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	v1
This version publication date	14 October 2018
First version publication date	14 October 2018

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	Median difference (final values)
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	Median difference (final values)
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	Median difference (final values)
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	Median difference (final values)
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 (Cmax,ss)

End point title	Population Pharmacokinetics (PK): Maximum Observed Drug Concentration at Steady State (Cmax,ss)[2]

End point description:

Plasma samples for pharmacokinetic (PK) analysis were obtained in week 0, week 4, week 8, week 16 and 24. Cmax 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	2 mg Baricitinib
Reporting group description: -	
Reporting group title	4 mg Baricitinib
Reporting group description: -	

Serious adverse events	Placebo	2 mg Baricitinib	4 mg Baricitinib
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 105 (4.76%)	11 / 105 (10.48%)	10 / 104 (9.62%)
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%)	0 / 105 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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%)	1 / 105 (0.95%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
abortion			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed[1]	0 / 99 (0.00%)	1 / 96 (1.04%)	0 / 99 (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
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%)	1 / 96 (1.04%)	0 / 99 (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
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 105 (0.95%)	0 / 104 (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
depression			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 105 (0.00%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
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%)	1 / 105 (0.95%)	0 / 104 (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
Investigations			
lipase increased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 105 (0.00%)	1 / 104 (0.96%)
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 20.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 105 (0.00%)	0 / 104 (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
joint dislocation			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 105 (0.95%)	0 / 104 (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
tibia fracture			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 105 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
angina pectoris			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 105 (0.95%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
migraine			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 105 (0.95%)	0 / 104 (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
syncope			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 105 (0.95%)	0 / 104 (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
Blood and lymphatic system disorders			
lymphadenopathy			

alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 105 (0.95%)	0 / 104 (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
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 105 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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%)	0 / 105 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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%)	0 / 105 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
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%)	0 / 105 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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 / 105 (0.00%)	0 / 104 (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%)	1 / 105 (0.95%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 105 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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 / 105 (0.00%)	0 / 104 (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%)	0 / 105 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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%)	0 / 105 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 105 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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 / 105 (0.00%)	0 / 104 (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%)	0 / 105 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
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%)	0 / 105 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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%)	1 / 105 (0.95%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
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 / 105 (0.00%)	0 / 104 (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 / 105 (0.95%)	1 / 104 (0.96%)
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	2 mg Baricitinib	4 mg Baricitinib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 105 (25.71%)	36 / 105 (34.29%)	32 / 104 (30.77%)
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 105 (2.86%)	6 / 105 (5.71%)	3 / 104 (2.88%)
occurrences (all)	3	8	4
Infections and infestations			
pharyngitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 105 (2.86%)	6 / 105 (5.71%)	5 / 104 (4.81%)
occurrences (all)	3	6	5
upper respiratory tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	6 / 105 (5.71%)	7 / 105 (6.67%)	8 / 104 (7.69%)
occurrences (all)	6	7	8
urinary tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	11 / 105 (10.48%)	10 / 105 (9.52%)	9 / 104 (8.65%)
occurrences (all)	15	12	15
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	4 / 105 (3.81%)	10 / 105 (9.52%)	10 / 104 (9.62%)
occurrences (all)	5	13	12

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