



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 |
|-----------------------|---------|

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 |
|------------------|----------------------|

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 |
|-----------------------|------------------------|

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.

| 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] |
|-----------------|--|

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 |
|----------------|---------|

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] |
|-----------------|---|

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 |
|----------------|---------|

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] |
|-----------------|---|

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 |
|----------------|---------|

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 |
|-----------------|------------|

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 occurrences (all) | 35 / 236 (14.83%) 47 | 66 / 475 (13.89%) 89 | 31 / 239 (12.97%) 42 |
| Vascular disorders HYPERTENSION subjects affected / exposed occurrences (all) | 14 / 236 (5.93%) 14 | 18 / 475 (3.79%) 18 | 4 / 239 (1.67%) 4 |
| Nervous system disorders HEADACHE subjects affected / exposed occurrences (all) | 15 / 236 (6.36%) 22 | 29 / 475 (6.11%) 38 | 14 / 239 (5.86%) 16 |
| Skin and subcutaneous tissue disorders ACNE subjects affected / exposed occurrences (all) DERMATITIS ATOPIC subjects affected / exposed occurrences (all) ECZEMA subjects affected / exposed occurrences (all) | 54 / 236 (22.88%) 65 45 / 236 (19.07%) 61 14 / 236 (5.93%) 32 | 103 / 475 (21.68%) 118 75 / 475 (15.79%) 109 27 / 475 (5.68%) 49 | 49 / 239 (20.50%) 53 30 / 239 (12.55%) 48 13 / 239 (5.44%) 17 |
| Infections and infestations COVID-19 subjects affected / exposed occurrences (all) HERPES SIMPLEX subjects affected / exposed occurrences (all) HERPES ZOSTER subjects affected / exposed occurrences (all) NASOPHARYNGITIS | 31 / 236 (13.14%) 34 12 / 236 (5.08%) 13 19 / 236 (8.05%) 20 | 63 / 475 (13.26%) 68 20 / 475 (4.21%) 23 44 / 475 (9.26%) 45 | 32 / 239 (13.39%) 34 8 / 239 (3.35%) 10 25 / 239 (10.46%) 25 |

| | | | |
|---|------------------------|------------------------|-------------------------|
| 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