Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Phase 3 Study of Baricitinib in Patients with Systemic Lupus Erythematosus

Summary

EudraCT number	2017-005027-25
Trial protocol	ES IT RO
Global end of trial date	20 October 2021

Results information

Result version number	v1 (current)
This version publication date	11 October 2022
First version publication date	11 October 2022

Trial information

Trial identification

Sponsor protocol code	I4V-MC-JAIA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03616964
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16677

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 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The reason for this study is to see how effective and safe the study drug known as baricitinib is in participants with systemic lupus erythematosus (SLE).

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	02 August 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 92
Country: Number of subjects enrolled	Chile: 34
Country: Number of subjects enrolled	Colombia: 48
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	India: 94
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Japan: 38
Country: Number of subjects enrolled	Philippines: 38
Country: Number of subjects enrolled	Poland: 93
Country: Number of subjects enrolled	Romania: 30
Country: Number of subjects enrolled	Serbia: 53
Country: Number of subjects enrolled	South Africa: 41
Country: Number of subjects enrolled	Korea, Republic of: 19
Country: Number of subjects enrolled	Spain: 30
Country: Number of subjects enrolled	United States: 149
Worldwide total number of subjects	775
EEA total number of subjects	169

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)	1
Adults (18-64 years)	733
From 65 to 84 years	41
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

As only year of birth was collected on case report form, for one participant, age at enrollment was calculated as 17 years old, using the imputed day and month of "01Jul ". Therefore, not necessarily indicating the participant's actual age.

Pre-assignment

Screening details:

Pharmacokinetic (PK) Population: 2 milligram (mg) Baricitinib (n=277), 4 mg Baricitinib (n=241). Participants with estimated glomerular filtration rate less than (<) 60 milliliter/minute (mL/min)/1.73 square meter (m2) at screening randomized to the 4 mg dose received a dose of 2 mg QD.

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 2 placebo tablets: one placebo tablet matching 4 mg baricitinib and one placebo tablet matching 2 mg baricitinib administered orally once daily (QD) for 52 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 2 placebo tablets: one placebo tablet matching 4 mg baricitinib and one placebo tablet matching 2 mg baricitinib administered orally QD for 52 weeks.

Arm title	2 mg Baricitinib

Arm description:

Participants received one 2 mg baricitinib tablet and one placebo tablet matching 4 mg baricitinib administered QD for 52 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:

Participants received one 2 mg baricitinib tablet and one placebo tablet matching 4 mg baricitinib administered orally QD for 52 weeks.

Arm title	4 mg Baricitinib

Arm description:

Participants received one 4 mg baricitinib tablet and one placebo tablet matching 2 mg baricitinib administered orally QD for 52 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:

Participants received one 4 mg baricitinib tablet and one placebo tablet matching 2 mg baricitinib administered QD for 52 weeks.

Number of subjects in period 1	Placebo	2 mg Baricitinib	4 mg Baricitinib
Started	256	261	258
Received at Least One Dose of Study Drug	256	261	258
Completed	212	222	205
Not completed	44	39	53
Adverse event, serious fatal	3	-	4
Consent withdrawn by subject	18	14	21
Physician decision	-	2	-
Adverse event, non-fatal	15	10	16
Due to Epidemic/Pandemic	-	1	-
Sponsor’s Decision	1	-	-
Withdrawal by Principal Investigator (PI)	1	1	1
Decreased Neutrophils due to SLE	-	1	-
Lost to follow-up	2	1	3
Lack of efficacy	4	8	8
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received 2 placebo tablets: one placebo tablet matching 4 mg baricitinib and one placebo tablet matching 2 mg baricitinib administered orally once daily (QD) for 52 weeks.	
Reporting group title	2 mg Baricitinib
Reporting group description:	
Participants received one 2 mg baricitinib tablet and one placebo tablet matching 4 mg baricitinib administered QD for 52 weeks.	
Reporting group title	4 mg Baricitinib
Reporting group description:	
Participants received one 4 mg baricitinib tablet and one placebo tablet matching 2 mg baricitinib administered orally QD for 52 weeks.	

Reporting group values	Placebo	2 mg Baricitinib	4 mg Baricitinib
Number of subjects	256	261	258
Age categorical			
Units: Subjects			
Age continuous			
Analysis population description (APD): All randomized participants who received at least one dose of study drug.			
Units: years			
arithmetic mean	43.50	42.80	42.20
standard deviation	± 13.47	± 12.99	± 12.11
Gender categorical			
APD: All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Female	241	246	245
Male	15	15	13
Ethnicity (NIH/OMB)			
APD: All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Hispanic or Latino	9	11	8
Not Hispanic or Latino	40	38	40
Unknown or Not Reported	207	212	210
Race (NIH/OMB)			
APD: All randomized participants who received at least one dose of study drug.			
Units: Subjects			
American Indian or Alaska Native	14	12	13
Asian	71	66	70
Native Hawaiian or Other Pacific Islander	0	0	1
Black or African American	17	23	26
White	145	152	140
More than one race	5	4	4
Unknown or Not Reported	4	4	4
Region of Enrollment			

APD: All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Argentina	34	29	29
Chile	8	14	12
Colombia	17	15	16
France	3	2	2
India	32	28	34
Italy	2	2	5
Japan	14	12	12
Philippines	13	14	11
Poland	26	36	31
Romania	12	11	7
Serbia	15	20	18
South Africa	14	15	12
South Korea	4	7	8
Spain	12	6	12
United States	50	50	49

Reporting group values	Total		
Number of subjects	775		
Age categorical Units: Subjects			

Age continuous			
Analysis population description (APD): All randomized participants who received at least one dose of study drug.			
Units: years arithmetic mean standard deviation	- -		
Gender categorical			
APD: All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Female	732		
Male	43		
Ethnicity (NIH/OMB)			
APD: All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Hispanic or Latino	28		
Not Hispanic or Latino	118		
Unknown or Not Reported	629		
Race (NIH/OMB)			
APD: All randomized participants who received at least one dose of study drug.			
Units: Subjects			
American Indian or Alaska Native	39		
Asian	207		
Native Hawaiian or Other Pacific Islander	1		
Black or African American	66		
White	437		
More than one race	13		
Unknown or Not Reported	12		
Region of Enrollment			

APD: All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Argentina	92		
Chile	34		
Colombia	48		
France	7		
India	94		
Italy	9		
Japan	38		
Philippines	38		
Poland	93		
Romania	30		
Serbia	53		
South Africa	41		
South Korea	19		
Spain	30		
United States	149		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received 2 placebo tablets: one placebo tablet matching 4 mg baricitinib and one placebo tablet matching 2 mg baricitinib administered orally once daily (QD) for 52 weeks.	
Reporting group title	2 mg Baricitinib
Reporting group description:	
Participants received one 2 mg baricitinib tablet and one placebo tablet matching 4 mg baricitinib administered QD for 52 weeks.	
Reporting group title	4 mg Baricitinib
Reporting group description:	
Participants received one 4 mg baricitinib tablet and one placebo tablet matching 2 mg baricitinib administered orally QD for 52 weeks.	
Subject analysis set title	2 mg Baricitinib
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Participants received one 2 mg baricitinib tablet and one placebo tablet matching 4 mg baricitinib administered QD for 52 weeks.	
Subject analysis set title	4 mg Baricitinib
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Participants received one 4 mg baricitinib tablet and one placebo tablet matching 2 mg baricitinib administered QD for 52 weeks.	

Primary: Percentage of Participants Achieving a Systemic Lupus Erythematosus Responder Index 4 (SRI-4) Response (4 mg Baricitinib)

End point title	Percentage of Participants Achieving a Systemic Lupus Erythematosus Responder Index 4 (SRI-4) Response (4 mg Baricitinib)[1]
End point description:	
SRI-4 response defined as 1)greater than or equal to (>=) 4-point reduction in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) total score 2)no new British Isles Lupus Assessment Group (BILAG) A and no more than 1 new BILAG B domain score and 3)no worsening in Physician Global Assessment (PGA) of Disease Activity (worsening defined as an increase of >=0.3 from baseline on a 0-3 visual analogue scale). SLEDAI-2K assessment consists of 24 items with total score of 0(no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity. BILAG Index: assessing clinical signs, symptoms,or laboratory parameters related to Systemic Lupus Erythematosus (SLE),divided into 9 organ systems. For each organ system A=severe disease,B=moderate disease,C=mild stable disease,D=inactive,but previously active,E=inactive and never affected. PGA assess disease activity on a visual analogue scale from 0 to 3 (1=mild, 2=moderate, 3=severe).	
End point type	Primary
End point timeframe:	
Week 52 APD: All randomized participants who received at least one dose of study drug (modified intent-to-treat (mITT) population). Missing data was imputed using the hybrid imputation method [nonresponder imputation (NRI) + multiple imputation (MI)].	

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: The endpoint is planned only for these reporting arms.

End point values	Placebo	4 mg Baricitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	258		
Units: percentage of participants				
number (not applicable)	45.6	47.1		

Statistical analyses

Statistical analysis title	SRI-4 Response (4 mg)
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	514
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.711
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.53

Secondary: Percentage of Participants Achieving SRI-4 Response (2 mg Baricitinib)

End point title	Percentage of Participants Achieving SRI-4 Response (2 mg Baricitinib)[2]

End point description:

SRI-4 response defined as 1)greater than or equal to (>=) 4-point reduction in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) total score 2)no new British Isles Lupus Assessment Group (BILAG) A and no more than 1 new BILAG B domain score and 3)no worsening in Physician Global Assessment (PGA) of Disease Activity (worsening defined as an increase of >=0.3 from baseline on a 0-3 visual analogue scale).
SLEDAI-2K assessment consists of 24 items with total score of 0(no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity. BILAG Index: assessing clinical signs, symptoms,or laboratory parameters related to Systemic Lupus Erythematosus (SLE),divided into 9 organ systems. For each organ system A=severe disease,B=moderate disease,C=mild stable disease,D=inactive,but previously active,E=inactive and never affected. PGA assess disease activity on a visual analogue scale from 0 to 3 (1=mild, 2=moderate, 3=severe).

End point type	Secondary

End point timeframe:

Week 52
APD: All randomized participants who received at least 1 dose of study drug (mITT population). Missing data was imputed using the hybrid imputation method [nonresponder imputation (NRI) + multiple imputation (MI)].

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: The endpoint is planned only for these reporting arms.

End point values	Placebo	2 mg Baricitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	261		
Units: percentage of participants				
number (not applicable)	45.6	46.3		

Statistical analyses

Statistical analysis title	SRI-4 Response (2 mg)
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.789
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.5

Secondary: Percentage of Participants Achieving a Lupus Low Disease Activity State (LLDAS)

End point title	Percentage of Participants Achieving a Lupus Low Disease Activity State (LLDAS)

End point description:

The LLDAS is a composite measure designed to identify patients achieving a state of low disease activity. The LLDAS response criteria were: (1) SLEDAI-2K <=4, with no activity in major organ systems (CNS, vascular, renal, cardiorespiratory and constitutional); where "no activity" is defined as all items of SLEDAI-2K within these major organ systems equal to 0. (2) no new features of lupus disease activity compared to previous occurred visit, where the "new feature" is defined as any of the SLEDAI-2K 24 items changed from 0 to greater than 0; (3) PGA (scale 0-3), <=1; (4) current prednisolone (or equivalent) dose <=7.5 mg daily. APD: All randomized participants who received at least 1 dose of study drug (mITT population). Missing data was imputed using the hybrid imputation method [nonresponder imputation (NRI) + multiple imputation (MI)].

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	256	261	258	
Units: percentage of participants				
number (not applicable)	23.2	24.0	25.4	

Statistical analyses

Statistical analysis title	Lupus Low Disease Activity State (2 mg)
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.673
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.68

Statistical analysis title	Lupus Low Disease Activity State (4 mg)
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	514
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.528
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.75

Secondary: Time to First Severe Flare

End point title	Time to First Severe Flare

End point description:

Time to first severe flare analyzed using a Cox proportional hazards model with treatment group, baseline disease activity [Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) <10; SLEDAI-2K ≥10], baseline corticosteroid dose (<10 mg/day; ≥10 mg/day prednisone or equivalent),

and region fitted as explanatory variables. Participants who did not have severe flare during the flare exposure time period were censored at the end of the flare exposure time. APD: All randomized participants who received at least 1 dose of study drug (mITT population). 9999=Data Not Available (N/A) as < 50% of participants experienced first flare, median was not reached, and 95% confidence interval could not be calculated.

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	256	251	258	
Units: weeks				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Whose Average Prednisone Dose Had Been Reduced by >=25% From Baseline to <=7.5 mg/Day During Weeks 40 Through 52 in Participants Receiving Greater Than 7.5 mg/Day at Baseline

End point title	Percentage of Participants Whose Average Prednisone Dose Had Been Reduced by >=25% From Baseline to <=7.5 mg/Day During Weeks 40 Through 52 in Participants Receiving Greater Than 7.5 mg/Day at Baseline

End point description:

For the analysis of steroid use, steroid dosages were converted to a prednisone equivalent in mg. A responder was defined as having a prednisone reduction by >=25% from Baseline to <=7.5 mg/day during Weeks 40 through 52. APD: All randomized participants who received at least 1 dose of study drug (mITT population) and had received >7.5 mg prednisone at baseline. Missing data was imputed using the hybrid imputation method [NRI + mLOCF (modified last observation carried forward)].

End point type	Secondary

End point timeframe:

Baseline, Week 40 through Week 52

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	104	114	105	
Units: percentage of participants				
number (not applicable)	31.7	29.8	34.3	

Statistical analyses

Statistical analysis title	Prednisone Dose Reduction (2 mg)
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.761
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.64

Statistical analysis title	Prednisone Dose Reduction (4 mg)
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	209
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.611
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	2.1

Secondary: Change from Baseline in Worst Pain Numeric Rating Scale (NRS)

End point title	Change from Baseline in Worst Pain Numeric Rating Scale (NRS)

End point description:

Participants assessed the worst pain in the last 24 hours on an 11-point numeric rating scale (NRS) ranging from 0 (no pain) to 10 (pain as bad as you can imagine). The average worst daily pain score was calculated as the mean of the scores over the last 7 days prior to each assessment time point. Higher score indicated severe pain. Least Squares (LS) mean was calculated using MMRM analysis with treatment, baseline disease activity (total SLEDAI-2K <10; >=10), baseline corticosteroid dose (<10 mg/day; >= 10 mg/day prednisone or equivalent), region (North America, Central/South, America/Mexico, Europe, Asia Rest of World), visit (as categorical variable), baseline value, treatment-by-visit interaction, and baseline value-by-visit interaction. APD: All randomized participants who received at least one dose of study drug (mITT population) and had baseline and post-baseline values at the specified time point. Missing data was imputed using the hybrid imputation method (NRI + MMRM).

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	183	182	179	
Units: score on a scale				
least squares mean (standard error)	-1.37 (± 0.14)	-1.45 (± 0.14)	-1.44 (± 0.14)	

Statistical analyses

Statistical analysis title	Change from Baseline in Worst Pain NRS (2 mg)
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.698
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.32
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Change from Baseline in Worst Pain NRS (4 mg)
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	362
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.744
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.33
Variability estimate	Standard error of the mean
Dispersion value	0.2

Secondary: Change from Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Total Score

End point title	Change from Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Total Score

End point description:

FACIT-Fatigue score calculated according to a 13-item questionnaire that assess self reported fatigue and its impact upon daily activities and function. It uses a 5-point Likert-type scale (0 = not at all; 1 = a little bit; 2 = somewhat; 3 = quite a bit; 4 = very much). The sum of all responses resulted in the FACIT-Fatigue score for a total possible score of 0 (worse possible score) to 52 (best score). A higher score reflected an improvement in the participant's health status. Least Squares (LS) mean was calculated using Mixed Model Repeated Measures (MMRM) analysis with treatment, baseline disease activity (total SLEDAI-2K <10; >=10), baseline corticosteroid dose (<10 mg/day; >= 10 mg/day prednisone or equivalent), region (North America, Central/South, America/Mexico, Europe, Asia Rest of World), visit (as categorical variable), baseline value, treatment-by-visit interaction, and baseline value-by-visit interaction.

End point type	Secondary

End point timeframe:

Baseline, Week 52
APD:All randomized participants who received at least one dose of study drug (mITT population) and had baseline and post-baseline values at the specified time point.Missing data was imputed using the hybrid imputation method (NRI+MMRM).

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	200	203	193	
Units: score on a scale				
least squares mean (standard error)	7.26 (± 0.60)	6.90 (± 0.60)	6.96 (± 0.61)	

Statistical analyses

Statistical analysis title	Change from Baseline in FACIT-Fatigue (2 mg)
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.665
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	1.28
Variability estimate	Standard error of the mean
Dispersion value	0.84

Statistical analysis title	Change from Baseline in FACIT-Fatigue (4 mg)
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.723
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.95
upper limit	1.35
Variability estimate	Standard error of the mean
Dispersion value	0.84

Secondary: Percentage of Participants with Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) Total Activity Score ≥10 at Baseline with ≥50% Reduction in CLASI Total Activity Score

End point title	Percentage of Participants with Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) Total Activity Score ≥10 at Baseline with ≥50% Reduction in CLASI Total Activity Score

End point description:

The CLASI is a single-page tool that separately quantifies disease activity and damage. For the activity score, points are given for the presence of erythema, scale, mucous membrane lesions, recent hair loss, and inflammatory alopecia. The total score represents the sum of the individual scores and ranges from 0 to 70. Higher scores are awarded for more severe manifestations. Analysis population description included all randomized participants who received at least one dose of study drug (mITT population) and had baseline CLASI score >=10. Missing data was imputed using NRI method. APD: All randomized participants who received at least one dose of study drug (mITT population) and had baseline CLASI score >=10. Missing data was imputed using NRI method.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	51	50	
Units: percentage of participants				
number (not applicable)	66.1	56.9	58.0	

Statistical analyses

Statistical analysis title	50% Reduction in CLASI (2 mg)
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.372
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	1.55

Statistical analysis title	50% Reduction in CLASI (4 mg)
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.555
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	1.78

Secondary: Change from Baseline in Tender Joint Count

End point title	Change from Baseline in Tender Joint Count

End point description:

The number of tender and painful joints is determined by examination of 28 joints (14 on each side) which include: the 2 shoulders, the 2 elbows, the 2 wrists, the 10 metacarpophalangeal joints, the 2 interphalangeal joints of the thumb, the 8 proximal interphalangeal joints, and the 2 knees. The joints are assessed and classified as tender or not tender. LS mean was calculated using Mixed Model Repeated Measures (MMRM) analysis with treatment, baseline disease activity (total SLEDAI-2K <10; >=10), baseline corticosteroid dose (<10 mg/day; >=10 mg/day prednisone or equivalent), region (North America, Central/South America/Mexico, Europe, Asia and Rest of World), visit (as categorical

variable), baseline value, treatment-by-visit interaction, and baseline value-by-visit interaction. APD: All randomized participants who received at least one dose of study drug (mITT population) and had baseline and post-baseline values at the specified time point.

End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	200	201	190	
Units: tender joint count				
least squares mean (standard error)	-6.92 (± 0.301)	-7.40 (± 0.300)	-7.83 (± 0.306)	

Statistical analyses

Statistical analysis title	Change from Baseline Tender joint Count (2 mg)
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.251
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	0.34
Variability estimate	Standard error of the mean
Dispersion value	0.422

Statistical analysis title	Change from Baseline Tender joint Count (4 mg)
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	390
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.333
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.91

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.74
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.425

Secondary: Change from Baseline in Swollen Joint Count

End point title	Change from Baseline in Swollen Joint Count

End point description:

The number of swollen joints is determined by examination of 28 joints (14 on each side) which include: the 2 shoulders, the 2 elbows, the 2 wrists, the 10 metacarpophalangeal joints, the 2 interphalangeal joints of the thumb, the 8 proximal interphalangeal joints, and the 2 knees. The joints are assessed and classified as swollen or not swollen. LS mean was calculated using MMRM analysis with treatment, baseline disease activity (total SLEDAI-2K <10; >=10), baseline corticosteroid dose (<10 mg/day; >=10 mg/day prednisone or equivalent), region (North America, Central/South America/Mexico, Europe, Asia and Rest of World), visit (as categorical variable), baseline value, treatment-by-visit interaction, and baseline value-by-visit interaction. Analysis population description included all randomized participants who received at least one dose of study drug (mITT population) and had baseline and post-baseline values at the specified time point.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	200	201	190	
Units: swollen joint count				
least squares mean (standard error)	-4.79 (± 0.202)	-5.10 (± 0.201)	-5.31 (± 0.205)	

Statistical analyses

Statistical analysis title	Change from Baseline Swollen joint Count (2 mg)
Comparison groups	2 mg Baricitinib v Placebo
Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.284
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	0.25
Variability estimate	Standard error of the mean
Dispersion value	0.282

Statistical analysis title	Change from Baseline Swollen joint Count (4 mg)
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	390
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.069
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.08
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.284

Secondary: Population Pharmacokinetics (PK): Area Under the Concentration-Time Curve for Dosing Interval of Baricitinib at Steady State (AUCtau,ss)

End point title	Population Pharmacokinetics (PK): Area Under the Concentration-Time Curve for Dosing Interval of Baricitinib at Steady State (AUCtau,ss)

End point description:

AUCtau,ss reported for participants who received multiple doses of mg baricitinib was derived by a population pharmacokinetics approach. APD: All randomized participants who received at least one dose of study drug with evaluable PK data. Analysis population description included all randomized participants who received at least one dose of study drug with evaluable PK data.

End point type	Secondary

End point timeframe:

Week 0 (Baseline): 15 minutes (min) and 60 min postdose; Week 4: 2 to 4 hours (hr) postdose; Week 8: 4 to 6 hr postdose; Week 12 and Week 16 predose

End point values	2 mg Baricitinib	4 mg Baricitinib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	277	241		
Units: nanogram*hour/milliliter (ng*h/mL)				
geometric mean (geometric coefficient of variation)	257 (± 48)	505 (± 50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Population PK: Maximum Observed Drug Concentration at Steady State (Cmax,ss)

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

End point description:

PK: Maximum Concentration of Baricitinib at steady-state (Cmax,ss) was derived by a population pharmacokinetics approach. APD: All randomized participants who received at least one dose of study drug with evaluable PK data. Analysis population description included all randomized participants who received at least one dose of study drug with evaluable PK data.

End point type	Secondary

End point timeframe:

Week 0 (Baseline): 15 minutes (min) and 60 min postdose; Week 4: 2 to 4 hours (hr) postdose; Week 8: 4 to 6 hr postdose; Week 12 and Week 16 predose

End point values	2 mg Baricitinib	4 mg Baricitinib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	277	241		
Units: nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)	27.0 (± 23)	54.1 (± 24)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline through Follow-up (Up to 56 Weeks)

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug and who did not discontinue from the study for the reason 'Lost to Follow-up' at the first postbaseline visit. Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received 2 placebo tablets: one placebo tablet matching 4 mg baricitinib and one placebo tablet matching 2 mg baricitinib administered orally QD for 52 weeks.

Reporting group title	2 mg Baricitinib

Reporting group description:

Participants received one 2 mg baricitinib tablet and one placebo tablet matching 4 mg baricitinib administered QD for 52 weeks.

Reporting group title	4 mg Baricitinib

Reporting group description:

Participants received one 4 mg baricitinib tablet and one placebo tablet matching 2 mg baricitinib administered QD for 52 weeks.

Serious adverse events	Placebo	2 mg Baricitinib	4 mg Baricitinib
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 256 (10.16%)	35 / 261 (13.41%)	32 / 258 (12.40%)
number of deaths (all causes)	3	0	4
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
basal cell carcinoma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
cervix carcinoma			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed[1]	0 / 241 (0.00%)	1 / 246 (0.41%)	0 / 245 (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
gastric cancer			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
squamous cell carcinoma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 256 (0.78%)	0 / 261 (0.00%)	0 / 258 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral ischaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
Surgical and medical procedures			
hip arthroplasty			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	2 / 261 (0.77%)	0 / 258 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
knee arthroplasty			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
rehabilitation therapy			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thyroidectomy			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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 spontaneous			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[2]	1 / 241 (0.41%)	1 / 246 (0.41%)	1 / 245 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
chest pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fatigue			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
oedema peripheral			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
Reproductive system and breast disorders			
genital prolapse			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
ovarian cyst			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[3]	0 / 241 (0.00%)	1 / 246 (0.41%)	0 / 245 (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
pelvic pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
postmenopausal haemorrhage			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[4]	1 / 241 (0.41%)	0 / 246 (0.00%)	0 / 245 (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
Respiratory, thoracic and mediastinal disorders			
acute respiratory failure			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
haemoptysis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
hyperventilation			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
pulmonary embolism			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	1 / 261 (0.38%)	0 / 258 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
psychotic disorder			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
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			
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
blood creatine phosphokinase increased			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
electrocardiogram t wave inversion			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
femur fracture			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
humerus fracture			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
lumbar vertebral fracture			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
post procedural haemorrhage			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
soft tissue injury			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
tendon rupture			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
atrial fibrillation			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac arrest			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myocardial infarction			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
headache			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
post herpetic neuralgia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
transient ischaemic attack			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
autoimmune haemolytic anaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
pancytopenia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	2 / 258 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
vertigo positional			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 256 (0.39%)	1 / 261 (0.38%)	0 / 258 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diarrhoea			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
food poisoning			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
gastritis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	1 / 261 (0.38%)	0 / 258 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intestinal pseudo-obstruction			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
pancreatitis acute			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

upper gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
vomiting			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
Hepatobiliary disorders			
cholelithiasis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	2 / 258 (0.78%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
lupus nephritis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
nephrotic syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
pelvi-ureteric obstruction			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ureterolithiasis			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
back pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
costochondritis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
foot deformity			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteoarthritis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteonecrosis			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
spinal stenosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
systemic lupus erythematosus			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	6 / 261 (2.30%)	3 / 258 (1.16%)
occurrences causally related to treatment / all	0 / 0	2 / 7	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
abscess jaw			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
appendicitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bronchitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
covid-19			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 256 (0.39%)	2 / 261 (0.77%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
covid-19 pneumonia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	1 / 261 (0.38%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
cellulitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
coronavirus infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cytomegalovirus colitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
disseminated varicella zoster virus infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
erysipelas			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastroenteritis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
gastroenteritis salmonella			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
herpes zoster meningomyelitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nasopharyngitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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
pneumonia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 256 (1.17%)	1 / 261 (0.38%)	2 / 258 (0.78%)
occurrences causally related to treatment / all	0 / 3	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
pneumonia bacterial			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 256 (0.78%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

pyelonephritis alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	0 / 258 (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
salmonellosis alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
sinusitis alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 256 (0.39%)	1 / 261 (0.38%)	0 / 258 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tubo-ovarian abscess alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[5]	0 / 241 (0.00%)	1 / 246 (0.41%)	0 / 245 (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
typhoid fever alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 256 (0.39%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urosepsis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	0 / 261 (0.00%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	1 / 258 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
hyponatraemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 256 (0.00%)	1 / 261 (0.38%)	0 / 258 (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

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: Gender specific events only occurring in male or female participants have had the number of participants at risk 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: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.
[3] - 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: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.
[4] - 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: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.
[5] - 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: Gender specific events only occurring in male or female participants have had the number of participants at risk 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	96 / 256 (37.50%)	100 / 261 (38.31%)	96 / 258 (37.21%)
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	9 / 256 (3.52%)	12 / 261 (4.60%)	13 / 258 (5.04%)
occurrences (all)	9	13	14
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	23 / 256 (8.98%)	25 / 261 (9.58%)	19 / 258 (7.36%)
occurrences (all)	26	28	21
Blood and lymphatic system disorders			
neutropenia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	7 / 256 (2.73%)	5 / 261 (1.92%)	13 / 258 (5.04%)
occurrences (all)	9	6	19
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	13 / 256 (5.08%)	20 / 261 (7.66%)	10 / 258 (3.88%)
occurrences (all)	14	25	11
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	6 / 256 (2.34%)	8 / 261 (3.07%)	15 / 258 (5.81%)
occurrences (all)	6	8	20
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	23 / 256 (8.98%)	18 / 261 (6.90%)	21 / 258 (8.14%)
occurrences (all)	28	20	27
upper respiratory tract infection			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	13 / 256 (5.08%)	17 / 261 (6.51%)	19 / 258 (7.36%)
occurrences (all)	16	18	22
urinary tract infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	26 / 256 (10.16%)	29 / 261 (11.11%)	19 / 258 (7.36%)
occurrences (all)	32	36	26

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 December 2018	- Modified logistic regression analyses; - Clarified the definition of post-menopausal; - Data from types of chest imaging other than x-ray can be accepted for tuberculosis screening; - Arterial thromboembolic events (ATEs) adjudicated by a blinded clinical event committee; - Analysis Methods were revised; - Language was revised for missing data imputation; - Subgroup analysis has been removed from the protocol.
20 April 2020	- Participant number and statistical analysis was revised to account for COVID-19 affected participants; - Protocol updated to include provisions put into place in order to assure the safety of trial participants and minimizing risks to trial integrity during the COVID-19 pandemic; - Schedule of activities was clarified; - Analysis of British Isles Lupus Assessment Group Based Composite Lupus Assessment (BICLA) endpoint was included in the protocol to supplement efficacy analyses; - Updated to clarify that while most concomitant medications should remain stable during the trial, reductions in dose for safety are permitted; - Updated to clarify that prohibited use of corticosteroids for SLE requires discontinuation from study drug, while use of prohibited doses of corticosteroids for other reasons may not require discontinuation of study drug; - An interim analysis has been added to assess the likelihood of trial failure time prior to trial conclusion in order to minimize participant exposure to an ineffective drug.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported