# Clinical trial results:
# A Phase 2a, Randomized, Double-Blind, Placebo-Controlled Study Investigating the Safety of Ritlecitinib (PF-06651600) in Adult Participants With Alopecia Areata

## Summary

| | |
|---|---|
| EudraCT number | 2020-001509-21 |
| Trial protocol | PL |
| Global end of trial date | |

### Results information

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 02 November 2022 |
| First version publication date | 02 November 2022 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | B7981037 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04517864 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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 | Interim |
| Date of interim/final analysis | 11 May 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 04 January 2022 |
| Global end of trial reached? | No |

Notes:

## General information about the trial

Main objective of the trial:

This was a Phase 2a, randomized, double-blind, parallel group, placebo-controlled safety study designed to evaluate the safety and tolerability of ritlecitinib, including the assessments of brainstem auditory evoked potential (BAEP) and intraepidermal nerve fiber (IENF), in adults 18 to ≤50 years of age with ≥25% scalp hair loss due to alopecia areata (AA).

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of subjects.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 15 September 2020 |
| 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 | Australia: 2 |
| Country: Number of subjects enrolled | Canada: 8 |
| Country: Number of subjects enrolled | Poland: 36 |
| Country: Number of subjects enrolled | United States: 25 |
| Worldwide total number of subjects | 71 |
| EEA total number of subjects | 36 |

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) | 71 |

| | |
|---|---|
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

A total of 71 subjects were enrolled and randomized to double-blind treatment and treated (36 in the Ritlecitinib 200/50 mg once daily [QD] arm and 35 in the Placebo -> Ritlecitinib 200/50 mg QD arm).

### Pre-assignment

Screening details:

A total of 131 subjects were screened for this study, among whom 71 subjects were randomized to double-blind treatment with 53 screen failures and 7 subjects were not screen failure but not randomized.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Ritlecitinib 200/50 mg QD |

Arm description:

In the 9-month Placebo-Controlled Phase, each subject received ritlecitinib 200 mg QD (50 mg/tablet ×4) during the initial 4-week period, and received 1 tablet of ritlecitinib 50 mg QD during the remainder of this treatment phase.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ritlecitinib |
| Investigational medicinal product code | PF-06651600 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Ritlecitinib 200 mg QD (50 mg/tablet ×4) was received during the initial 4-week period, and 1 tablet of ritlecitinib 50 mg QD was received during the remainder of the Placebo-Controlled Phase.

| | |
|---|---|
| **Arm title** | Placebo -> Ritlecitinib 200/50 mg QD |

Arm description:

In the 9-month Placebo-Controlled Phase, each subject received a total of 4 tablets of placebo QD during the initial 4-week period, and received 1 tablet of placebo QD during the remainder of this treatment phase.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

A total of 4 tablets of Placebo QD were received during the initial 4-week period, and 1 tablet of Placebo QD was received during the remainder of the Placebo-Controlled Phase.

| Number of subjects in period 1 | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD |
|---|---|---|
| Started | 36 | 35 |
| Completed | 32 | 33 |
| Not completed | 4 | 2 |
| Consent withdrawn by subject | 1 | 1 |
| Adverse event, non-fatal | 1 | - |
| Lost to follow-up | 1 | 1 |
| Protocol deviation | 1 | - |

## Period 2

| | |
|---|---|
| Period 2 title | Active Therapy Extension Phase |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Ritlecitinib 200/50 mg QD |

Arm description:

In the 15-month Active Therapy Extension Phase, each subject received 1 tablet of ritlecitinib 50 mg QD and 3 tablets of placebo QD during the initial 4-week period, and then received 1 tablet of Ritlecitinib 50 mg QD during the remainder of this treatment phase.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ritlecitinib |
| Investigational medicinal product code | PF-06651600 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

One tablet of ritlecitinib 50 mg QD and 3 tablets of placebo QD were received during the initial 4-week period, and 1 tablet of ritlecitinib 50 mg QD was received during the remainder of the Active Therapy Extension Phase.

| | |
|---|---|
| **Arm title** | Placebo -> Ritlecitinib 200/50 mg QD |

Arm description:

In the 15-month Active Therapy Extension Phase, each subject received ritlecitinib 200 mg QD (50 mg/tablet ×4) during the initial 4-week period, and then received 1 tablet of ritlecitinib 50 mg QD during the remainder of this treatment phase.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ritlecitinib |
| Investigational medicinal product code | PF-06651600 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Ritlecitinib 200 mg QD (50 mg/tablet ×4) was received during the initial 4-week period, and 1 tablet of ritlecitinib 50 mg QD was received during the remainder of the Active Therapy Extension Phase.

| **Number of subjects in period 2[1]** | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD |
|---|---|---|
| Started | 32 | 31 |
| Completed | 31 | 33 |
| Not completed | 1 | 0 |
| Adverse event, non-fatal | 1 | - |
| Joined | 0 | 2 |
| Not yet entered at the time of the PCD data-cut | - | 2 |

Notes:

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

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Ritlecitinib 200/50 mg QD |
| Reporting group description: | |
| In the 9-month Placebo-Controlled Phase, each subject received ritlecitinib 200 mg QD (50 mg/tablet ×4) during the initial 4-week period, and received 1 tablet of ritlecitinib 50 mg QD during the remainder of this treatment phase. | |
| Reporting group title | Placebo -> Ritlecitinib 200/50 mg QD |
| Reporting group description: | |
| In the 9-month Placebo-Controlled Phase, each subject received a total of 4 tablets of placebo QD during the initial 4-week period, and received 1 tablet of placebo QD during the remainder of this treatment phase. | |

| Reporting group values | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | Total |
|---|---|---|---|
| Number of subjects | 36 | 35 | 71 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 36 | 35 | 71 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 35.1 | 34.2 | |
| standard deviation | ± 9.64 | ± 8.95 | - |
| Sex: Female, Male<br>Units: Subjects | | | |
| Female | 25 | 25 | 50 |
| Male | 11 | 10 | 21 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 3 | 0 | 3 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 7 | 4 | 11 |
| White | 26 | 28 | 54 |
| More than one race | 0 | 2 | 2 |
| Unknown or Not Reported | 0 | 1 | 1 |
| Baseline Percentage of Nerve Fibers With Axonal Swelling<br>Units: Percentage | | | |

| | | | |
|---|---|---|---|
| arithmetic mean | 1.8 | 1.8 | |
| standard deviation | ± 2.48 | ± 2.07 | - |
| Baseline Intraepidermal Nerve Fiber Density (IENFD) | | | |
| Units: /mm | | | |
| arithmetic mean | 10.2 | 11.0 | |
| standard deviation | ± 3.81 | ± 3.95 | - |
| Baseline Severity of Alopecia Tool (SALT) Scores for Non-AT/AU Subjects | | | |
| AT=alopecia totalis; AU=alopecia universalis. | | | |
| Units: Units on a scale | | | |
| arithmetic mean | 59.6 | 53.7 | |
| standard deviation | ± 30.31 | ± 24.18 | - |

## End points

### End points reporting groups

| Reporting group title | Ritlecitinib 200/50 mg QD |
|---|---|
| Reporting group description: | |
| In the 9-month Placebo-Controlled Phase, each subject received ritlecitinib 200 mg QD (50 mg/tablet ×4) during the initial 4-week period, and received 1 tablet of ritlecitinib 50 mg QD during the remainder of this treatment phase. | |
| Reporting group title | Placebo -> Ritlecitinib 200/50 mg QD |
| Reporting group description: | |
| In the 9-month Placebo-Controlled Phase, each subject received a total of 4 tablets of placebo QD during the initial 4-week period, and received 1 tablet of placebo QD during the remainder of this treatment phase. | |
| Reporting group title | Ritlecitinib 200/50 mg QD |
| Reporting group description: | |
| In the 15-month Active Therapy Extension Phase, each subject received 1 tablet of ritlecitinib 50 mg QD and 3 tablets of placebo QD during the initial 4-week period, and then received 1 tablet of Ritlecitinib 50 mg QD during the remainder of this treatment phase. | |
| Reporting group title | Placebo -> Ritlecitinib 200/50 mg QD |
| Reporting group description: | |
| In the 15-month Active Therapy Extension Phase, each subject received ritlecitinib 200 mg QD (50 mg/tablet ×4) during the initial 4-week period, and then received 1 tablet of ritlecitinib 50 mg QD during the remainder of this treatment phase. | |

### Primary: Change From Baseline in I-V Interwave Latency on Brainstem Auditory Evoked Potentials (BAEP) at a Stimulus Intensity of 80 dB From the Right Side at Month 9

| End point title | Change From Baseline in I-V Interwave Latency on Brainstem Auditory Evoked Potentials (BAEP) at a Stimulus Intensity of 80 dB From the Right Side at Month 9 |
|---|---|
| End point description: | |
| BAEP interwave I-V latency was the primary endpoint for this study. High-intensity stimulation (80dB) was used. Subjects had BAEP evaluations performed at the same evaluation center, by the same audiology professional using the same equipment, during the study. Audiology and BAEP evaluations were done on the same day, with audiology assessment first. If they could not be done on the same day, assessments had to be within 7 days of each other. A central reader was used for BAEP to confirm that locally read BAEP waves were labelled appropriately and at their peak so that latency were accurate. Central reading also ensured consistency in BAEP interpretation. Analysis population included all subjects who received at least 1 dose of study intervention. Number of subjects analyzed signifies number of subjects who were evaluable for this endpoint. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline, Month 9 (Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase) | |

| End point values | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 32 | | |
| Units: Millisecond (ms) | | | | |
| least squares mean (confidence interval | | | | |

| | | | | |
|---|---|---|---|---|
| 95%) | | | | |
| Month 9 | 0.011 (-0.043 to 0.065) | -0.010 (-0.063 to 0.043) | | |

### Statistical analyses

| **Statistical analysis title** | LS Mean Difference (Ritlecitinib vs Placebo) |
|---|---|
| Statistical analysis description: | |
| Linear mixed-effects model with baseline, treatment group, visit (Month 6 and Month 9) and treatment group by visit interaction as fixed effects, and subject as a random effect with an unstructured covariance matrix assumption was used. | |
| Comparison groups | Ritlecitinib 200/50 mg QD v Placebo -> Ritlecitinib 200/50 mg QD |
| Number of subjects included in analysis | 63 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | 0.021 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.056 |
| upper limit | 0.097 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0382 |

## Primary: Change From Baseline in I-V Interwave Latency on BAEP at a Stimulus Intensity of 80 dB From the Left Side at Month 9

| End point title | Change From Baseline in I-V Interwave Latency on BAEP at a Stimulus Intensity of 80 dB From the Left Side at Month 9 |
|---|---|
| End point description: | |
| BAEP interwave I-V latency was the primary endpoint for this study. High-intensity stimulation (80dB) was used. Subjects had BAEP evaluations performed at the same evaluation center, by the same audiology professional using the same equipment, during the study. Audiology and BAEP evaluations were done on the same day, with audiology assessment first. If they could not be done on the same day, assessments had to be within 7 days of each other. A central reader was used for BAEP to confirm that locally read BAEP waves were labelled appropriately and at their peak so that latency were accurate. Central reading also ensured consistency in BAEP interpretation. Analysis population included all subjects who received at least 1 dose of study intervention. Number of subjects analyzed signifies number of subjects who were evaluable for this endpoint. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline, Month 9 (Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase) | |

| End point values | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 32 | | |
| Units: ms | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Month 9 | 0.031 (-0.012 to 0.075) | 0.022 (-0.020 to 0.065) | | |

**Statistical analyses**

| Statistical analysis title | LS Mean Difference (Ritlecitinib vs Placebo) |
|---|---|

Statistical analysis description:

Linear mixed-effects model with baseline, treatment group, visit (Month 6 and Month 9) and treatment group by visit interaction as fixed effects, and subject as a random effect with an unstructured covariance matrix assumption was used.

| | |
|---|---|
| Comparison groups | Ritlecitinib 200/50 mg QD v Placebo -> Ritlecitinib 200/50 mg QD |
| Number of subjects included in analysis | 63 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | 0.009 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.052 |
| upper limit | 0.07 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0307 |

**Secondary: Change From Baseline in I-V Interwave Latency on BAEP at 80 dB from the Right Side at Month 6**

| End point title | Change From Baseline in I-V Interwave Latency on BAEP at 80 dB from the Right Side at Month 6 |
|---|---|

End point description:

High-intensity stimulation (80dB) was used. Subjects had BAEP evaluations performed at the same evaluation center, by the same audiology professional using the same equipment, during the study. Audiology and BAEP evaluations were done on the same day, with audiology assessment first. If they could not be done on the same day, assessments had to be within 7 days of each other. A central reader was used for BAEP to confirm that locally read BAEP waves were labelled appropriately and at their peak so that latency were accurate. Central reading also ensured consistency in BAEP interpretation. Analysis population included all subjects who received at least 1 dose of study intervention. Number of subjects analyzed signifies number of subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Month 6 (Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase)

| End point values | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 34 | 34 | | |
| Units: ms | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Month 6 | -0.030 (-0.072 to 0.011) | -0.024 (-0.065 to 0.017) | | |

### Statistical analyses

| Statistical analysis title | LS Mean Difference (Ritlecitinib vs Placebo) |
|---|---|

Statistical analysis description:

Linear mixed-effects model with baseline, treatment group, visit (Month 6 and Month 9) and treatment group by visit interaction as fixed effects, and subject as a random effect with an unstructured covariance matrix assumption was used.

| | |
|---|---|
| Comparison groups | Ritlecitinib 200/50 mg QD v Placebo -> Ritlecitinib 200/50 mg QD |
| Number of subjects included in analysis | 68 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.006 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.065 |
| upper limit | 0.053 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0297 |

### Secondary: Change From Baseline in I-V Interwave Latency on BAEP at 80 dB from the Left Side at Month 6

| End point title | Change From Baseline in I-V Interwave Latency on BAEP at 80 dB from the Left Side at Month 6 |
|---|---|

End point description:

High-intensity stimulation (80dB) was used. Subjects had BAEP evaluations performed at the same evaluation center, by the same audiology professional using the same equipment, during the study. Audiology and BAEP evaluations were done on the same day, with audiology assessment first. If they could not be done on the same day, assessments had to be within 7 days of each other. A central reader was used for BAEP to confirm that locally read BAEP waves were labelled appropriately and at their peak so that latency were accurate. Central reading also ensured consistency in BAEP interpretation. Analysis population included all subjects who received at least 1 dose of study intervention. Number of subjects analyzed signifies number of subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Month 6 (Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase)

| **End point values** | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 34 | 34 | | |
| Units: ms | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Month 6 | 0.021 (-0.011 to 0.054) | -0.020 (-0.053 to 0.012) | | |

**Statistical analyses**

| **Statistical analysis title** | LS Mean Difference (Ritlecitinib vs Placebo) |
|---|---|

Statistical analysis description:

Linear mixed-effects model with baseline, treatment group, visit (Month 6 and Month 9) and treatment group by visit interaction as fixed effects, and participant as a random effect with an unstructured covariance matrix assumption was used.

| Comparison groups | Ritlecitinib 200/50 mg QD v Placebo -> Ritlecitinib 200/50 mg QD |
|---|---|
| Number of subjects included in analysis | 68 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | 0.042 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.005 |
| upper limit | 0.088 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0235 |

**Secondary: Change From Baseline in Percentage of Intra-epidermal Nerve Fiber (IENF) With Axonal Swelling in Skin Punch Biopsies at Month 9**

| End point title | Change From Baseline in Percentage of Intra-epidermal Nerve Fiber (IENF) With Axonal Swelling in Skin Punch Biopsies at Month 9 |
|---|---|

End point description:

The endpoint “axonal dystrophy” referred to the percentage of IENF with axonal swellings. Axonal swellings were evaluated in peripheral skin punch biopsies from the distal part of lower extremities. Axonal swellings were counted by axon. Any IENF with single or multiple swellings was counted as a

single event, ie, a single axon with axonal swellings. For each subject, data were reported as the percentage of IENF with any number of swellings. IENF was assessed at Day 1 and Month 9. Subjects who had entered the Active Therapy Extension Phase at Month 6 had a skin punch biopsy taken at Month 6 for IENF assessments instead of at Month 9. The skin biopsy must have been collected before the start of Active Therapy Extension Phase. Analysis population included all subjects who received at least 1 dose of study intervention. Number of subjects analyzed signifies number of subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Month 9 (Month 6 for the 2 subjects who entered the Active Therapy Extension Phase at Month 6). Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase.

| **End point values** | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 33 | | |
| Units: Percentage of Nerve Fibers | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| End of Placebo-controlled Phase (EOP) | 0.0 (-0.5 to 2.5) | 0.0 (-2.0 to 1.0) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Intraepidermal Nerve Fiber Density (IENFD) in Skin Punch Biopsies at Month 9

| End point title | Change From Baseline in Intraepidermal Nerve Fiber Density (IENFD) in Skin Punch Biopsies at Month 9 |
|---|---|

End point description:

IENFD was evaluated in peripheral skin punch biopsies from the distal part of lower extremities. IENFD was measured by counting the number of fibers and fiber branches that independently crossed the dermal-epidermal barrier (basement membrane). Secondary branching was excluded from quantification and fragments were not counted. The length of the histology section was measured (mm) and the linear epidermal nerve fiber density was reported as number of intraepidermal nerve fibers/mm. Analysis population included all subjects who received at least 1 dose of study intervention. Number of subjects analyzed signifies number of subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Month 9 (Month 6 for the 2 subjects who entered the Active Therapy Extension Phase at Month 6). Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase.

| End point values | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 33 | | |
| Units: fibers/mm | | | | |
| arithmetic mean (standard deviation) | | | | |
| End of Placebo-controlled Phase (EOP) | -0.4 (± 3.90) | -0.2 (± 2.72) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Amplitude of Wave V on BAEP at a Stimulus Intensity of 80 dB From the Right Side at Month 6 and Month 9

| End point title | Change From Baseline in Amplitude of Wave V on BAEP at a Stimulus Intensity of 80 dB From the Right Side at Month 6 and Month 9 |
|---|---|

End point description:

High-intensity stimulation (80dB) was used. Subjects had BAEP evaluations performed at the same evaluation center, by the same audiology professional using the same equipment, during the study. Audiology and BAEP evaluations were done on the same day, with audiology assessment first. If they could not be done on the same day, assessments had to be within 7 days of each other. A central reader was used for BAEP to confirm that locally read BAEP waves were labelled appropriately and at their peak so that amplitude data were accurate. Central reading also ensured consistency in BAEP interpretation. Analysis population included all subjects who received at least 1 dose of study intervention. Number of subjects analyzed signifies number of subjects who were evaluable for this endpoint. n = x, y in the following table represents the number of evaluable subjects in the Ritlecitinib 200/50 mg QD and Placebo arms, respectively.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Month 6 and Month 9 (Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase)

| End point values | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 34 | 34 | | |
| Units: Microvolts (µV) | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Month 6 (n = 34, 34) | -0.031 (-0.063 to 0) | -0.017 (-0.048 to 0.015) | | |
| Month 9 (n = 31, 32) | -0.051 (-0.085 to -0.018) | 0.008 (-0.025 to 0.041) | | |

## Statistical analyses

| Statistical analysis title | LS Mean Difference (Ritlecitinib vs Placebo) |
|---|---|
| Statistical analysis description: | |
| Month 9 | |
| Comparison groups | Ritlecitinib 200/50 mg QD v Placebo -> Ritlecitinib 200/50 mg QD |
| Number of subjects included in analysis | 68 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[1] |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.107 |
| upper limit | -0.012 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0236 |

Notes:

[1] - Linear mixed-effects model with baseline, treatment group, visit (Month 6 and Month 9) and treatment group by visit interaction as fixed effects, and subject as a random effect with an unstructured covariance matrix assumption was used.

| Statistical analysis title | LS Mean Difference (Ritlecitinib vs Placebo) |
|---|---|
| Statistical analysis description: | |
| Month 6 | |
| Comparison groups | Ritlecitinib 200/50 mg QD v Placebo -> Ritlecitinib 200/50 mg QD |
| Number of subjects included in analysis | 68 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[2] |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.015 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.059 |
| upper limit | 0.03 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0224 |

Notes:

[2] - Linear mixed-effects model with baseline, treatment group, visit (Month 6 and Month 9) and treatment group by visit interaction as fixed effects, and subject as a random effect with an unstructured covariance matrix assumption was used.

## Secondary: Change From Baseline in Amplitude of Wave V on BAEP at a Stimulus Intensity of 80 dB From the Left Side at Month 6 and Month 9

| End point title | Change From Baseline in Amplitude of Wave V on BAEP at a Stimulus Intensity of 80 dB From the Left Side at Month 6 and Month 9 |
|---|---|

End point description:

High-intensity stimulation (80dB) was used. Subjects had BAEP evaluations performed at the same evaluation center, by the same audiology professional using the same equipment, during the study. Audiology and BAEP evaluations were done on the same day, with audiology assessment first. If they

could not be done on the same day, assessments had to be within 7 days of each other. A central reader was used for BAEP to confirm that locally read BAEP waves were labelled appropriately and at their peak so that amplitude data were accurate. Central reading also ensured consistency in BAEP interpretation. Analysis population included all subjects who received at least 1 dose of study intervention. Number of subjects analyzed signifies number of subjects who were evaluable for this endpoint. n = x, y in the following table represents the number of evaluable subjects in the Ritlecitinib 200/50 mg QD and Placebo arms, respectively.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Month 6 and Month 9 (Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase)

| **End point values** | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 34 | 34 | | |
| Units: Microvolts (µV) | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Month 6 (n = 34, 34) | -0.047 (-0.082 to -0.013) | -0.019 (-0.053 to 0.015) | | |
| Month 9 (n = 31, 32) | -0.045 (-0.082 to -0.008) | -0.049 (-0.085 to -0.012) | | |

**Statistical analyses**

| **Statistical analysis title** | LS Mean Difference (Ritlecitinib vs Placebo) |
|---|---|

Statistical analysis description:

Month 9

| Comparison groups | Ritlecitinib 200/50 mg QD v Placebo -> Ritlecitinib 200/50 mg QD |
|---|---|
| Number of subjects included in analysis | 68 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | 0.003 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.049 |
| upper limit | 0.056 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0261 |

| **Statistical analysis title** | LS Mean Difference (Ritlecitinib vs Placebo) |
|---|---|

| | |
|---|---|
| Statistical analysis description:<br>Month 6 | |
| Comparison groups | Ritlecitinib 200/50 mg QD v Placebo -> Ritlecitinib 200/50 mg QD |
| Number of subjects included in analysis | 68 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.028 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.076 |
| upper limit | 0.02 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0242 |

## Secondary: Number of Subjects With Absence of Wave V on BAEP at Stimulus Intensities Ranging From 80 dB to 40 dB From Right Side up to Month 9

| | |
|---|---|
| End point title | Number of Subjects With Absence of Wave V on BAEP at Stimulus Intensities Ranging From 80 dB to 40 dB From Right Side up to Month 9 |

End point description:

Absence of wave V on BAEP at stimulus intensities ranging from 80dB to 40dB were summarized descriptively using number of subjects by treatment group at each intensity level. Analysis population included all subjects who received at least 1 dose of study intervention. Number of subjects analyzed signifies number of subjects who were evaluable for this endpoint. n = x, y in the following table represents the number of subjects at each visit in the Ritlecitinib 200/50 mg QD and Placebo arms, respectively.
One subject had fluctuating absence of Wave V at lower intensities. Hearing sensitivity remained normal from screening through Month 9. The case was reviewed by a panel of neuroaudiology experts who concluded that there was no evidence of neural transmission abnormality in the auditory nerve or auditory brainstem and that the likely explanation for the absence of Wave V was that the evoked response amplitude was too small for it to be identified within the electroencephalogram (EEG).

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline, Month 6 and Month 9

| **End point values** | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 36 | 35 | | |
| Units: Subjects | | | | |
| Baseline-80dB normal hearing level (nHL) (n=36,35) | 0 | 0 | | |
| Baseline - 70 dB nHL (n = 36, 35) | 0 | 0 | | |
| Baseline - 60 dB nHL (n = 36, 35) | 0 | 0 | | |
| Baseline - 50 dB nHL (n = 36, 35) | 0 | 0 | | |
| Baseline - 40 dB nHL (n = 36, 35) | 0 | 0 | | |

| | | | | |
|---|---|---|---|---|
| Month 6 - 80 dB nHL (n = 34, 34) | 0 | 0 | | |
| Month 6 - 70 dB nHL (n = 34, 34) | 0 | 0 | | |
| Month 6 - 60 dB nHL (n = 34, 34) | 0 | 0 | | |
| Month 6 - 50 dB nHL (n = 34, 34) | 0 | 0 | | |
| Month 6 - 40 dB nHL (n = 34, 34) | 0 | 0 | | |
| Month 9 - 80 dB nHL (n = 31, 32) | 0 | 0 | | |
| Month 9 - 70 dB nHL (n = 31, 32) | 0 | 0 | | |
| Month 9 - 60 dB nHL (n = 31, 32) | 0 | 0 | | |
| Month 9 - 50 dB nHL (n = 31, 32) | 0 | 0 | | |
| Month 9 - 40 dB nHL (n = 31, 32) | 1 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Absence of Wave V on BAEP at Stimulus Intensities Ranging From 80 dB to 40 dB From Left Side up to Month 9

| End point title | Number of Subjects With Absence of Wave V on BAEP at Stimulus Intensities Ranging From 80 dB to 40 dB From Left Side up to Month 9 |
|---|---|

End point description:

Absence of wave V on BAEP at stimulus intensities ranging from 80dB to 40dB were summarized descriptively using number of subjects by treatment group at each intensity level. Analysis population included all subjects who received at least 1 dose of study intervention. Number of subjects analyzed signifies number of subjects who were evaluable for this endpoint. n = x, y in the following table represents the number of evaluable subjects in the Ritlecitinib 200/50 mg QD and Placebo arms, respectively.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Month 6 and Month 9

| End point values | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 36 | 35 | | |
| Units: Subjects | | | | |
| Baseline - 80 dB nHL (n = 36, 35) | 0 | 0 | | |
| Baseline - 70 dB nHL (n = 36, 35) | 0 | 0 | | |
| Baseline - 60 dB nHL (n = 36, 35) | 0 | 0 | | |
| Baseline - 50 dB nHL (n = 36, 35) | 0 | 0 | | |
| Baseline - 40 dB nHL (n = 36, 35) | 0 | 0 | | |
| Month 6 - 80 dB nHL (n = 34, 34) | 0 | 0 | | |
| Month 6 - 70 dB nHL (n = 34, 34) | 0 | 0 | | |
| Month 6 - 60 dB nHL (n = 34, 34) | 0 | 0 | | |
| Month 6 - 50 dB nHL (n = 34, 34) | 0 | 0 | | |
| Month 6 - 40 dB nHL (n = 34, 34) | 0 | 0 | | |
| Month 9 - 80 dB nHL (n = 31, 32) | 0 | 0 | | |
| Month 9 - 70 dB nHL (n = 31, 32) | 0 | 0 | | |

| | | | | |
|---|---|---|---|---|
| Month 9 - 60 dB nHL (n = 31, 32) | 0 | 0 | | |
| Month 9 - 50 dB nHL (n = 31, 32) | 0 | 0 | | |
| Month 9 - 40 dB nHL (n = 31, 32) | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse events (TESAEs)

| End point title | Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse events (TESAEs) |
|---|---|

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Seriousness of an AE was assessed under the criteria of serious adverse event (SAE). An SAE was defined as any untoward medical occurrence that, at any dose: resulted in death; was life-threatening; required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent disability/incapacity; was a congenital anomaly/birth defect, etc. Treatment-emergent events were with onset date occurring during the on-treatment period. Relatedness to study treatment was determined by the investigator. Analysis population included all subjects taking at least 1 dose of study intervention.

| End point type | Secondary |
|---|---|

End point timeframe:

24 months

| End point values | Ritlecitinib 200/50 mg QD | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 36 | 32 | 35 | 31 |
| Units: Subjects | | | | |
| TEAE (All-Causality) | 29 | 3 | 22 | 3 |
| TEAE (Treatment-Related) | 9 | 0 | 5 | 1 |
| TESAE (All-Causality) | 0 | 1 | 1 | 0 |
| TESAE (Treatment-Related) | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects Who Discontinued From Study Due to Adverse Event (AEs)

| End point title | Number of Subjects Who Discontinued From Study Due to Adverse Event (AEs) |
|---|---|

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Subjects who had an AE

record that indicated that the AE caused the subject to be discontinued from the study. Relatedness to study treatment was determined by the investigator. Analysis population included all subjects taking at least 1 dose of study intervention.

| End point type | Secondary |
|---|---|

End point timeframe:

24 months

| **End point values** | Ritlecitinib 200/50 mg QD | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 36 | 32 | 35 | 31 |
| Units: Subjects | | | | |
| Due to All-Causality AEs | 0 | 1 | 0 | 0 |
| Due to Treatment-Related AEs | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects Who Discontinued Study Drug Due to AE and Continued Study

| End point title | Number of Subjects Who Discontinued Study Drug Due to AE and Continued Study |
|---|---|

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study intervention, whether or not considered related to the study intervention. This Outcome Measures presented the number of subjects who had an AE record that indicated that action taken with study treatment was drug withdrawn but AE did not cause the subject to be discontinued from study. Relatedness to study treatment was determined by the investigator. Analysis population included all subjects taking at least 1 dose of study intervention.

| End point type | Secondary |
|---|---|

End point timeframe:

24 months

| **End point values** | Ritlecitinib 200/50 mg QD | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 36 | 32 | 35 | 31 |
| Units: Subjects | | | | |
| Due to All-Causality AEs | 1 | 0 | 0 | 0 |
| Due to Treatment-Related AEs | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Temporary Drug Discontinuation Due to AEs

| End point title | Number of Subjects With Temporary Drug Discontinuation Due to AEs |
|---|---|

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The number of subjects with temporary drug discontinuation due to both all-causality and treatment-related AEs are presented below. Relatedness to study treatment was determined by the investigator. Analysis population included all subjects taking at least 1 dose of study intervention.

| End point type | Secondary |
|---|---|

End point timeframe:

24 months

| End point values | Ritlecitinib 200/50 mg QD | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 36 | 32 | 35 | 31 |
| Units: Subjects | | | | |
| Due to All-Causality AEs | 6 | 0 | 1 | 0 |
| Due to Treatment-Related AEs | 3 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Clinically Significant Abnormalities in Vital Signs

| End point title | Number of Subjects With Clinically Significant Abnormalities in Vital Signs |
|---|---|

End point description:

Oral, tympanic, or axillary temperature, pulse rate, respiratory rate, and blood pressure (BP) were assessed. BP and pulse measurements were assessed in a chair, back supported and arms bared (free of restrictions such as rolled-up sleeves, etc) and supported at heart level. Measurements were taken on the same arm at each visit (preferably non-dominant) with a completely automated device. Pulse rate was measured at approximately the same time as BP for a minimum of 30 seconds. BP and pulse measurements should be preceded by at least 5 minutes of rest for the subject in a quiet setting without distractions (eg, television, cell phones). Subjects refrained from smoking or ingesting caffeine during the 30 minutes preceding the measurements. The clinical significance was determined by the investigator. Analysis population included all subjects taking at least 1 dose of study intervention.

| End point type | Secondary |
|---|---|

End point timeframe:

24 months

| End point values | Ritlecitinib 200/50 mg QD | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 36 | 32 | 35 | 31 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Clinically Significant Abnormalities in Clinical Laboratory Values

| End point title | Number of Subjects With Clinically Significant Abnormalities in Clinical Laboratory Values |
|---|---|

End point description:

Safety laboratory assessments included the categories of Hematology, Chemistry, Urinalysis and other tests. The clinical significance was determined by the investigator. Analysis population included all subjects taking at least 1 dose of study intervention.

| End point type | Secondary |
|---|---|

End point timeframe:

24 months

| End point values | Ritlecitinib 200/50 mg QD | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 36 | 32 | 35 | 31 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Overall Severity of Alopecia Tool (SALT) Scores up to Month 9

| End point title | Change From Baseline in Overall Severity of Alopecia Tool (SALT) Scores up to Month 9 |
|---|---|

End point description:

SALT is a quantitative assessment of AA severity based on scalp terminal hair loss. The overall SALT score included hair loss regardless of etiology (ie, scalp hair loss due to both non-AA and AA) and was collected at study visits. The Overall SALT Score ranged from 0 to 100%, with higher scores representing greater amount of hair loss. Analysis population included all randomized subjects taking at least 1 dose of study intervention. Number of subjects analyzed signifies number of subjects who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Months 3, 6 and 9 (Baseline was defined as the last non-missing measurement obtained

before the first dose in the placebo-controlled phase)

| **End point values** | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 35 | 35 | | |
| Units: Units on a scale | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Month 3 | -23.0 (-29.70 to -16.25) | -2.7 (-9.39 to 4.06) | | |
| Month 6 | -35.2 (-44.55 to -25.81) | -5.1 (-14.44 to 4.18) | | |
| Month 9 | -38.2 (-47.46 to -28.86) | -6.8 (-16.08 to 2.40) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Alopecia Areata - Severity of Alopecia Tool (AA-SALT) Score up to Month 9

| End point title | Change From Baseline in Alopecia Areata - Severity of Alopecia Tool (AA-SALT) Score up to Month 9 |
|---|---|

End point description:

SALT is a quantitative assessment of AA severity based on scalp terminal hair loss. AA-SALT is amount of scalp hair loss due to AA. AA-SALT score in Placebo-Controlled Phase = overall SALT score – non-AA SALT score at Month 6 (for those subjects who entered Active Therapy Extension Phase at Month 6) or Month 9 (non-AA SALT: scalp hair loss other than that due to AA). AA-SALT Score ranged from 0 to 100%, with higher scores representing greater amount of hair loss. Analysis population included all randomized subjects taking at least 1 dose of study intervention. Number of subjects analyzed signifies number of subjects who were evaluable for this endpoint. n = x, y below represents the number of evaluable subjects in Ritlecitinib 200/50 mg and Placebo arms, respectively.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Months 3, 6 and 9 (Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase)

| **End point values** | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 35 | 35 | | |
| Units: Units on a scale | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Month 3 (n = 35, 35) | -23.0 (-29.70 to -16.25) | -2.7 (-9.39 to 4.06) | | |

| | | | | |
|---|---|---|---|---|
| Month 6 (n = 34, 35) | -35.2 (-44.55 to -25.81) | -5.1 (-14.44 to 4.18) | | |
| Month 9 (n = 32, 31) | -38.2 (-47.46 to -28.87) | -6.8 (-16.08 to 2.40) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Patient's Global Impression of Change (PGI-C) Response up to Month 9

| End point title | Number of Subjects With Patient's Global Impression of Change (PGI-C) Response up to Month 9 |
|---|---|

End point description:

The PGI-C asked the subjects to evaluate the improvement or worsening of their AA as compared to the start of the study using a single item, “Since the start of the study, my alopecia areata has: …”. The subjects selected one of seven responses ranging from "greatly improved" to "greatly worsened". This Outcome Measure presented the number of subjects with PGI-C response which was defined as "greatly improved" or "moderately improved". Subjects with missing PGI-C scores were considered as non-responders. Analysis population included all randomized subjects taking at least 1 dose of study intervention.

| End point type | Secondary |
|---|---|

End point timeframe:

Months 1, 3, 6 and 9

| End point values | Ritlecitinib 200/50 mg QD | Placebo -> Ritlecitinib 200/50 mg QD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 36 | 35 | | |
| Units: Subjects | | | | |
| Month 1 | 4 | 3 | | |
| Month 3 | 20 | 6 | | |
| Month 6 | 21 | 10 | | |
| Month 9 | 19 | 6 | | |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

24 months

Adverse event reporting additional description:

Same event may appear as both an AE and a serious AE (SAE). However, what is presented are distinct events. An event may be categorized as serious in 1 subject and as non-serious in another subject, or 1 subject may have experienced both serious and non-serious event during the study.

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Placebo -> Ritlecitinib 200/50 mg QD |

Reporting group description:

In the 9-month Placebo-Controlled Phase, each subject received a total of 4 tablets of Placebo QD during the initial 4-week period, and received 1 tablet of Placebo QD during the remainder of that study phase. In the 15-month Active Therapy Extension Phase, each subject received Ritlecitinib 200 mg QD (50 mg/tablet ×4) during the initial 4-week period, and then received 1 tablet of Ritlecitinib 50 mg QD during the remainder of this phase.

| | |
|---|---|
| Reporting group title | Ritlecitinib 200/50 mg QD |

Reporting group description:

In the 9-month Placebo-Controlled Phase, each subject received Ritlecitinib 200 mg QD (50 mg/tablet ×4) during the initial 4-week period, and received 1 tablet of Ritlecitinib 50 mg QD during the remainder of that study phase. In the 15-month Active Therapy Extension Phase, each subject received 1 tablet QD of Ritlecitinib 50 mg and 3 tablets of placebo QD during the initial 4-week period, and then received 1 tablet of Ritlecitinib 50 mg QD during the remainder of this phase.

| **Serious adverse events** | Placebo -> Ritlecitinib 200/50 mg QD | Ritlecitinib 200/50 mg QD | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | 1 / 36 (2.78%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | 0 / 36 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Takayasu's arteritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 35 (0.00%) | 1 / 36 (2.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Placebo -> Ritlecitinib 200/50 mg QD | Ritlecitinib 200/50 mg QD | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 23 / 35 (65.71%) | 29 / 36 (80.56%) | |
| Investigations | | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | 2 / 36 (5.56%) | |
| occurrences (all) | 0 | 2 | |
| Injury, poisoning and procedural complications | | | |
| Limb injury | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | 0 / 36 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | 3 / 36 (8.33%) | |
| occurrences (all) | 1 | 3 | |
| Headache | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | 4 / 36 (11.11%) | |
| occurrences (all) | 1 | 5 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 3 / 35 (8.57%) | 1 / 36 (2.78%) | |
| occurrences (all) | 4 | 1 | |
| Blood and lymphatic system disorders | | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | 0 / 36 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Ear and labyrinth disorders | | | |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | 2 / 36 (5.56%) | |
| occurrences (all) | 0 | 2 | |

| | | | |
|---|---|---|---|
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | 3 / 36 (8.33%) | |
| occurrences (all) | 0 | 4 | |
| Nausea | | | |
| subjects affected / exposed | 3 / 35 (8.57%) | 1 / 36 (2.78%) | |
| occurrences (all) | 4 | 1 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | 3 / 36 (8.33%) | |
| occurrences (all) | 1 | 3 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | 2 / 36 (5.56%) | |
| occurrences (all) | 0 | 2 | |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | 2 / 36 (5.56%) | |
| occurrences (all) | 2 | 2 | |
| Pruritus | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | 0 / 36 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | 2 / 36 (5.56%) | |
| occurrences (all) | 0 | 2 | |
| Infections and infestations | | | |
| Acne pustular | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | 4 / 36 (11.11%) | |
| occurrences (all) | 0 | 5 | |
| COVID-19 | | | |
| subjects affected / exposed | 3 / 35 (8.57%) | 3 / 36 (8.33%) | |
| occurrences (all) | 3 | 3 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | 3 / 36 (8.33%) | |
| occurrences (all) | 3 | 4 | |
| Tonsillitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 35 (0.00%) | 2 / 36 (5.56%) | |
| occurrences (all) | 0 | 2 | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | 2 / 36 (5.56%) | |
| occurrences (all) | 1 | 2 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | 3 / 36 (8.33%) | |
| occurrences (all) | 1 | 3 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 35 (8.57%) | 0 / 36 (0.00%) | |
| occurrences (all) | 4 | 0 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 20 April 2021 | Updated Schedule of Activities and Section 4.1 Study Design; revised Inclusion and Exclusion Criteria; Section 6.2.1 Preparation and Dispensing was updated to add that at the EOP visit; updated Section 6.5.3 Vaccinations, Section 8.2.6 Audiological Evaluations, Section 8.2.7 Brainstem Auditory Evoked Potential Evaluations, Section 8.2.10.1.3 Subsequent Tuberculosis Testing, Section 8.2.11.1. Columbia Suicide Severity Rating Scale (C-SSRS); Section 8.2.9.2.2 Canfield Rash Manual was updated to Canfield Photography User Manual; In Section 8.2.14 The name of the 'Rater Qualifications Manual' was updated to 'Rater Assessment Manual'; Section 8.3.6 Cardiovascular and Death Events, was updated to reflect the adjudication process; Section 8.3.8 Adverse Events of Special Interest, was updated to add a reference to the section with the definition and the reporting process; deleted Section 8.10 Health Economics; updated Appendix 4, 6, 7, 9. |
| 28 April 2022 | In order to allow study subjects continued access to study intervention with collection of additional long-term safety and efficacy data, study duration was extended up to 60 months (or until availability of commercial product in the country or until the sponsor terminates the study in that country). The endpoints were updated as a result of the study extension. Added ECG analysis under safety endpoints at TP1 and TP2 phases only. Added detail on permanent discontinuation and defined the Observation Period. Update was made in alignment with Investigator Brochure version 8.0 December 2021, and also to clarify the safety of PF-06651600.<br>Update was made to clarify the safety of PF-06651600. Mean Clinical AUC and Calculated Safety Margin updated. Added additional clarifications on the contraception check. Updated the blinding approach in the study. Updated the amount of blood to be collected from each subject. Clarified when an interim analysis may be needed. Updated language regarding events requiring submission to an adjudication/review committee, and text regarding confirmation of post-menopausal status during the study. Updated hemoglobin values requiring re-testing in Table 3. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study is still ongoing. This report reflects data collected up to PCD (04 January 2022), and will be updated after completion of the whole study.

Notes: