Clinical trial results:
An Open-label Multiple-Dose Study to Evaluate the Pharmacokinetics, Safety, and Tolerability of Upadacitinib in Pediatric Subjects with Severe Atopic Dermatitis

Summary

EudraCT number	2018-004409-17
Trial protocol	NO NL
Global end of trial date	29 August 2024

Results information

Result version number	v1 (current)
This version publication date	22 February 2025
First version publication date	22 February 2025

Trial information

Trial identification

Sponsor protocol code	M16-049

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03646604
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	1 North Waukegan Road, North Chicago, IL, United States, 60064
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001741-PIP04-17
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 August 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part 1:
- To evaluate the pharmacokinetics, activity, safety and tolerability of multiple doses of upadacitinib in pediatric subjects with severe atopic dermatitis.
- To evaluate the palatability of upadacitinib oral solution in pediatric subjects.
Part 2:
- To evaluate the long-term safety and tolerability of multiple doses of upadacitinib in pediatric subjects with severe atopic dermatitis.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 January 2019
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	Puerto Rico: 3
Country: Number of subjects enrolled	United States: 32
Worldwide total number of subjects	35
EEA total number of subjects	0

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)	35
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Within 35 days prior to the Baseline/Day 1 Visit, subject and subject's legally authorized representative received a full explanation of the study design and study procedures, provided a written informed consent/assent, and underwent the screening procedures outlined in the protocol.

Period 1

Period 1 title	Part 1
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Low Dose Upadacitinib, 6 to < 12 years

Arm description:

Participants, 6 to <12 years of age, received weight-dependent low dose of upadacitinib.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib (ABT-494)
Investigational medicinal product code	ABT-494
Other name	RINVOQ
Pharmaceutical forms	Film-coated tablet, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Low Dose: 10 < 20 kg body weight: 3 mg twice daily (BID; oral solution); 20 < 30 kg body weight: 4 mg BID (oral solution); >=30 kg body weight: 15 mg once daily (QD; tablet) or 6 mg BID (oral solution) if unable to swallow tablet.

Arm title	Cohort 2: High Dose Upadacitinib, 6 to < 12 years

Arm description:

Participants, 6 to <12 years of age, received weight-dependent high dose of upadacitinib.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib (ABT-494)
Investigational medicinal product code	ABT-494
Other name	RINVOQ
Pharmaceutical forms	Film-coated tablet, Oral solution
Routes of administration	Oral use

Dosage and administration details:

High Dose: 10 < 20 kg body weight: 6 mg BID (oral solution); 20 < 30 kg body weight: 8 mg BID (oral solution); >=30 kg body weight: 30 mg (QD) or 12 mg BID (oral solution) if unable to swallow tablet.

Arm title	Cohort 3: Low Dose Upadacitinib, 2 < 6 years

Arm description:

Participants, 2 to <6 years of age, received weight-dependent low dose of upadacitinib.

Arm type	Experimental

Investigational medicinal product name	Upadacitinib (ABT-494)
Investigational medicinal product code	ABT-494
Other name	RINVOQ
Pharmaceutical forms	Film-coated tablet, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Low Dose: 10 < 20 kg body weight: 3 mg twice daily (BID; oral solution); 20 < 30 kg body weight: 4 mg BID (oral solution); >=30 kg body weight: 15 mg once daily (QD; tablet) or 6 mg BID (oral solution) if unable to swallow tablet.

Arm title	Cohort 4: High Dose Upadacitinib, 2 < 6 years

Arm description:

Participants, 2 to <6 years of age, received weight-dependent high dose of upadacitinib.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib (ABT-494)
Investigational medicinal product code	ABT-494
Other name	RINVOQ
Pharmaceutical forms	Film-coated tablet, Oral solution
Routes of administration	Oral use

Dosage and administration details:

High Dose: 10 < 20 kg body weight: 6 mg BID (oral solution); 20 < 30 kg body weight: 8 mg BID (oral solution); >=30 kg body weight: 30 mg (QD) or 12 mg BID (oral solution) if unable to swallow tablet.

Number of subjects in period 1	Cohort 1: Low Dose Upadacitinib, 6 to < 12 years	Cohort 2: High Dose Upadacitinib, 6 to < 12 years	Cohort 3: Low Dose Upadacitinib, 2 < 6 years
Started	9	8	9
Completed	9	8	8
Not completed	0	0	1
Consent withdrawn by subject	-	-	1
Study drug noncompliance	-	-	-

Number of subjects in period 1	Cohort 4: High Dose Upadacitinib, 2 < 6 years
Started	9
Completed	8
Not completed	1
Consent withdrawn by subject	-
Study drug noncompliance	1

Period 2

Period 2 title	Part 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 2: Aged 6 to < 12 years

Arm description:

Eligible participants, aged 6 to < 12 years, who completed Part 1 received weight-dependent low dose of upadacitinib.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib (ABT-494)
Investigational medicinal product code	ABT-494
Other name	RINVOQ
Pharmaceutical forms	Film-coated tablet, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Low Dose: 10 < 20 kg body weight: 3 mg twice daily (BID; oral solution); 20 < 30 kg body weight: 4 mg BID (oral solution); >=30 kg body weight: 15 mg once daily (QD; tablet) or 6 mg BID (oral solution) if unable to swallow tablet.

Arm title	Part 2: Aged 2 to < 6 Years

Arm description:

Eligible participants, aged 2 to < 6 years, who completed Part 1 received weight-dependent low dose of upadacitinib.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib (ABT-494)
Investigational medicinal product code	ABT-494
Other name	RINVOQ
Pharmaceutical forms	Film-coated tablet, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Low Dose: 10 < 20 kg body weight: 3 mg twice daily (BID; oral solution); 20 < 30 kg body weight: 4 mg BID (oral solution); >=30 kg body weight: 15 mg once daily (QD; tablet) or 6 mg BID (oral solution) if unable to swallow tablet.

Number of subjects in period 2	Part 2: Aged 6 to < 12 years	Part 2: Aged 2 to < 6 Years
Started	17	16
Completed	10	9
Not completed	7	7
Consent withdrawn by subject	1	2
Adverse event	3	1
FDA recommended discontinuation (> 3 years)	-	2
Lost to follow-up	1	-
Lack of efficacy	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: Low Dose Upadacitinib, 6 to < 12 years
Reporting group description: Participants, 6 to <12 years of age, received weight-dependent low dose of upadacitinib.	
Reporting group title	Cohort 2: High Dose Upadacitinib, 6 to < 12 years
Reporting group description: Participants, 6 to <12 years of age, received weight-dependent high dose of upadacitinib.	
Reporting group title	Cohort 3: Low Dose Upadacitinib, 2 < 6 years
Reporting group description: Participants, 2 to <6 years of age, received weight-dependent low dose of upadacitinib.	
Reporting group title	Cohort 4: High Dose Upadacitinib, 2 < 6 years
Reporting group description: Participants, 2 to <6 years of age, received weight-dependent high dose of upadacitinib.	

Reporting group values	Cohort 1: Low Dose Upadacitinib, 6 to < 12 years	Cohort 2: High Dose Upadacitinib, 6 to < 12 years	Cohort 3: Low Dose Upadacitinib, 2 < 6 years
Number of subjects	9	8	9
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	8.3	8.0	4.0
standard deviation	± 1.58	± 1.77	± 1.00
Gender categorical Units: Subjects			
Female	6	6	5
Male	3	2	4

Reporting group values	Cohort 4: High Dose Upadacitinib, 2 < 6 years	Total	
Number of subjects	9	35	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	3.2		
standard deviation	± 0.83	-	
Gender categorical Units: Subjects			
Female	2	19	
Male	7	16	

End points

End points reporting groups

Reporting group title	Cohort 1: Low Dose Upadacitinib, 6 to < 12 years
Reporting group description:	
Participants, 6 to <12 years of age, received weight-dependent low dose of upadacitinib.	
Reporting group title	Cohort 2: High Dose Upadacitinib, 6 to < 12 years
Reporting group description:	
Participants, 6 to <12 years of age, received weight-dependent high dose of upadacitinib.	
Reporting group title	Cohort 3: Low Dose Upadacitinib, 2 < 6 years
Reporting group description:	
Participants, 2 to <6 years of age, received weight-dependent low dose of upadacitinib.	
Reporting group title	Cohort 4: High Dose Upadacitinib, 2 < 6 years
Reporting group description:	
Participants, 2 to <6 years of age, received weight-dependent high dose of upadacitinib.	
Reporting group title	Part 2: Aged 6 to < 12 years
Reporting group description:	
Eligible participants, aged 6 to < 12 years, who completed Part 1 received weight-dependent low dose of upadacitinib.	
Reporting group title	Part 2: Aged 2 to < 6 Years
Reporting group description:	
Eligible participants, aged 2 to < 6 years, who completed Part 1 received weight-dependent low dose of upadacitinib.	
Subject analysis set title	Cohort 1, QD Regimen: Pharmacokinetics (PK)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with viable PK data in Cohort 1 who received the upadacitinib tablet QD regimen.	
Subject analysis set title	Cohort 1, BID Regimen: PK
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with viable PK data in Cohort 1 who received the upadacitinib solution BID regimen.	
Subject analysis set title	Cohort 1, QD and BID Regimen Combined: PK
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with viable PK data in Cohort 1 who received the upadacitinib tablet QD and/or solution BID regimen.	
Subject analysis set title	Cohort 2, QD Regimen: PK
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with viable PK data in Cohort 2 who received the upadacitinib tablet QD regimen.	
Subject analysis set title	Cohort 2, BID Regimen: PK
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with viable PK data in Cohort 2 who received the upadacitinib solution BID regimen.	
Subject analysis set title	Cohort 2, QD and BID Regimen Combined: PK
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with viable PK data in Cohort 2 who received the upadacitinib tablet QD and/or solution BID regimen.	
Subject analysis set title	Cohort 3, BID Regimen: PK
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with viable PK data in Cohort 3 who received the upadacitinib solution BID regimen.

Subject analysis set title	Cohort 3, QD and BID Regimen Combined: PK
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with viable PK data in Cohort 3 who received the upadacitinib tablet QD and/or solution BID regimen.

Subject analysis set title	Cohort 4, BID Regimen: PK
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with viable PK data in Cohort 4 who received the upadacitinib solution BID regimen.

Subject analysis set title	Cohort 4, QD and BID Regimen Combined: PK
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with viable PK data in Cohort 4 who received the upadacitinib tablet QD and/or solution BID regimen.

Primary: Time to Maximum Observed Plasma Concentration (Tmax)

End point title	Time to Maximum Observed Plasma Concentration (Tmax)[1]

End point description:

End point type	Primary

End point timeframe:

Part 1, Day 7

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics planned per protocol are presented in the data table.

End point values	Cohort 1, QD Regimen: Pharmacokinetics (PK)	Cohort 1, BID Regimen: PK	Cohort 1, QD and BID Regimen Combined: PK	Cohort 2, QD Regimen: PK
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	5	9	5
Units: hours				
median (full range (min-max))	3.12 (1.00 to 4.05)	1.00 (0.500 to 1.92)	1.17 (0.500 to 4.05)	2.00 (0.567 to 3.38)

End point values	Cohort 2, BID Regimen: PK	Cohort 2, QD and BID Regimen Combined: PK	Cohort 3, BID Regimen: PK	Cohort 3, QD and BID Regimen Combined: PK
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	8	8	8
Units: hours				
median (full range (min-max))	2.00 (0.250 to 4.00)	2.00 (0.250 to 4.00)	2.00 (1.00 to 4.07)	2.00 (1.00 to 4.07)

End point values	Cohort 4, BID Regimen: PK	Cohort 4, QD and BID Regimen Combined: PK		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	7		
Units: hours				
median (full range (min-max))	0.500 (0.317 to 1.08)	0.500 (0.317 to 1.08)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Plasma Concentration (Cmax)

End point title	Maximum Plasma Concentration (Cmax)[2]

End point description:

End point type	Primary

End point timeframe:

Part 1, Day 7

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics planned per protocol are presented in the data table.

End point values	Cohort 1, QD Regimen: Pharmacokinetics (PK)	Cohort 1, BID Regimen: PK	Cohort 1, QD and BID Regimen Combined: PK	Cohort 2, QD Regimen: PK
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	5	9	5
Units: ng/mL				
geometric mean (geometric coefficient of variation)	47.7 (± 71.5)	24.7 (± 53.1)	33.1 (± 76.4)	154 (± 50.1)

End point values	Cohort 2, BID Regimen: PK	Cohort 2, QD and BID Regimen Combined: PK	Cohort 3, BID Regimen: PK	Cohort 3, QD and BID Regimen Combined: PK
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	8	8	8
Units: ng/mL				
geometric mean (geometric coefficient of variation)	43.2 (± 42.7)	95.5 (± 73.2)	35.9 (± 97.3)	35.9 (± 97.3)

End point values	Cohort 4, BID Regimen: PK	Cohort 4, QD and BID		

		Regimen Combined: PK		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	7		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	108 (± 57.9)	108 (± 57.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-Time Curve Within a Dosing Interval (AUCtau)

End point title	Area Under the Plasma Concentration-Time Curve Within a Dosing Interval (AUCtau)[3]

End point description:

The area under the plasma concentration-time curve (AUCtau) is a method of measurement of the total exposure of a drug in plasma. For QD regimens, AUCtau = AUC0-24; for BID regimens, AUCtau = AUC0-12 and AUC0-24 = AUC0-12 × 2.

End point type	Primary

End point timeframe:

Part 1, Day 7

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics planned per protocol are presented in the data table.

End point values	Cohort 1, QD Regimen: Pharmacokinetics (PK)	Cohort 1, BID Regimen: PK	Cohort 1, QD and BID Regimen Combined: PK	Cohort 2, QD Regimen: PK
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	5	9	5
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	284 (± 22.9)	111 (± 52.0)	169 (± 54.5)	675 (± 21.1)

End point values	Cohort 2, BID Regimen: PK	Cohort 2, QD and BID Regimen Combined: PK	Cohort 3, BID Regimen: PK	Cohort 3, QD and BID Regimen Combined: PK
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	8	6	6
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	174 (± 25.4)	406 (± 57.8)	146 (± 102)	146 (± 102)

End point values	Cohort 4, BID Regimen: PK	Cohort 4, QD and BID Regimen Combined: PK		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	7		
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	326 (± 39.0)	326 (± 39.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Oral Clearance at Steady State (CLss/F)

End point title	Apparent Oral Clearance at Steady State (CLss/F)[4]

End point description:

End point type	Primary

End point timeframe:

Part 1, Day 7

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics planned per protocol are presented in the data table.

End point values	Cohort 1, QD Regimen: Pharmacokinetics (PK)	Cohort 1, BID Regimen: PK	Cohort 1, QD and BID Regimen Combined: PK	Cohort 2, QD Regimen: PK
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	5	9	5
Units: L/h				
geometric mean (geometric coefficient of variation)	31.4 (± 47.5)	19.5 (± 30.1)	24.1 (± 49.2)	38.7 (± 37.4)

End point values	Cohort 2, BID Regimen: PK	Cohort 2, QD and BID Regimen Combined: PK	Cohort 3, BID Regimen: PK	Cohort 3, QD and BID Regimen Combined: PK
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	8	6	6
Units: L/h				
geometric mean (geometric coefficient of variation)	23.0 (± 27.2)	31.9 (± 44.5)	14.1 (± 61.3)	14.1 (± 61.3)

End point values	Cohort 4, BID Regimen: PK	Cohort 4, QD and BID		

		Regimen Combined: PK		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	7		
Units: L/h				
geometric mean (geometric coefficient of variation)	18.4 (± 70.6)	18.4 (± 70.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAE)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAE)[5]

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product which does not necessarily have a causal relationship with this treatment. The investigator assesses the relationship of each event to the use of study drug as either probably related, possibly related, probably not related or not related. A serious adverse event (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the participant and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent adverse events (TEAEs) are defined as AEs with an onset date that is after the first dose of study drug, and no more than 30 days of the drug after the last dose of study drug.

End point type	Primary

End point timeframe:

Part 1: For a median of 7 days (+ 30 days of follow up for those not advancing to Part 2).
Part 2: For a median of 748 days + 30 days of follow-up.

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics planned per protocol are presented in the data table.

End point values	Cohort 1: Low Dose Upadacitinib, 6 to < 12 years	Cohort 2: High Dose Upadacitinib, 6 to < 12 years	Cohort 3: Low Dose Upadacitinib, 2 < 6 years	Cohort 4: High Dose Upadacitinib, 2 < 6 years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	8	9	9
Units: participants				
AE	1	1	5	0
AE with reasonable possibility of = drug related	0	0	1	0
Severe AE	0	0	0	0
SAE	0	0	0	0
SAE with reasonable possibility of = drug related	0	0	0	0
AE leading to discontinuation of study drug	0	0	0	0
AE leading to death	0	0	0	0
All deaths	0	0	0	0

End point values	Part 2: Aged 6 to < 12 years	Part 2: Aged 2 to < 6 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: participants				
AE	15	14		
AE with reasonable possibility of = drug related	2	7		
Severe AE	3	1		
SAE	3	0		
SAE with reasonable possibility of = drug related	1	0		
AE leading to discontinuation of study drug	3	1		
AE leading to death	0	0		
All deaths	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part 1: For a median of 7 days (+ 30 days of follow up for those not advancing to Part 2).
Part 2: For a median of 748 days + 30 days of follow-up.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Cohort 1: Low Dose Upadacitinib, 6 to < 12 years

Reporting group description:

Participants, 6 to <12 years of age, received weight-dependent low dose of upadacitinib.

Reporting group title	Part 2: Aged 2 to < 6 Years

Reporting group description:

Eligible participants, aged 2 to < 6 years, who completed Part 1 received weight-dependent low dose of upadacitinib.

Reporting group title	Cohort 4: High Dose Upadacitinib, 2 < 6 years

Reporting group description:

Participants, 2 to <6 years of age, received weight-dependent high dose of upadacitinib.

Reporting group title	Part 2: Aged 6 to < 12 years

Reporting group description:

Eligible participants, aged 6 to < 12 years, who completed Part 1 received weight-dependent low dose of upadacitinib.

Reporting group title	Cohort 2: High Dose Upadacitinib, 6 to < 12 years

Reporting group description:

Participants, 6 to <12 years of age, received weight-dependent high dose of upadacitinib.

Reporting group title	Cohort 3: Low Dose Upadacitinib, 2 < 6 years

Reporting group description:

Participants, 2 to <6 years of age, received weight-dependent low dose of upadacitinib.

Serious adverse events	Cohort 1: Low Dose Upadacitinib, 6 to < 12 years	Part 2: Aged 2 to < 6 Years	Cohort 4: High Dose Upadacitinib, 2 < 6 years
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Psychiatric disorders			
MAJOR DEPRESSION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (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			

COVID-19			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (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
OPHTHALMIC HERPES ZOSTER			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2: Aged 6 to < 12 years	Cohort 2: High Dose Upadacitinib, 6 to < 12 years	Cohort 3: Low Dose Upadacitinib, 2 < 6 years
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 17 (17.65%)	0 / 8 (0.00%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Psychiatric disorders			
MAJOR DEPRESSION			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OPHTHALMIC HERPES ZOSTER			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (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

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

Non-serious adverse events	Cohort 1: Low Dose Upadacitinib, 6 to < 12 years	Part 2: Aged 2 to < 6 Years	Cohort 4: High Dose Upadacitinib, 2 < 6 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)	14 / 16 (87.50%)	0 / 9 (0.00%)

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SKIN PAPILLOMA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
FATIGUE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CYST			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PYREXIA			
subjects affected / exposed	0 / 9 (0.00%)	2 / 16 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
SWELLING			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Immune system disorders			
HYPERSENSITIVITY			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	0 / 9 (0.00%)	3 / 16 (18.75%)	0 / 9 (0.00%)
occurrences (all)	0	6	0
COUGH			
subjects affected / exposed	0 / 9 (0.00%)	5 / 16 (31.25%)	0 / 9 (0.00%)
occurrences (all)	0	5	0
RHINORRHOEA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PRODUCTIVE COUGH			

subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
COUGH VARIANT ASTHMA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DYSPNOEA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
EPISTAXIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
ELECTROCARDIOGRAM ST SEGMENT ELEVATION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HEART RATE IRREGULAR			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
ANIMAL BITE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

FOOT FRACTURE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SKIN WOUND			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
LEFT VENTRICULAR HYPERTROPHY			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
LYMPHADENITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LYMPHADENOPATHY			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
NEUTROPENIA			
subjects affected / exposed	0 / 9 (0.00%)	2 / 16 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
THROMBOCYTOSIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
DENTAL CARIES			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

GASTRITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
TOOTH DISORDER			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	0 / 9 (0.00%)	3 / 16 (18.75%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Skin and subcutaneous tissue disorders			
DERMATITIS ATOPIC			
subjects affected / exposed	0 / 9 (0.00%)	2 / 16 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
ALOPECIA AREATA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SKIN EROSION			
subjects affected / exposed	1 / 9 (11.11%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
RASH			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ERYTHEMA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
ECZEMA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
URTICARIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			

URINARY INCONTINENCE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
CONJUNCTIVITIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
CELLULITIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
BACTERIAL INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
EAR INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ECZEMA HERPETICUM			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HAND-FOOT-AND-MOUTH DISEASE			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HERPES ZOSTER			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
OTITIS EXTERNA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
MOLLUSCUM CONTAGIOSUM			
subjects affected / exposed	0 / 9 (0.00%)	2 / 16 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
INFLUENZA			

subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
IMPETIGO			
subjects affected / exposed	0 / 9 (0.00%)	2 / 16 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
HORDEOLUM			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SCARLET FEVER			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
SINUSITIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
SKIN INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SWEATING FEVER			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	2 / 16 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
VIRAL INFECTION			

subjects affected / exposed	0 / 9 (0.00%)	1 / 16 (6.25%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 9 (0.00%)	2 / 16 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 16 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 2: Aged 6 to < 12 years	Cohort 2: High Dose Upadacitinib, 6 to < 12 years	Cohort 3: Low Dose Upadacitinib, 2 < 6 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 17 (82.35%)	1 / 8 (12.50%)	5 / 9 (55.56%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SKIN PAPILLOMA			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
PAIN			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
FATIGUE			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
CYST			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SWELLING			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			

HYPERSENSITIVITY			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
COUGH			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
COUGH VARIANT ASTHMA			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
DYSPNOEA			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
EPISTAXIS			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

ELECTROCARDIOGRAM ST SEGMENT ELEVATION			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HEART RATE IRREGULAR			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
ANIMAL BITE			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
FALL			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
FOOT FRACTURE			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
SKIN WOUND			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
LEFT VENTRICULAR HYPERTROPHY			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	3 / 17 (17.65%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	7	0	0
Blood and lymphatic system disorders			
LYMPHADENITIS			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
LYMPHADENOPATHY			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NEUTROPENIA			

subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
THROMBOCYTOSIS			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
DENTAL CARIES			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
GASTRITIS			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
NAUSEA			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
TOOTH DISORDER			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
VOMITING			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
DERMATITIS ATOPIC			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
ALOPECIA AREATA			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
SKIN EROSION			

subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RASH			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
ERYTHEMA			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ECZEMA			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
URTICARIA			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
URINARY INCONTINENCE			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Infections and infestations			
CONJUNCTIVITIS			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
CELLULITIS			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
BACTERIAL INFECTION			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	3 / 17 (17.65%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
EAR INFECTION			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
ECZEMA HERPETICUM			

subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HAND-FOOT-AND-MOUTH DISEASE			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HERPES ZOSTER			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
OTITIS EXTERNA			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
MOLLUSCUM CONTAGIOSUM			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
IMPETIGO			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HORDEOLUM			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
NASOPHARYNGITIS			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
RESPIRATORY SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
SCARLET FEVER			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

SKIN INFECTION			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
SWEATING FEVER			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	5	0	0
VIRAL INFECTION			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 December 2018	The purpose of this amendment is to correct minor clerical errors for consistency throughout the protocol in addition to the following: - Add pharmacodynamic assessment and palatability evaluation of upadacitinib oral solution to Part 1 objectives in Section 1 (Synopsis) and Section 3.1 (Objectives). - Add statistical analyses of palatability evaluation to Section 7.5 - Add minimum enrollment of 4 subjects to each bodyweight category to Section 1 (Synopsis) and Section 4.1 (Investigational Plan). - Add additional details regarding limiting subject discomfort in Section 4.2 (Discussion of Study Design), on discontinuation of subjects in Section 5.6 (Withdrawal of Subjects and Discontinuation of Study), on QTc criterion in Section 6.2 (Toxicity Management and on end of study in Section 11 (Completion of Study). - Section 5.2 Contraception Requirements for Females. Additional description for females of childbearing potential. - Section 6.1 (Complaints and Adverse Events). Updated information on CTCAE and pregnancy. - Removed "in a blinded manner" from cardiovascular paragraph. Section 6.2 (Toxicity Management). - Added Section 6.3 (Data Monitoring Committee and Cardiovascular Adjudication Committee)" to Section 6.4. - Update abbreviations in Appendix A (Study Specific Abbreviations and Terms). - Update Appendix D (Study Activities Table) to clarify study activities including addition of a ± 7 day window to study visits in Part 2 - Operations Manual. Section 3.16, Follow-Up. Remove telephone follow-up. - Operations Manual. Section 3.18, Dispense Study Drug. Move section and add additional details. - Operations Manual. Section 5.2, Packaging and Labeling. Specified that upadacitinib oral solution should be protected from freezing and add temperature excursion information. - Operations Manual. Section 5.3, Method of Assigning Subjects to Treatment Groups. Update the subject identification number from 6 to 8 digits.
21 December 2018	(continued) - Operations Manual. Section 5, Study Drug, Subsections 5.4, 5.5 and 5.6. Provide additional information regarding study drug procedures. - Operations Manual. Replace TB RISK ASSESSMENT FORM EXAMPLE and TANNER STAGES. - Operations Manual. Update the definitions in ECZEMA AREA AND SEVERITY INDEX (EASI) SCORING EXAMPLE. - Added two appendices to Operations Manual ORAL SOLUTION DOSING INFORMATION WITH REQUIRED SYRINGE SIZE and INSTRUCTIONS FOR USE: ORAL SOLUTION. - Operations Manual. Added to appendices of protocol.
26 February 2020	The purpose of this amendment is to correct minor clerical errors for consistency throughout the protocol in addition to the following: - Update the study design to include an additional group of subjects 6 months to less than 2 years of age. - Add a new oral upadacitinib formulation of 0.5 mg/mL. - Update the safety related language throughout the protocol. - Update language for moderate/strong inhibitors. - Update Section 5.6: Treatment Compliance in the Operations Manual.

11 February 2021	The purpose of this amendment is to correct minor clerical errors for consistency throughout the protocol in addition to the following: - Updated sponsor/emergency medical contact. - Updated dose levels and body weight categories in Table 2 for subjects 2 to < 12 years of age and added dosing recommendations for subjects 6 months to < 2 years in cohorts 5 and 6 in Table 3. - Added citation to selection of doses discussion. - Added summary of conclusions on efficacy and safety from the available Phase 3 AD studies in Section 2.1, Benefits and Risks to Subjects. - Updated Eligibility Criterion 3 to have separate weight limits based on age. - Added information regarding development of oral solutions. - Added information regarding COVID-19 procedures throughout the document. - Replace PF 04965842 with abrocitinib in JAK inhibitor list in Prior/Concomitant Therapy - Added information regarding adjudication committee used to assess potential gastrointestinal perforation AEs. - Updated language regarding study drug withdrawal criterion and toxicity management related to gastrointestinal perforation. - Added a study stopping criteria related to elevations in creatinine phosphokinase: Two or more subjects administered study drug experience a confirmed symptomatic creatinine phosphokinase (CPK) elevation ≥ 4x upper limit of normal considered related to study drug. - Updated sample size estimation. - Added additional text regarding dose adjustment for subjects in Part 1 of the study. - Updated text for re-screening procedure in Appendix F, Section 3.2 - Added text to collect full date of birth to Appendix F, Section 3.3. - Removed home urine pregnancy test paragraph from Appendix F, Section 3.13, Clinical Laboratory Tests. - Added information regarding at self-scoring of Tanner stage in Appendix F, Section 3.12. - Updated table in Operations Manual Appendix G with new weight categories.
19 July 2021	The purpose of this amendment is to correct minor clerical errors for consistency throughout the protocol in addition to the following: - Clarified that for the calculation of the EASI score, the age at the respective visit is used (Appendix E of the Operations Manual). - Changed the contact information for reporting protocol deviations and product complaints in the operations manual.
15 December 2021	The purpose of this amendment is to correct minor clerical errors for consistency throughout the protocol in addition to the following: - SPONSOR/EMERGENCY MEDICAL CONTACT updated. - Updated the safety team's email address. - Changed central laboratory to Labcorp Central Laboratory Services Limited Partnership. - In Eligibility criterion number 3, updated minimum age to 3 years of age starting with protocol version 6.0. - In Eligibility criteria number 12, added "history of retinopathy of prematurity, congenital structural abnormalities of the eye (e.g., Marfan's Syndrome), inherited vitreoretinal degenerations or vitreoretinopathies (e.g., Stickler syndrome) or prior history of retinal detachment" as exclusionary conditions. - Throughout the document updated minimum age of subjects in study to 2 years of age - Removed Cohorts 5 and 6 from the study design and all language related to these cohorts throughout the document. - Added ophthalmology assessment every 3 months to check visual acuity of subjects that are < 3 years old until they reach their third year of age, or as needed for subjects ≥ 3 years of age.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported