Clinical trial results:
A Phase 2b Multicenter, Randomized, Placebo-Controlled, Double-Blind Dose-Ranging Study to Evaluate ABT-494 (Upadacitinib) in Adult Subjects with Moderate to Severe Atopic Dermatitis

Summary

EudraCT number	2016-002451-21
Trial protocol	NL FI IE BE ES
Global end of trial date	31 January 2019

Results information

Result version number	v2 (current)
This version publication date	15 August 2020
First version publication date	08 February 2020
Version creation reason	• New data added to full data set Correction to study arms in safety section.

Trial information

Trial identification

Sponsor protocol code	M16-048

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02925117
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Abbvie Deutschland GmbH & Co.KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 011 800-633-9110,
Scientific contact	Alvina Chu, MD, AbbVie, alvina.chu@abbvie.com

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	31 January 2019

Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	31 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to evaluate the safety and efficacy of multiple doses of upadacitinib monotherapy versus placebo in the treatment of adults with moderate to severe atopic dermatitis (AD).

Protection of trial subjects:

All subjects entering the study had to sign an informed consent that was explained to them and questions encouraged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 October 2016
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	Spain: 1
Country: Number of subjects enrolled	United States: 75
Country: Number of subjects enrolled	Australia: 17
Country: Number of subjects enrolled	Canada: 41
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Japan: 10
Country: Number of subjects enrolled	Netherlands: 17
Worldwide total number of subjects	167
EEA total number of subjects	24

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)	152
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 36 sites in 8 countries (Australia, Canada, Finland, Germany, Japan, Netherlands, Spain, and the United States [US]).
The study included a 16-week double-blind treatment period (period 1) followed by a a 72-week double-blind treatment period (Period 2) for a total of 88 weeks of treatment.

Pre-assignment

Screening details:

Participants were randomized in a 1:1:1:1 ratio, stratified by geographic region (US and Canada; European Union and Australia; and Japan). Participants who completed Period 1 were re-randomized at Week 16 within their original treatment group assignments to either upadacitinib or placebo in a 1:1 ratio. Rescue therapy was provided from Week 20.

Period 1

Period 1 title	Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants randomized to receive placebo once daily (QD) for 16 weeks in Period 1.

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:

Administered orally once a day

Arm title	Upadacitinib 7.5 mg

Arm description:

Participants randomized to receive upadacitinib 7.5 mg once daily for 16 weeks in Period 1.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	ABT-494
Other name	RINVOQ™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once a day

Arm title	Upadacitinib 15 mg

Arm description:

Participants randomized to receive upadacitinib 15 mg once daily for 16 weeks in Period 1.

Arm type	Experimental

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	ABT-494
Other name	RINVOQ™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Administered orally once a day

Arm title	Upadacitinib 30 mg

Arm description:
Participants randomized to receive upadacitinib 30 mg once daily for 16 weeks in Period 1.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	ABT-494
Other name	RINVOQ™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Administered orally once a day

Number of subjects in period 1	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg
Started	41	42	42
Received Treatment	40	42	42
Completed	23	31	37
Not completed	18	11	5
Other	5	4	1
Adverse event, non-fatal	1	3	1
Consent withdrawn by subject	10	3	3
Lost to follow-up	2	1	-

Number of subjects in period 1	Upadacitinib 30 mg
Started	42
Received Treatment	42
Completed	39
Not completed	3
Other	1
Adverse event, non-fatal	2
Consent withdrawn by subject	-
Lost to follow-up	-

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo / Placebo

Arm description:

Participants originally randomized to placebo were re-randomized at Week 16 to receive placebo tablets once a day for 72 weeks in Period 2.

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:

Administered orally once a day

Arm title	Placebo / Upadacitinib 30 mg

Arm description:

Participants originally randomized to placebo were re-randomized at Week 16 to receive 30 mg upadacitinib once a day for 72 weeks in Period 2.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	ABT-494
Other name	RINVOQ™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once a day

Arm title	Upadacitinib 7.5 mg / Placebo

Arm description:

Participants originally randomized to 7.5 mg upadacitinib were re-randomized at Week 16 to receive placebo tablets once a day for 72 weeks in Period 2.

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:

Administered orally once a day

Arm title	Upadacitinib 7.5 mg / Upadacitinib 7.5 mg

Arm description:

Participants originally randomized to 7.5 mg upadacitinib were re-randomized at Week 16 to receive 7.5 mg upadacitinib once a day for 72 weeks in Period 2.

Arm type	Experimental

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	ABT-494
Other name	RINVOQ™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once a day

Arm title	Upadacitinib 15 mg / Placebo

Arm description:

Participants originally randomized to 15 mg upadacitinib were re-randomized at Week 16 to receive placebo tablets once a day for 72 weeks in Period 2.

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:

Administered orally once a day

Arm title	Upadacitinib 15 mg / Upadacitinib 15 mg

Arm description:

Participants originally randomized to 15 mg upadacitinib were re-randomized at Week 16 to receive 15 mg upadacitinib once a day for 72 weeks in Period 2.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	ABT-494
Other name	RINVOQ™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once a day

Arm title	Upadacitinib 30 mg / Placebo

Arm description:

Participants originally randomized to 30 mg upadacitinib were re-randomized at Week 16 to receive placebo tablets once a day for 72 weeks in Period 2.

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:

Administered orally once a day

Arm title	Upadacitinib 30 mg / Upadacitinib 30 mg

Arm description:

Participants originally randomized to 30 mg upadacitinib were re-randomized at Week 16 to receive 30 mg upadacitinib once a day for 72 weeks in Period 2.

Arm type	Experimental

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	ABT-494
Other name	RINVOQ™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once a day

Number of subjects in period 2[1]	Placebo / Placebo	Placebo / Upadacitinib 30 mg	Upadacitinib 7.5 mg / Placebo
Started	10	10	15
Received Treatment	10	10	15
Rescued by Upadacitinib 30 mg	8	1 [2]	13
Completed	8	5	9
Not completed	2	5	6
Other	1	1	1
Adverse event, non-fatal	-	1	-
Consent withdrawn by subject	-	1	4
Lost to follow-up	1	2	1

Number of subjects in period 2[1]	Upadacitinib 7.5 mg / Upadacitinib 7.5 mg	Upadacitinib 15 mg / Placebo	Upadacitinib 15 mg / Upadacitinib 15 mg
Started	16	19	18
Received Treatment	16	19	18
Rescued by Upadacitinib 30 mg	12	17	12
Completed	11	13	12
Not completed	5	6	6
Other	1	3	4
Adverse event, non-fatal	-	-	-
Consent withdrawn by subject	3	2	2
Lost to follow-up	1	1	-

Number of subjects in period 2[1]	Upadacitinib 30 mg / Placebo	Upadacitinib 30 mg / Upadacitinib 30 mg
Started	19	19
Received Treatment	19	19
Rescued by Upadacitinib 30 mg	14	4 [3]
Completed	11	14
Not completed	8	5
Other	3	-
Adverse event, non-fatal	3	2
Consent withdrawn by subject	2	2

Lost to follow-up	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Four participants completed Week 16 but were not re-randomized into Period 2.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: One participant re-randomized to 30 mg upadacitinib was rescued during Period 2; 5 participants completed Period 2.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Four participants re-randomized to 30 mg upadacitinib were rescued during Period 2; 14 participants completed Period 2.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants randomized to receive placebo once daily (QD) for 16 weeks in Period 1.	
Reporting group title	Upadacitinib 7.5 mg
Reporting group description:	
Participants randomized to receive upadacitinib 7.5 mg once daily for 16 weeks in Period 1.	
Reporting group title	Upadacitinib 15 mg
Reporting group description:	
Participants randomized to receive upadacitinib 15 mg once daily for 16 weeks in Period 1.	
Reporting group title	Upadacitinib 30 mg
Reporting group description:	
Participants randomized to receive upadacitinib 30 mg once daily for 16 weeks in Period 1.	

Reporting group values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg
Number of subjects	41	42	42
Age categorical Units: Subjects			
< 40 years	25	22	25
40 - 64 years	11	16	14
≥ 65 years	5	4	3
Age continuous Units: years			
arithmetic mean	39.9	41.5	38.5
standard deviation	± 17.52	± 15.36	± 15.24
Gender categorical Units: Subjects			
Female	17	14	12
Male	24	28	30
Race Units: Subjects			
White	28	24	21
Black or African American	6	7	10
Asian	7	9	9
American Indian/Alaska Native	0	0	1
Native Hawaiian or Other Pacific Islander	0	2	1
Ethnicity Units: Subjects			
Hispanic or Latino	0	2	2
Not Hispanic or Latino	41	40	40
Geographic Region Units: Subjects			
US/Canada	29	29	29
EU/Australia	10	11	10
Japan	2	2	3

Duration of Atopic Dermatitis Diagnosis			
n = 40 in the placebo group			
Units: years			
arithmetic mean	26.84	30.44	22.59
standard deviation	± 18.76	± 18.07	± 15.78
Eczema Area and Severity Index (EASI)			
EASI is a tool to measure the extent and severity of atopic eczema based on assessments of the head/neck, trunk, upper limbs and lower limbs. For each region the percentage of skin affected, and the severity of eczema (scored as none [0], mild [1], moderate [2], or severe [3]) for redness, thickness, scratching, and lichenification are assessed. The EASI score is the sum of the scores for each region and ranges from 0 to 72, where higher scores represent worse disease.			
Units: scores on a scale			
arithmetic mean	32.62	31.42	31.40
standard deviation	± 14.49	± 15.76	± 12.26

Reporting group values	Upadacitinib 30 mg	Total	
Number of subjects	42	167	
Age categorical			
Units: Subjects			
< 40 years	22	94	
40 - 64 years	17	58	
≥ 65 years	3	15	
Age continuous			
Units: years			
arithmetic mean	39.9		
standard deviation	± 15.30	-	
Gender categorical			
Units: Subjects			
Female	20	63	
Male	22	104	
Race			
Units: Subjects			
White	23	96	
Black or African American	6	29	
Asian	13	38	
American Indian/Alaska Native	0	1	
Native Hawaiian or Other Pacific Islander	0	3	
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	5	
Not Hispanic or Latino	41	162	
Geographic Region			
Units: Subjects			
US/Canada	29	116	
EU/Australia	10	41	
Japan	3	10	
Duration of Atopic Dermatitis Diagnosis			
n = 40 in the placebo group			
Units: years			
arithmetic mean	24.24		
standard deviation	± 13.58	-	
Eczema Area and Severity Index (EASI)			

EASI is a tool to measure the extent and severity of atopic eczema based on assessments of the head/neck, trunk, upper limbs and lower limbs. For each region the percentage of skin affected, and the severity of eczema (scored as none [0], mild [1], moderate [2], or severe [3]) for redness, thickness, scratching, and lichenification are assessed. The EASI score is the sum of the scores for each region and ranges from 0 to 72, where higher scores represent worse disease.			
Units: scores on a scale			
arithmetic mean	28.15		
standard deviation	± 11.62	-	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants randomized to receive placebo once daily (QD) for 16 weeks in Period 1.	
Reporting group title	Upadacitinib 7.5 mg
Reporting group description:	
Participants randomized to receive upadacitinib 7.5 mg once daily for 16 weeks in Period 1.	
Reporting group title	Upadacitinib 15 mg
Reporting group description:	
Participants randomized to receive upadacitinib 15 mg once daily for 16 weeks in Period 1.	
Reporting group title	Upadacitinib 30 mg
Reporting group description:	
Participants randomized to receive upadacitinib 30 mg once daily for 16 weeks in Period 1.	
Reporting group title	Placebo / Placebo
Reporting group description:	
Participants originally randomized to placebo were re-randomized at Week 16 to receive placebo tablets once a day for 72 weeks in Period 2.	
Reporting group title	Placebo / Upadacitinib 30 mg
Reporting group description:	
Participants originally randomized to placebo were re-randomized at Week 16 to receive 30 mg upadacitinib once a day for 72 weeks in Period 2.	
Reporting group title	Upadacitinib 7.5 mg / Placebo
Reporting group description:	
Participants originally randomized to 7.5 mg upadacitinib were re-randomized at Week 16 to receive placebo tablets once a day for 72 weeks in Period 2.	
Reporting group title	Upadacitinib 7.5 mg / Upadacitinib 7.5 mg
Reporting group description:	
Participants originally randomized to 7.5 mg upadacitinib were re-randomized at Week 16 to receive 7.5 mg upadacitinib once a day for 72 weeks in Period 2.	
Reporting group title	Upadacitinib 15 mg / Placebo
Reporting group description:	
Participants originally randomized to 15 mg upadacitinib were re-randomized at Week 16 to receive placebo tablets once a day for 72 weeks in Period 2.	
Reporting group title	Upadacitinib 15 mg / Upadacitinib 15 mg
Reporting group description:	
Participants originally randomized to 15 mg upadacitinib were re-randomized at Week 16 to receive 15 mg upadacitinib once a day for 72 weeks in Period 2.	
Reporting group title	Upadacitinib 30 mg / Placebo
Reporting group description:	
Participants originally randomized to 30 mg upadacitinib were re-randomized at Week 16 to receive placebo tablets once a day for 72 weeks in Period 2.	
Reporting group title	Upadacitinib 30 mg / Upadacitinib 30 mg
Reporting group description:	
Participants originally randomized to 30 mg upadacitinib were re-randomized at Week 16 to receive 30 mg upadacitinib once a day for 72 weeks in Period 2.	

Primary: Percent Change from Baseline in Eczema Area and Severity Index (EASI) Score at Week 16

End point title	Percent Change from Baseline in Eczema Area and Severity Index (EASI) Score at Week 16

End point description:

EASI is a tool used to measure the extent (area) and severity of atopic eczema based on assessments of the head/neck, trunk, upper limbs and lower limbs. For each region the area score is recorded as the percentage of skin affected by eczema. For each region, the severity score is calculated as the sum of the intensity scores (scored as none (0), mild (1), moderate (2), or severe (3)) for Redness (erythema, inflammation), Thickness (induration, papulation, swelling – acute eczema), Scratching (excoriation), and Lichenification (lined skin, prurigo nodules – chronic eczema).
The total EASI score for each region is calculated by multiplying the severity score by the area score, with adjustment for the proportion of the body region to the whole body. The final EASI score is the sum of the 4 region scores and ranges from 0 to 72 where higher scores represent worse disease; a negative change from baseline indicates improvement. Last observation carried forward (LOCF) imputation was used.

End point type	Primary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39[1]	42	42	42
Units: percent change				
least squares mean (standard error)	-23.0 (± 6.42)	-39.4 (± 6.24)	-61.7 (± 6.12)	-74.4 (± 6.13)

Notes:

[1] - Randomized participants with at least one post-baseline assessment

Statistical analyses

Statistical analysis title	Analysis of % Change From Baseline in EASI
Comparison groups	Upadacitinib 30 mg v Placebo
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [2]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-51.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-66.5
upper limit	-36.3
Variability estimate	Standard error of the mean
Dispersion value	7.65

Notes:

[2] - Analysis of covariance (ANCOVA) with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change From Baseline in EASI

Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-38.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.7
upper limit	-23.6
Variability estimate	Standard error of the mean
Dispersion value	7.61

Notes:

[3] - Analysis of covariance (ANCOVA) with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change From Baseline in EASI
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.032 [4]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-16.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.4
upper limit	-1.4
Variability estimate	Standard error of the mean
Dispersion value	7.61

Notes:

[4] - Analysis of covariance (ANCOVA) with stratum (geographic region), baseline value, and treatment in the model.

Secondary: Percentage of Participants who Achieved a 75% Reduction in EASI Score (EASI 75) at Week 16

End point title	Percentage of Participants who Achieved a 75% Reduction in EASI Score (EASI 75) at Week 16

End point description:

EASI is a tool to measure the extent and severity of atopic eczema based on assessments of the head/neck, trunk, upper limbs and lower limbs. For each region the percentage of skin affected, and the severity of eczema (scored as none [0], mild [1], moderate [2], or severe [3]) for redness, thickness, scratching, and lichenification are assessed. The EASI score is the sum of the scores for each region and ranges from 0 to 72, where higher scores represent worse disease.
An EASI 75 response is defined as at least a 75% reduction (improvement) in EASI score relative to the Baseline value.
Participants with missing values at Week 16 were counted as non-responders in this analysis (non-responder imputation).

End point type	Secondary

End point timeframe:

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	42	42	42
Units: percentage of participants				
number (not applicable)	9.8	28.6	52.4	69.0

Statistical analyses

Statistical analysis title	Analysis of EASI 75 at Week 16
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	58.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	42.5
upper limit	74.8

Notes:

[5] - Cochran-Mantel-Haenszel test, adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 75 at Week 16
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	42.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.5
upper limit	59.6

Notes:

[6] - Cochran-Mantel-Haenszel test, adjusted for stratum (geographic region).

	Analysis of EASI 75 at Week 16

Statistical analysis title	
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	18.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.7
upper limit	34.7

Notes:

[7] - Cochran-Mantel-Haenszel test, adjusted for stratum (geographic region).

Secondary: Percentage of Participants Achieving an Investigator Global Assessment (IGA) of "0" or "1" at Week 16

End point title	Percentage of Participants Achieving an Investigator Global Assessment (IGA) of "0" or "1" at Week 16

End point description:

Investigator's Global Assessment for Atopic Dermatitis (IGA) was scored on the following scale:
0: Clear (No inflammatory signs of atopic dermatitis)
1: Almost Clear (Just perceptible erythema and just perceptible papulation/infiltration)
2: Mild (Mild erythema and mild papulation/infiltration)
3: Moderate (Moderate erythema and moderate papulation/infiltration)
4: Severe (Severe erythema and severe papulation/infiltration with or without oozing/crusting)
The percentage of participants with a score of 0 or 1 at Week 16 is reported.
Non-responder imputation was used.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	42	42	42
Units: percentage of participants				
number (not applicable)	2.4	14.3	31.0	50.0

Statistical analyses

Statistical analysis title	Analysis of IGA Response at Week 16
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority

P-value	< 0.001 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	46.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.1
upper limit	62.7

Notes:

[8] - Cochran-Mantel-Haenszel test, adjusted for stratum (geographic region).

Statistical analysis title	Analysis of IGA Response at Week 16
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	28.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.8
upper limit	43.4

Notes:

[9] - Cochran-Mantel-Haenszel test, adjusted for stratum (geographic region).

Statistical analysis title	Analysis of IGA Response at Week 16
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	11.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	23.5

Notes:

[10] - Cochran-Mantel-Haenszel test, adjusted for stratum (geographic region).

Secondary: Percent Change from Baseline to Weeks 2, 8, and 16 in Pruritus Numerical Rating Scale (NRS)

End point title	Percent Change from Baseline to Weeks 2, 8, and 16 in Pruritus Numerical Rating Scale (NRS)

End point description:

Participants were asked to rate itch in the past 24 hours on a daily basis using a scale from 0 to 10, with 0 being no itch and 10 being the worst imaginable itch. The percent change from Baseline at each week was calculated from a rolling weekly average.
Last observation carried forward (LOCF) imputation was used.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 8, and 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37[11]	40	37	42
Units: units on a scale				
least squares mean (standard error)				
Week 2 (n = 37, 39, 37, 42)	1.7 (± 5.59)	-29.3 (± 5.45)	-46.0 (± 5.44)	-57.6 (± 5.24)
Week 8 (n = 37, 40, 37, 42)	-6.7 (± 7.51)	-35.5 (± 7.28)	-45.1 (± 7.32)	-73.1 (± 7.05)
Week 16 (n = 37, 40, 37, 42)	-9.7 (± 8.30)	-39.6 (± 8.04)	-48.0 (± 8.08)	-68.9 (± 7.79)

Notes:

[11] - Participants with at least one post-baseline measurement

Statistical analyses

Statistical analysis title	Analysis of % Change in Pruritus NRS at Week 2
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [12]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-59.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-72.3
upper limit	-46.3
Variability estimate	Standard error of the mean
Dispersion value	6.58

Notes:

[12] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in Pruritus NRS at Week 2
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [13]
Method	ANCOVA

Parameter estimate	LS Mean Difference
Point estimate	-47.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-61.1
upper limit	-34.3
Variability estimate	Standard error of the mean
Dispersion value	6.78

Notes:

[13] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in Pruritus NRS at Week 2

Statistical analysis description:

The number of subjects included in the analysis of the comparison of Placebo vs Upadacitinib 7.5 mg at Week 2 is 76 subjects, rather than 77 subjects, since 1 subject in the Upadacitinib 7.5 mg had missing data at Week 2.

Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [14]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-31.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.3
upper limit	-17.8
Variability estimate	Standard error of the mean
Dispersion value	6.7

Notes:

[14] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in Pruritus NRS at Week 8
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [15]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-66.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-83.9
upper limit	-48.9
Variability estimate	Standard error of the mean
Dispersion value	8.85

Notes:
[15] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in Pruritus NRS at Week 8
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [16]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-38.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-56.4
upper limit	-20.4
Variability estimate	Standard error of the mean
Dispersion value	9.13

Notes:
[16] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in Pruritus NRS at Week 8
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [17]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-28.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.6
upper limit	-11.2
Variability estimate	Standard error of the mean
Dispersion value	8.96

Notes:
[17] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in Pruritus NRS at Week 16
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [18]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-59.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-78.6
upper limit	-39.9
Variability estimate	Standard error of the mean
Dispersion value	9.78

Notes:

[18] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in Pruritus NRS at Week 16
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [19]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-38.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.3
upper limit	-18.4
Variability estimate	Standard error of the mean
Dispersion value	10.08

Notes:

[19] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in Pruritus NRS at Week 16
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [20]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-29.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.4
upper limit	-10.3
Variability estimate	Standard error of the mean
Dispersion value	9.9

Notes:

[20] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Secondary: Percent Change from Baseline in EASI Score at Week 8

End point title	Percent Change from Baseline in EASI Score at Week 8

End point description:

EASI is a tool used to measure the extent (area) and severity of atopic eczema based on assessments of the head/neck, trunk, upper limbs and lower limbs. For each region the area score is recorded as the percentage of skin affected by eczema. For each region, the severity score is calculated as the sum of the intensity scores (scored as none (0), mild (1), moderate (2), or severe (3)) for Redness (erythema, inflammation), Thickness (induration, papulation, swelling – acute eczema), Scratching (excoriation), and Lichenification (lined skin, prurigo nodules – chronic eczema).
The total EASI score for each region is calculated by multiplying the severity score by the area score, with adjustment for the proportion of the body region to the whole body. The final EASI score is the sum of the 4 region scores and ranges from 0 to 72 where higher scores represent worse disease; a negative change from baseline indicates improvement. Last observation carried forward (LOCF) imputation was used.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39[21]	42	42	42
Units: percent change				
least squares mean (standard error)	-17.5 (± 6.27)	-43.7 (± 6.09)	-65.4 (± 5.97)	-82.8 (± 5.98)

Notes:

[21] - Participants with at least one post-baseline measurement

Statistical analyses

Statistical analysis title	Analysis of % Change in EASI at Week 8
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [22]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-65.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-80
upper limit	-50.5
Variability estimate	Standard error of the mean
Dispersion value	7.46

Notes:

[22] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in EASI at Week 8
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority

P-value	< 0.001 [23]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-47.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.6
upper limit	-33.3
Variability estimate	Standard error of the mean
Dispersion value	7.42

Notes:

[23] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in EASI at Week 8
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [24]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-26.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.8
upper limit	-11.5
Variability estimate	Standard error of the mean
Dispersion value	7.42

Notes:

[24] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Secondary: Percent Change from Baseline in SCORing Atopic Dermatitis (SCORAD) Score at Weeks 8 and 16

End point title	Percent Change from Baseline in SCORing Atopic Dermatitis (SCORAD) Score at Weeks 8 and 16

End point description:

SCORAD is a clinical tool used to assess the extent and severity of eczema (SCORing Atopic Dermatitis). The extent is assessed using the rule of 9 to calculate the affected area (A) as a percentage of the whole body (0-100%). The intensity part of the SCORAD (B) consists of 6 items: erythema, oedema/papulation, excoriations, lichenification, oozing/crusts and dryness, each graded on a scale from 0 (none) to 3 (severe), for a total score of 0 to 18. Subjective items (C) include daily pruritus and sleeplessness, each scored on a visual analogue scale (VAS) from 0 to 10 (total score 0-20). SCORAD is calculated as A/5 + 7B/2 + C, and ranges from 0 to 103 (worst). A negative change from Baseline indicates improvement.
Last observation carried forward imputation was used.

End point type	Secondary

End point timeframe:

Baseline and Weeks 8 and 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33[25]	39	36	40
Units: percent change				
least squares mean (standard error)				
Week 8	-7.0 (± 5.84)	-35.4 (± 5.53)	-44.1 (± 5.69)	-65.3 (± 5.52)
Week 16	-12.4 (± 5.97)	-32.5 (± 5.66)	-46.9 (± 5.82)	-60.4 (± 5.65)

Notes:

[25] - Participants with Baseline and at least one post-baseline measurement

Statistical analyses

Statistical analysis title	Analysis of % Change in SCORAD at Week 8
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [26]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-58.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-71.7
upper limit	-44.9
Variability estimate	Standard error of the mean
Dispersion value	6.78

Notes:

[26] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in SCORAD at Week 8
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [27]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-37.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.8
upper limit	-23.4
Variability estimate	Standard error of the mean
Dispersion value	6.94

Notes:

[27] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in SCORAD at Week 8
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [28]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-28.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.9
upper limit	-15
Variability estimate	Standard error of the mean
Dispersion value	6.81

Notes:

[28] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in SCORAD at Week 16
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [29]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-61.7
upper limit	-34.3
Variability estimate	Standard error of the mean
Dispersion value	6.93

Notes:

[29] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in SCORAD at Week 16
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [30]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-34.5
Confidence interval	
level	95 %
sides	2-sided

lower limit	-48.5
upper limit	-20.5
Variability estimate	Standard error of the mean
Dispersion value	7.1

Notes:

[30] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of % Change in SCORAD at Week 16
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [31]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-20.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.9
upper limit	-6.4
Variability estimate	Standard error of the mean
Dispersion value	6.96

Notes:

[31] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Secondary: Percentage of Participants who Achieved an EASI 75 Response at Week 8

End point title	Percentage of Participants who Achieved an EASI 75 Response at Week 8

End point description:

EASI is a tool to measure the extent and severity of atopic eczema based on assessments of the head/neck, trunk, upper limbs and lower limbs. For each region the percentage of skin affected, and the severity of eczema (scored as none [0], mild [1], moderate [2], or severe [3]) for redness, thickness, scratching, and lichenification are assessed. The EASI score is the sum of the scores for each region and ranges from 0 to 72, where higher scores represent worse disease.
An EASI 75 response is defined as at least a 75% reduction (improvement) in EASI score relative to the Baseline value.
Participants with missing values at Week 8 were counted as non-responders in this analysis (non-responder imputation).

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	42	42	42
Units: percentage of participants				
number (not applicable)	7.3	31.0	52.4	81.0

Statistical analyses

Statistical analysis title	Analysis of EASI 75 Response at Week 8
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [32]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	72.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	58.3
upper limit	87.1

Notes:

[32] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 75 Response at Week 8
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [33]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	44.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.9
upper limit	61.9

Notes:

[33] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 75 Response at Week 8
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [34]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference

Point estimate	23.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.5
upper limit	39.4

Notes:

[34] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Secondary: Percentage of Participants who Achieved an EASI 50 Response at Weeks 8 and 16

End point title	Percentage of Participants who Achieved an EASI 50 Response at Weeks 8 and 16

End point description:

EASI is a tool to measure the extent and severity of atopic eczema based on assessments of the head/neck, trunk, upper limbs and lower limbs. For each region the percentage of skin affected, and the severity of eczema (scored as none [0], mild [1], moderate [2], or severe [3]) for redness, thickness, scratching, and lichenification are assessed. The EASI score is the sum of the scores for each region and ranges from 0 to 72, where higher scores represent worse disease.
An EASI 50 response is defined as at least a 50% reduction (improvement) in EASI score relative to the Baseline value.
Participants with missing values at each time point were counted as non-responders in this analysis (non-responder imputation).

End point type	Secondary

End point timeframe:

Baseline and Weeks 8 and 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	42	42	42
Units: percentage of participants				
number (not applicable)				
Week 8	22.0	54.8	71.4	92.9
Week 16	22.0	50.0	71.4	83.3

Statistical analyses

Statistical analysis title	Analysis of EASI 50 Response at Week 8
Comparison groups	Upadacitinib 30 mg v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [35]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	70.7
Confidence interval	
level	95 %

sides	2-sided
lower limit	56.2
upper limit	85.2

Notes:

[35] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 50 Response at Week 8
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [36]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	49
Confidence interval	
level	95 %
sides	2-sided
lower limit	30.8
upper limit	67.3

Notes:

[36] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 50 Response at Week 8
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [37]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	32.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.4
upper limit	52.2

Notes:

[37] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 50 Response at Week 16
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [38]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	60.6
Confidence interval	

level	95 %
sides	2-sided
lower limit	45.3
upper limit	75.9

Notes:

[38] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 50 Response at Week 16
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [39]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	48.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.3
upper limit	65.9

Notes:

[39] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 50 Response at Week 16
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [40]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	28.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.8
upper limit	46.6

Notes:

[40] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Secondary: Percentage of Participants who Achieved an EASI 90 Response at Weeks 8 and 16

End point title	Percentage of Participants who Achieved an EASI 90 Response at Weeks 8 and 16

End point description:

EASI is a tool to measure the extent and severity of atopic eczema based on assessments of the head/neck, trunk, upper limbs and lower limbs. For each region the percentage of skin affected, and the severity of eczema (scored as none [0], mild [1], moderate [2], or severe [3]) for redness, thickness, scratching, and lichenification are assessed. The EASI score is the sum of the scores for each region and ranges from 0 to 72, where higher scores represent worse disease.
An EASI 90 response is defined as at least a 90% reduction (improvement) in EASI score relative to the

Baseline value.
Participants with missing values at Week 16 were counted as non-responders in this analysis (non-responder imputation).

End point type	Secondary

End point timeframe:

Baseline and Weeks 8 and 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	42	42	42
Units: percentage of participants				
number (not applicable)				
Week 8	0.0	9.5	26.2	45.2
Week 16	2.4	14.3	26.2	50.0

Statistical analyses

Statistical analysis title	Analysis of EASI 90 Response at Week 8
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [41]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	43.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	29.1
upper limit	58.5

Notes:

[41] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 90 Response at Week 8
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [42]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	26.1
Confidence interval	
level	95 %
sides	2-sided

lower limit	12.6
upper limit	39.6

Notes:

[42] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 90 Response at Week 8
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.051 [43]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	18.8

Notes:

[43] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 90 Response at Week 16
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [44]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	46.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.3
upper limit	62.4

Notes:

[44] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 90 Response at Week 16
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [45]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	23.8
Confidence interval	
level	95 %

sides	2-sided
lower limit	9.6
upper limit	38.1

Notes:

[45] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of EASI 90 Response at Week 16
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.049 [46]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	11.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	23.6

Notes:

[46] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Secondary: Percentage of Participants who Achieved a SCORAD 50 Response at Weeks 8 and 16

End point title	Percentage of Participants who Achieved a SCORAD 50 Response at Weeks 8 and 16

End point description:

A SCORAD 50 response is defined as at least a 50% reduction (improvement) in SCORAD score relative to the Baseline value.
SCORAD is a clinical tool used to assess the extent and severity of eczema (SCORing Atopic Dermatitis). The extent is assessed using the rule of 9 to calculate the affected area (A) as a percentage of the whole body (0-100%). The intensity part of the SCORAD (B) consists of 6 items: erythema, oedema/papulation, excoriations, lichenification, oozing/crusts and dryness, each graded on a scale from 0 (none) to 3 (severe), for a total score of 0 to 18. Subjective items (C) include daily pruritus and sleeplessness, each scored on a visual analogue scale (VAS) from 0 to 10 (total score 0-20). SCORAD is calculated as A/5 + 7B/2 + C, and ranges from 0 to 103 (worst).
Non-responder imputation was used.

End point type	Secondary

End point timeframe:

Baseline and Weeks 8 and 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	42	42	42
Units: percentage of participants				
number (not applicable)				
Week 8	7.3	33.3	42.9	76.2
Week 16	7.3	28.6	42.9	61.9

Statistical analyses

Statistical analysis title	Analysis of SCORAD 50 Response at Week 8
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [47]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	68.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	54
upper limit	82.8

Notes:

[47] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 50 Response at Week 8
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [48]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	35.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.5
upper limit	52.2

Notes:

[48] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 50 Response at Week 8
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [49]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference

Point estimate	25.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.6
upper limit	41.7

Notes:

[49] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 50 Response at Week 16
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [50]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	54.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	39
upper limit	69.9

Notes:

[50] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 50 Response at Week 16
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [51]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	35.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.1
upper limit	52.5

Notes:

[51] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 50 Response at Week 16
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008 [52]
Method	Cochran-Mantel-Haenszel

Parameter estimate	Adjusted Difference
Point estimate	21.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.7
upper limit	36.8

Notes:

[52] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Secondary: Percentage of Participants who Achieved a SCORAD 75 Response at Weeks 8 and 16

End point title	Percentage of Participants who Achieved a SCORAD 75 Response at Weeks 8 and 16

End point description:

A SCORAD 75 response is defined as at least a 75% reduction (improvement) in SCORAD score relative to the Baseline value.
SCORAD is a clinical tool used to assess the extent and severity of eczema (SCORing Atopic Dermatitis). The extent is assessed using the rule of 9 to calculate the affected area (A) as a percentage of the whole body (0-100%). The intensity part of the SCORAD (B) consists of 6 items: erythema, oedema/papulation, excoriations, lichenification, oozing/crusts and dryness, each graded on a scale from 0 (none) to 3 (severe), for a total score of 0 to 18. Subjective items (C) include daily pruritus and sleeplessness, each scored on a visual analogue scale (VAS) from 0 to 10 (total score 0-20). SCORAD is calculated as A/5 + 7B/2 + C, and ranges from 0 to 103 (worst).
Non-responder imputation was used.

End point type	Secondary

End point timeframe:

Baseline and Weeks 8 and 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	42	42	42
Units: percentage of participants				
number (not applicable)				
Week 8	0.0	9.5	9.5	31.0
Week 16	2.4	4.8	21.4	40.5

Statistical analyses

Statistical analysis title	Analysis of SCORAD 75 Response at Week 8
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [53]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	30.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	16.2
upper limit	44.6

Notes:

[53] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 75 Response at Week 8
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.052 [54]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	18.9

Notes:

[54] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 75 Response at Week 8
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.048 [55]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	9.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	18.5

Notes:

[55] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 75 Response at Week 16
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [56]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference

Point estimate	37.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.2
upper limit	53.3

Notes:

[56] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 75 Response at Week 16
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [57]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	19
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.6
upper limit	32.5

Notes:

[57] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 75 Response at Week 16
Comparison groups	Upadacitinib 7.5 mg v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.581 [58]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	10.8

Notes:

[58] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Secondary: Percentage of Participants who Achieved a SCORAD 90 Response at Weeks 8 and 16

End point title	Percentage of Participants who Achieved a SCORAD 90 Response at Weeks 8 and 16

End point description:

A SCORAD 90 response is defined as at least a 90% reduction (improvement) in SCORAD score relative to the Baseline value.
SCORAD is a clinical tool used to assess the extent and severity of eczema (SCORing Atopic Dermatitis).

The extent is assessed using the rule of 9 to calculate the affected area (A) as a percentage of the whole body (0-100%). The intensity part of the SCORAD (B) consists of 6 items: erythema, oedema/papulation, excoriations, lichenification, oozing/crusts and dryness, each graded on a scale from 0 (none) to 3 (severe), for a total score of 0 to 18. Subjective items (C) include daily pruritus and sleeplessness, each scored on a visual analogue scale (VAS) from 0 to 10 (total score 0-20). SCORAD is calculated as A/5 + 7B/2 + C, and ranges from 0 to 103 (worst).
Non-responder imputation was used.

End point type	Secondary

End point timeframe:

Baseline and Weeks 8 and 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	42	42	42
Units: percentage of participants				
number (not applicable)				
Week 8	0.0	4.8	2.4	14.3
Week 16	0.0	2.4	9.5	23.8

Statistical analyses

Statistical analysis title	Analysis of SCORAD 90 Response at Week 8
Comparison groups	Upadacitinib 30 mg v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012 [59]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	14.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.2
upper limit	25.2

Notes:

[59] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 90 Response at Week 8
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.428 [60]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	2.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	8

Notes:

[60] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 90 Response at Week 8
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.206 [61]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	11.8

Notes:

[61] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 90 Response at Week 16
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [62]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	23.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.4
upper limit	36.2

Notes:

[62] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 90 Response at Week 16
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.048 [63]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference

Point estimate	9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	18.8

Notes:

[63] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of SCORAD 90 Response at Week 16
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.426 [64]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	8.1

Notes:

[64] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Secondary: Change from Baseline in Percentage of Body Surface Area (BSA) Affected by Atopic Dermatitis at Week 16

End point title	Change from Baseline in Percentage of Body Surface Area (BSA) Affected by Atopic Dermatitis at Week 16

End point description:

Body surface area (BSA) affected by atopic dermatitis was assessed by the physician and is expressed as a percentage of the total BSA. For purposes of the estimation, the total surface of the participant's palm plus five digits was assumed to be approximately equivalent to 1% BSA.
Last observation carried forward imputation was used.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39[65]	42	42	42
Units: percentage of body surface area				
least squares mean (standard error)	-4.1 (± 3.58)	-11.7 (± 3.48)	-27.1 (± 3.43)	-30.7 (± 3.43)

Notes:

[65] - Participants with at least one post-baseline measurement

Statistical analyses

Statistical analysis title	Analysis of Change in BSA at Week 16
Comparison groups	Upadacitinib 30 mg v Placebo
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [66]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-26.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.9
upper limit	-18.1
Variability estimate	Standard error of the mean
Dispersion value	4.25

Notes:

[66] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of Change in BSA at Week 16
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [67]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.4
upper limit	-14.6
Variability estimate	Standard error of the mean
Dispersion value	4.27

Notes:

[67] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Statistical analysis title	Analysis of Change in BSA at Week 16
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.075 [68]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-7.6
Confidence interval	
level	95 %

sides	2-sided
lower limit	-16
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	4.25

Notes:

[68] - ANCOVA with stratum (geographic region), baseline value, and treatment in the model.

Secondary: Percentage of Participants with Reduction of ≥ 4 Points from Baseline in Pruritus NRS at Week 16

End point title	Percentage of Participants with Reduction of ≥ 4 Points from Baseline in Pruritus NRS at Week 16

End point description:

Participants were asked to rate itch in the past 24 hours on a daily basis using a scale from 0 to 10, with 0 being no itch and 10 being the worst imaginable itch. The percentage of participants with reduction of ≥ 4 points from Baseline in pruritus NRS was assessed in participants with a baseline pruritus NRS of ≥ 4. Non-responder imputation was used.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[69]	37	32	36
Units: percentage of participants				
number (not applicable)	5.7	24.3	59.4	52.8

Notes:

[69] - Participants with Baseline pruritus NRS of ≥ 4

Statistical analyses

Statistical analysis title	Analysis of Reduction in Pruritus NRS ≥ 4 Points
Comparison groups	Placebo v Upadacitinib 30 mg
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [70]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	47.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	29.6
upper limit	65.2

Notes:

[70] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of Reduction in Pruritus NRS ≥ 4 Points
Comparison groups	Placebo v Upadacitinib 15 mg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [71]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	53.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	35.5
upper limit	71.3

Notes:

[71] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Statistical analysis title	Analysis of Reduction in Pruritus NRS ≥ 4 Points
Comparison groups	Placebo v Upadacitinib 7.5 mg
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021 [72]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	18.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	34.3

Notes:

[72] - Cochran-Mantel-Haenszel test adjusted for stratum (geographic region).

Secondary: Percent Change from Re-randomization (Week 16) in EASI Score in Period 2

End point title	Percent Change from Re-randomization (Week 16) in EASI Score in Period 2

End point description:

EASI is a tool used to measure the extent (area) and severity of atopic eczema based on assessments of the head/neck, trunk, upper limbs and lower limbs. For each region the area score is recorded as the percentage of skin affected by eczema. For each region, the severity score is calculated as the sum of the intensity scores (scored as none (0), mild (1), moderate (2), or severe (3)) for Redness (erythema, inflammation), Thickness (induration, papulation, swelling – acute eczema), Scratching (excoriation), and Lichenification (lined skin, prurigo nodules – chronic eczema).
The total EASI score for each region is calculated by multiplying the severity score by the area score, with adjustment for the proportion of the body region to the whole body. The final EASI score is the sum of the 4 region scores and ranges from 0 to 72 where higher scores represent worse disease; a negative change from baseline indicates improvement. Last observation carried forward imputation was used.

End point type	Secondary

End point timeframe:

Re-randomization (Week 16) and Weeks 20, 24, 32, 40, 52, 64, 76, and 88

End point values	Placebo / Placebo	Placebo / Upadacitinib 30 mg	Upadacitinib 7.5 mg / Placebo	Upadacitinib 7.5 mg / Upadacitinib 7.5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	15	15
Units: percent change				
least squares mean (standard error)				
Week 20	50.7 (± 33.50)	11.8 (± 30.59)	186.0 (± 46.53)	79.1 (± 48.42)
Week 24	13.5 (± 17.13)	-67.5 (± 15.64)	189.6 (± 44.17)	59.0 (± 45.97)
Week 32	-2.3 (± 15.15)	-83.1 (± 13.83)	181.5 (± 44.74)	63.5 (± 46.56)
Week 40	-31.2 (± 18.16)	-92.0 (± 16.58)	200.9 (± 41.58)	77.6 (± 43.27)
Week 52	-29.8 (± 17.74)	-90.1 (± 16.20)	189.1 (± 43.65)	74.4 (± 45.42)
Week 64	-35.8 (± 17.34)	-91.4 (± 15.83)	179.9 (± 44.91)	71.8 (± 46.74)
Week 76	-37.3 (± 19.09)	-90.3 (± 17.43)	201.4 (± 41.89)	77.7 (± 43.60)
Week 88	-37.7 (± 19.18)	-84.6 (± 17.51)	170.7 (± 46.87)	69.1 (± 48.78)

End point values	Upadacitinib 15 mg / Placebo	Upadacitinib 15 mg / Upadacitinib 15 mg	Upadacitinib 30 mg / Placebo	Upadacitinib 30 mg / Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	18[73]	14[74]	19[75]
Units: percent change				
least squares mean (standard error)				
Week 20	582.3 (± 172.19)	65.7 (± 178.24)	791.5 (± 262.34)	-73.8 (± 215.54)
Week 24	607.3 (± 169.49)	72.6 (± 175.44)	898.5 (± 248.78)	-69.6 (± 200.01)
Week 32	613.3 (± 169.63)	151.7 (± 175.59)	771.5 (± 252.90)	-28.8 (± 210.78)
Week 40	608.8 (± 169.95)	154.1 (± 175.92)	778.9 (± 344.45)	140.6 (± 293.17)
Week 52	613.8 (± 166.85)	104.1 (± 164.05)	799.5 (± 254.30)	-13.3 (± 216.44)
Week 64	614.6 (± 166.57)	104.1 (± 163.78)	802.1 (± 278.76)	63.6 (± 237.26)
Week 76	614.0 (± 168.03)	130.2 (± 169.29)	787.8 (± 262.89)	24.4 (± 219.11)
Week 88	617.5 (± 165.84)	99.3 (± 163.06)	769.7 (± 265.64)	39.0 (± 226.10)

Notes:

[73] - n = 16 at Weeks 20, 24, 32, and 40; n = 17 at Week 76

[74] - n = 13 at Weeks 20, 24

[75] - n = 18 at Weeks 20, 40, 52, 64, and 88

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an EASI 75 Response in Period 2 in Participants who were Re-randomized as EASI 75 Non-responders at Week 16

End point title	Percentage of Participants with an EASI 75 Response in Period 2 in Participants who were Re-randomized as EASI 75 Non-responders at Week 16

End point description:

EASI is a tool to measure the extent and severity of atopic eczema based on assessments of the head/neck, trunk, upper limbs and lower limbs. For each region the percentage of skin affected, and the severity of eczema (scored as none [0], mild [1], moderate [2], or severe [3]) for redness, thickness, scratching, and lichenification are assessed. The EASI score is the sum of the scores for each region and ranges from 0 to 72, where higher scores represent worse disease.
An EASI 75 response is defined as at least a 75% reduction (improvement) in EASI score relative to the Baseline value, and was analyzed in participants who were re-randomized at Week 16 and were EASI 75 non-responders at Week 16.

End point type	Secondary

End point timeframe:

Weeks 20, 24, 32, 40, 52, 64, 76, and 88

End point values	Placebo / Placebo	Placebo / Upadacitinib 30 mg	Upadacitinib 7.5 mg / Placebo	Upadacitinib 7.5 mg / Upadacitinib 7.5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	8	10	11
Units: percentage of participants				
number (not applicable)				
Week 20 (n = 9, 8, 10, 11, 7, 8, 5, 4)	11.1	12.5	0	9.1
Week 24 (n = 1, 7, 0, 3, 1, 2, 3, 3)	100	85.7	0	33.3
Week 32 (n = 1, 6, 0, 2, 1, 2, 2, 2)	100	100	0	0
Week 40 (n = 1, 6, 0, 0, 1, 1, 1, 2)	100	66.7	0	0
Week 52 (n = 1, 6, 0, 0, 1, 1, 0, 2)	100	66.7	0	0
Week 64 (n = 1, 5, 0, 0, 1, 1, 0, 1)	100	80.0	0	0
Week 76 (n = 1, 3, 0, 0, 1, 1, 0, 1)	100	100	0	0
Week 88 (n = 1, 2, 0, 0, 1, 1, 0, 1)	100	100	0	0

End point values	Upadacitinib 15 mg / Placebo	Upadacitinib 15 mg / Upadacitinib 15 mg	Upadacitinib 30 mg / Placebo	Upadacitinib 30 mg / Upadacitinib 30 mg

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	8	5	4
Units: percentage of participants				
number (not applicable)				
Week 20 (n = 9, 8, 10, 11, 7, 8, 5, 4)	0	12.5	20.0	25.0
Week 24 (n = 1, 7, 0, 3, 1, 2, 3, 3)	0	0	33.3	33.3
Week 32 (n = 1, 6, 0, 2, 1, 2, 2, 2)	0	50.0	50.0	50.0
Week 40 (n = 1, 6, 0, 0, 1, 1, 1, 2)	0	100	0	50.0
Week 52 (n = 1, 6, 0, 0, 1, 1, 0, 2)	0	100	0	50.0
Week 64 (n = 1, 5, 0, 0, 1, 1, 0, 1)	0	100	0	100
Week 76 (n = 1, 3, 0, 0, 1, 1, 0, 1)	0	100	0	100
Week 88 (n = 1, 2, 0, 0, 1, 1, 0, 1)	0	100	0	100

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved a Dermatology Life Quality Index (DLQI) = "0" or "1" at Weeks 8 and 16

End point title	Percentage of Participants who Achieved a Dermatology Life Quality Index (DLQI) = "0" or "1" at Weeks 8 and 16

End point description:

The DLQI is a 10-item questionnaire that asks participants to evaluate the degree that psoriasis has affected their quality of life in the last week in the following 6 aspects: symptoms and feelings, daily activities, leisure, work or school activities, personal relationships and treatment related feelings. Participants answer the 10 questions on a scale from 0 (not at all) to 3 (very much). The DLQI is calculated by summing the scores of the 10 questions, resulting in a maximum of 30 and a minimum of 0 with higher scores indicating more impaired quality of life. A score of 0 or 1 means that the disease has no effect at all.
Dermatology Life Quality Index outcomes were defined but are not reported because of an error in the programming of the electronic device used to administer the questionnaire that precluded determination of these outcomes.

End point type	Secondary

End point timeframe:

Baseline and Weeks 8 and 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[76]	0[77]	0[78]	0[79]
Units: percentage of participants				
number (not applicable)				

Notes:

[76] - Not reported due to an error in the electronic device used to administer the questionnaire

[77] - Not reported due to an error in the electronic device used to administer the questionnaire

[78] - Not reported due to an error in the electronic device used to administer the questionnaire

[79] - Not reported due to an error in the electronic device used to administer the questionnaire

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DLQI at Weeks 8 and 16

End point title	Change from Baseline in DLQI at Weeks 8 and 16

End point description:

The DLQI is a 10-item questionnaire that asks participants to evaluate the degree that psoriasis has affected their quality of life in the last week in the following 6 aspects: symptoms and feelings, daily activities, leisure, work or school activities, personal relationships and treatment related feelings. Participants answer the 10 questions on a scale from 0 (not at all) to 3 (very much). The DLQI is calculated by summing the scores of the 10 questions, resulting in a maximum of 30 and a minimum of 0 with higher scores indicating more impaired quality of life. A negative change from Baseline indicates improvement.
Dermatology Life Quality Index outcomes were defined but are not reported because of an error in the programming of the electronic device used to administer the questionnaire that precluded determination of these outcomes.

End point type	Secondary

End point timeframe:

Baseline and Weeks 8 and 16

End point values	Placebo	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[80]	0[81]	0[82]	0[83]
Units: scores on a scale				
least squares mean (standard error)	()	()	()	()

Notes:

[80] - Not reported due to an error in the electronic device used to administer the questionnaire

[81] - Not reported due to an error in the electronic device used to administer the questionnaire

[82] - Not reported due to an error in the electronic device used to administer the questionnaire

[83] - Not reported due to an error in the electronic device used to administer the questionnaire

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Loss of EASI 50 Response Relative to Baseline Among Participants Re-randomized as EASI 75 Responders at Week 16

End point title	Time to Loss of EASI 50 Response Relative to Baseline Among Participants Re-randomized as EASI 75 Responders at Week 16

End point description:

Time to loss of EASI 50 response in Period 2 relative to Baseline among those who were re-randomized as EASI 75 responders at Week 16.
Time to loss of EASI 50 response was measured from Week 16 to the date of the first assessment in Period 2 where a participant's EASI score was higher than 50% of their Baseline score.
Participants with no loss of response were censored at their last treatment visit or the start of rescue treatment, whichever occurred first. "99999" indicates data that could not be estimated due to a low number of events.

End point type	Secondary

End point timeframe:

From re-randomization at Week 16 until Week 88

End point values	Placebo / Placebo	Placebo / Upadacitinib 30 mg	Upadacitinib 7.5 mg / Placebo	Upadacitinib 7.5 mg / Upadacitinib 7.5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	2	5	5
Units: days				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)	29 (27 to 99999)	99999 (29 to 99999)

End point values	Upadacitinib 15 mg / Placebo	Upadacitinib 15 mg / Upadacitinib 15 mg	Upadacitinib 30 mg / Placebo	Upadacitinib 30 mg / Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	14	15
Units: days				
median (confidence interval 95%)	30 (17 to 55)	114 (29 to 99999)	28 (25 to 36)	99999 (99999 to 99999)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug up to 30 days after last dose. Period 1: 16 weeks, Period 2: 72 weeks.

Adverse event reporting additional description:

Any AE that occurred on or after the first dose of upadacitinib 30 mg rescue therapy is counted in the Period 1+2: Upadacitinib 30 mg group. Participants who received rescue therapy after placebo, upadacitinib 7.5 or 15 mg treatment in Period 2 are counted in both Period 1+2: Placebo/Upadacitinib 7.5/15 mg and Period 1+2: Upadacitinib 30 mg groups.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Period 1: Placebo

Reporting group description:

Participants received placebo once daily (QD) for 16 weeks in Period 1.

Reporting group title	Period 1: Upadacitinib 15 mg

Reporting group description:

Participants received upadacitinib 15 mg once daily for 16 weeks in Period 1.

Reporting group title	Period 1: Upadacitinib 7.5 mg

Reporting group description:

Participants received upadacitinib 7.5 mg once daily for 16 weeks in Period 1.

Reporting group title	Period 1: Upadacitinib 30 mg

Reporting group description:

Participants received upadacitinib 30 mg once daily for 16 weeks in Period 1.

Reporting group title	Period 1+2: Upadacitinib 7.5 mg

Reporting group description:

Participants originally randomized to upadacitinib 7.5 mg received upadacitinib 7.5 mg once daily for 16 weeks in Period 1; Participants re-randomized to upadacitinib 7.5 mg in Period 2 continued to receive upadacitinib 7.5 mg for 72 weeks in Period 2 or until rescue.

Reporting group title	Period 1+2: Upadacitinib 15 mg

Reporting group description:

Participants originally randomized to upadacitinib 15 mg received upadacitinib 15 mg once daily for 16 weeks in Period 1; Participants re-randomized to upadacitinib 15 mg in Period 2 continued to receive upadacitinib 15 mg for 72 weeks in Period 2 or until rescue.

Reporting group title	Period 1+2: Upadacitinib 30 mg

Reporting group description:

Participants originally randomized to upadacitinib 30 mg received upadacitinib 30 mg once daily for 16 weeks in Period 1. Participants re-randomized to upadacitinib 30 mg in Period 2 continued to receive upadacitinib 30 mg for 72 weeks in Period 2. Participants originally randomized to placebo and re-randomized to upadacitinib 30 mg at Week 16 received upadacitinib 30 mg from Week 16 to Week 88. Participants re-randomized to upadacitinib 7.5 mg or 15 mg at Week 16 who were rescued starting at Week 20 or later received upadacitinib 30 mg until Week 88.

Reporting group title	Period 1+2: Placebo

Reporting group description:

Participants originally randomized to placebo received placebo once daily for 16 weeks in Period 1. Participants re-randomized to placebo in Period 2 continued to receive placebo for 72 weeks in Period 2 or until rescue.

Serious adverse events	Period 1: Placebo	Period 1: Upadacitinib 15 mg	Period 1: Upadacitinib 7.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 40 (2.50%)	1 / 42 (2.38%)	2 / 42 (4.76%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 40 (2.50%)	0 / 42 (0.00%)	0 / 42 (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
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
PERICARDITIS			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Respiratory, thoracic and mediastinal disorders			
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Gastrointestinal disorders			
OESOPHAGEAL FISTULA			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Renal and urinary disorders			

URETEROLITHIASIS			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS ATOPIC			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	1 / 42 (2.38%)
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			
OSTEOARTHRITIS			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Infections and infestations			
APPENDICITIS			
subjects affected / exposed	0 / 40 (0.00%)	1 / 42 (2.38%)	0 / 42 (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
PERICORONITIS			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN INFECTION			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1

deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Period 1: Upadacitinib 30 mg	Period 1+2: Upadacitinib 7.5 mg	Period 1+2: Upadacitinib 15 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 42 (0.00%)	2 / 42 (4.76%)	1 / 42 (2.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
PERICARDITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Respiratory, thoracic and mediastinal disorders			
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Gastrointestinal disorders			
OESOPHAGEAL FISTULA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Renal and urinary disorders			
URETEROLITHIASIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS ATOPIC			
subjects affected / exposed	0 / 42 (0.00%)	1 / 42 (2.38%)	0 / 42 (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
Musculoskeletal and connective tissue disorders			
OSTEOARTHRITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Infections and infestations			
APPENDICITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICORONITIS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 42 (2.38%)	0 / 42 (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
SEPSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN INFECTION			

subjects affected / exposed	0 / 42 (0.00%)	1 / 42 (2.38%)	0 / 42 (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

Serious adverse events	Period 1+2: Upadacitinib 30 mg	Period 1+2: Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 114 (6.14%)	1 / 93 (1.08%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events	2	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	1 / 114 (0.88%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 114 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	1 / 114 (0.88%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
PERICARDITIS			
subjects affected / exposed	1 / 114 (0.88%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 114 (0.88%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
OESOPHAGEAL FISTULA			

subjects affected / exposed	1 / 114 (0.88%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Renal and urinary disorders			
URETEROLITHIASIS			
subjects affected / exposed	1 / 114 (0.88%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
DERMATITIS ATOPIC			
subjects affected / exposed	0 / 114 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
OSTEOARTHRITIS			
subjects affected / exposed	1 / 114 (0.88%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ROTATOR CUFF SYNDROME			
subjects affected / exposed	1 / 114 (0.88%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
APPENDICITIS			
subjects affected / exposed	0 / 114 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICORONITIS			
subjects affected / exposed	0 / 114 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	1 / 114 (0.88%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	

deaths causally related to treatment / all	1 / 1	0 / 0	
SKIN INFECTION			
subjects affected / exposed	0 / 114 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Period 1: Placebo	Period 1: Upadacitinib 15 mg	Period 1: Upadacitinib 7.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 40 (37.50%)	17 / 42 (40.48%)	21 / 42 (50.00%)
Injury, poisoning and procedural complications			
LIGAMENT SPRAIN			
subjects affected / exposed	2 / 40 (5.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	2 / 40 (5.00%)	3 / 42 (7.14%)	0 / 42 (0.00%)
occurrences (all)	2	3	0
Respiratory, thoracic and mediastinal disorders			
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	3 / 42 (7.14%)
occurrences (all)	0	0	3
Nervous system disorders			
HEADACHE			
subjects affected / exposed	1 / 40 (2.50%)	3 / 42 (7.14%)	3 / 42 (7.14%)
occurrences (all)	1	3	3
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	2 / 40 (5.00%)	2 / 42 (4.76%)	2 / 42 (4.76%)
occurrences (all)	2	4	2
NAUSEA			
subjects affected / exposed	1 / 40 (2.50%)	1 / 42 (2.38%)	3 / 42 (7.14%)
occurrences (all)	1	1	3
Renal and urinary disorders			

HAEMATURIA			
subjects affected / exposed	2 / 40 (5.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
PROTEINURIA			
subjects affected / exposed	2 / 40 (5.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	1 / 40 (2.50%)	2 / 42 (4.76%)	4 / 42 (9.52%)
occurrences (all)	1	2	6
DERMATITIS ATOPIC			
subjects affected / exposed	2 / 40 (5.00%)	2 / 42 (4.76%)	5 / 42 (11.90%)
occurrences (all)	2	2	6
DERMATITIS CONTACT			
subjects affected / exposed	2 / 40 (5.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
Infections and infestations			
HERPES ZOSTER			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
IMPETIGO			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
INFLUENZA			
subjects affected / exposed	0 / 40 (0.00%)	0 / 42 (0.00%)	3 / 42 (7.14%)
occurrences (all)	0	0	3
NASOPHARYNGITIS			
subjects affected / exposed	1 / 40 (2.50%)	4 / 42 (9.52%)	2 / 42 (4.76%)
occurrences (all)	1	5	2
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	4 / 40 (10.00%)	5 / 42 (11.90%)	7 / 42 (16.67%)
occurrences (all)	4	5	7
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 40 (0.00%)	2 / 42 (4.76%)	2 / 42 (4.76%)
occurrences (all)	0	2	2

Non-serious adverse events	Period 1: Upadacitinib 30 mg	Period 1+2: Upadacitinib 7.5 mg	Period 1+2: Upadacitinib 15 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 42 (50.00%)	23 / 42 (54.76%)	22 / 42 (52.38%)
Injury, poisoning and procedural complications			
LIGAMENT SPRAIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	4 / 42 (9.52%)	0 / 42 (0.00%)	3 / 42 (7.14%)
occurrences (all)	4	0	3
Respiratory, thoracic and mediastinal disorders			
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 42 (0.00%)	3 / 42 (7.14%)	0 / 42 (0.00%)
occurrences (all)	0	3	0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	4 / 42 (9.52%)	3 / 42 (7.14%)	3 / 42 (7.14%)
occurrences (all)	4	3	3
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	0 / 42 (0.00%)	2 / 42 (4.76%)	2 / 42 (4.76%)
occurrences (all)	0	2	5
NAUSEA			
subjects affected / exposed	3 / 42 (7.14%)	3 / 42 (7.14%)	1 / 42 (2.38%)
occurrences (all)	3	3	1
Renal and urinary disorders			
HAEMATURIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
PROTEINURIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	6 / 42 (14.29%)	4 / 42 (9.52%)	2 / 42 (4.76%)
occurrences (all)	7	6	2

DERMATITIS ATOPIC			
subjects affected / exposed	4 / 42 (9.52%)	6 / 42 (14.29%)	5 / 42 (11.90%)
occurrences (all)	5	7	5
DERMATITIS CONTACT			
subjects affected / exposed	1 / 42 (2.38%)	0 / 42 (0.00%)	1 / 42 (2.38%)
occurrences (all)	1	0	1
Infections and infestations			
HERPES ZOSTER			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
IMPETIGO			
subjects affected / exposed	2 / 42 (4.76%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
INFLUENZA			
subjects affected / exposed	0 / 42 (0.00%)	3 / 42 (7.14%)	0 / 42 (0.00%)
occurrences (all)	0	3	0
NASOPHARYNGITIS			
subjects affected / exposed	3 / 42 (7.14%)	3 / 42 (7.14%)	5 / 42 (11.90%)
occurrences (all)	3	3	6
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	5 / 42 (11.90%)	7 / 42 (16.67%)	7 / 42 (16.67%)
occurrences (all)	9	7	7
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 42 (2.38%)	2 / 42 (4.76%)	2 / 42 (4.76%)
occurrences (all)	1	2	2

Non-serious adverse events	Period 1+2: Upadacitinib 30 mg	Period 1+2: Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 114 (59.65%)	19 / 93 (20.43%)	
Injury, poisoning and procedural complications			
LIGAMENT SPRAIN			
subjects affected / exposed	1 / 114 (0.88%)	2 / 93 (2.15%)	
occurrences (all)	1	2	
Investigations			

BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	7 / 114 (6.14%)	3 / 93 (3.23%)	
occurrences (all)	8	3	
Respiratory, thoracic and mediastinal disorders			
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 114 (0.00%)	0 / 93 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
HEADACHE			
subjects affected / exposed	7 / 114 (6.14%)	2 / 93 (2.15%)	
occurrences (all)	7	2	
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	2 / 114 (1.75%)	2 / 93 (2.15%)	
occurrences (all)	2	2	
NAUSEA			
subjects affected / exposed	6 / 114 (5.26%)	2 / 93 (2.15%)	
occurrences (all)	8	2	
Renal and urinary disorders			
HAEMATURIA			
subjects affected / exposed	1 / 114 (0.88%)	2 / 93 (2.15%)	
occurrences (all)	1	2	
PROTEINURIA			
subjects affected / exposed	1 / 114 (0.88%)	2 / 93 (2.15%)	
occurrences (all)	1	2	
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	13 / 114 (11.40%)	1 / 93 (1.08%)	
occurrences (all)	14	1	
DERMATITIS ATOPIC			
subjects affected / exposed	22 / 114 (19.30%)	2 / 93 (2.15%)	
occurrences (all)	25	2	
DERMATITIS CONTACT			
subjects affected / exposed	2 / 114 (1.75%)	2 / 93 (2.15%)	
occurrences (all)	2	2	
Infections and infestations			

HERPES ZOSTER			
subjects affected / exposed	10 / 114 (8.77%)	0 / 93 (0.00%)	
occurrences (all)	10	0	
IMPETIGO			
subjects affected / exposed	8 / 114 (7.02%)	0 / 93 (0.00%)	
occurrences (all)	8	0	
INFLUENZA			
subjects affected / exposed	3 / 114 (2.63%)	0 / 93 (0.00%)	
occurrences (all)	4	0	
NASOPHARYNGITIS			
subjects affected / exposed	11 / 114 (9.65%)	1 / 93 (1.08%)	
occurrences (all)	16	1	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	26 / 114 (22.81%)	5 / 93 (5.38%)	
occurrences (all)	47	5	
URINARY TRACT INFECTION			
subjects affected / exposed	6 / 114 (5.26%)	0 / 93 (0.00%)	
occurrences (all)	8	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 July 2016	- Updated contraception timeline requirements for females and clarified consent requirements in Japan. - Updated Exclusion Criteria for topical treatment criteria. - Updated list of prohibited therapies to remove non-atopic dermatitis related treatments. Updated tanning booth and extended sun exposure criteria. Updated live vaccine timeline requirements for Japan. - Updated requirements for allowed topical corticosteroids for rescue therapy.
18 October 2016	- Updated details regarding upadacitinib pharmacokinetic data. - Added discontinuation criteria during Period 1 and Period 2. - Added secondary endpoints for Period 2.
16 December 2016	- Updated rescue therapy and Premature Discontinuation Visits for subjects who prematurely discontinue from study drug to improve readability and provide clarity. - Updated Inclusion Criteria to clarify diagnosis, pregnancy testing, and contraception requirements. - Updated Exclusion Criteria - Updated text to clarify administration criteria for vaccines for Prior and Concomitant Therapy - Updated Prohibited Therapy to clarify exceptions for administering live vaccines. - Updated contraception requirements. - Added three new PRO questionnaires. - Added a Week 16 primary endpoint analysis.
07 June 2017	- Extended the study from 40 weeks to 88 weeks of treatment. Added visits every 12 weeks post Week 40 (Week 52, Week 64, Week 76, and Week 88). Removed optional visits at Week 28 and Week 36 and added optional Visit 4 weeks post topical rescue therapy. - Updated list of examples of biologic therapies for Prohibited Therapy. - Updated language to require a Visit 4 weeks after receiving topical rescue therapy instead of at Week 28 or Week 36. - Updated blood samples collection schedule to reduce patient burden. - Updated list of AEs of special interest to be consistent with the product safety statistical analysis plan. - Removed Week 8 interim analysis language that is no longer planned. Added Week 32 interim analysis language.
30 August 2017	- Updated list of AEs of special interest to be consistent with the current AbbVie list of AEs of special interest.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported