EU Clinical Trials Register

Clinical trial results:
A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Baricitinib in Adult Patients with Moderate to Severe Atopic Dermatitis

Summary

EudraCT number	2017-000870-12
Trial protocol	CZ DE FR DK IT
Global end of trial date	16 August 2019

Results information

Result version number	v1 (current)
This version publication date	23 August 2020
First version publication date	23 August 2020

Trial information

Trial identification

Sponsor protocol code	I4V-MC-JAHL

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03334396
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16580

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, 1 877-CTLilly,
Scientific contact	Available Mon-Fri 9 AM - 5 PM EST, Eli Lilly, 1 877-285-4559,

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	16 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 December 2018
Global end of trial reached?	Yes
Global end of trial date	16 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy and safety of baricitinib as monotherapy in participants with moderate to severe atopic dermatitis.

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 was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 November 2017
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	Japan: 111
Country: Number of subjects enrolled	Taiwan: 63
Country: Number of subjects enrolled	Italy: 44
Country: Number of subjects enrolled	Mexico: 73
Country: Number of subjects enrolled	India: 46
Country: Number of subjects enrolled	Russian Federation: 30
Country: Number of subjects enrolled	Czech Republic: 76
Country: Number of subjects enrolled	France: 39
Country: Number of subjects enrolled	Germany: 178
Worldwide total number of subjects	660
EEA total number of subjects	337

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)	643
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants who completed double blind treatment phase had option to enter extension study I4V-MC-JAHN, EU#: 2017-000873-35

Pre-assignment

Screening details:

No Text

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:

Placebo administered orally once daily.

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:

Placebo administered orally once daily.

Arm title	1 mg Baricitinib

Arm description:

1 mg Baricitinib administered orally once daily.

Arm type	Experimental
Investigational medicinal product name	1 mg Baricitinib
Investigational medicinal product code	LY3009104
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg Baricitinib administered orally once daily.

Arm title	2 mg Baricitinib

Arm description:

2 mg Baricitinib administered orally once daily.

Arm type	Experimental
Investigational medicinal product name	2 mg Baricitinib
Investigational medicinal product code	LY3009104
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 mg Baricitinib administered orally once daily.

Arm title	4 mg Baricitinib

Arm description:

4 mg Baricitinib administered orally once daily.

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:

4 mg Baricitinib administered orally once daily.

Arm title	Placebo Maximum Extended Enrollment (MEE)

Arm description:

Placebo administered orally once daily.

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:

Placebo administered orally once daily.

Arm title	1 mg Baricitinib MEE

Arm description:

1 mg Baricitinib administered orally once daily.

Arm type	Experimental
Investigational medicinal product name	1 mg Baricitinib
Investigational medicinal product code	LY3009104
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg Baricitinib administered orally once daily.

Arm title	2 mg Baricitinib MEE

Arm description:

2 mg Baricitinib administered orally once daily.

Arm type	Experimental
Investigational medicinal product name	2 mg Baricitinib
Investigational medicinal product code	LY3009104
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 mg Baricitinib administered orally once daily.

Arm title	4 mg Baricitinib MEE

Arm description:	
4 mg Baricitinib administered orally once daily.	
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:

4 mg Baricitinib administered orally once daily.

Number of subjects in period 1	Placebo	1 mg Baricitinib	2 mg Baricitinib
Started	249	127	123
Received at Least One Dose of Study Drug	249	127	123
Completed	226	116	113
Not completed	23	11	10
Ineligible	-	1	-
Physician decision	1	-	-
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	1	-	1
Started new job	1	-	-
Pregnancy	-	1	-
Lost to follow-up	-	-	1
Lack of efficacy	10	4	1
Withdrawal by subject	10	5	7

Number of subjects in period 1	4 mg Baricitinib	Placebo Maximum Extended Enrollment (MEE)	1 mg Baricitinib MEE
Started	125	15	5
Received at Least One Dose of Study Drug	125	15	5
Completed	120	12	4
Not completed	5	3	1
Ineligible	-	-	-
Physician decision	-	-	-
Consent withdrawn by subject	-	2	1
Adverse event, non-fatal	-	-	-
Started new job	-	-	-
Pregnancy	-	-	-
Lost to follow-up	-	-	-
Lack of efficacy	3	1	-

Withdrawal by subject	2	-	-

Number of subjects in period 1	2 mg Baricitinib MEE	4 mg Baricitinib MEE
Started	8	8
Received at Least One Dose of Study Drug	8	8
Completed	5	7
Not completed	3	1
Ineligible	-	-
Physician decision	-	-
Consent withdrawn by subject	2	-
Adverse event, non-fatal	-	-
Started new job	-	-
Pregnancy	-	-
Lost to follow-up	1	-
Lack of efficacy	-	1
Withdrawal by subject	-	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo administered orally once daily.	
Reporting group title	1 mg Baricitinib
Reporting group description:	
1 mg Baricitinib administered orally once daily.	
Reporting group title	2 mg Baricitinib
Reporting group description:	
2 mg Baricitinib administered orally once daily.	
Reporting group title	4 mg Baricitinib
Reporting group description:	
4 mg Baricitinib administered orally once daily.	
Reporting group title	Placebo Maximum Extended Enrollment (MEE)
Reporting group description:	
Placebo administered orally once daily.	
Reporting group title	1 mg Baricitinib MEE
Reporting group description:	
1 mg Baricitinib administered orally once daily.	
Reporting group title	2 mg Baricitinib MEE
Reporting group description:	
2 mg Baricitinib administered orally once daily.	
Reporting group title	4 mg Baricitinib MEE
Reporting group description:	
4 mg Baricitinib administered orally once daily.	

Reporting group values	Placebo	1 mg Baricitinib	2 mg Baricitinib
Number of subjects	249	127	123
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	242	127	118
From 65-84 years	7	0	5
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	101	49	41
Male	148	78	82

Race			
Units: Subjects			
American Indian or Alaska Native	14	7	7
Asian	73	40	35
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	147	74	75
More than one race	13	6	5
Unknown or Not Reported	2	0	0
Region of Enrollment			
Units: Subjects			
Czechia	36	11	11
Japan	45	23	21
Taiwan	25	13	13
Italy	17	8	6
Mexico	32	15	17
France	15	4	13
Germany	67	44	37
India	1	2	1
Russia	11	7	4

Reporting group values	4 mg Baricitinib	Placebo Maximum Extended Enrollment (MEE)	1 mg Baricitinib MEE
Number of subjects	125	15	5
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	121	15	5
From 65-84 years	4	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	42	6	2
Male	83	9	3
Race			
Units: Subjects			
American Indian or Alaska Native	2	0	0
Asian	41	15	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	0
White	70	0	0
More than one race	10	0	0
Unknown or Not Reported	1	0	0
Region of Enrollment			

Units: Subjects			
Czechia	18	0	0
Japan	22	0	0
Taiwan	12	0	0
Italy	13	0	0
Mexico	9	0	0
France	7	0	0
Germany	30	0	0
India	6	15	5
Russia	8	0	0

Reporting group values	2 mg Baricitinib MEE	4 mg Baricitinib MEE	Total
Number of subjects	8	8	660
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	8	643
From 65-84 years	1	0	17
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	0	2	243
Male	8	6	417
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	30
Asian	8	8	225
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	2
White	0	0	366
More than one race	0	0	34
Unknown or Not Reported	0	0	3
Region of Enrollment			
Units: Subjects			
Czechia	0	0	76
Japan	0	0	111
Taiwan	0	0	63
Italy	0	0	44
Mexico	0	0	73
France	0	0	39
Germany	0	0	178
India	8	8	46
Russia	0	0	30

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo administered orally once daily.	
Reporting group title	1 mg Baricitinib
Reporting group description:	
1 mg Baricitinib administered orally once daily.	
Reporting group title	2 mg Baricitinib
Reporting group description:	
2 mg Baricitinib administered orally once daily.	
Reporting group title	4 mg Baricitinib
Reporting group description:	
4 mg Baricitinib administered orally once daily.	
Reporting group title	Placebo Maximum Extended Enrollment (MEE)
Reporting group description:	
Placebo administered orally once daily.	
Reporting group title	1 mg Baricitinib MEE
Reporting group description:	
1 mg Baricitinib administered orally once daily.	
Reporting group title	2 mg Baricitinib MEE
Reporting group description:	
2 mg Baricitinib administered orally once daily.	
Reporting group title	4 mg Baricitinib MEE
Reporting group description:	
4 mg Baricitinib administered orally once daily.	

Primary: Percentage of Participants Achieving Investigator's Global Assessment (IGA) of 0 or 1 With a ≥ 2 Point Improvement (2 mg and 4 mg Baricitinib)

End point title	Percentage of Participants Achieving Investigator's Global Assessment (IGA) of 0 or 1 With a ≥ 2 Point Improvement (2 mg and 4 mg Baricitinib)[1]

End point description:

The IGA measures the investigator's global assessment of the participant's overall severity of their Atopic Dermatitis (AD), based on a static, numeric 5-point scale from 0 (clear skin) to 4 (severe disease). The score is based on an overall assessment of the degree of erythema, papulation/induration, oozing/crusting, and lichenification.

Analysis Population Description(APD): All participants randomized to placebo, 2 mg, or 4 mg of study drug.

End point type	Primary

End point timeframe:

16 Weeks

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: Per protocol, the primary outcome measure was to compare the response in participants who received the 2 mg and 4 mg doses of Baricitinib to the response of participants who received placebo.

A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into

the analysis of the global study cohort.

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	249	123	125	
Units: percentage of participants				
number (not applicable)	4.8	11.4	16.8	

Statistical analyses

Statistical analysis title	IGA of 0 or 1: 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	5.84

Statistical analysis title	IGA of 0 or 1: 4 mg Baricitinib
Comparison groups	4 mg Baricitinib v Placebo
Number of subjects included in analysis	374
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.93
upper limit	8.7

Secondary: Percentage of Participants Achieving IGA of 0 or 1 With a ≥ 2 Point Improvement (1 mg Baricitinib)

End point title	Percentage of Participants Achieving IGA of 0 or 1 With a ≥ 2 Point Improvement (1 mg Baricitinib)[2]

End point description:

The IGA measures the investigator's global assessment of the participant's overall severity of their AD, based on a static, numeric 5-point scale from 0 (clear skin) to 4 (severe disease). The score is based on an overall assessment of the degree of erythema, papulation/induration, oozing/crusting, and lichenification.

Analysis Population Description: All participants randomized to placebo or 1 mg of study drug .

End point type	Secondary

End point timeframe:

16 Weeks

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: Per protocol, the secondary outcome measure was to compare the response in participants who received the 1 mg dose of Baricitinib to the response of participants who received placebo.

A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	249	127		
Units: percentage of participants				
number (not applicable)	4.8	11.8		

Statistical analyses

Statistical analysis title	IGA of 0 or 1 - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	6.01

Secondary: Percentage of Participants Achieving Eczema Area and Severity Index 75 (EASI75)

End point title	Percentage of Participants Achieving Eczema Area and Severity Index 75 (EASI75)[3]

End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent and clinical signs affected: 0 = 0%; 1 = 1-9%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6 = 90-100% and the severity of 4 clinical signs: (1) erythema, (2) edema/papulation, (3) excoriation, and (4) lichenification each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head/neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2, and 3. The final EASI score was obtained by weight-averaging these 4 scores and will range from 0 to 72 (severe). The EASI75 is defined as a ≥ 75% improvement from baseline in the EASI score.

Analysis Population Description: All randomized participants.

End point type	Secondary

End point timeframe:

16 Weeks

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	249	127	123	125
Units: percentage of participants				
number (not applicable)	8.8	17.3	18.7	24.8

Statistical analyses

Statistical analysis title	EASI75 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.032
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	3.88

Statistical analysis title	EASI75 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib

Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.29
upper limit	4.67

Statistical analysis title	EASI75 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	374
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.01
upper limit	6.89

Secondary: Percentage of Participants Achieving EASI90

End point title	Percentage of Participants Achieving EASI90[4]

End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent and clinical signs affected: 0 = 0%; 1 = 1-9%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6 = 90-100% and the severity of 4 clinical signs: (1) erythema, (2) edema/papulation, (3) excoriation, and (4) lichenification each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head/neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2, and 3. The final EASI score was obtained by weight-averaging these 4 scores and will range from 0 to 72 (severe). The EASI90 is defined as a ≥ 90% improvement from baseline in the EASI score.

Analysis Population Description : All randomized participants.

End point type	Secondary

End point timeframe:

16 Weeks

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	249	127	123	125
Units: percentage of participants				
number (not applicable)	4.8	8.7	10.6	16.0

Statistical analyses

Statistical analysis title	EASI90 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.21
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	4.05

Statistical analysis title	EASI90 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	5.7

Statistical analysis title	EASI90 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib

Number of subjects included in analysis	374
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.91
upper limit	8.91

Secondary: Percent Change From Baseline (PCFB) in EASI Score

End point title	Percent Change From Baseline (PCFB) in EASI Score[5]

End point description:

The EASI assesses objective physician estimates of 2 dimensions of AD - disease extent and clinical signs affected: 0 = 0%; 1 = 1-9%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6 = 90-100% and the severity of 4 clinical signs: (1) erythema, (2) edema/papulation, (3) excoriation, and (4) lichenification each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head/neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2, and 3. The final EASI score was obtained by weight-averaging these 4 scores and will range from 0 to 72 (severe).

Least Square (LS) Means were calculated using a mixed model repeated measures (MMRM) model with treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit-interaction as fixed categorical effects and baseline and baseline-by- visit-interaction as fixed continuous effects.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

Analysis Population Description: All randomized participants who had Week 16 EASI data.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	71	52	52	70
Units: percentage of participants				
least squares mean (standard error)	-34.82 (± 3.64)	-48.22 (± 4.52)	51.89 (± 4.29)	-59.36 (± 3.84)

Statistical analyses

Statistical analysis title	PCFB EASI - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-13.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.77
upper limit	-2.03
Variability estimate	Standard error of the mean
Dispersion value	5.78

Statistical analysis title	PCFB EASI - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-17.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.05
upper limit	-6.01
Variability estimate	Standard error of the mean
Dispersion value	5.57

Statistical analysis title	PCFB EASI - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-24.54

Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.84
upper limit	-14.24
Variability estimate	Standard error of the mean
Dispersion value	5.23

Secondary: Percentage of Participants Achieving SCORing Atopic Dermatitis 75 (SCORAD75)

End point title	Percentage of Participants Achieving SCORing Atopic Dermatitis 75 (SCORAD75)[6]

End point description:

The SCORAD index uses the rule of nines to assess disease extent and evaluates 6 clinical characteristics to determine disease severity: (1) erythema, (2) edema/papulation, (3) oozing/crusts, (4) excoriation, (5) lichenification, and (6) dryness on a scale of 0 to 3 (0=absence, 1=mild, 2=moderate, 3=severe). The SCORAD index also assesses subjective symptoms of pruritus and sleep loss with visual analog scale (VAS) where 0 is no itching or no trouble sleeping and 10 is unbearable itching or a lot of trouble sleeping. These 3 aspects: extent of disease (A: 0-1-2), disease severity (B: 0-18), & subjective symptoms (C: 0-20) combine using A/5 + 7*B/2+ C to give a maximum possible score of 103, where 0 = no disease and 103 = severe disease. The SCORAD75 responder is defined as a participant who achieves a ≥ 75% improvement from baseline in the SCORAD score.

Analysis Population Description: All randomized participants.

End point type	Secondary

End point timeframe:

16 Weeks

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	249	127	123	125
Units: percentage of participants				
number (not applicable)	1.2	5.5	7.3	10.4

Statistical analyses

Statistical analysis title	SCORAD 75 - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib

Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	15.24

Statistical analysis title	SCORAD 75 - 2 mg Baricitinib
Comparison groups	2 mg Baricitinib v Placebo
Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.79
upper limit	20.99

Statistical analysis title	SCORAD 75 - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	374
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	8.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.68
upper limit	28.58

Secondary: Percentage of Participants Achieving a 4-Point Improvement in Itch

Numeric Rating Scale (NRS)

End point title	Percentage of Participants Achieving a 4-Point Improvement in Itch Numeric Rating Scale (NRS)[7]

End point description:

The Itch Numeric Rating Scale (NRS) is a participant-administered, 11-point horizontal scale anchored at 0 and 10, with 0 representing "no itch" and 10 representing "worst itch imaginable." Overall severity of a participant's itching is indicated by selecting the number, using a daily diary, that best describes the worst level of itching in the past 24 hours.

Analysis Population Description: All randomized participants with a Baseline Itch NRS score >=4

End point type	Secondary

End point timeframe:

16 Weeks

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	222	105	100	107
Units: percentage of participants				
number (not applicable)	7.2	10.5	12.0	21.5

Statistical analyses

Statistical analysis title	Itch NRS - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	327
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.246
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	3.56

Statistical analysis title	Itch NRS - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib

Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.169
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	3.77

Statistical analysis title	Itch NRS - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	329
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.82
upper limit	7.18

Secondary: Change From Baseline (CFB) in the Score of Item 2 of the Atopic Dermatitis Sleep Scale (ADSS)

End point title	Change From Baseline (CFB) in the Score of Item 2 of the Atopic Dermatitis Sleep Scale (ADSS)[8]

End point description:

The ADSS is a 3-item, participant-administered questionnaire developed to assess the impact of itch on sleep including difficulty falling asleep, frequency of waking, and difficulty getting back to sleep last night. Item 2, frequency of waking last night is reported by selecting the number of times they woke up each night, ranging from 0 to 29 times. The ADSS is designed to be completed daily, using a daily diary, with respondents thinking about sleep "last night." Each item is scored individually.

LS Means were calculated using a MMRM model with adjustments made for treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit-interaction as fixed categorical effects and baseline and baseline-by-visit-interaction as fixed continuous effects.

Analysis Population Description: All randomized participants with Week 16 ADSS Item 2 (frequency of waking) data.

End point type	Secondary

End point timeframe:	

Baseline, 16 Weeks

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	52	50	50
Units: units on a scale				
least squares mean (standard error)	-0.84 (± 0.15)	-1.21 (± 0.18)	-1.04 (± 0.17)	-1.42 (± 0.16)

Statistical analyses

Statistical analysis title	CFB ADSS - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.103
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	0.08

Statistical analysis title	CFB ADSS - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.352
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.23

Statistical analysis title	CFB ADSS - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.17

Secondary: Change from Baseline (CFB) in the Skin Pain Numeric Rating Scale (NRS)

End point title	Change from Baseline (CFB) in the Skin Pain Numeric Rating Scale (NRS)[9]

End point description:

Skin Pain NRS is a participant-administered, 11-point horizontal scale anchored at 0 and 10, with 0 representing "no pain" and 10 representing "worst pain imaginable." Overall severity of a participant's skin pain is indicated by selecting the number, using a daily diary, that best describes the worst level of skin pain in the past 24 hours.

LS Means were calculated using a MMRM model with treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit-interaction as fixed categorical effects and baseline and baseline-by-visit-interaction as fixed continuous effects.

Analysis Population Description: All randomized participants with Week 16 Skin Pain NRS data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

Notes:

[9] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	52	50	68
Units: units on a scale				
least squares mean (standard error)	-0.84 (± 0.24)	-1.92 (± 0.30)	-1.58 (± 0.29)	-1.93 (± 0.26)

Statistical analyses

Statistical analysis title	CFB Skin Pain NRS - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.84
upper limit	-0.32

Statistical analysis title	CFB Skin Pain NRS - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.051
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.48
upper limit	0

Statistical analysis title	CFB Skin Pain NRS - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.79
upper limit	-0.39

Secondary: Percentage of Participants Achieving EASI50

End point title	Percentage of Participants Achieving EASI50[10]

End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent and clinical signs affected: 0 = 0%; 1 = 1-9%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6 = 90-100%) and the severity of 4 clinical signs (erythema, edema/papulation, excoriation, and lichenification) each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head and neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2 and 3. The final EASI score was obtained by weight-averaging these 4 scores and will range from 0 to 72 (severe). The EASI50 is defined as a ≥ 50% improvement from baseline in EASI score.

Analysis Population Description: All randomized participants.

End point type	Secondary

End point timeframe:

16 Weeks

Notes:

[10] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	249	127	123	125
Units: percentage of participants				
number (not applicable)	15.3	26.0	30.1	41.6

Statistical analyses

Statistical analysis title	EASI50 - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	3.25

Statistical analysis title	EASI50 - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Mean difference (final values)
Point estimate	2.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.44
upper limit	4.14

Statistical analysis title	EASI50 - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	374
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Mean difference (final values)
Point estimate	4.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.51
upper limit	6.96

Secondary: Percentage of Participants Achieving IGA of 0

End point title	Percentage of Participants Achieving IGA of 0[11]

End point description:

The IGA measures the investigator's global assessment of the patient's overall severity of their AD, based on a static, numeric 5-point scale from 0 (clear skin) to 4 (severe disease). The score is based on an overall assessment of the degree of erythema, papulation/induration, oozing/crusting, and lichenification.

Analysis Population Description: All randomized participants.

End point type	Secondary

End point timeframe:

16 Weeks

Notes:

[11] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	249	127	123	125
Units: percentage of participants				
number (not applicable)	0.8	1.6	2.4	1.6

Statistical analyses

Statistical analysis title	IGA of 0 - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.424
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	10.63

Statistical analysis title	IGA of 0 - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.182
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	13.75

Statistical analysis title	IGA of 0 - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	374
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.441
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	10.41

Secondary: Change from Baseline (CFB) in SCORAD

End point title	Change from Baseline (CFB) in SCORAD[12]

End point description:

The SCORAD index uses the rule of nines to assess disease extent and evaluates 6 clinical characteristics to determine disease severity: (1) erythema, (2)edema/papulation, (3) oozing/crusts, (4) excoriation, (5) lichenification, and (6) dryness on a scale of 0 to 3 (0=absence, 1=mild, 2=moderate, 3=severe). The SCORAD index also assesses subjective symptoms of pruritus and sleep loss with VAS where 0 is no itching or no trouble sleeping and 10 is unbearable itching or a lot of trouble sleeping. These 3 aspects: extent of disease (A: 0- 1-2), disease severity (B: 0-18), & subjective symptoms (C: 0-20) combine using A/5 + 7*B/2+ C to give a maximum possible score of 103, where 0 = no disease and 103 = severe disease. LSMean was calculated using MMRM model with treatment, region, baseline disease severity (IGA), visit, & treatment-by-visit-interaction as fixed categorical effects, baseline and baseline-by-visit-interaction as fixed continuous effects.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks
Analysis Population Description: All randomized participants with Week 16 SCORAD data.

Notes:

[12] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	71	52	52	70
Units: units on scale				
least squares mean (standard error)	-13.51 (± 2.00)	-18.85 (± 2.48)	-21.47 (± 2.36)	-28.30 (± 2.10)

Statistical analyses

Statistical analysis title	CFB SCORAD - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.093
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.57
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	3.17

Statistical analysis title	CFB SCORAD - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-7.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.01
upper limit	-1.92
Variability estimate	Standard error of the mean
Dispersion value	3.07

Statistical analysis title	CFB SCORAD - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib

Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-14.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.46
upper limit	-9.13
Variability estimate	Standard error of the mean
Dispersion value	2.88

Secondary: Percentage of Participants Achieving SCORAD90

End point title	Percentage of Participants Achieving SCORAD90[13]

End point description:

The SCORAD index uses the rule of nines to assess disease extent and evaluates 6 clinical characteristics to determine disease severity: (1) erythema, (2) edema/papulation, (3) oozing/crusts, (4) excoriation, (5) lichenification, and (6) dryness on a scale of 0 to 3 (0=absence, 1=mild, 2=moderate, 3=severe). The SCORAD index also assesses subjective symptoms of pruritus and sleep loss in the last 72 hours on visual analogue scales (VAS) of 0 to 10 where 0 is no itching or no trouble sleeping and 10 is unbearable itching or a lot of trouble sleeping. These 3 aspects: extent of disease (A: 0-1-2), disease severity (B: 0-18), & subjective symptoms (C: 0-20) combine using A/5 + 7*B/2+ C to give a maximum possible score of 103, where 0 = no disease and 103 = severe disease. SCORAD90 is defined as having ≥ 90% improvement in SCORAD from baseline.

Analysis Population Description: All randomized participants.

End point type	Secondary

End point timeframe:

16 Weeks

Notes:

[13] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	249	127	123	125
Units: percentage of participants				
number (not applicable)	0.8	0.8	2.4	2.4

Statistical analyses

Statistical analysis title	SCORAD90 - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.874
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	7.77

Statistical analysis title	SCORAD90 - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.176
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	13.36

Statistical analysis title	SCORAD90 - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	374
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.201
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	12.65

Secondary: Change From Baseline (CFB) in Body Surface Area (BSA) Affected

End point title	Change From Baseline (CFB) in Body Surface Area (BSA) Affected[14]

End point description:

Body surface area (BSA) affected by AD will be assessed for 4 separate body regions and is collected as part of the EASI assessment: head and neck, trunk (including genital region), upper extremities, and lower extremities (including the buttocks). Each body region will be assessed for disease extent ranging from 0% to 100% involvement. The overall total percentage will be reported based off of all 4 body regions combined, after applying specific multipliers to the different body regions to account for the percent of the total BSA represented by each of the 4 regions. Use the percentage of skin affected for each region (0 to 100%) in EASI as follows: BSA Total = 0.1*BSAhead and neck + 0.3*BSAtrunk + 0.2* BSAupper limbs + 0.4*BSAlower limbs.

LSMean were calculated using MMRM model with treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit-interaction as fixed categorical effects and baseline and baseline-by-visit-interaction as fixed continuous effects.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

Analysis Population Description: All randomized participants with Week 16 BSA.

Notes:

[14] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	71	52	52	70
Units: units on a scale				
least squares mean (standard error)	-14.80 (± 1.82)	-20.79 (± 2.26)	-20.14 (± 2.16)	-25.96 (± 1.93)

Statistical analyses

Statistical analysis title	CFB BSA - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.039
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.67
upper limit	-0.31
Variability estimate	Standard error of the mean
Dispersion value	2.88

Statistical analysis title	CFB BSA - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.058
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.86
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	2.8

Statistical analysis title	CFB BSA - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-11.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.33
upper limit	-5.98
Variability estimate	Standard error of the mean
Dispersion value	2.63

Secondary: Percentage of Participants Developing Skin Infections Requiring Antibiotic Treatment

End point title	Percentage of Participants Developing Skin Infections Requiring Antibiotic Treatment[15]
End point description:	

Percentage of participants developing skin infections requiring antibiotic treatment.

Analysis Population Description: All randomized participants.

End point type	Secondary
End point timeframe:	

16 Weeks

Notes:

[15] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	249	127	123	125
Units: percentage of partcipants				
number (not applicable)	4.4	0.8	4.9	3.2

Statistical analyses

Statistical analysis title	Skin Infections - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.067
Method	Fisher exact

Statistical analysis title	Skin Infections - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.799
Method	Fisher exact

Statistical analysis title	Skin Infections - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib

Number of subjects included in analysis	374
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.782
Method	Fisher exact

Secondary: Percent Change From Baseline (PCFB) in Itch NRS

End point title	Percent Change From Baseline (PCFB) in Itch NRS[16]

End point description:

The Itch NRS is a participant-administered, 11-point horizontal scale, anchored at 0 and 10, with 0 representing "no itch" and 10 representing "worst itch imaginable." Overall severity of a participant's itching is indicated by selecting the number, using a daily diary, that best describes the worst level of itching in the past 24 hours.

LS Means were calculated using a MMRM model with treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit-interaction as fixed categorical effects and baseline and baseline-by-visit-interaction as fixed continuous effects.

Analysis Population Description: All randomized participants with Week 16 Itch NRS data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

Notes:

[16] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	52	50	68
Units: units on a scale				
least squares mean (standard error)	-12.04 (± 4.65)	-31.30 (± 5.70)	-29.43 (± 5.45)	-36.55 (± 4.88)

Statistical analyses

Statistical analysis title	PCFB Itch NRS - 1 mg Baricitinib
Comparison groups	1 mg Baricitinib v Placebo
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-19.25

Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.69
upper limit	-4.81
Variability estimate	Standard error of the mean
Dispersion value	7.33

Statistical analysis title	PCFB Itch NRS - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-17.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.43
upper limit	-3.35
Variability estimate	Standard error of the mean
Dispersion value	7.13

Statistical analysis title	PCFB Itch NRS - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-24.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.71
upper limit	-11.3
Variability estimate	Standard error of the mean
Dispersion value	6.71

Secondary: Change From Baseline (CFB) in the Total Score of the Patient Oriented Eczema Measure (POEM)

End point title	Change From Baseline (CFB) in the Total Score of the Patient Oriented Eczema Measure (POEM)[17]

End point description:

The POEM is a 7-item self-assessment questionnaire that assesses disease symptoms (dryness, itching, flaking, cracking, sleep loss, bleeding and weeping) on a scale ranging from 0-4 (0 = no days, 1 = 1-2 days, 2 = 3-4 days, 3 = 5-6 days, 4 = everyday). The sum of the 7 items gives the total POEM score of 0 (absent disease) to 28 (severe disease). High scores are indicative of more severe disease and poor quality of life.
LS Means were calculated using a MMRM model with treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit-interaction as fixed categorical effects and baseline and baseline-by-visit-interaction as fixed continuous effects.

Analysis Population Description: All randomized participants with Week 16 POEM data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

Notes:

[17] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	53	52	70
Units: units on a scale				
least squares mean (standard error)	-2.68 (± 0.76)	-5.32 (± 0.93)	-6.26 (± 0.91)	-7.84 (± 0.80)

Statistical analyses

Statistical analysis title	CFB POEM - 1 mg Baricitinib
Comparison groups	1 mg Baricitinib v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.028
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.98
upper limit	-0.29
Variability estimate	Standard error of the mean
Dispersion value	1.19

Statistical analysis title	CFB POEM - 2 mg Baricitinib

Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.89
upper limit	-1.27
Variability estimate	Standard error of the mean
Dispersion value	1.17

Statistical analysis title	CFB POEM - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.33
upper limit	-2.99
Variability estimate	Standard error of the mean
Dispersion value	1.1

Secondary: Change from Baseline (CFB) in the Patient Global Impression of Severity—Atopic Dermatitis (PGI-S-AD) Score

End point title	Change from Baseline (CFB) in the Patient Global Impression of Severity—Atopic Dermatitis (PGI-S-AD) Score[18]

End point description:

The PGI-S-AD asked the participant to evaluate the severity of the disease at that point in time on a single-item, 5-point scale, using a daily diary. The same category labels used in the Physician's Global Assessment were used for the PGI-S-AD, i.e.,"(0) no symptoms", "(1) very mild", "(2) mild" "(3) moderate", and "(4) severe."

LS Means were calculated using a MMRM model with treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit-interaction as fixed categorical effects and baseline and baseline-by-visit-interaction as fixed continuous effects.

Analysis Population Description: All randomized participants with Week 16 PGI-S-AD score.

End point type	Secondary

End point timeframe:
Baseline, 16 Weeks

Notes:

[18] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	52	50	68
Units: units on a scale				
least squares mean (standard error)	-0.31 (± 0.09)	-0.58 (± 0.12)	-0.58 (± 0.11)	-0.77 (± 0.10)

Statistical analyses

Statistical analysis title	CFB PGI-S-AD - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.069
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	CFB PGI-S-AD - 2mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.066
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.27

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	CFB PGI-S-AD - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	-0.19
Variability estimate	Standard error of the mean
Dispersion value	0.14

Secondary: Change From Baseline (CFB) on the Hospital Anxiety and Depression Scale (HADS)

End point title	Change From Baseline (CFB) on the Hospital Anxiety and Depression Scale (HADS)[19]

End point description:

The HADS is a participant-rated instrument used to assess both anxiety and depression. This instrument consists of 14 item questionnaire, each item is rated on a 4-point scale, giving maximum scores of 21 for anxiety and depression. Scores of 11 or more on either subscale are considered to be a significant 'case' of psychological morbidity, while scores of 8-10 represent 'borderline' and 0-7, 'normal.
 LS Means were calculated using a MMRM model with treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit-interaction as fixed categorical effects and baseline and baseline-by-visit-interaction as fixed continuous effects.

Analysis Population Description: All randomized participants with Week 16 HADS data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

Notes:

[19] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	71	51	52	70
Units: units on a scale				
least squares mean (standard error)				
Anxiety	-0.90 (± 0.28)	-1.35 (± 0.34)	-1.83 (± 0.33)	-2.05 (± 0.30)
Depression	-0.37 (± 0.27)	-1.04 (± 0.34)	-1.40 (± 0.32)	-1.50 (± 0.29)

Statistical analyses

Statistical analysis title	CFB HADS Anxiety - 1 mg Baricitinib
Statistical analysis description:	
HADS Anxiety	
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.305
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.43

Statistical analysis title	CFB HADS Anxiety - 2 mg Baricitinib
Statistical analysis description:	
HADS Anxiety	
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.77
upper limit	-0.1

Variability estimate	Standard error of the mean
Dispersion value	0.42

Statistical analysis title	CFB HADS Anxiety - 4 mg Baricitinib
Statistical analysis description:	
HADS Anxiety	
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.93
upper limit	-0.36
Variability estimate	Standard error of the mean
Dispersion value	0.4

Statistical analysis title	CFB HADS Depression - 1 mg Baricitinib
Statistical analysis description:	
HADS Depression	
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.113
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.51
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.43

Statistical analysis title	CFB HADS Depression - 2 mg Baricitinib
Statistical analysis description:	
HADS Depression	

Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.85
upper limit	-0.22
Variability estimate	Standard error of the mean
Dispersion value	0.42

Statistical analysis title	CFB HADS Depression - 4 mg Baricitinib
Statistical analysis description:	
HADS Depression	
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.91
upper limit	-0.37
Variability estimate	Standard error of the mean
Dispersion value	0.39

Secondary: Change From Baseline (CFB) in the Dermatology Life Quality Index (DLQI)

End point title	Change From Baseline (CFB) in the Dermatology Life Quality Index (DLQI)[20]

End point description:

The DLQI is a simple, participant-administered, 10 question, validated, quality-of-life questionnaire that covers 6 domains: symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. The recall period of this scale is over the "last week". Response categories include "not at all," "a lot," and "very much," with corresponding scores of 1, 2, and 3, respectively, and unanswered ("not relevant") responses scored as "0." Totals range from 0 to 30 (less to more impairment), and a 4-point change from baseline is considered as the minimal clinically important difference threshold.

LS Means were calculated using a MMRM model with treatment, region, baseline disease severity (IGA),

visit, and treatment-by-visit-interaction as fixed categorical effects and baseline and baseline-by-visit-interaction as fixed continuous effects.

Analysis Population Description: All randomized participants with Week 16 DLQI data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

Notes:

[20] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	71	52	52	70
Units: units on a scale				
least squares mean (standard error)	-2.46 (± 0.57)	-4.64 (± 0.70)	-4.30 (± 0.68)	-6.76 (± 0.60)

Statistical analyses

Statistical analysis title	CFB DLQI - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.92
upper limit	-0.42
Variability estimate	Standard error of the mean
Dispersion value	0.89

Statistical analysis title	CFB DLQI - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib

Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.56
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.87

Statistical analysis title	CFB DLQI - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.91
upper limit	-2.69
Variability estimate	Standard error of the mean
Dispersion value	0.82

Secondary: Change from Baseline (CFB) on the Work Productivity and Activity Impairment - Atopic Dermatitis (WPAI-AD) Questionnaire

End point title	Change from Baseline (CFB) on the Work Productivity and Activity Impairment - Atopic Dermatitis (WPAI-AD) Questionnaire[21]

End point description:

The WPAI-AD participant questionnaire was developed to measure the effect of general health and symptom severity on work productivity and regular activities in the 7 days prior to the visit. The WPAI-AD consists of 6 items grouped into 4 domains: absenteeism (work time missed), presenteeism (impairment at work/reduced on-the-job effectiveness), work productivity loss (overall work impairment/absenteeism plus presenteeism), and activity impairment, that range from 0% to 100%, with higher values indicating greater impairment.
LS Mean were calculated using a MMRM model with treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit-interaction as fixed categorical effects and baseline and baseline-by-visit-interaction as fixed continuous effects.

Analysis Population Description: All randomized participants with Week 16 WPAI-AD data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

Notes:

[21] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	51	52	70
Units: units on a scale				
least squares mean (standard error)				
Absenteeism (48, 30, 27, 40)	-0.49 (± 1.68)	4.54 (± 2.15)	-0.84 (± 2.23)	-3.89 (± 1.88)
Presenteeism(48, 30, 27, 40)	-2.98 (± 2.60)	-9.75 (± 3.37)	-11.53 (± 3.44)	-15.57 (± 2.95)
Work Productivity Loss (48, 30, 27, 39)	-2.57 (± 2.60)	-11.23 (± 3.75)	-9.06 (± 3.83)	-13.85 (± 3.29)
Activity Impairment (70, 51, 52, 70)	-5.67 (± 2.16)	-12.98 (± 2.63)	-10.80 (± 2.57)	-22.20 (± 2.30)

Statistical analyses

Statistical analysis title	CFB Absenteeism - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.136
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-4.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.39
upper limit	1.29
Variability estimate	Standard error of the mean
Dispersion value	2.7

Statistical analysis title	CFB Absenteeism - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib

Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.898
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.81
upper limit	5.1
Variability estimate	Standard error of the mean
Dispersion value	2.76

Statistical analysis title	CFB Absenteeism - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.174
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.32
upper limit	1.52
Variability estimate	Standard error of the mean
Dispersion value	2.49

Statistical analysis title	CFB Presenteeism - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.104
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-6.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.13
upper limit	1.41

Variability estimate	Standard error of the mean
Dispersion value	4.19

Statistical analysis title	CFB Presenteeism - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.045
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-8.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.09
upper limit	-0.19
Variability estimate	Standard error of the mean
Dispersion value	4.28

Statistical analysis title	CFB Presenteeism - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-12.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.97
upper limit	-4.59
Variability estimate	Standard error of the mean
Dispersion value	3.9

Notes:

[22] - Presentisms

Statistical analysis title	CFB Work Productivity Loss - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib

Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.066
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-8.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.89
upper limit	0.57
Variability estimate	Standard error of the mean
Dispersion value	4.67

Statistical analysis title	CFB Work Productivity Loss - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.175
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-6.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.89
upper limit	2.91
Variability estimate	Standard error of the mean
Dispersion value	4.76

Statistical analysis title	CFB Work Productivity Loss - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-11.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.84
upper limit	-2.72

Variability estimate	Standard error of the mean
Dispersion value	4.94

Statistical analysis title	CFB Activity Impairment - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-7.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.93
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	3.36

Statistical analysis title	CFB Activity Impairment - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.122
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.65
upper limit	1.39
Variability estimate	Standard error of the mean
Dispersion value	3.31

Statistical analysis title	CFB Activity Impairment - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-16.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.64
upper limit	-10.41
Variability estimate	Standard error of the mean
Dispersion value	3.11

Secondary: Change From Baseline (CFB) on the European Quality of Life–5 Dimensions 5 Levels (EQ-5D-5L) Index Score United States and United Kingdom Algorithm

End point title	Change From Baseline (CFB) on the European Quality of Life–5 Dimensions 5 Levels (EQ-5D-5L) Index Score United States and United Kingdom Algorithm[23]

End point description:

EQ-5D-5L is a 2-part measurement. The first part is comprised of the following 5 participant-reported dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. Responses are used to derive the health state index scores using the United Kingdom (UK) algorithm, scores range from -0.594 to 1, and the United States (US) algorithm, scores range from -0.109 to 1. Higher scores indicate better health state.

LS Mean were calculated using MMRM model with treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit-interaction as fixed categorical effects and baseline and baseline-by-visit-interaction as fixed continuous effects.

Analysis Population Description: All randomized participants with Week 16 EQ-5D-5L health state index US and UK data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

Notes:

[23] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	51	52	70
Units: units on a scale				
least squares mean (standard error)				
Health State Index Score US (70, 51, 52, 70)	0.01 (± 0.01)	0.05 (± 0.02)	0.05 (± 0.02)	0.09 (± 0.01)
Health State Index Score UK (70, 51, 52, 70)	0.01 (± 0.02)	0.07 (± 0.02)	0.07 (± 0.02)	0.13 (± 0.02)

Statistical analyses

Statistical analysis title	CFB Health State Index US - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.061
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	CFB Health State Index US - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	CFB Health State Index US - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	CFB Health State Index UK - 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.046
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.03

Statistical analysis title	CFB Health State Index UK - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.059
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.11

Variability estimate	Standard error of the mean
Dispersion value	0.03

Statistical analysis title	CFB Health State Index UK - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.03

Secondary: Change From Baseline (CFB) on the European Quality of Life−5 Dimensions 5 Levels (EQ-5D-5L) Visual Analog Score (VAS)

End point title	Change From Baseline (CFB) on the European Quality of Life−5 Dimensions 5 Levels (EQ-5D-5L) Visual Analog Score (VAS)[24]

End point description:

EQ-5D-5L is a 2-part measurement. The second part is assessed using a visual analog scale (VAS) that ranged from 0 to 100 millimeter (mm), where 0 is the worst health you can imagine and 100 is the best health you can imagine.

LS Mean were calculated using MMRM model with treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit-interaction as fixed categorical effects and baseline and baseline-by-visit-interaction as fixed continuous effects.

Analysis Population Description: All randomized participants with Week 16 EQ-5D-5L VAS data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

Notes:

[24] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	51	52	70
Units: millimeters				
least squares mean (standard error)	2.00 (± 2.04)	4.97 (± 2.53)	3.35 (± 2.41)	9.05 (± 2.17)

Statistical analyses

Statistical analysis title	CFB EQ-5D-5L VAS - 1mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.356
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.36
upper limit	9.3
Variability estimate	Standard error of the mean
Dispersion value	3.21

Statistical analysis title	CFB EQ-5D-5L VAS - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.688
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.81
upper limit	7.5
Variability estimate	Standard error of the mean
Dispersion value	3.13

Statistical analysis title	CFB EQ-5D-5L VAS - 4 mg Baricitinib

Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	7.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.25
upper limit	12.86
Variability estimate	Standard error of the mean
Dispersion value	2.95

Secondary: Percentage of Participants Achieving Investigator's Global Assessment (IGA) of 0 or 1 With a ≥ 2 Point Improvement

End point title	Percentage of Participants Achieving Investigator's Global Assessment (IGA) of 0 or 1 With a ≥ 2 Point Improvement[25]

End point description:

The IGA measures the investigator's global assessment of the participant's overall severity of their Atopic Dermatitis (AD), based on a static, numeric 5-point scale from 0 (clear skin) to 4 (severe disease). The score is based on an overall assessment of the degree of erythema, papulation/induration, oozing/crusting, and lichenification.

Analysis Population Description: All randomized participants

End point type	Secondary

End point timeframe:

Week 4

Notes:

[25] - 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: A Maximum Extended Enrollment (MEE) cohort is implemented in countries to meet regulatory requirements for submission. Data from any MEE country-specific cohort will not be incorporated into the analysis of the global study cohort.

End point values	Placebo	1 mg Baricitinib	2 mg Baricitinib	4 mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	249	127	123	125
Units: Percentage of Participants				
number (not applicable)	2.4	3.1	8.9	10.4

Statistical analyses

Statistical analysis title	IGA of 0 or 1 (Wk 4): 1 mg Baricitinib
Comparison groups	Placebo v 1 mg Baricitinib

Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.603
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	4.71

Statistical analysis title	IGA of 0 or 1 (Wk 4): 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	11.12

Statistical analysis title	IGA of 0 or 1 (Wk 4): 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	374
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.78
upper limit	12.35

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
Baseline Up to 20 weeks	
Adverse event reporting additional description:	
I4V-MC-JAHL	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	1 mg Baricitinib
Reporting group description: -	
Reporting group title	2 mg Baricitinib
Reporting group description: -	
Reporting group title	4 mg Baricitinib
Reporting group description: -	
Reporting group title	Placebo Maximum Extended Enrollment (MEE)
Reporting group description: -	
Reporting group title	1 mg Baricitinib MEE
Reporting group description: -	
Reporting group title	2 mg Baricitinib MEE
Reporting group description: -	
Reporting group title	4 mg Baricitinib MEE

Reporting group description: -

Serious adverse events	Placebo	1 mg Baricitinib	2 mg Baricitinib
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 249 (2.41%)	1 / 127 (0.79%)	0 / 123 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
breast cancer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 249 (0.40%)	0 / 127 (0.00%)	0 / 123 (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
papillary thyroid cancer			
alternative dictionary used: MedDRA 21.1			

	4 mg Baricitinib	Placebo Maximum Extended Enrollment (MEE)	1 mg Baricitinib MEE
subjects affected / exposed	1 / 249 (0.40%)	0 / 127 (0.00%)	0 / 123 (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

alcohol poisoning

alternative dictionary used: MedDRA 21.1

	4 mg Baricitinib	Placebo MEE	1 mg Baricitinib MEE
subjects affected / exposed	0 / 249 (0.00%)	0 / 127 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

clavicle fracture

alternative dictionary used: MedDRA 21.1

	4 mg Baricitinib	Placebo MEE	1 mg Baricitinib MEE
subjects affected / exposed	1 / 249 (0.40%)	0 / 127 (0.00%)	0 / 123 (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

rib fracture

alternative dictionary used: MedDRA 21.1

	4 mg Baricitinib	Placebo MEE	1 mg Baricitinib MEE
subjects affected / exposed	1 / 249 (0.40%)	0 / 127 (0.00%)	0 / 123 (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

Skin and subcutaneous tissue disorders

dermatitis atopic

alternative dictionary used: MedDRA 21.1

	4 mg Baricitinib	Placebo MEE	1 mg Baricitinib MEE
subjects affected / exposed	2 / 249 (0.80%)	1 / 127 (0.79%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders

suicide attempt

alternative dictionary used: MedDRA 21.1

	4 mg Baricitinib	Placebo MEE	1 mg Baricitinib MEE
subjects affected / exposed	1 / 249 (0.40%)	0 / 127 (0.00%)	0 / 123 (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

Serious adverse events	4 mg Baricitinib	Placebo Maximum Extended Enrollment (MEE)	1 mg Baricitinib MEE

Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 125 (1.60%)	0 / 15 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
breast cancer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 125 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
papillary thyroid cancer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 125 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
alcohol poisoning			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 125 (0.80%)	0 / 15 (0.00%)	0 / 5 (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
clavicle fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 125 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rib fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 125 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
dermatitis atopic			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 125 (0.80%)	0 / 15 (0.00%)	0 / 5 (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
Psychiatric disorders			
suicide attempt			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 125 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	2 mg Baricitinib MEE	4 mg Baricitinib MEE	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
breast cancer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
papillary thyroid cancer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
alcohol poisoning			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
clavicle fracture			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0

rib fracture

alternative dictionary used: MedDRA 21.1

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0

Skin and subcutaneous tissue disorders

dermatitis atopic

alternative dictionary used: MedDRA 21.1

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0

Psychiatric disorders

suicide attempt

alternative dictionary used: MedDRA 21.1

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	1 mg Baricitinib	2 mg Baricitinib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 249 (22.09%)	37 / 127 (29.13%)	34 / 123 (27.64%)
Investigations			
weight decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 249 (0.00%)	0 / 127 (0.00%)	0 / 123 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	16 / 249 (6.43%)	7 / 127 (5.51%)	14 / 123 (11.38%)
occurrences (all)	17	8	15

Blood and lymphatic system disorders

anaemia

alternative dictionary used: MedDRA 21.1

subjects affected / exposed	1 / 249 (0.40%)	0 / 127 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0

leukopenia

alternative dictionary used: MedDRA 21.1

subjects affected / exposed	0 / 249 (0.00%)	0 / 127 (0.00%)	0 / 123 (0.00%)
occurrences (all)	0	0	0

lymphopenia

alternative dictionary used: MedDRA 21.1

subjects affected / exposed	0 / 249 (0.00%)	0 / 127 (0.00%)	1 / 123 (0.81%)
occurrences (all)	0	0	1

neutropenia

alternative dictionary used: MedDRA 21.1

subjects affected / exposed	1 / 249 (0.40%)	0 / 127 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0

General disorders and administration site conditions

oedema

alternative dictionary used: MedDRA 21.1

subjects affected / exposed	1 / 249 (0.40%)	0 / 127 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0

oedema peripheral

alternative dictionary used: MedDRA 21.1

subjects affected / exposed	1 / 249 (0.40%)	0 / 127 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0

pyrexia

alternative dictionary used: MedDRA 21.1

subjects affected / exposed	0 / 249 (0.00%)	1 / 127 (0.79%)	3 / 123 (2.44%)
occurrences (all)	0	1	3

Gastrointestinal disorders

abdominal pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 249 (0.40%)	2 / 127 (1.57%)	3 / 123 (2.44%)
occurrences (all)	1	2	4
diarrhoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	7 / 249 (2.81%)	9 / 127 (7.09%)	0 / 123 (0.00%)
occurrences (all)	8	9	0
nausea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 249 (0.80%)	1 / 127 (0.79%)	1 / 123 (0.81%)
occurrences (all)	2	1	1
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 249 (0.80%)	0 / 127 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 249 (0.40%)	2 / 127 (1.57%)	1 / 123 (0.81%)
occurrences (all)	1	2	1
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	26 / 249 (10.44%)	22 / 127 (17.32%)	12 / 123 (9.76%)
occurrences (all)	28	25	14
oral herpes			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 249 (0.00%)	3 / 127 (2.36%)	2 / 123 (1.63%)
occurrences (all)	0	4	2
skin infection			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 249 (0.40%)	0 / 127 (0.00%)	1 / 123 (0.81%)
occurrences (all)	1	0	1

urinary tract infection
alternative dictionary used: MedDRA 21.1

subjects affected / exposed	4 / 249 (1.61%)	1 / 127 (0.79%)	2 / 123 (1.63%)
occurrences (all)	4	1	2

vulvovaginal candidiasis
alternative dictionary used: MedDRA 21.1

subjects affected / exposed[1]	1 / 101 (0.99%)	0 / 49 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	4 mg Baricitinib	Placebo Maximum Extended Enrollment (MEE)	1 mg Baricitinib MEE
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 125 (23.20%)	3 / 15 (20.00%)	1 / 5 (20.00%)
Investigations			
weight decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 125 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	10 / 125 (8.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	11	0	0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 125 (0.80%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
leukopenia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 125 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
lymphopenia			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 125 (0.80%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0

neutropenia

alternative dictionary used:
MedDRA 21.1

subjects affected / exposed	0 / 125 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

General disorders and administration site conditions

oedema

alternative dictionary used:
MedDRA 21.1

subjects affected / exposed	0 / 125 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

oedema peripheral

alternative dictionary used:
MedDRA 21.1

subjects affected / exposed	0 / 125 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

pyrexia

alternative dictionary used:
MedDRA 21.1

subjects affected / exposed	1 / 125 (0.80%)	0 / 15 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1

Gastrointestinal disorders

abdominal pain

alternative dictionary used:
MedDRA 21.1

subjects affected / exposed	0 / 125 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

diarrhoea

alternative dictionary used:
MedDRA 21.1

subjects affected / exposed	4 / 125 (3.20%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	4	1	0

nausea

alternative dictionary used:
MedDRA 21.1

subjects affected / exposed	1 / 125 (0.80%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Respiratory, thoracic and mediastinal disorders

cough			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	4 / 125 (3.20%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	4	1	0

Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 125 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	12 / 125 (9.60%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	17	0	0
oral herpes			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 125 (1.60%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
skin infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 125 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
urinary tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	4 / 125 (3.20%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	7	0	0
vulvovaginal candidiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[1]	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	2 mg Baricitinib MEE	4 mg Baricitinib MEE	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	3 / 8 (37.50%)	
Investigations			

weight decreased		
alternative dictionary used: MedDRA 21.1		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0

Nervous system disorders

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

Blood and lymphatic system disorders

anaemia		
alternative dictionary used: MedDRA 21.1		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
leukopenia		
alternative dictionary used: MedDRA 21.1		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
lymphopenia		
alternative dictionary used: MedDRA 21.1		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
neutropenia		
alternative dictionary used: MedDRA 21.1		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0

General disorders and administration site conditions

oedema		
alternative dictionary used: MedDRA 21.1		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
oedema peripheral		
alternative dictionary used: MedDRA 21.1		
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1

pyrexia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
diarrhoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
nausea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
oral herpes			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0

skin infection
alternative dictionary used:
MedDRA 21.1

subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	3

urinary tract infection
alternative dictionary used:
MedDRA 21.1

subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	1	1

vulvovaginal candidiasis
alternative dictionary used:
MedDRA 21.1

subjects affected / exposed[1]	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0

Notes:

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

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly. The 2 mg Baricitinib MEE reporting group had 8 male and 0 female participants. The number of participants exposed should be zero, however the EudraCT Results Database requires a value of greater than or equal to 1 for this field. The number of participants exposed cannot be adjusted to zero for this gender specific adverse event due to a system issue.

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