



Clinical trial results:

A Phase 3b, Open-Label Treatment Extension Study of Upadacitinib for the Treatment of Adult Subjects with Moderate to Severe Atopic Dermatitis Who Completed Treatment in Study M16-046

Summary

EudraCT number	2019-001227-12
Trial protocol	IE FI HU CZ ES NL FR GB HR IT NO
Global end of trial date	11 September 2023

Results information

Result version number	v1
This version publication date	21 September 2024
First version publication date	21 September 2024

Trial information

Trial identification

Sponsor protocol code	M19-850
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04195698
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Services, AbbVie, Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@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	11 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 September 2023
Global end of trial reached?	Yes
Global end of trial date	11 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a study for adults (18-75 years) who have successfully completed treatment either with Dupilumab or with Upadacitinib in the study M16-046. At the end of M16-046, they have the option to receive Upadacitinib with a duration of 52 weeks beyond the timeframe of Study M16-046. There will be a 30 day follow-up visit after the treatment period is completed.

Main objective of this study is to assess long-term safety, tolerability and efficacy of upadacitinib in participants with moderate to severe atopic dermatitis who successfully completed treatment in the study M16-046.

Protection of trial subjects:

The investigator or his/her representative will explain the nature of the study to the subject and answer all questions regarding this study. Prior to any study-related procedures being performed on the subject or any medications being discontinued by the subject in order to participate in this study, the informed consent statement will be reviewed, signed, and dated by the subject, the person who administered the informed consent, and any other signatories according to local requirements. A copy of the signed informed consent will be given to the subject and the original will be placed in the subject's medical record.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 35
Country: Number of subjects enrolled	Canada: 67
Country: Number of subjects enrolled	Croatia: 5
Country: Number of subjects enrolled	Czechia: 16
Country: Number of subjects enrolled	Finland: 16
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Germany: 33
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	Ireland: 5
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Malaysia: 20

Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	New Zealand: 26
Country: Number of subjects enrolled	Norway: 5
Country: Number of subjects enrolled	Poland: 31
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Spain: 32
Country: Number of subjects enrolled	Taiwan: 8
Country: Number of subjects enrolled	Ukraine: 8
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	United States: 94
Worldwide total number of subjects	475
EEA total number of subjects	198

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)	456
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 475 participants were enrolled at 114 sites located in 22 countries (Australia, Canada, Croatia, Czechia, Finland, France, Germany, Hungary, Ireland, Israel, Italy, Malaysia, Netherlands, New Zealand, Norway, Poland, Singapore, Spain, Taiwan, Ukraine, United Kingdom, and the US).

Pre-assignment

Screening details:

Participants originally randomized to upa or dupi in Parent Study M16-046 and continued in this study. The ITT Population consists of all enrolled participants who received at least 1 dose of study drug in the study and is used for all efficacy analyses. The Safety Population is the same as the ITT Population and is used for all safety analyses.

Period 1

Period 1 title	Overall Study Period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	DUPI 300mg to UPA 30mg

Arm description:

All participants in this study received upadacitinib 30 mg once a day (QD). Participants were grouped by previous treatment in Parent Study M16-046. Participants who received dupilumab (DUPI) in Parent Study M16-046 are included in the DUPI 300 mg Q2W/UPA 30 mg QD (DUPI/UPA) group.

Arm type	Experimental
Investigational medicinal product name	upadacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

All participants in this study received upadacitinib 30 mg once a day (QD). Participants were grouped by previous treatment in Parent Study M16-046. Participants who received dupilumab (DUPI) in Parent Study M16-046 are included in the DUPI 300 mg Q2W/UPA 30 mg QD (DUPI/UPA) group.

Arm title	UPA 30mg to UPA 30mg
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Arm description:

All participants in this study received upadacitinib 30 mg once a day (QD). Participants were grouped by previous treatment in Parent Study M16-046. Participants who received upadacitinib (UPA) in Parent Study M16-046 are included in the UPA 30 mg QD/UPA 30 mg QD (UPA/UPA) group.

Arm type	Experimental
Investigational medicinal product name	upadacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

All participants in this study received upadacitinib 30 mg once a day (QD). Participants were grouped by previous treatment in Parent Study M16-046. Participants who received upadacitinib (UPA) in Parent Study M16-046 are included in the UPA 30 mg QD/UPA 30 mg QD (UPA/UPA) group.

Number of subjects in period 1	DUPI 300mg to UPA 30mg	UPA 30mg to UPA 30mg
Started	239	236
Completed	214	197
Not completed	25	39
Consent withdrawn by subject	9	10
Adverse event, non-fatal	4	11
Not specified	5	4
Lost to follow-up	5	4
Lack of efficacy	2	10

Baseline characteristics

Reporting groups

Reporting group title	DUPI 300mg to UPA 30mg
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Reporting group description:

All participants in this study received upadacitinib 30 mg once a day (QD). Participants were grouped by previous treatment in Parent Study M16-046. Participants who received dupilumab (DUPI) in Parent Study M16-046 are included in the DUPI 300 mg Q2W/UPA 30 mg QD (DUPI/UPA) group.

Reporting group title	UPA 30mg to UPA 30mg
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Reporting group description:

All participants in this study received upadacitinib 30 mg once a day (QD). Participants were grouped by previous treatment in Parent Study M16-046. Participants who received upadacitinib (UPA) in Parent Study M16-046 are included in the UPA 30 mg QD/UPA 30 mg QD (UPA/UPA) group.

Reporting group values	DUPI 300mg to UPA 30mg	UPA 30mg to UPA 30mg	Total
Number of subjects	239	236	475
Age categorical			
Units: Subjects			
< 40 years	167	156	323
≥ 40 to < 65 years	66	70	136
≥ 65 years	6	10	16
Age continuous			
Units: years			
arithmetic mean	35.3	36.1	
standard deviation	± 12.90	± 14.41	-
Gender categorical			
Units: Subjects			
Female	100	104	204
Male	139	132	271
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	17	16	33
Not Hispanic or Latino	222	220	442
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	1	2
Asian	49	46	95
Native Hawaiian or Other Pacific Islander	1	2	3
Black or African American	11	14	25
White	172	170	342
More than one race	5	3	8
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	DUPI 300mg to UPA 30mg
Reporting group description: All participants in this study received upadacitinib 30 mg once a day (QD). Participants were grouped by previous treatment in Parent Study M16-046. Participants who received dupilumab (DUPI) in Parent Study M16-046 are included in the DUPI 300 mg Q2W/UPA 30 mg QD (DUPI/UPA) group.	
Reporting group title	UPA 30mg to UPA 30mg
Reporting group description: All participants in this study received upadacitinib 30 mg once a day (QD). Participants were grouped by previous treatment in Parent Study M16-046. Participants who received upadacitinib (UPA) in Parent Study M16-046 are included in the UPA 30 mg QD/UPA 30 mg QD (UPA/UPA) group.	

Primary: Number of Participants With Adverse Events

End point title	Number of Participants With Adverse Events ^[1]
End point description: An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. The investigator assessed 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 subject and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent events (TEAEs/TESAEs) are defined as any event that began or worsened in severity after the first dose of study drug and no more than 30 days after the last dose of the study drug.	
End point type	Primary
End point timeframe: From Baseline to 30 days following last dose of study drug (Week 52)	

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: There will be no statistical testing for all of the efficacy and safety endpoints.

End point values	DUPI 300mg to UPA 30mg	UPA 30mg to UPA 30mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	236		
Units: count of participants				
number (not applicable)				
Any TEAE	205	223		
TESAE	14	17		
AE leading to discontinuation of study drug	12	18		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Adverse Events of Special Interest (AESI)

End point title	Number of Participants With Adverse Events of Special Interest (AESI) ^[2]
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End point description:

Adverse events will be monitored throughout the study to identify any of special interest that may indicate a trend or risk to participants such as the following: serious infections, opportunistic infections, herpes zoster, active tuberculosis, malignancy (all types), adjudicated gastrointestinal perforations, adjudicated cardiovascular events (e.g., major adverse cardiovascular event [MACE]), anemia, neutropenia, lymphopenia, renal dysfunction, hepatic disorders, elevated creatine phosphokinase (CPK), adjudicated embolic and thrombotic events (non-cardiac, non-central nervous system) and COVID-19 (consider while pandemic is ongoing).

MACE defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

VTE include deep vein thrombosis (DVT) and pulmonary embolism (PE)(fatal and non-fatal).

End point type	Primary
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End point timeframe:

From Baseline to 30 days following last dose of study drug (Week 52)

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: There will be no statistical testing for all of the efficacy and safety endpoints.

End point values	DUPI 300mg to UPA 30mg	UPA 30mg to UPA 30mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	236		
Units: Count of participants				
number (not applicable)				
Serious infections	7	8		
Opportunistic infection excluding TB & Herpes	6	4		
Malignancy	1	0		
Non-melanoma skin cancer (NMSC)	0	0		
Malignancy excluding NMSC	1	0		
Lymphoma	0	0		
Hepatic disorder	19	15		
Adjudicated gastrointestinal perforations	0	0		
Anemia	7	8		
Neutropenia	10	8		
Lymphopenia	4	5		
Herpes zoster	26	25		
Creatine phosphokinase (CPK) elevation	31	44		
Renal dysfunction	0	0		
Active tuberculosis	0	1		
Adjudicated MACE	0	0		
Adjudicated VTE	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Potentially Clinically Important (PCI)

Laboratory Values as Assessed by the Investigator

End point title	Percentage of Participants With Potentially Clinically Important (PCI) Laboratory Values as Assessed by the Investigator ^[3]
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End point description:

Clinical laboratory test values are considered PCI if they meet either the lower-limit or higher-limit PCI criteria defined in the categories below. Percentage of participants with PCI laboratory values are summarized for hematology and chemistry.

The Number Analyzed is defined as the number of participants with at least one post-baseline value for the specific criteria.

Post-baseline grade must also be more extreme (worse) than the baseline grade in order to be included in the count. If a participant does not have a baseline value then the participant would be counted in the numerator if the participant had at least one post-baseline.

xULN = Times upper limit of the normal range.

Amino = Aminotransferase

End point type	Primary
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End point timeframe:

From Baseline to 30 days following last dose of study drug (Week 52)

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: There will be no statistical testing for all of the efficacy and safety endpoints.

End point values	DUPI 300mg to UPA 30mg	UPA 30mg to UPA 30mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239 ^[4]	236		
Units: Percentage of participants				
number (not applicable)				
Hemoglobin (G/L): Grade 3 (<80)	0	0.8		
Hemoglobin (G/L): Grade 3 or above	0	0.8		
Platelets (10 ⁹ /L): Grade 3 (25-<50)	0	0.4		
Platelets (10 ⁹ /L): Grade 4 (<25)	0	0		
Platelets (10 ⁹ /L): Grade 3 or above	0	0.4		
Leukocytes (10 ⁹ /L): Grade 3 (1.0-<2.0)	0	1.3		
Leukocytes (10 ⁹ /L): Grade 4 (<1.0)	0	0		
Leukocytes (10 ⁹ /L): Grade 3 or above	0	1.3		
Neutrophils (10 ⁹ /L): Grade 3 (0.5-<1.0)	2.5	3.4		
Neutrophils (10 ⁹ /L): Grade 4 (<0.5)	0.4	0.4		
Neutrophils (10 ⁹ /L): Grade 3 or above	2.9	3.8		
Lymphocytes (10 ⁹ /L): Grade 3 (0.2-<0.5)	0.8	3.4		
Lymphocytes (10 ⁹ /L): Grade 4 (<0.2)	0	0		
Lymphocytes (10 ⁹ /L): Grade 3 or above	0.8	3.4		
Alanine Amino (U/L): Grade 3 (>5.0-20.0xULN)	0.4	0.4		
Alanine Amino (U/L): Grade 4 (>20.0xULN)	0	0		
Alanine Amino (U/L): Grade 3 or above	0.4	0.4		
Aspartate Amino (U/L): Grade 3 (>5.0-20.0xULN)	0	1.3		
Aspartate Amino (U/L): Grade 4 (>20.0xULN)	0	0		

Aspartate Amino (U/L): Grade 3 or above	0	1.3		
Alkaline Phosphatase (U/L):Grade 3(>5.0-20.0 xULN)	0	0		
Alkaline Phosphatase (U/L): Grade 4 (>20.0 xULN)	0	0		
Alkaline Phosphatase (U/L): Grade 3 or above	0	0		
Creatine Kinase (U/ L): Grade 3 (>5.0-10.0xULN)	4.2	8.1		
Creatine Kinase (U/L): Grade 4 (>10.0 xULN)	3.8	5.1		
Creatine Kinase (U/L): Grade 3 or above	8.0	13.1		
Creatinine (UMOL/L): (>3.0-6.0 xULN OR >3.0xBL)	0	0.8		
Creatinine (UMOL/L): Grade 4 (>6.0 xULN)	0	0.4		
Creatinine (UMOL/L): Grade 3 or above	0	1.3		
Phosphate (MMOL/L): Grade 3 (0.3-<0.6)	1.7	1.3		
Phosphate (MMOL/L): Grade 4 (<0.3)	0	0		
Phosphate (MMOL/L): Grade 3 or above	1.7	1.3		
Calcium Hyper (MMOL/L): Grade 3 (>3.1-3.4)	0	0.4		
Calcium Hyper (MMOL/L): Grade 4 (>3.4)	0	0		
Calcium Hyper (MMOL/L): Grade 3 or above	0	0.4		
Calcium Hypo (MMOL/L): Grade 3 (1.5-<1.75)	0	0		
Calcium Hypo (MMOL/L): Grade 4 (<1.5)	0	0.4		
Calcium Hypo (MMOL/L): Grade 3 or above	0	0.4		
Sodium Hyper (MMOL/L): Grade 3 (>155-160)	0.5	0		
Sodium Hyper (MMOL/L): Grade 4 (>160)	0	0		
Sodium Hyper (MMOL/L): Grade 3 or above	0.5	0		
Sodium Hypo (MMOL/L): Grade 3 (120-<130)	0	0.4		
Sodium Hypo (MMOL/L): Grade 4 (<120)	0	0		
Sodium Hypo (MMOL/L): Grade 3 or above	0	0.4		
Potassium Hyper (MMOL/L): Grade 3 (>6.0-7.0)	0	0		
Potassium Hyper (MMOL/L): Grade 4 (>7.0)	0	0		
Potassium Hyper (MMOL/L): Grade 3 or above	0	0		
Potassium Hypo (MMOL/L): Grade 3 (2.5-<3.0)	0	0		
Potassium Hypo (MMOL/L): Grade 4 (<2.5)	0	0		
Potassium Hypo (MMOL/L): Grade 3 or above	0	0		
Glucose Hyper (MMOL/L): Grade 3 (>13.9-27.8)	1.3	0.4		

Glucose Hyper (MMOL/L): Grade 4 (>27.8)	0	0		
Glucose Hyper (MMOL/L): Grade 3 or above	1.3	0.4		
Glucose Hypo (MMOL/L): Grade 3 (1.7-<2.2)	0	0		
Glucose Hypo (MMOL/L): Grade 4 (<1.7)	0	0		
Glucose Hypo (MMOL/L): Grade 3 or above	0	0		
Albumin (G/L): Grade 3(<20)	0	0		
Albumin (G/L): Grade 3 or above	0	0		
Cholesterol (MMOL/L): Grade 3 (10.34<-12.92)	1.3	0		
Cholesterol (MMOL/L): Grade 4 (>12.92)	0	0		
Cholesterol (MMOL/L): Grade 3 or above	1.3	0		
Triglycerides (MMOL/L): Grade 3 (>5.7-11.4)	3.4	5.1		
Triglycerides (MMOL/L): Grade 4 (>11.4)	0	0		
Triglycerides (MMOL/L): Grade 3 or above	3.4	5.1		

Notes:

[4] - N=238 for all except Sodium Hyper/Hypo & Potassium Hyper/Hypo are N=212.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Potentially Clinically Important (PCI) Vital Sign Measurements and Physical Examination Findings as Assessed by the Investigator

End point title	Percentage of Participants With Potentially Clinically Important (PCI) Vital Sign Measurements and Physical Examination Findings as Assessed by the Investigator ^[5]
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End point description:

PCI post-baseline vital sign values are summarized for categories: systolic and diastolic blood pressures [sitting], pulse rate [sitting], and weight. Only those categories where at least 1 person had a non-PCI value at Baseline and met the PCI criterion at least once during post-baseline are reported.

The Number Analyzed is defined as the number of participants with at least one post-baseline value for the specific criteria.

Post-baseline grade must also be more extreme (worse) than the baseline grade in order to be included in the count. If a participant does not have a baseline value then the participant would be counted in the numerator if the participant had at least one post-baseline.

BP = Blood Pressure

End point type	Primary
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End point timeframe:

From Baseline to 30 days following last dose of study drug (Week 52)

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: There will be no statistical testing for all of the efficacy and safety endpoints.

End point values	DUPI 300mg to UPA 30mg	UPA 30mg to UPA 30mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239 ^[6]	236		
Units: Percentage of participants				
number (not applicable)				
Sitting Systolic BP (MMHG): ≤90 & ≥20 Decrease	0.4	0.8		
Sitting Systolic BP (MMHG): ≥160 & ≥20 Increase	2.5	5.5		
Sitting Diastolic BP (MMHG): ≤50 & ≥10 Decrease	0.4	1.3		
Sitting Diastolic BP (MMHG): ≥100 & ≥10 Increase	2.1	9.3		
Sitting Pulse Rate (BEATS/MIN): ≤50 & ≥15 Decrease	1.7	4.7		
Sitting Pulse Rate (BEATS/MIN): ≥120 & ≥15 Increase	0	2.1		
Weight (KG): >7% Decrease	5.5	7.6		
Weight (KG): >7% Increase	22.5	39.0		

Notes:

[6] - N=238 for all except Weight is N=236.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality and adverse event tables include events reported from the time of informed consent to the end of the study. The median time on follow-up was 398 and 399 days for UPA/UPA and DUPI/UPA, respectively.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	UPA 30mg to UPA 30mg
Reporting group description: -	
Reporting group title	Total
Reporting group description: -	
Reporting group title	DUPI 300mg to UPA 30mg
Reporting group description: -	

Serious adverse events	UPA 30mg to UPA 30mg	Total	DUPI 300mg to UPA 30mg
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 236 (5.51%)	27 / 475 (5.68%)	14 / 239 (5.86%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	1	1	0
Investigations			
HAEMOGLOBIN DECREASED			
subjects affected / exposed	1 / 236 (0.42%)	1 / 475 (0.21%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
PROSTATE CANCER			
subjects affected / exposed	0 / 236 (0.00%)	1 / 475 (0.21%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE LEIOMYOMA			
subjects affected / exposed	0 / 236 (0.00%)	2 / 475 (0.42%)	2 / 239 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural			

complications			
FOOT FRACTURE			
subjects affected / exposed	0 / 236 (0.00%)	1 / 475 (0.21%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
ESSENTIAL HYPERTENSION			
subjects affected / exposed	1 / 236 (0.42%)	1 / 475 (0.21%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
ABORTION INDUCED			
subjects affected / exposed	1 / 236 (0.42%)	1 / 475 (0.21%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	0 / 236 (0.00%)	1 / 475 (0.21%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
FOOD ALLERGY			
subjects affected / exposed	1 / 236 (0.42%)	1 / 475 (0.21%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
PANCREATITIS			
subjects affected / exposed	1 / 236 (0.42%)	1 / 475 (0.21%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
ADNEXAL TORSION			
subjects affected / exposed	0 / 236 (0.00%)	1 / 475 (0.21%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOMETRIOSIS			

subjects affected / exposed	1 / 236 (0.42%)	1 / 475 (0.21%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS ATOPIC			
subjects affected / exposed	1 / 236 (0.42%)	2 / 475 (0.42%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	1 / 1	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
BULLOUS IMPETIGO			
subjects affected / exposed	1 / 236 (0.42%)	1 / 475 (0.21%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE TUBERCULOSIS			
subjects affected / exposed	1 / 236 (0.42%)	1 / 475 (0.21%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
APPENDICITIS			
subjects affected / exposed	0 / 236 (0.00%)	1 / 475 (0.21%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABSCESS JAW			
subjects affected / exposed	0 / 236 (0.00%)	1 / 475 (0.21%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICHONDritis			
subjects affected / exposed	0 / 236 (0.00%)	1 / 475 (0.21%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 236 (0.00%)	1 / 475 (0.21%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYSIPELAS			

subjects affected / exposed	0 / 236 (0.00%)	1 / 475 (0.21%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ECZEMA HERPETICUM			
subjects affected / exposed	1 / 236 (0.42%)	3 / 475 (0.63%)	2 / 239 (0.84%)
occurrences causally related to treatment / all	1 / 1	3 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 PNEUMONIA			
subjects affected / exposed	3 / 236 (1.27%)	3 / 475 (0.63%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 236 (0.00%)	1 / 475 (0.21%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PILONIDAL DISEASE			
subjects affected / exposed	1 / 236 (0.42%)	1 / 475 (0.21%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 236 (0.00%)	1 / 475 (0.21%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	1 / 236 (0.42%)	1 / 475 (0.21%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	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	UPA 30mg to UPA 30mg	Total	DUPI 300mg to UPA 30mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	154 / 236 (65.25%)	303 / 475 (63.79%)	149 / 239 (62.34%)
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	35 / 236 (14.83%)	66 / 475 (13.89%)	31 / 239 (12.97%)
occurrences (all)	47	89	42
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	14 / 236 (5.93%)	18 / 475 (3.79%)	4 / 239 (1.67%)
occurrences (all)	14	18	4
Nervous system disorders			
HEADACHE			
subjects affected / exposed	15 / 236 (6.36%)	29 / 475 (6.11%)	14 / 239 (5.86%)
occurrences (all)	22	38	16
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	54 / 236 (22.88%)	103 / 475 (21.68%)	49 / 239 (20.50%)
occurrences (all)	65	118	53
DERMATITIS ATOPIC			
subjects affected / exposed	45 / 236 (19.07%)	75 / 475 (15.79%)	30 / 239 (12.55%)
occurrences (all)	61	109	48
ECZEMA			
subjects affected / exposed	14 / 236 (5.93%)	27 / 475 (5.68%)	13 / 239 (5.44%)
occurrences (all)	32	49	17
Infections and infestations			
COVID-19			
subjects affected / exposed	31 / 236 (13.14%)	63 / 475 (13.26%)	32 / 239 (13.39%)
occurrences (all)	34	68	34
HERPES SIMPLEX			
subjects affected / exposed	12 / 236 (5.08%)	20 / 475 (4.21%)	8 / 239 (3.35%)
occurrences (all)	13	23	10
HERPES ZOSTER			
subjects affected / exposed	19 / 236 (8.05%)	44 / 475 (9.26%)	25 / 239 (10.46%)
occurrences (all)	20	45	25
NASOPHARYNGITIS			

subjects affected / exposed occurrences (all)	15 / 236 (6.36%) 23	41 / 475 (8.63%) 58	26 / 239 (10.88%) 35
UPPER RESPIRATORY TRACT INFECTION subjects affected / exposed occurrences (all)	12 / 236 (5.08%) 13	26 / 475 (5.47%) 37	14 / 239 (5.86%) 24
Metabolism and nutrition disorders HYPERCHOLESTEROLAEMIA subjects affected / exposed occurrences (all)	13 / 236 (5.51%) 14	14 / 475 (2.95%) 15	1 / 239 (0.42%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 August 2019	Version 2: Changes included clarifying that the safety endpoints were the primary endpoints for the study, further clarifying adverse reaction and SAE definitions, and clarifying management of study drug and subject treatment for herpes zoster or serious reactivated infection of any herpes virus.
28 January 2020	Version 3: Updated the number of sites and subjects to expand to all countries participating in Study M16-046. Other changes included updating benefits and risks to subjects to reflect updated safety language across the upadacitinib program, updating language for prohibited use of vaccines and strong CYP3A inhibitors or inducers, adding discontinuation criterion around confirmed thrombosis diagnosis and adding safety precautions around risk of thromboembolic events, clarifying language for AESIs, and updating toxicity management language to match updated Investigator's Brochure.
06 March 2020	Version 4: Clarified biomarker sample collection, updated study drug discontinuation criteria for subjects with worsening EASI score, added eczema herpeticum electronic case report form, and clarified the activity schedule to allow flexibility in return visits.
07 January 2021	Version 5: Incorporated necessary protocol modifications due to the COVID-19 pandemic, added an interim analysis, incorporated additional description about management of gastrointestinal perforation and serious herpes zoster, and provided clarification about the timing of efficacy assessments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported