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

Summary

EudraCT number	2018-001726-26
Trial protocol	DE AT ES PL IT
Global end of trial date	22 August 2019

Results information

Result version number	v1 (current)
This version publication date	09 August 2020
First version publication date	09 August 2020

Trial information

Trial identification

Sponsor protocol code	I4V-MC-JAIY

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03733301
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17100

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	22 August 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 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 in combination with topical corticosteroids (TCS) 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:

Participants were allowed to use approved low to moderate potency topical corticosteroids (TCS) as background therapy. Triamcinolone 0.1% cream and /or hydrocortisone 2.5% ointment were provided by the sponsor for use as background therapy. In the event of these specific TCS being unavailable, and alternate equivalent-potency TCS may be provided.

Evidence for comparator: -

Actual start date of recruitment	16 November 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 25
Country: Number of subjects enrolled	Korea, Republic of: 63
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Japan: 63
Country: Number of subjects enrolled	Taiwan: 36
Country: Number of subjects enrolled	Poland: 26
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	Germany: 47
Country: Number of subjects enrolled	Spain: 15
Worldwide total number of subjects	329
EEA total number of subjects	115

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)	322
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants who completed the 16-week treatment period had an option to enter extension study JAHN (NCT03334435).

Pre-assignment

Screening details:

No Text Available

Period 1

Period 1 title	Overall (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 in combination with topical corticosteroids (TCS).

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	2 mg Baricitinib

Arm description:

2 mg Baricitinib administered orally once daily in combination with TCS. Placebo administered orally once daily to match 4 mg Baricitinib.

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:

2 mg Baricitinib administered orally once daily.

Arm title	4 mg Baricitinib

Arm description:

4 mg Baricitinib administered orally once daily in combination with TCS. Placebo administered orally once daily to match 2 mg Baricitinib.

Arm type	Experimental

Investigational medicinal product name	4 mg 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	2 mg Baricitinib	4 mg Baricitinib
Started	109	109	111
Received at Least One Dose of Study Drug	108	109	111
Completed	102	100	107
Not completed	7	9	4
Screen Fail	1	-	-
Consent withdrawn by subject	3	5	1
Adverse event, non-fatal	-	1	3
Non-compliance	1	-	-
Lack of efficacy	2	3	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo administered orally once daily in combination with topical corticosteroids (TCS).	
Reporting group title	2 mg Baricitinib
Reporting group description:	
2 mg Baricitinib administered orally once daily in combination with TCS. Placebo administered orally once daily to match 4 mg Baricitinib.	
Reporting group title	4 mg Baricitinib
Reporting group description:	
4 mg Baricitinib administered orally once daily in combination with TCS. Placebo administered orally once daily to match 2 mg Baricitinib.	

Reporting group values	Placebo	2 mg Baricitinib	4 mg Baricitinib
Number of subjects	109	109	111
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	106	105	111
>=65 years	3	4	0
Gender categorical Units: Subjects			
Female	38	39	36
Male	71	70	75
Race/Ethnicity, Customized Units: Subjects			
Asian	57	57	54
Multiple	6	2	3
White	46	50	54
Region of Enrollment Units: Subjects			
Argentina	8	6	11
South Korea	29	19	15
Austria	2	1	5
Japan	21	20	22
Taiwan	9	12	15
Poland	11	9	6
Italy	7	6	6
Australia	4	14	9
Germany	12	18	17
Spain	6	4	5

Reporting group values	Total		
Number of subjects	329		
Age categorical Units: Subjects			
<=18 years	0		

Between 18 and 65 years	322		
>=65 years	7		

Gender categorical Units: Subjects			
Female	113		
Male	216		
Race/Ethnicity, Customized Units: Subjects			
Asian	168		
Multiple	11		
White	150		
Region of Enrollment Units: Subjects			
Argentina	25		
South Korea	63		
Austria	8		
Japan	63		
Taiwan	36		
Poland	26		
Italy	19		
Australia	27		
Germany	47		
Spain	15		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo administered orally once daily in combination with topical corticosteroids (TCS).	
Reporting group title	2 mg Baricitinib
Reporting group description:	
2 mg Baricitinib administered orally once daily in combination with TCS. Placebo administered orally once daily to match 4 mg Baricitinib.	
Reporting group title	4 mg Baricitinib
Reporting group description:	
4 mg Baricitinib administered orally once daily in combination with TCS. Placebo administered orally once daily to match 2 mg Baricitinib.	

Primary: 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 investigators 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) 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 randomized participants.	
End point type	Primary
End point timeframe:	
Week 16	

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	109	111	
Units: percentage of participants				
number (not applicable)	14.7	23.9	30.6	

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	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.082
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	3.85

Statistical analysis title	IGA of 0 or 1 - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	5.56

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/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.

APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	109	111	
Units: percentage of participants				
number (not applicable)	22.9	43.1	47.7	

Statistical analyses

Statistical analysis title	EASI75 - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.44
upper limit	4.76

Statistical analysis title	EASI75 - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	5.97

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/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.

APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	109	111	
Units: percentage of participants				
number (not applicable)	13.8	16.5	24.3	

Statistical analyses

Statistical analysis title	EASI90 - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.574
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	2.62

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

Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.045
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	4.02

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

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

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).

Least Squares Mean (LSM) were calculated using mixed model repeated measures (MMRM) with treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit interaction as fixed categorical effects and baseline score and baseline score-by-visit interaction as fixed continuous effects.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	100	100	
Units: percent change				
least squares mean (standard error)	-45.08 (± 3.828)	-58.16 (± 3.689)	-67.21 (± 3.679)	

Statistical analyses

Statistical analysis title	PCFB EASI - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib

Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.013
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-13.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.42
upper limit	-2.73
Variability estimate	Standard error of the mean
Dispersion value	5.256

Statistical analysis title	PCFB EASI - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-22.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.48
upper limit	-11.78
Variability estimate	Standard error of the mean
Dispersion value	5.259

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 a visual analogue scales (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), and subjective symptoms (C: 0-20) combine A/5+7^B/2+C to give a maximum possible score of 103, where 0 = no disease & 103 = severe disease. The SCORAD 75 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:
Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	109	111	
Units: percentage of participants				
number (not applicable)	7.3	11.0	18.0	

Statistical analyses

Statistical analysis title	SCORAD75 - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.364
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	3.81

Statistical analysis title	SCORAD 75 - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	6.34

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 NRS is a patient-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 patient'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.

APD: All randomized participants with Baseline Itch Score >= 4.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	104	97	100	
Units: percentage of participants				
number (not applicable)	20.2	38.1	44.0	

Statistical analyses

Statistical analysis title	NRS - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.48
upper limit	5.61

Statistical analysis title	NRS - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib

Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.98
upper limit	7.46

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)

End point description:

The ADSS is a 3-item, patient-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. Patients report their frequency of waking last night, item 2, by selecting the number of times they woke up each night, ranging from 0 to 29 times, where the higher a number indicates a worse outcome. The ADSS is designed to be completed each day, using a daily diary, with respondents thinking about sleep "last night." Each item is scored individually. LS Mean were calculated using MMRM with treatment, region, baseline disease severity (IGA), visit, and treatment-by-visit interaction as fixed categorical effects and baseline score and baseline score-by-visit interaction as fixed continuous effects.

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

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	98	94	
Units: units on a scale				
least squares mean (standard error)	-0.51 (± 0.151)	-1.33 (± 0.147)	-1.42 (± 0.147)	

Statistical analyses

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

Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	-0.41
Variability estimate	Standard error of the mean
Dispersion value	0.209

Statistical analysis title	CFB ADSS - 4 mg
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	-0.51
Variability estimate	Standard error of the mean
Dispersion value	0.209

Secondary: Change from Baseline in Skin Pain NRS

End point title	Change from Baseline in Skin Pain NRS

End point description:

The Skin Pain NRS is a patient-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 patient'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.

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

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	98	94	
Units: units on a scale				
least squares mean (standard error)	-2.06 (± 0.231)	-3.22 (± 0.224)	-3.73 (± 0.226)	

Statistical analyses

Statistical analysis title	CFB NRS - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	-1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.78
upper limit	-0.52
Variability estimate	Standard error of the mean
Dispersion value	0.319

Statistical analysis title	CFB NRS - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	0.322

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/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 the EASI score.

APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	109	111	
Units: percentage of participants				
number (not applicable)	41.3	64.2	70.3	

Statistical analyses

Statistical analysis title	EASI50 - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.57
Confidence interval	
level	Other: 96 %
sides	2-sided
lower limit	1.47
upper limit	4.49

Statistical analysis title	EASI50 - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib

Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	6.32

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 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.

APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	109	111	
Units: percentage of participants				
number (not applicable)	2.8	3.7	8.1	

Statistical analyses

Statistical analysis title	IGA of 0 - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.715
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	5.31

Statistical analysis title	IGA of 0 - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.083
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	10.56

Secondary: Change from Baseline in SCORAD

End point title	Change from Baseline in SCORAD

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, & (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.

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

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[1]	100[2]	99[3]	
Units: units on a scale				
least squares mean (standard error)	-21.40 (± 1.941)	-29.88 (± 1.867)	-35.78 (± 1.862)	

Notes:
[1] - APD: All randomized participants with Week 16 SCORAD data.
[2] - APD: All randomized participants with Week 16 SCORAD data.
[3] - APD: All randomized participants with Week 16 SCORAD data.

Statistical analyses

Statistical analysis title	CFB SCORAD - 2 mg Baricitinib
Comparison groups	2 mg Baricitinib v Placebo
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-8.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.72
upper limit	-3.24
Variability estimate	Standard error of the mean
Dispersion value	2.663

Statistical analysis title	CFB SCORAD - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-14.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.62
upper limit	-9.14
Variability estimate	Standard error of the mean
Dispersion value	2.662

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 in the last 72 hours on visual analogue scales (VAS) of 0 to 10 where 0 is no itch or sleep loss and 10 is worst imaginable itch or sleep loss. These 3 aspects: (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 SCORAD90 is defined as a ≥ 90% improvement from baseline in the SCORAD score.
APD: All randomized participants.

End point type	Secondary
End point timeframe:	
Week 16	

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	109	111	
Units: percentage of participants				
number (not applicable)	0.9	3.7	7.2	

Statistical analyses

Statistical analysis title	SCORAD90 - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.204
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	19.37

Statistical analysis title	SCORAD90 - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	38.53

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:

The 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.

LS Means 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,Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[4]	100[5]	100[6]	
Units: units on a scale				
least squares mean (standard error)	-18.03 (± 1.888)	-27.00 (± 1.825)	-29.73 (± 1.814)	

Notes:

[4] - APD: All randomized participants with Week 16 BSA data.

[5] - APD: All randomized participants with Week 16 BSA data.

[6] - APD: All randomized participants with Week 16 BSA data.

Statistical analyses

Statistical analysis title	CFB BSA - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-8.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.07
upper limit	-3.87
Variability estimate	Standard error of the mean
Dispersion value	2.591

Statistical analysis title	CFB BSA - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-11.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.78
upper limit	-6.61
Variability estimate	Standard error of the mean
Dispersion value	2.584

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:

Percentage of participants developing skin infections requiring antibiotic treatment.

APD: All randomized participants who receive at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	108	109	111	
Units: percentage of participants				
number (not applicable)	2.8	4.6	2.7	

Statistical analyses

Statistical analysis title	Skin Infections - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.721
Method	Fisher exact

Statistical analysis title	Skin Infections - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Fisher exact

Secondary: Mean Gram Quantity of Moderate Potency Background Topical Corticosteroids (TCS) Used (Tube Weights)

End point title	Mean Gram Quantity of Moderate Potency Background Topical Corticosteroids (TCS) Used (Tube Weights)

End point description:

Average weights of full tubes were used to determine the dispensed weights for each region. Returned tubes were weighed with cap without carton to determine the amount of TCS in grams (g) used at each visit. Analysis was done via analysis of variance (ANOVA), with geographic region, baseline disease severity (IGA) and treatment as factors in the model.

APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 0 through Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	109	111	
Units: gram				
least squares mean (standard error)	252.75 (± 17.536)	187.59 (± 17.508)	161.61 (± 17.280)	

Statistical analyses

Statistical analysis title	Moderate Potency Background TCS - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	218
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0073
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-65.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-112.87
upper limit	-17.65
Variability estimate	Standard error of the mean
Dispersion value	24.149

Statistical analysis title	Moderate Potency Background TCS - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	220
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0002
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-91.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-138.43
upper limit	-43.85
Variability estimate	Standard error of the mean
Dispersion value	24.038

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.

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

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

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	98	94	
Units: percent change				
least squares mean (standard error)	-27.00 (± 3.370)	-43.44 (± 3.263)	-51.22 (± 3.280)	

Statistical analyses

Statistical analysis title	PCFB Itch NRS - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-16.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.6
upper limit	-7.27
Variability estimate	Standard error of the mean
Dispersion value	4.658

Statistical analysis title	PCFB Itch NRS - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib

Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-24.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.42
upper limit	-15.03
Variability estimate	Standard error of the mean
Dispersion value	4.672

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.

LS Means 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.

APD: All randomized participants with Week 16 POEM data.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	99	99	
Units: units on a scale				
least squares mean (standard error)	-5.60 (± 0.764)	-8.50 (± 0.736)	-10.83 (± 0.730)	

Statistical analyses

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

Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.96
upper limit	-0.84
Variability estimate	Standard error of the mean
Dispersion value	1.046

Statistical analysis title	CFB POEM - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.28
upper limit	-3.18
Variability estimate	Standard error of the mean
Dispersion value	1.043

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 is a single-item question asking the participant how they would rate their overall AD symptoms over the past 24 hours, using a daily diary. The 5 categories of responses are "(0) no symptoms", "(1) very mild", "(2) mild" "(3) moderate", and "(4) severe."

LS Means 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.

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

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	98	94	
Units: units on a scale				
least squares mean (standard error)	-0.69 (± 0.094)	-1.06 (± 0.091)	-1.18 (± 0.091)	

Statistical analyses

Statistical analysis title	CFB PGI-S-AD - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	CFB PGI-S-AD - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	-0.24
Variability estimate	Standard error of the mean
Dispersion value	0.13

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 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 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 Week 16 HADS data.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	99	99	
Units: units on a scale				
least squares mean (standard error)				
Depression	-1.31 (± 0.311)	-2.05 (± 0.298)	-2.33 (± 0.296)	
Anxiety	-1.89 (± 0.304)	-2.70 (± 0.292)	-2.80 (± 0.289)	

Statistical analyses

Statistical analysis title	CFB HADS - 2 mg Baricitinib

Statistical analysis description:

HADS Depression

Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.083
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.57
upper limit	0.1

Variability estimate	Standard error of the mean
Dispersion value	0.425

Statistical analysis title	CFB HADS - 4 mg Baricitinib
Statistical analysis description:	
HADS Depression	
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.85
upper limit	-0.19
Variability estimate	Standard error of the mean
Dispersion value	0.423

Statistical analysis title	CFB HADS - 2 mg Baricitinib
Statistical analysis description:	
HADS Anxiety	
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.051
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.63
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.415

Notes:
[7] - HADS Anxiety

Statistical analysis title	CFB HADS - 4 mg Baricitinib
Statistical analysis description:	
HADS Anxiety	

Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.028
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.72
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.413

Notes:

[8] - HADS Anxiety

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 including 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 at unanswered ("not relevant") responses scored as "0." Scores 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 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 Week 16 DLQI data.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	99	99	
Units: units on a scale				
least squares mean (standard error)	-5.58 (± 0.608)	-7.50 (± 0.584)	-8.89 (± 0.851)	

Statistical analyses

Statistical analysis title	DLQI - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.56
upper limit	-0.28
Variability estimate	Standard error of the mean
Dispersion value	0.832

Statistical analysis title	DLQI - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.94
upper limit	-1.68
Variability estimate	Standard error of the mean
Dispersion value	0.829

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.

LS Means 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.

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

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

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	99	111	
Units: units on a scale				
least squares mean (standard error)				
Absenteeism (n=47, 57, 57)	-6.27 (± 1.897)	-4.25 (± 1.741)	-5.29 (± 1.737)	
Presenteeism (n=46, 54, 54)	-13.15 (± 3.203)	-21.28 (± 2.978)	-23.89 (± 2.955)	
Work Productivity Loss (n=46, 54, 54)	-14.25 (± 3.300)	-22.17 (± 3.070)	-24.96 (± 3.051)	
Activity Impairment (n=87, 99, 98)	-16.75 (± 2.570)	-26.55 (± 2.458)	-27.25 (± 2.447)	

Statistical analyses

Statistical analysis title	WPAI-AD Absenteeism - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.435
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.06
upper limit	7.08
Variability estimate	Standard error of the mean
Dispersion value	2.569

Statistical analysis title	WPAI-AD Absenteeism - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib

Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.706
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	6.04
Variability estimate	Standard error of the mean
Dispersion value	2.569

Statistical analysis title	WPAI-AD Presenteeism - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.066
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-8.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.78
upper limit	0.54
Variability estimate	Standard error of the mean
Dispersion value	4.384

Statistical analysis title	WPAI-AD Presenteeism - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-10.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.3
upper limit	-2.17

Variability estimate	Standard error of the mean
Dispersion value	4.336

Statistical analysis title	WPAI-AD Work Productivity Loss - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.081
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-7.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.84
upper limit	0.99
Variability estimate	Standard error of the mean
Dispersion value	4.511

Statistical analysis title	WPAI-AD Work Productivity Loss - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-10.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.55
upper limit	1.88
Variability estimate	Standard error of the mean
Dispersion value	4.473

Statistical analysis title	WPAI-AD Activity Impairment - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib

Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-9.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.71
upper limit	-2.89
Variability estimate	Standard error of the mean
Dispersion value	3.511

Statistical analysis title	WPAI-AD Activity Impairment - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-10.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.39
upper limit	-3.61
Variability estimate	Standard error of the mean
Dispersion value	3.5

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, with higher score indicating better health state.

LS Means 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.

APD: All randomized participants with Week 16 EQ-5D-5L Health State Index US and UK data.

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

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	99	98	
Units: units on a scale				
least squares mean (standard error)				
Health State Index Score (US Algorithm)	0.09 (± 0.013)	0.12 (± 0.012)	0.14 (± 0.012)	
Health State Index Score (UK Algorithm)	0.13 (± 0.018)	0.17 (± 0.017)	0.21 (± 0.017)	

Statistical analyses

Statistical analysis title	Health State Index US - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.176
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.017

Statistical analysis title	Health State Index US - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.017

Statistical analysis title	Health State Index UK - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.176
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.024

Statistical analysis title	Health State Index UK - 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.024

Secondary: Change from Baseline on the EQ-5D-5L Visual Analog Scale (VAS)	
End point title	Change from Baseline on the EQ-5D-5L Visual Analog Scale

	(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.

LS Means 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.

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

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	99	98	
Units: milliliters				
least squares mean (standard error)	11.00 (± 1.903)	15.12 (± 1.806)	17.06 (± 1.805)	

Statistical analyses

Statistical analysis title	CFB EQ-5D-5L VAS - 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.113
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	4.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	9.23
Variability estimate	Standard error of the mean
Dispersion value	2.593

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

Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	6.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	11.16
Variability estimate	Standard error of the mean
Dispersion value	2.592

Secondary: Mean Number of Days Without Use of Background TCS

End point title	Mean Number of Days Without Use of Background TCS

End point description:

The ANCOVA model includes treatment, region, and baseline disease severity (IGA) as factors.

APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 0 through Week 16

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	109	111	
Units: Days				
least squares mean (standard error)	12.45 (± 3.17)	22.49 (± 3.16)	29.78 (± 3.12)	

Statistical analyses

Statistical analysis title	Background TCS 2 mg Baricitinib
Comparison groups	Placebo v 2 mg Baricitinib
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	10.04

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	18.36
Variability estimate	Standard error of the mean
Dispersion value	4.36

Statistical analysis title	Background TCS 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	17.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.79
upper limit	25.88
Variability estimate	Standard error of the mean
Dispersion value	4.34

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

End point title	Percentage of Participants Achieving IGA of 0 or 1 With a ≥ 2 Point Improvement

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) 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:

Week 4

End point values	Placebo	2 mg Baricitinib	4 mg Baricitinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	109	111	
Units: Participants				
number (not applicable)	5.5	17.4	19.8	

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	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	10.03

Statistical analysis title	IGA of 0 or 1: 4 mg Baricitinib
Comparison groups	Placebo v 4 mg Baricitinib
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.77
upper limit	11.87

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline 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	4mg Baricitinib
Reporting group description:	
4 mg Baricitinib administered orally once daily.	
Reporting group title	2mg Baricitinib
Reporting group description:	
2 mg Baricitinib administered orally once daily.	

Serious adverse events	Placebo	4mg Baricitinib	2mg Baricitinib
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 108 (3.70%)	4 / 111 (3.60%)	2 / 109 (1.83%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
skin laceration			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 108 (0.00%)	0 / 111 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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 / 108 (0.00%)	1 / 111 (0.90%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

abdominal pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 108 (0.93%)	0 / 111 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
asthma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 108 (0.00%)	1 / 111 (0.90%)	0 / 109 (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
pulmonary embolism			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 108 (0.00%)	1 / 111 (0.90%)	0 / 109 (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
Skin and subcutaneous tissue disorders			
dermatitis atopic			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 108 (0.00%)	0 / 111 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 108 (0.00%)	1 / 111 (0.90%)	0 / 109 (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
intervertebral disc protrusion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 108 (0.93%)	0 / 111 (0.00%)	0 / 109 (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			
eye infection toxoplasmal			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 108 (0.93%)	0 / 111 (0.00%)	0 / 109 (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
postoperative abscess			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 108 (0.93%)	0 / 111 (0.00%)	0 / 109 (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

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

Non-serious adverse events	Placebo	4mg Baricitinib	2mg Baricitinib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 108 (13.89%)	26 / 111 (23.42%)	24 / 109 (22.02%)
Infections and infestations			
folliculitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 108 (0.00%)	6 / 111 (5.41%)	4 / 109 (3.67%)
occurrences (all)	0	6	4
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	13 / 108 (12.04%)	17 / 111 (15.32%)	12 / 109 (11.01%)
occurrences (all)	14	18	16
upper respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 108 (1.85%)	3 / 111 (2.70%)	8 / 109 (7.34%)
occurrences (all)	2	4	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