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 Patients with Moderate to Severe Atopic Dermatitis

Summary

EudraCT number	2017-000871-10
Trial protocol	HU AT ES PL
Global end of trial date	12 December 2018

Results information

Result version number	v1 (current)
This version publication date	27 December 2019
First version publication date	27 December 2019

Trial information

Trial identification

Sponsor protocol code	I4V-MC-JAHM

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03334422
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16581

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 December 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 December 2018
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 is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 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	Argentina: 67
Country: Number of subjects enrolled	Korea, Republic of: 55
Country: Number of subjects enrolled	Austria: 31
Country: Number of subjects enrolled	Hungary: 52
Country: Number of subjects enrolled	Japan: 112
Country: Number of subjects enrolled	Poland: 118
Country: Number of subjects enrolled	Israel: 34
Country: Number of subjects enrolled	Australia: 67
Country: Number of subjects enrolled	Switzerland: 25
Country: Number of subjects enrolled	Spain: 54
Worldwide total number of subjects	615
EEA total number of subjects	255

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)	596
From 65 to 84 years	19
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 (NCT03334435).

Pre-assignment

Screening details:

NA

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	Investigator, Subject

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	1mg Baricitinib

Arm description:

1 milligram (mg) Baricitinib administered orally once daily.

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

Dosage and administration details:

1mg Baricitinib administered orally once daily.

Arm title	2mg Baricitinib

Arm description:

2mg Baricitinib administered orally once daily.

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

Dosage and administration details:

2mg Baricitinib administered orally once daily.

Arm title	4mg Baricitinib
Arm description:	
4mg Baricitinib administered orally once daily.	
Arm type	Experimental
Investigational medicinal product name	Baricitinib
Investigational medicinal product code	
Other name	LY3009104
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

4mg Baricitinib administered orally once daily.

Number of subjects in period 1	Placebo	1mg Baricitinib	2mg Baricitinib
Started	244	125	123
Received at least one dose of study drug	244	124	123
Completed	225	115	113
Not completed	19	10	10
Consent withdrawn by subject	8	3	1
Adverse event, non-fatal	1	3	2
inability to obtain laboratory samples	-	1	-
Pregnancy	-	1	-
Lost to follow-up	-	-	-
Lack of efficacy	10	2	7

Number of subjects in period 1	4mg Baricitinib
Started	123
Received at least one dose of study drug	123
Completed	117
Not completed	6
Consent withdrawn by subject	-
Adverse event, non-fatal	2
inability to obtain laboratory samples	-
Pregnancy	-
Lost to follow-up	1
Lack of efficacy	3

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo administered orally once daily.	
Reporting group title	1mg Baricitinib
Reporting group description:	
1 milligram (mg) Baricitinib administered orally once daily.	
Reporting group title	2mg Baricitinib
Reporting group description:	
2mg Baricitinib administered orally once daily.	
Reporting group title	4mg Baricitinib
Reporting group description:	
4mg Baricitinib administered orally once daily.	

Reporting group values	Placebo	1mg Baricitinib	2mg Baricitinib
Number of subjects	244	125	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)	235	124	118
From 65-84 years	9	1	5
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	90	45	58
Male	154	80	65
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	72	36	37
Native Hawaiian or Other Pacific Islander	0	1	0
Black or African American	0	0	0
White	169	85	85
More than one race	3	3	1
Unknown or Not Reported	0	0	0
Region of Enrollment			
Units: Subjects			
Argentina	28	14	13
South Korea	24	11	11
Austria	13	7	4

Hungary	23	10	11
Japan	45	22	22
Poland	41	27	21
Israel	12	7	6
Australia	24	14	15
Switzerland	13	5	5
Spain	21	8	15

Reporting group values	4mg Baricitinib	Total	
Number of subjects	123	615	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	119	596	
From 65-84 years	4	19	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	41	234	
Male	82	381	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	38	183	
Native Hawaiian or Other Pacific Islander	0	1	
Black or African American	0	0	
White	82	421	
More than one race	3	10	
Unknown or Not Reported	0	0	
Region of Enrollment			
Units: Subjects			
Argentina	12	67	
South Korea	9	55	
Austria	7	31	
Hungary	8	52	
Japan	23	112	
Poland	29	118	
Israel	9	34	
Australia	14	67	
Switzerland	2	25	
Spain	10	54	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo administered orally once daily.	
Reporting group title	1mg Baricitinib
Reporting group description:	
1 milligram (mg) Baricitinib administered orally once daily.	
Reporting group title	2mg Baricitinib
Reporting group description:	
2mg Baricitinib administered orally once daily.	
Reporting group title	4mg Baricitinib
Reporting group description:	
4mg Baricitinib administered orally once daily.	

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

End point description:

The IGA measures the investigator's global assessment of the participants 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 participants randomized to placebo, 2mg, or 4mg 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.

End point values	Placebo	2mg Baricitinib	4mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	244	123	123	
Units: percentage of participants				
number (not applicable)	4.5	10.6	13.8	

Statistical analyses

Statistical analysis title	IGA of 0 or 1: 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib

Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	5.92

Statistical analysis title	IGA of 0 or 1: 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.64
upper limit	8.05

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

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

End point description:

The IGA measures the investigator's global assessment of the participants 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.

APD: All participants randomized to placebo or 1mg 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.

End point values	Placebo	1mg Baricitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244	125		
Units: percentage of participants				
number (not applicable)	4.5	8.8		

Statistical analyses

Statistical analysis title	IGA of 0 or 1 - 1mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	5.02

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)

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 and neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2 and 3.The final EASI score is 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.

APD:All randomized participants.

End point type	Secondary

End point timeframe:

16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	244	125	123	123
Units: percentage of participants				
number (not applicable)	6.1	12.8	17.9	21.1

Statistical analyses

Statistical analysis title	EASI75 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.024
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	4.93

Statistical analysis title	EASI75 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.73
upper limit	7.04

Statistical analysis title	EASI75 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib

Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.22
upper limit	8.76

Secondary: Percentage of Participants Achieving EASI90

End point title	Percentage of Participants Achieving EASI90

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 and neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2 and 3. The final EASI score is 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. APD: All randomized participants.

End point type	Secondary

End point timeframe:

16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	244	125	123	123
Units: percentage of participants				
number (not applicable)	2.5	6.4	8.9	13.0

Statistical analyses

Statistical analysis title	EASI90 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.053
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	7.97

Statistical analysis title	EASI90 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.44
upper limit	10.41

Statistical analysis title	EASI90 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.42
upper limit	15.91

Secondary: Percent Change from Baseline (PFCB) on EASI Score

End point title	Percent Change from Baseline (PFCB) on EASI Score

End point description:

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 and neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2 and 3. The final EASI score is 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	
APD: All randomized participants who had a week 16 EASI data.	

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	34	40	49
Units: Percent Change				
least squares mean (standard error)	-28.91 (± 4.32)	-41.68 (± 5.33)	-54.80 (± 4.99)	-54.88 (± 4.56)

Statistical analyses

Statistical analysis title	PCFB EASI - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.062
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-12.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.19
upper limit	0.66
Variability estimate	Standard error of the mean
Dispersion value	6.81

Statistical analysis title	PCFB EASI - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-25.89

Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.78
upper limit	-12.99
Variability estimate	Standard error of the mean
Dispersion value	6.54

Statistical analysis title	PCFB EASI - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-25.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.29
upper limit	-13.65
Variability estimate	Standard error of the mean
Dispersion value	6.24

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

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

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 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.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	244	125	123	123
Units: percentage of participants				
number (not applicable)	1.6	4.8	7.3	11.4

Statistical analyses

Statistical analysis title	SCORAD 75 - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.086
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	9.76

Statistical analysis title	SCORAD 75 - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.58
upper limit	15.49

Statistical analysis title	SCORAD 75 - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib

Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.51
upper limit	21.83

Secondary: Percentage of Participants Achieving a 4-Point Improvement on the Itch Numeric Rating Scale (NRS)

End point title	Percentage of Participants Achieving a 4-Point Improvement on the Itch Numeric Rating Scale (NRS)

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 participants itching is indicated by selecting the number, using a daily diary, that best describes the worst level of itching in the past 24 hours.

APD: All randomized participants with a baseline Itch NRS score ≥ 4.

End point type	Secondary

End point timeframe:

16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	213	100	106	107
Units: percentage of participants				
number (not applicable)	4.7	6.0	15.1	18.7

Statistical analyses

Statistical analysis title	Itch NRS - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.505
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.41

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	3.87

Statistical analysis title	Itch NRS - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	8.27

Statistical analysis title	Itch NRS - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.22
upper limit	10.86

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

End point title	Change from Baseline in the Score of Item 2 of the Atopic Dermatitis Sleep Scale (ADSS)

End point description:

Atopic Dermatitis Sleep Scale (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 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

APD: All randomized participants with a Week 16 ADSS Item 2 (frequency of waking) data.

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	208	103	105	112
Units: units on a scale				
least squares mean (standard error)	-0.8 (± 0.09)	-1.10 (± 0.12)	-1.21 (± 0.12)	-1.38 (± 0.12)

Statistical analyses

Statistical analysis title	CFB ADSS - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.074
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.15

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

Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	-0.09
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	CFB ADSS - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	-0.26
Variability estimate	Standard error of the mean
Dispersion value	0.15

Secondary: Change from Baseline in Skin Pain NRS

End point title	Change from Baseline in Skin Pain NRS

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.

LSMean was 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.

APD: All randomized participants with a Week 16 Skin Pain NRS data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	31	38	47
Units: units on a scale				
least squares mean (standard error)	-0.86 (± 0.26)	-1.09 (± 0.32)	-2.61 (± 0.30)	-2.49 (± 0.28)

Statistical analyses

Statistical analysis title	CFB Skin Pain NRS - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.58
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	0.59
Variability estimate	Standard error of the mean
Dispersion value	0.41

Statistical analysis title	CFB Skin Pain NRS - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.54
upper limit	-0.96
Variability estimate	Standard error of the mean
Dispersion value	0.4

Statistical analysis title	CFB Skin Pain NRS - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.37
upper limit	-0.87
Variability estimate	Standard error of the mean
Dispersion value	0.38

Secondary: Percentage of Participants Achieving EASI50

End point title	Percentage of Participants Achieving EASI50

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 and neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2 and 3. Each body site will have a score that ranges from 0 to 72, and the final EASI score was obtained by weight-averaging these 4 scores. Hence, the final EASI score will range from 0 to 72 (Severe). The EASI 50 is defined as ≥50% improvement from baseline in EASI score.

APD: All randomized participants.

End point type	Secondary

End point timeframe:

16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	244	125	123	123
Units: percentage of participants				
number (not applicable)	12.3	18.4	27.6	29.3

Statistical analyses

Statistical analysis title	EASI50 - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.094
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	3.04

Statistical analysis title	EASI50 - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.65
upper limit	5.11

Statistical analysis title	EASI50 - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	5.51

Secondary: Percentage of Participants Achieving IGA of 0

End point title	Percentage of Participants Achieving IGA of 0
End point description:	

The IGA measures the investigator's global assessment of the participants 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.

End point type	Secondary
End point timeframe:	

16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	244	125	123	123
Units: percentage of participants				
number (not applicable)	1.6	2.4	4.1	4.1

Statistical analyses

Statistical analysis title	IGA of 0 - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.528
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	6.31

Statistical analysis title	IGA of 0 - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib

Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.142
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	8.95

Statistical analysis title	IGA of 0 - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.123
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	9.37

Secondary: Change from Baseline in SCORing Atopic Dermatitis (SCORAD)

End point title	Change from Baseline in SCORing Atopic Dermatitis (SCORAD)

End point description:

SCORAD index uses the rule of nines to assess disease extent & evaluates 6 clinical characteristics to determine disease severity: (1) erythema (2) edema/papulation (3) oozing/crusts (4) excoriation (5) lichenification & (6) dryness on a scale of 0 to 3 (0=absence, 1=mild, 2=moderate, 3=severe). SCORAD index also assesses subjective symptoms of pruritus & sleep loss with VAS where 0 is no itching or no trouble sleeping & 10 is unbearable itching or 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 & baseline-by-visit-interaction as fixed continuous effects.
APD: All randomized participants with a Week 16 SCORAD data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	34	40	49
Units: units on a scale				
least squares mean (standard error)	-13.35 (± 2.31)	-20.23 (± 2.84)	-27.83 (± 2.62)	-27.50 (± 2.41)

Statistical analyses

Statistical analysis title	CFB SCORAD - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.059
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-6.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.03
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	3.63

Statistical analysis title	CFB SCORAD - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-14.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.32
upper limit	-7.63
Variability estimate	Standard error of the mean
Dispersion value	3.47

Statistical analysis title	CFB SCORAD - 4 mg Baricitinib

Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-14.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.69
upper limit	-7.61
Variability estimate	Standard error of the mean
Dispersion value	3.32

Secondary: Percentage of Participants Achieving SCORAD90

End point title	Percentage of Participants Achieving SCORAD90

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 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 defined as a ≥ 90% improvement from baseline in the SCORAD score. APD: All randomized participants.

End point type	Secondary

End point timeframe:

16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	244	125	123	123
Units: percentage of participants				
number (not applicable)	1.2	3.2	4.1	4.9

Statistical analyses

Statistical analysis title	SCORAD90 - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib

Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.193
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	10.45

Statistical analysis title	SCORAD90 - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.042
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	16.03

Statistical analysis title	SCORAD90 - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	14.57

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

End point title	Change from Baseline in Body Surface Area (BSA) Affected

End point description:

Body surface area 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

APD: All randomized participants with week 16 BSA.

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	34	40	49
Units: units on a scale				
median (standard error)	12.82 (± 2.07)	-18.98 (± 2.53)	-22.12 (± 2.37)	-23.98 (± 2.17)

Statistical analyses

Statistical analysis title	CFB BSA - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.058
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-6.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.53
upper limit	0.21
Variability estimate	Standard error of the mean
Dispersion value	3.23

Statistical analysis title	CFB BSA - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-9.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.42
upper limit	-3.18
Variability estimate	Standard error of the mean
Dispersion value	3.1

Statistical analysis title	CFB BSA - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-11.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.03
upper limit	-5.3
Variability estimate	Standard error of the mean
Dispersion value	2.98

Secondary: Percentage of Participants Developing Skin Infections Requiring Antibiotic Treatment

End point title	Percentage of Participants Developing Skin Infections Requiring Antibiotic Treatment

End point description:

Number of participants developing skin infections requiring antibiotic treatment.

APD: All randomized participants.

End point type	Secondary

End point timeframe:

16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	244	125	123	123
Units: Percentage of participants				
number (not applicable)	7.8	4.8	7.3	4.9

Statistical analyses

Statistical analysis title	Skin Infections - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.189
Method	Fisher exact

Statistical analysis title	Skin Infections - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Statistical analysis title	Skin Infections - 4 mg Baricitinib
Comparison groups	4mg Baricitinib v Placebo
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.383
Method	Fisher exact

Secondary: Percent Change from Baseline in Itch NRS

End point title	Percent Change from Baseline in Itch NRS

End point description:

The Itch NRS is a participant-administered, 11-point horizontal scale, 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.
LSMean were 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.

APD: All randomized participants with week 16 Itch NRS data.

End point type	Secondary
End point timeframe:	
Baseline, 16 Weeks	

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	31	38	47
Units: Percent Change				
least squares mean (standard error)	-16.58 (± 5.45)	-31.39 (± 6.61)	47.24 (± 6.10)	46.87 (± 5.43)

Statistical analyses

Statistical analysis title	PCFB Itch NRS - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.081
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-14.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.45
upper limit	1.85
Variability estimate	Standard error of the mean
Dispersion value	8.46

Statistical analysis title	PCFB Itch NRS - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-30.66

Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.62
upper limit	-14.7
Variability estimate	Standard error of the mean
Dispersion value	8.11

Statistical analysis title	PCFB Itch NRS - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-30.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.29
upper limit	-15.27
Variability estimate	Standard error of the mean
Dispersion value	7.63

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

End point title	Change from Baseline in the Total Score of the Patient Oriented Eczema Measure (POEM)

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.
LSMean were 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.
APD: All randomized participants with week 16 POEM data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	34	40	48
Units: units on a scale				
least squares mean (standard error)	-1.48 (± 0.84)	-3.85 (± 1.04)	-7.06 (± 0.96)	-7.56 (± 0.88)

Statistical analyses

Statistical analysis title	CFB POEM - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.075
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-2.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.97
upper limit	0.24
Variability estimate	Standard error of the mean
Dispersion value	1.32

Statistical analysis title	CFB POEM - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-5.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.07
upper limit	-3.08
Variability estimate	Standard error of the mean
Dispersion value	1.27

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

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-6.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.47
upper limit	-3.68
Variability estimate	Standard error of the mean
Dispersion value	1.21

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

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

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 was used for the PGI-S-AD, ie, "No symptoms (0)", "Very mild (1)", "mild (2)", "moderate (3)", "severe (4)".
LSMean were 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.

APD: All randomized participants with Week 16 PGI-S-AD data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	31	38	47
Units: units on a scale				
least squares mean (standard error)	-0.27 (± 0.11)	-0.53 (± 0.14)	-0.88 (± 0.13)	-0.96 (± 0.12)

Statistical analyses

Statistical analysis title	CFB PGI-S-AD - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	CFB PGI-S-AD - 2mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	-0.28
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	CFB PGI-S-AD - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.38

Variability estimate	Standard error of the mean
Dispersion value	0.16

Secondary: Change from Baseline on the Hospital Anxiety Depression Scale (HADS)

End point title	Change from Baseline on the Hospital Anxiety Depression Scale (HADS)

End point description:

The HADS is a participant-rated instrument used to assess both anxiety and depression. This instrument consists of 14 items 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. LSMean were 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.

APD: All randomized participants with week 16 HADS data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	34	40	48
Units: units on a scale				
least squares mean (standard error)				
Anxiety	-0.99 (± 0.33)	-1.93 (± 0.40)	-1.92 (± 0.38)	-2.30 (± 0.35)
Depression	-0.28 (± 0.32)	-0.78 (± 0.40)	-0.99 (± 0.38)	-1.46 (± 0.35)

Statistical analyses

Statistical analysis title	CFB HADS Anxiety - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.067
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.95
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.51

Notes:

[3] - HADS Anxiety.

Statistical analysis title	CFB HADS Anxiety - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.06
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.89
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.49

Notes:

[4] - HADS Anxiety.

Statistical analysis title	CFB HADS Anxiety - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.006
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.23
upper limit	-0.38
Variability estimate	Standard error of the mean
Dispersion value	0.47

Notes:

[5] - HADS Anxiety.

Statistical analysis title	CFB HADS Depression - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.321
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.49
Variability estimate	Standard error of the mean
Dispersion value	0.51

Notes:

[6] - HADS Depression.

Statistical analysis title	CFB HADS Depression - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.143
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.67
upper limit	0.24
Variability estimate	Standard error of the mean
Dispersion value	0.49

Notes:

[7] - HADS Depression.

Statistical analysis title	CFB HADS Depression - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.012
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.11
upper limit	-0.26
Variability estimate	Standard error of the mean
Dispersion value	0.47

Notes:

[8] - HADS Depression.

Secondary: Change from Baseline on the Dermatology Life Quality Index (DLQI)

End point title	Change from Baseline on the Dermatology Life Quality Index

	(DLQI)

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.

LSMean were 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.

APD: All randomized participants with week 16 DLQI data.

End point type	Secondary

End point timeframe:

Baseline, 16 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	34	40	48
Units: units on a scale				
least squares mean (standard error)	-3.35 (± 0.62)	-5.11 (± 0.76)	-7.44 (± 0.71)	-7.56 (± 0.66)

Statistical analyses

Statistical analysis title	CFB DLQI - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.071
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.67
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.97

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

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-4.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.92
upper limit	-2.26
Variability estimate	Standard error of the mean
Dispersion value	0.93

Statistical analysis title	CFB DLQI - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-4.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.98
upper limit	-2.45
Variability estimate	Standard error of the mean
Dispersion value	0.9

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

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

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 in 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. LSMean were 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.

APD: All randomized participants with week 16 WPAI-AD data.

End point type	Secondary

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52[9]	34[10]	39[11]	49[12]
Units: units on a scale				
least squares mean (standard error)				
Absenteeism(25,21,22,33)	-4.40 (± 3.45)	-5.31 (± 3.91)	-3.39 (± 3.68)	0.76 (± 3.08)
Presenteeism(23,21,22,32)	-6.15 (± 3.87)	-9.27 (± 4.08)	-19.71 (± 3.90)	-19.28 (± 3.37)
Work Productivity Loss(23,21,22,32)	-7.15 (± 4.65)	-8.96 (± 4.86)	-16.63 (± 4.65)	-16.28 (± 3.96)
Activity Impairment(52,34,39,49)	-8.94 (± 2.74)	-11.21 (± 3.34)	-23.25 (± 3.12)	-23.41 (± 2.82)

Notes:

[9] - N=25,23,23,52.

[10] - N=21,21,21,34.

[11] - N=22,22,22,39.

[12] - N=33,32,32,49.

Statistical analyses

Statistical analysis title	CFB Absenteeism - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.861
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.16
upper limit	9.34
Variability estimate	Standard error of the mean
Dispersion value	5.17

Notes:

[13] - Percentage of Absenteeism Change from Baseline.

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

Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.841 [15]
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.94
upper limit	10.97
Variability estimate	Standard error of the mean
Dispersion value	5.03

Notes:

[14] - Percentage of Absenteeism Change from Baseline.

[15] - Absenteeism

Statistical analysis title	CFB Absenteeism - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	= 0.264
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	5.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.95
upper limit	14.26
Variability estimate	Standard error of the mean
Dispersion value	4.6

Notes:

[16] - Percentage of Absenteeism Change from Baseline.

Statistical analysis title	CFB Presenteeism - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.58
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-3.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.26
upper limit	8.02

Variability estimate	Standard error of the mean
Dispersion value	5.63

Statistical analysis title	CFB Presenteeism - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-13.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.45
upper limit	-2.86
Variability estimate	Standard error of the mean
Dispersion value	5.5

Statistical analysis title	CFB Presenteeism - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-13.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.2
upper limit	-3.06
Variability estimate	Standard error of the mean
Dispersion value	5.08

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

Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.788
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.12
upper limit	11.49
Variability estimate	Standard error of the mean
Dispersion value	6.71

Statistical analysis title	CFB Work Productivity Loss - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.152
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-9.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.51
upper limit	3.55
Variability estimate	Standard error of the mean
Dispersion value	6.57

Statistical analysis title	CFB Work Productivity Loss - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.135
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-9.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.17
upper limit	2.9

Variability estimate	Standard error of the mean
Dispersion value	6.07

Statistical analysis title	CFB Activity Impairment - 1 mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.595
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-2.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.65
upper limit	6.12
Variability estimate	Standard error of the mean
Dispersion value	4.25

Statistical analysis title	CFB Activity Impairment - 2 mg Baricitinib
Comparison groups	2mg Baricitinib v Placebo
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.43
upper limit	-6.17
Variability estimate	Standard error of the mean
Dispersion value	4.12

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

Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-14.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.11
upper limit	-6.83
Variability estimate	Standard error of the mean
Dispersion value	3.88

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

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. The responses are used to derive the health state index scores using the United Kingdom (UK) algorithm, with scores ranging from -0.594 to 1, and the United States (US) algorithm, with scores ranging from -0.109 to 1. A higher score indicates better health state.
LSMean were 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.

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

End point type	Secondary

End point timeframe:

Baseline, 16 weeks

APD:All randomized participants with week 16 EQ-5D-5L health state index US & UK score.

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	34	39	49
Units: units on a scale				
least squares mean (standard deviation)				
Health State Index Score (US Algorithm)	0.02 (± 0.02)	0.05 (± 0.02)	0.10 (± 0.02)	0.10 (± 0.02)
Health State Index Score (UK Algorithm)	0.03 (± 0.02)	0.06 (± 0.03)	0.14 (± 0.02)	0.14 (± 0.02)

Statistical analyses

Statistical analysis title	CFB Health State Index US - 1 mg Baricitinib
Statistical analysis description: Health State Index Score (US Algorithm)	
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.295
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	CFB Health State Index US - 2 mg Baricitinib
Statistical analysis description: Health State Index Score (US Algorithm)	
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.12
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 4mg Baricitinib
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
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 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.334
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.1
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 2mg Baricitinib
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.03

Statistical analysis title	CFB Health State Index UK - 4 mg Baricitinib

Statistical analysis description:

Health State Index Score (UK Algorithm)

Comparison groups	Placebo v 4mg Baricitinib
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.03

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

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

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.

LSMean were 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.

APD: All randomized participants with week 16 EQ-5D-5L VAS data.

End point type	Secondary

End point timeframe:

Baseline, 16 weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	34	39	49
Units: Millimeter (mm)				
least squares mean (standard error)	2.34 (± 2.22)	2.75 (± 2.71)	10.54 (± 2.53)	11.16 (± 2.30)

Statistical analyses

Statistical analysis title	CFB EQ-5D-5L VAS - 1mg Baricitinib
Comparison groups	Placebo v 1mg Baricitinib
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.907
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.44
upper limit	7.25
Variability estimate	Standard error of the mean
Dispersion value	3.47

Statistical analysis title	CFB EQ-5D-5L VAS - 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	8.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.63
upper limit	14.76
Variability estimate	Standard error of the mean
Dispersion value	3.33

Statistical analysis title	CFB EQ-5D-5L VAS - 4 mg Baricitinib
Comparison groups	Placebo v 4mg Baricitinib

Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	8.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.62
upper limit	15.01
Variability estimate	Standard error of the mean
Dispersion value	3.14

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

End point description:

The IGA measures the investigator's global assessment of the participants 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.

APD: All randomized participants.

End point type	Secondary

End point timeframe:

4 Weeks

End point values	Placebo	1mg Baricitinib	2mg Baricitinib	4mg Baricitinib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	244	125	123	123
Units: percentage of participants				
number (not applicable)	3.7	3.2	8.1	15.4

Statistical analyses

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

Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.905
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	2.93

Statistical analysis title	IGA of 0 or 1 (Wk 4): 2 mg Baricitinib
Comparison groups	Placebo v 2mg Baricitinib
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.064
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	5.92

Statistical analysis title	IGA of 0 or 1 (Wk 4): 4 mg Baricitinib
Comparison groups	4mg Baricitinib v Placebo
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.01
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.25
upper limit	11.74

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
Baseline to end of study (Up to 20 weeks)	
Adverse event reporting additional description:	
All randomized participants who received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo administered orally once daily.	
Reporting group title	1mg Baricitinib
Reporting group description:	
1mg Baricitinib administered orally once daily.	
Reporting group title	2mg Baricitinib
Reporting group description:	
2mg Baricitinib administered orally once daily.	
Reporting group title	4mg Baricitinib
Reporting group description:	
4mg Baricitinib administered orally once daily.	

Serious adverse events	Placebo	1mg Baricitinib	2mg Baricitinib
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 244 (3.69%)	9 / 124 (7.26%)	3 / 123 (2.44%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 244 (0.41%)	0 / 124 (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
Blood and lymphatic system disorders			
lymphadenopathy			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 244 (0.00%)	1 / 124 (0.81%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
cataract			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 244 (0.00%)	1 / 124 (0.81%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
retinal detachment			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 244 (0.41%)	0 / 124 (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
Gastrointestinal disorders			
diverticulum			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 244 (0.00%)	1 / 124 (0.81%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
asthma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 244 (0.00%)	1 / 124 (0.81%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
angioedema			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 244 (0.00%)	1 / 124 (0.81%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dermatitis atopic			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	3 / 244 (1.23%)	1 / 124 (0.81%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 3	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dermatitis exfoliative generalised			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 244 (0.41%)	0 / 124 (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
drug eruption			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 244 (0.00%)	1 / 124 (0.81%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
depression			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 244 (0.00%)	0 / 124 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
panic attack			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 244 (0.00%)	0 / 124 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
intervertebral disc protrusion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 244 (0.41%)	0 / 124 (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
Infections and infestations			
eczema herpeticum			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	2 / 244 (0.82%)	2 / 124 (1.61%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
encephalitis viral			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 244 (0.00%)	1 / 124 (0.81%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peritonsillitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 244 (0.00%)	1 / 124 (0.81%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tonsillitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 244 (0.00%)	0 / 124 (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

Serious adverse events	4mg Baricitinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 123 (0.81%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
lymphadenopathy			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Eye disorders

cataract

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

retinal detachment

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders

diverticulum

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders

asthma

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Skin and subcutaneous tissue disorders

angioedema

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

dermatitis atopic

alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
dermatitis exfoliative generalised			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
drug eruption			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
depression			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
panic attack			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
intervertebral disc protrusion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
eczema herpeticum			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
encephalitis viral			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
peritonsillitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
tonsillitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	1mg Baricitinib	2mg Baricitinib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 244 (13.93%)	23 / 124 (18.55%)	27 / 123 (21.95%)
Investigations			
blood creatine phosphokinase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 244 (0.41%)	4 / 124 (3.23%)	1 / 123 (0.81%)
occurrences (all)	1	4	1
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	5 / 244 (2.05%)	6 / 124 (4.84%)	9 / 123 (7.32%)
occurrences (all)	8	6	9

Infections and infestations			
herpes simplex			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 244 (0.82%)	2 / 124 (1.61%)	7 / 123 (5.69%)
occurrences (all)	3	2	7
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	30 / 244 (12.30%)	13 / 124 (10.48%)	16 / 123 (13.01%)
occurrences (all)	33	13	16

Non-serious adverse events	4mg Baricitinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 123 (23.58%)		
Investigations			
blood creatine phosphokinase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	7 / 123 (5.69%)		
occurrences (all)	7		
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	11 / 123 (8.94%)		
occurrences (all)	14		
Infections and infestations			
herpes simplex			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	3 / 123 (2.44%)		
occurrences (all)	3		
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	10 / 123 (8.13%)		
occurrences (all)	12		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol?   No

---

Interruptions (globally)

Were there any global interruptions to the trial?   No

Limitations and caveats

 None reported