |
| Participants were defined as responders as follows using SLEDAI-2K definitions of arthritis and rash. If only arthritis is present at baseline, then arthritis must be absent at Week 24 to meet the primary endpoint. If only rash is present at baseline, then rash must be absent at Week 24 to meet the primary endpoint. If both arthritis and rash are present at baseline, then the primary endpoint is met if either arthritis, or rash, or both arthritis and rash are absent at Week 24. Analysis Population Description: All randomized participants who received at least 1 dose of study drug with baseline and post-baseline values at the specified time point for remission of arthritis and/or rash. | |
| End point type | Primary |
| End point timeframe: | |
| Week 24 | |

| End point values | Placebo | 2 mg Baricitinib | 4 mg Baricitinib | |
|-----------------------------------|-----------------|------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 105 | 105 | 104 | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 53.3 | 58.1 | 67.3 | |

Statistical analyses

| | |
|----------------------------|------------------------------------|
| Statistical analysis title | Remission of Arthritis and/or Rash |
| Comparison groups | Placebo v 2 mg Baricitinib |

| | |
|---|----------------------|
| Number of subjects included in analysis | 210 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.392 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.73 |
| upper limit | 2.27 |

| | |
|---|------------------------------------|
| Statistical analysis title | Remission of Arthritis and/or Rash |
| Comparison groups | Placebo v 4 mg Baricitinib |
| Number of subjects included in analysis | 209 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.041 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.02 |
| upper limit | 3.29 |

Secondary: Percentage of Participants who Achieve SLE Responder Index 4 (SRI-4) Response

| | |
|--|---|
| End point title | Percentage of Participants who Achieve SLE Responder Index 4 (SRI-4) Response |
| End point description: The SRI-4 is a composite index used to assess disease activity in SLE. SRI-4 response is defined as: 1) Reduction of ≥ 4 points from baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score; 2) no new British Isles Lupus Assessment Group (BILAG) A or no more than 1 new BILAG B disease activity scores; and 3) no worsening (defined as an increase of ≥ 0.3 points [10 mm] from baseline) in Physician's Global Assessment of Disease Activity. Analysis Population Description: All randomized participants who received at least 1 dose of study drug with baseline and post-baseline values at the specified time point for SRI-4 response. | |
| End point type | Secondary |
| End point timeframe: Week 24 | |

| End point values | Placebo | 2 mg Baricitinib | 4 mg Baricitinib | |
|-----------------------------------|-----------------|------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 105 | 105 | 104 | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 47.6 | 51.4 | 64.4 | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | SLE Responder Index-4 Response |
| Comparison groups | Placebo v 2 mg Baricitinib |
| Number of subjects included in analysis | 210 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.44 |
| Method | Regression, Logistic |
| Parameter estimate | Log odds ratio |
| Point estimate | 1.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.71 |
| upper limit | 2.19 |

| | |
|---|--------------------------------|
| Statistical analysis title | SLE Responder Index-4 Response |
| Comparison groups | Placebo v 4 mg Baricitinib |
| Number of subjects included in analysis | 209 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.015 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.15 |
| upper limit | 3.62 |

Secondary: Change from Baseline in SLEDAI-2K Score

| | |
|-----------------|---|
| End point title | Change from Baseline in SLEDAI-2K Score |
|-----------------|---|

End point description:

SLE Disease Activity Index 2000 (SLEDAI-2K) score is a weighted, cumulative index of lupus disease activity. SLEDAI-2K is calculated from 24 individual descriptors across 9 organ systems; 0 indicates inactive disease and the maximum theoretical score is 105. Least Squares (LS) mean was determined

by mixed-model repeated measures (MMRM) model with baseline of response, region, baseline disease activity (SLEDAI-2K <10, ≥10), baseline anti-dsDNA status (positive, negative), treatment, time, treatment*time (type III sum of squares).

Analysis Population Description: All randomized participants who received at least 1 dose of study drug with baseline and post-baseline values at the specified time point for SLEDAI-2K.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 24 | |

| End point values | Placebo | 2 mg Baricitinib | 4 mg Baricitinib | |
|-------------------------------------|-----------------|------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 86 | 88 | 86 | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | -3.82 (± 0.352) | -4.07 (± 0.356) | -4.39 (± 0.353) | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Change From Baseline in SLEDAI-2K Score |
| Comparison groups | Placebo v 2 mg Baricitinib |
| Number of subjects included in analysis | 174 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference (Final Vaules) |
| Point estimate | -0.26 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.23 |
| upper limit | 0.71 |

| | |
|---|---|
| Statistical analysis title | Change From Baseline in SLEDAI-2K Score |
| Comparison groups | Placebo v 4 mg Baricitinib |
| Number of subjects included in analysis | 172 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.243 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference (Final Vaules) |
| Point estimate | -0.58 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.55 |
| upper limit | 0.39 |

Secondary: Change from Baseline in Patient's Global Assessment of Disease Activity

| | |
|-----------------|---|
| End point title | Change from Baseline in Patient's Global Assessment of Disease Activity |
|-----------------|---|

End point description:

The Patient's Global Assessment of Disease Activity is a single-item, patient reported scale developed for the assessment of the patient's overall rating of their disease activity due to SLE. The scale measures disease activity through a 5 point Likert scale ranging from 0 ("No disease activity") to 4 ("Severe disease activity") at its worst over the past 7 days. LS mean was determined by MMRM model with baseline of response, region, baseline disease activity (SLEDAI-2K <10, >=10), baseline anti-dsDNA status (positive, negative), treatment, time, treatment*time (type III sum of squares).

Analysis Population Description: All randomized participants who received at least 1 dose of study drug with baseline and post-baseline values at the specified time point for Patient's Global Assessment of Disease Activity.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 24

| End point values | Placebo | 2 mg Baricitinib | 4 mg Baricitinib | |
|-------------------------------------|-----------------|------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 84 | 86 | 86 | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | -0.67 (± 0.105) | -0.83 (± 0.107) | -1.00 (± 0.105) | |

Statistical analyses

| | |
|---|-----------------------------------|
| Statistical analysis title | Change From Baseline in PGA |
| Comparison groups | Placebo v 2 mg Baricitinib |
| Number of subjects included in analysis | 170 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.285 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference (Final Vaules) |
| Point estimate | -0.16 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.45 |
| upper limit | 0.13 |

| | |
|---|-----------------------------------|
| Statistical analysis title | Change From Baseline in PGA |
| Comparison groups | Placebo v 4 mg Baricitinib |
| Number of subjects included in analysis | 170 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.026 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference (Final Vaules) |
| Point estimate | -0.33 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.62 |
| upper limit | -0.04 |

Secondary: Population Pharmacokinetics (PK): Area Under the Concentration-Time Curve of Baricitinib at Steady State (AUC_{T, ss})

| | |
|-----------------|---|
| End point title | Population Pharmacokinetics (PK): Area Under the Concentration-Time Curve of Baricitinib at Steady State (AUC _{T, ss}) ^[1] |
|-----------------|---|

End point description:

Plasma samples for pharmacokinetic (PK) analysis were obtained in week 0, week 4, week 8, week 16 and 24. AUC takes all time points post dose into account and one value is reported.

Analysis Population Description: All randomized participants who received at least one dose of study drug and had evaluable PK (pharmacokinetics) data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week (Wk) 0: 15-30 minutes (min) postdose; Wk 4: Predose, 1.5 - 4 hour (hr) postdose; Wk 8: 1 - 3 hr postdose; Wk 16: Predose.

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No arm comparison analyses were planned or conducted.

| End point values | 2 mg Baricitinib | 4 mg Baricitinib | | |
|---|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 104 | 104 | | |
| Units: nanogram*hour per milliliter (ng*h/mL) | | | | |
| geometric mean (geometric coefficient of variation) | 265 (± 55) | 569 (± 50) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Population Pharmacokinetics (PK): Maximum Observed Drug Concentration at Steady State (C_{max,ss})

| | |
|-----------------|---|
| End point title | Population Pharmacokinetics (PK): Maximum Observed Drug Concentration at Steady State (C _{max,ss}) ^[2] |
|-----------------|---|

End point description:

Plasma samples for pharmacokinetic (PK) analysis were obtained in week 0, week 4, week 8, week 16 and 24. C_{max} takes all time points post dose into account and one value is reported.

Analysis Population Description: All randomized participants who received at least one dose of study drug and had evaluable PK (pharmacokinetics) data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week (Wk) 0: 15-30 minutes (min) postdose; Wk 4: Predose, 1.5 - 4 hour (hr) postdose; Wk 8: 1 - 3 hr postdose; Wk 16: Predose.

Notes:

[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: No arm comparison analyses were planned or conducted.

| End point values | 2 mg Baricitinib | 4 mg Baricitinib | | |
|---|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 104 | 104 | | |
| Units: nanogram per milliliter (ng/mL) | | | | |
| geometric mean (geometric coefficient of variation) | 29.0 (± 30) | 59.2 (± 24) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

I4V-MC-JAHH

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| | |
|-----------------------|------------------|
| Reporting group title | 4 mg Baricitinib |
|-----------------------|------------------|

Reporting group description: -

| | |
|-----------------------|------------------|
| Reporting group title | 2 mg Baricitinib |
|-----------------------|------------------|

Reporting group description: -

| Serious adverse events | Placebo | 4 mg Baricitinib | 2 mg Baricitinib |
|---|-----------------|------------------|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 105 (4.76%) | 10 / 104 (9.62%) | 11 / 105 (10.48%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| deep vein thrombosis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 0 / 105 (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 |
| hypertension | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 0 / 104 (0.00%) | 1 / 105 (0.95%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| abortion | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|---|-----------------|-----------------|
| subjects affected / exposed ^[1] | 0 / 99 (0.00%) | 0 / 99 (0.00%) | 1 / 96 (1.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| cervical dysplasia | Additional description: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly. | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed ^[2] | 0 / 99 (0.00%) | 0 / 99 (0.00%) | 1 / 96 (1.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| anxiety | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 0 / 104 (0.00%) | 1 / 105 (0.95%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| depression | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 2 / 104 (1.92%) | 0 / 105 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| mental status changes | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 0 / 104 (0.00%) | 1 / 105 (0.95%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| lipase increased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 0 / 105 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|-----------------------------------|-----------------------------------|-----------------------------------|
| ankle fracture alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 105 (0.95%) 0 / 1 0 / 0 | 0 / 104 (0.00%) 0 / 0 0 / 0 | 0 / 105 (0.00%) 0 / 0 0 / 0 |
| joint dislocation alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 105 (0.00%) 0 / 0 0 / 0 | 0 / 104 (0.00%) 0 / 0 0 / 0 | 1 / 105 (0.95%) 0 / 1 0 / 0 |
| tibia fracture alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 105 (0.95%) 0 / 1 0 / 0 | 1 / 104 (0.96%) 0 / 1 0 / 0 | 0 / 105 (0.00%) 0 / 0 0 / 0 |
| Cardiac disorders angina pectoris alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 105 (0.00%) 0 / 0 0 / 0 | 0 / 104 (0.00%) 0 / 0 0 / 0 | 1 / 105 (0.95%) 0 / 1 0 / 0 |
| Nervous system disorders migraine alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 105 (0.00%) 0 / 0 0 / 0 | 0 / 104 (0.00%) 0 / 0 0 / 0 | 1 / 105 (0.95%) 0 / 1 0 / 0 |
| syncope alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 105 (0.00%) 0 / 0 0 / 0 | 0 / 104 (0.00%) 0 / 0 0 / 0 | 1 / 105 (0.95%) 1 / 1 0 / 0 |
| Blood and lymphatic system disorders lymphadenopathy | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 0 / 104 (0.00%) | 1 / 105 (0.95%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 0 / 105 (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 |
| gastric ulcer | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 0 / 105 (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 |
| intestinal perforation | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 0 / 105 (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 |
| nausea | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 0 / 105 (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 |
| umbilical hernia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 105 (0.95%) | 0 / 104 (0.00%) | 0 / 105 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| volvulus | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 105 (0.00%) | 0 / 104 (0.00%) | 1 / 105 (0.95%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| acute kidney injury | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 0 / 105 (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 |
| lupus nephritis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 105 (0.95%) | 0 / 104 (0.00%) | 0 / 105 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| osteonecrosis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 0 / 105 (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 |
| pain in extremity | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 0 / 105 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| appendicitis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 0 / 105 (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 |
| cellulitis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 105 (0.95%) | 0 / 104 (0.00%) | 0 / 105 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| diverticulitis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 0 / 105 (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 |
| influenza | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 0 / 105 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pneumonia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 2 / 104 (1.92%) | 1 / 105 (0.95%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| tooth abscess | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 105 (0.95%) | 0 / 104 (0.00%) | 0 / 105 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 105 (0.00%) | 1 / 104 (0.96%) | 1 / 105 (0.95%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Notes:

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

Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects

exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

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

| Non-serious adverse events | Placebo | 4 mg Baricitinib | 2 mg Baricitinib |
|---|-------------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 27 / 105 (25.71%) | 32 / 104 (30.77%) | 36 / 105 (34.29%) |
| Nervous system disorders | | | |
| headache | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 3 / 105 (2.86%) | 3 / 104 (2.88%) | 6 / 105 (5.71%) |
| occurrences (all) | 3 | 4 | 8 |
| Infections and infestations | | | |
| pharyngitis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 3 / 105 (2.86%) | 5 / 104 (4.81%) | 6 / 105 (5.71%) |
| occurrences (all) | 3 | 5 | 6 |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 6 / 105 (5.71%) | 8 / 104 (7.69%) | 7 / 105 (6.67%) |
| occurrences (all) | 6 | 8 | 7 |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 11 / 105 (10.48%) | 9 / 104 (8.65%) | 10 / 105 (9.52%) |
| occurrences (all) | 15 | 15 | 12 |
| viral upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 4 / 105 (3.81%) | 10 / 104 (9.62%) | 10 / 105 (9.52%) |
| occurrences (all) | 5 | 12 | 13 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported