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	v2
This version publication date	01 May 2024
First version publication date	02 November 2022
Version creation reason	

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	13 September 2023
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

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
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 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	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	Ritlecitinib 50 mg QD	Ritlecitinib 200/50 mg QD
Started	32	33
Completed	1	0
Not completed	31	33
Physician decision	1	-
Consent withdrawn by subject	8	8
Remained Ongoing in Active Therapy Extension Phase	20	24
Adverse event, non-fatal	1	-
Lost to follow-up	-	1
Lack of efficacy	1	-

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
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	Total
Number of subjects	36	35	71
Age categorical Units: Subjects			
Adults (18-64 years)	36	35	71
Age Continuous Units: years			
arithmetic mean	35.1	34.2	
standard deviation	± 9.64	± 8.95	-
Sex: Female, Male Units: Subjects			
Female	25	25	50
Male	11	10	21
Race (NIH/OMB) Units: Subjects			
Asian	3	0	3
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 Units: Percentage of Nerve Fibers			
arithmetic mean	1.8	1.8	
standard deviation	± 2.48	± 2.07	-
Baseline Severity of Alopecia Tool (SALT) Scores for Non-AT/AU Subjects			
Baseline SALT score for non-alopecia totalis (AT)/alopecia universalis (AU) subjects: SALT was a quantitative assessment of alopecia severity based on scalp terminal hair loss performed by an experienced and qualified rater. Score parameters utilized a visual aid showing the division of the scalp hair into 4 quadrants (back, top of scalp, and both sides), with each of 4 quadrants given an accurate determination of the % of scalp surface area covered, representing 24%, 40%, 18%, and 18% of the total scalp surface area, respectively. Higher SALT score represents greater amount of hair loss.			
Units: Units on a scale			
arithmetic mean	59.6	53.7	
standard deviation	± 30.31	± 24.18	-
Baseline Intraepidermal Nerve Fiber Density (IENFD)			

Units: fibers/mm			
arithmetic mean	10.2	11.0	
standard deviation	± 3.81	± 3.95	-

Subject analysis sets

Subject analysis set title	Ritlecitinib 200/50/50 mg QD
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in 2 treatment periods:
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. 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.

Subject analysis set title	Placebo -> Ritlecitinib 200/50 mg QD
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in 2 treatment periods:
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. 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.

Reporting group values	Ritlecitinib 200/50/50 mg QD	Placebo -> Ritlecitinib 200/50 mg QD	
Number of subjects	36	35	
Age categorical Units: Subjects			
Adults (18-64 years)	36	35	
Age Continuous Units: years			
arithmetic mean	35.1	34.2	
standard deviation	± 9.64	± 8.95	
Sex: Female, Male Units: Subjects			
Female	25	25	
Male	11	10	
Race (NIH/OMB) Units: Subjects			
Asian	3	0	
Black or African American	7	4	
White	26	28	
More than one race	0	2	
Unknown or Not Reported	0	1	
Baseline Percentage of Nerve Fibers With Axonal Swelling Units: Percentage of Nerve Fibers			
arithmetic mean	1.8	1.8	
standard deviation	± 2.48	± 2.07	
Baseline Severity of Alopecia Tool (SALT) Scores for Non-AT/AU Subjects			
Baseline SALT score for non-alopecia totalis (AT)/alopecia universalis (AU) subjects: SALT was a			

quantitative assessment of alopecia severity based on scalp terminal hair loss performed by an experienced and qualified rater. Score parameters utilized a visual aid showing the division of the scalp hair into 4 quadrants (back, top of scalp, and both sides), with each of 4 quadrants given an accurate determination of the % of scalp surface area covered, representing 24%, 40%, 18%, and 18% of the total scalp surface area, respectively. Higher SALT score represents greater amount of hair loss.			
Units: Units on a scale			
arithmetic mean	59.6	53.7	
standard deviation	± 30.31	± 24.18	
Baseline Intraepidermal Nerve Fiber Density (IENFD)			
Units: fibers/mm			
arithmetic mean	10.2	11.0	
standard deviation	± 3.81	± 3.95	

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

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 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	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.

Subject analysis set title	Ritlecitinib 200/50/50 mg QD
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in 2 treatment periods:
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. 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.

Subject analysis set title	Placebo -> Ritlecitinib 200/50 mg QD
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in 2 treatment periods:
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. 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 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		
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
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

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		
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
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

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		
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
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 Right Side at Month 9E and 15E

End point title	Change From Baseline in I-V Interwave Latency on BAEP at 80 dB From the Right Side at Month 9E and 15E

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. n = x, y in the following table represents the number of evaluable subjects in the Ritlecitinib 200/50/50 mg QD and Placebo->Ritlecitinib 200/50 mg QD arms, respectively.

End point type	Secondary

End point timeframe:

Baseline, Months 9E and 15E (Month 9/15 in the Active Therapy Extension Phase). Baseline was defined as the last non-missing measurement obtained before the first dose in the Placebo-controlled Phase.

End point values	Ritlecitinib 200/50/50 mg QD	Placebo -> Ritlecitinib 200/50 mg QD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36	35		
Units: millisecond (ms)				
arithmetic mean (standard deviation)				
Month 9E (n=25, 30)	0.010 (± 0.1233)	-0.033 (± 0.2448)		
Month 15E (n=24, 28)	0.051 (± 0.1188)	0.034 (± 0.2224)		

Statistical analyses

No statistical analyses for this end point

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		
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 subject as a random effect with an unstructured covariance matrix assumption was used.

Comparison groups	Ritlecitinib 200/50 mg QD v Placebo
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 I-V Interwave Latency on BAEP at 80 dB From the Left Side at Month 9E and 15E

End point title	Change From Baseline in I-V Interwave Latency on BAEP at 80 dB From the Left Side at Month 9E and 15E

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. n = x, y in the following table represents the number of evaluable subjects in the Ritlecitinib 200/50/50 mg QD and Placebo->Ritlecitinib 200/50 mg QD arms, respectively.

End point type	Secondary

End point timeframe:

Baseline, Month 9E and 15E (Month 9/15 in the Active Therapy Extension Phase). Baseline was defined as the last non-missing measurement obtained before the first dose in the Placebo-controlled Phase.

End point values	Ritlecitinib 200/50/50 mg QD	Placebo -> Ritlecitinib 200/50 mg QD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36	35		
Units: millisecond (ms)				
arithmetic mean (standard deviation)				
Month 9E (n=25, 30)	0.006 (± 0.1109)	0.056 (± 0.1694)		
Month 15E (n=24, 28)	0.024 (± 0.1044)	0.017 (± 0.2339)		

Statistical analyses

No statistical analyses for this end point

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		
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 Percentage of IENFs With Axonal Swelling in Skin Punch Biopsies at Month 15E

End point title	Change From Baseline in Percentage of IENFs With Axonal Swelling in Skin Punch Biopsies at Month 15E

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. 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 200/50/50 mg QD and Placebo->Ritlecitinib 200/50 mg QD arms, respectively.

End point type	Secondary

End point timeframe:

Baseline, Month 15E (Month 15 in the Active Therapy Extension Phase). Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase.

End point values	Ritlecitinib 200/50/50 mg QD	Placebo -> Ritlecitinib 200/50 mg QD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36	35		
Units: Percentage of Nerve Fibers				
median (inter-quartile range (Q1-Q3))				
Month 15E (n=22, 25)	0 (-1.0 to 0)	0 (-1.0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in IENFD in Skin Punch Biopsies at Month 15E

End point title	Change From Baseline in IENFD in Skin Punch Biopsies at Month 15E

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. n = x, y in the following table represents the number of evaluable subjects in the Ritlecitinib 200/50/50 mg QD and Placebo->Ritlecitinib 200/50 mg QD arms, respectively.

End point type	Secondary

End point timeframe:

Baseline, Month 15E (Month 15 in the Active Therapy Extension Phase). Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase.

End point values	Ritlecitinib 200/50/50 mg QD	Placebo -> Ritlecitinib 200/50 mg QD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36	35		
Units: fibers/mm				
arithmetic mean (standard deviation)				
Month 15E (n=22, 25)	0.2 (± 2.85)	-1.1 (± 3.51)		

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		
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		
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

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
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 Right Side at Month 9E and 15E

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 9E and 15E

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 200/50/50 mg QD and Placebo->Ritlecitinib 200/50 mg QD arms, respectively.

End point type	Secondary

End point timeframe:

Baseline, Month 9E and 15E (Month 9 and 15 in the Active Therapy Extension Phase). Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase.

End point values	Ritlecitinib 200/50/50 mg QD	Placebo -> Ritlecitinib 200/50 mg QD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36	35		
Units: µV				
arithmetic mean (standard deviation)				
Month 9E (n = 25, 30)	-0.052 (± 0.1109)	-0.025 (± 0.1649)		
Month 15E (n = 24, 28)	-0.065 (± 0.1513)	-0.042 (± 0.1214)		

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 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		
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
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: Month 6	
Comparison groups	Ritlecitinib 200/50 mg QD v Placebo
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: Change From Baseline in Amplitude of Wave V on BAEP at a Stimulus Intensity of 80 dB From the Left Side at Month 9E and 15E

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 9E and 15E

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 200/50/50 mg QD and Placebo->Ritlecitinib 200/50 mg QD arms, respectively.

End point type	Secondary

End point timeframe:

Baseline, Month 9E and 15E (Month 9 and 15 in the Active Therapy Extension Phase). Baseline was defined as the last non-missing measurement obtained before the first dose in the placebo-controlled phase.

End point values	Ritlecitinib 200/50/50 mg QD	Placebo -> Ritlecitinib 200/50 mg QD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36	35		
Units: µV				
arithmetic mean (standard deviation)				
Month 9E (25, 30)	-0.058 (± 0.1209)	-0.025 (± 0.1307)		
Month 15E (n = 24, 28)	-0.047 (± 0.1314)	-0.023 (± 0.1217)		

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 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		
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 Right Side at Baseline, Month 3E, 6E, 9E and 15E

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 at Baseline, Month 3E, 6E, 9E and 15E

End point description:

Absence of wave V on BAEP at stimulus intensities ranging from 80dB to 40dB were summarized using number of subjects by treatment group at each intensity level.
All subjects had Wave V on BAEP present at stimulus intensities ranging from 80 dB to 40 dB up to Month 15E except for 1 subject. Hearing sensitivity remained normal from screening through Month 15E bilaterally. 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 200/50/50 mg QD and Placebo->Ritlecitinib 200/50 mg QD arms, respectively.

End point type	Secondary

End point timeframe:

Baseline, Month 3E, 6E, 9E and 15E (Month 3/6/9/15 in the Active Therapy Extension Phase). Baseline was defined as the last non-missing measurement obtained before the first dose in the Placebo-Controlled Phase.

End point values	Ritlecitinib 200/50/50 mg QD	Placebo -> Ritlecitinib 200/50 mg QD		
Subject group type	Subject analysis set	Subject analysis set		
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 3E - 80 dB nHL (n=1, 0)	0	0		
Month 3E - 70 dB nHL (n=1, 0)	0	0		
Month 3E - 60 dB nHL (n=1, 0)	0	0		
Month 3E - 50 dB nHL (n=1, 0)	0	0		
Month 3E - 40 dB nHL (n=1, 0)	0	0		
Month 6E - 80 dB nHL (n=1, 1)	0	0		
Month 6E - 70 dB nHL (n=1, 1)	0	0		
Month 6E - 60 dB nHL (n=1, 1)	0	0		
Month 6E - 50 dB nHL (n=1, 1)	0	0		
Month 6E - 40 dB nHL (n=1, 1)	0	0		
Month 9E - 80 dB nHL (n=25, 30)	0	0		
Month 9E - 70 dB nHL (n=25, 30)	0	0		
Month 9E - 60 dB nHL (n=25, 30)	0	0		
Month 9E - 50 dB nHL (n=25, 30)	1	0		
Month 9E - 40 dB nHL (n=25, 30)	1	0		
Month 15E - 80 dB nHL (n=24, 28)	0	0		
Month 15E - 70 dB nHL (n=24, 28)	0	0		
Month 15E - 60 dB nHL (n=24, 28)	0	0		
Month 15E - 50 dB nHL (n=24, 28)	0	0		
Month 15E - 40 dB nHL (n=24, 28)	0	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		
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 Absence of Wave V on BAEP at Stimulus Intensities Ranging From 80 dB to 40 dB From Left Side at Baseline, Month 3E, 6E, 9E and 15E

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 at Baseline, Month 3E, 6E, 9E and 15E

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.
All participants had Wave V on BAEP present at stimulus intensities ranging from 80 dB to 40 dB up to Month 15E except for 1 subject. Hearing sensitivity remained normal from screening through Month 15E bilaterally. 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 200/50/50 mg QD and Placebo->Ritlecitinib 200/50 mg QD arms, respectively.

End point type	Secondary

End point timeframe:

Baseline, Month 3E, 6E, 9E and 15E (Month 3/6/9/15 in the Active Therapy Extension Phase). Baseline was defined as the last non-missing measurement obtained before the first dose in the Placebo-Controlled Phase.

End point values	Ritlecitinib 200/50/50 mg QD	Placebo -> Ritlecitinib 200/50 mg QD		
Subject group type	Subject analysis set	Subject analysis set		
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 3E - 80 dB nHL (n=1, 0)	0	0		
Month 3E - 70 dB nHL (n=1, 0)	0	0		
Month 3E - 60 dB nHL (n=1, 0)	0	0		
Month 3E - 50 dB nHL (n=1, 0)	0	0		
Month 3E - 40 dB nHL (n=1, 0)	0	0		
Month 6E - 80 dB nHL (n=1, 1)	0	0		
Month 6E - 70 dB nHL (n=1, 1)	0	0		
Month 6E - 60 dB nHL (n=1, 1)	0	0		
Month 6E - 50 dB nHL (n=1, 1)	0	0		
Month 6E - 40 dB nHL (n=1, 1)	0	0		
Month 9E - 80 dB nHL (n=25, 30)	0	0		
Month 9E - 70 dB nHL (n=25, 30)	0	0		
Month 9E - 60 dB nHL (n=25, 30)	0	0		
Month 9E - 50 dB nHL (n=25, 30)	0	0		
Month 9E - 40 dB nHL (n=25, 30)	0	0		
Month 15E - 80 dB nHL (n=24, 28)	0	0		
Month 15E - 70 dB nHL (n=24, 28)	0	0		
Month 15E - 60 dB nHL (n=24, 28)	0	0		
Month 15E - 50 dB nHL (n=24, 28)	0	0		
Month 15E - 40 dB nHL (n=24, 28)	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:

Approximately 16 months

End point values	Ritlecitinib 200/50 mg QD	Ritlecitinib 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 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:

Approximately 16 months

End point values	Ritlecitinib 200/50 mg QD	Ritlecitinib 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 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:

Approximately 16 months

End point values	Ritlecitinib 200/50 mg QD	Ritlecitinib 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:

Approximately 16 months

End point values	Ritlecitinib 200/50 mg QD	Ritlecitinib 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:

Approximately 16 months

End point values	Ritlecitinib 200/50 mg QD	Ritlecitinib 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		
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: 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:

Approximately 16 months

End point values	Ritlecitinib 200/50 mg QD	Ritlecitinib 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 SALT Scores at Month 3E, 6E, 9E, 12E and 15E

End point title	Change From Baseline in Overall SALT Scores at Month 3E, 6E, 9E, 12E and 15E

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. n = x, y in the following table represents the number of evaluable subjects in the Ritlecitinib 200/50/50 mg QD and Placebo->Ritlecitinib 200/50 mg QD arms, respectively.

End point type	Secondary

End point timeframe:

Baseline, Month 3E, 6E, 9E, 12E and 15E (Month 3/6/9/12/15 in the Active Therapy Extension Phase). Baseline was defined as the last non-missing measurement obtained before the first dose in the Placebo-Controlled Phase.

End point values	Ritlecitinib 200/50/50 mg QD	Placebo -> Ritlecitinib 200/50 mg QD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36	35		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Month 3E (n = 32, 33)	-41.7 (± 33.98)	-38.7 (± 33.49)		
Month 6E (n = 29, 30)	-38.0 (± 29.88)	-43.4 (± 34.13)		
Month 9E (n = 26, 30)	-38.7 (± 29.90)	-46.6 (± 34.14)		
Month 12E (n = 25, 29)	-41.6 (± 29.67)	-48.9 (± 34.77)		
Month 15E (n = 24, 28)	-44.6 (± 28.51)	-49.9 (± 34.40)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in AA-SALT Score at Month 3E, 6E, 9E, 12E and 15E

End point title	Change From Baseline in AA-SALT Score at Month 3E, 6E, 9E, 12E and 15E

End point description:

SALT is a quantitative assessment of AA severity based on scalp terminal hair loss. AA-SALT is the amount of scalp hair loss due to AA. AA SALT score in Placebo-Controlled Phase = overall SALT score – non-AA SALT score (The non-AA SALT score only took into account scalp hair loss other than that due to AA and was required to be assessed only at Month 9 [or Month 6 for those who entered the Active Therapy Extension Phase at Month 6] in Placebo-Controlled Phase). The 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 in the following table represents the number of evaluable subjects in the Ritlecitinib 200/50/50 mg QD and Placebo->Ritlecitinib 200/50 mg QD arms, respectively.

End point type	Secondary

End point timeframe:

Baseline, Month 3E, 6E, 9E, 12E and 15E (Month 3/6/9/12/15 in the Active Therapy Extension Phase). Baseline was defined as the last non-missing measurement obtained before the first dose in the Placebo-Controlled Phase.

End point values	Ritlecitinib 200/50/50 mg QD	Placebo -> Ritlecitinib 200/50 mg QD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36	35		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Month 3E (n = 32, 33)	-41.7 (± 33.97)	-39.4 (± 32.89)		
Month 6E (n = 29, 30)	-38.0 (± 29.87)	-44.2 (± 33.37)		
Month 9E (n = 26, 30)	-38.7 (± 29.90)	-47.4 (± 33.36)		
Month 12E (n = 25, 29)	-41.6 (± 29.70)	-49.7 (± 33.92)		
Month 15E (n = 24, 28)	-44.8 (± 28.37)	-50.8 (± 33.49)		

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		
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		
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

Secondary: Number of Subjects With PGI-C Response at Month 3E, 6E, 9E, 12E and 15E

End point title	Number of Subjects With PGI-C Response at Month 3E, 6E, 9E, 12E and 15E

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:

Month 3E, 6E, 9E, 12E and 15E (Month 3/6/9/12/15 in the Active Therapy Extension Phase)

End point values	Ritlecitinib 200/50/50 mg QD	Placebo -> Ritlecitinib 200/50 mg QD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36	35		
Units: Subjects				
Month 3E	22	22		
Month 6E	16	20		
Month 9E	20	18		
Month 12E	17	18		
Month 15E	17	18		

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	26.0

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 this treatment 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 treatment phase.

Reporting group title	Ritlecitinib 200/50/50 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. 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 phase.

Serious adverse events	Placebo -> Ritlecitinib 200/50 mg QD	Ritlecitinib 200/50/50 mg QD	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 35 (5.71%)	3 / 36 (8.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	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	
Hepatobiliary disorders			
Biliary colic			
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	
Skin and subcutaneous tissue disorders			
Chronic pigmented purpura			
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	

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

Non-serious adverse events	Placebo -> Ritlecitinib 200/50 mg QD	Ritlecitinib 200/50/50 mg QD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 35 (68.57%)	27 / 36 (75.00%)	
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	
Joint dislocation			

subjects affected / exposed	2 / 35 (5.71%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 35 (0.00%)	3 / 36 (8.33%)	
occurrences (all)	0	3	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 35 (2.86%)	3 / 36 (8.33%)	
occurrences (all)	1	3	
Headache			
subjects affected / exposed	4 / 35 (11.43%)	4 / 36 (11.11%)	
occurrences (all)	4	5	
Hypoaesthesia			
subjects affected / exposed	3 / 35 (8.57%)	2 / 36 (5.56%)	
occurrences (all)	4	4	
Paraesthesia			
subjects affected / exposed	1 / 35 (2.86%)	4 / 36 (11.11%)	
occurrences (all)	1	4	
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	
Vertigo			
subjects affected / exposed	2 / 35 (5.71%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 35 (2.86%)	4 / 36 (11.11%)	
occurrences (all)	1	4	
Nausea			
subjects affected / exposed	3 / 35 (8.57%)	1 / 36 (2.78%)	
occurrences (all)	4	1	

Diarrhoea			
subjects affected / exposed	0 / 35 (0.00%)	3 / 36 (8.33%)	
occurrences (all)	0	4	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	1 / 35 (2.86%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
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	3 / 35 (8.57%)	2 / 36 (5.56%)	
occurrences (all)	3	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	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 35 (2.86%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Back pain			
subjects affected / exposed	1 / 35 (2.86%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Infections and infestations			
COVID-19			
subjects affected / exposed	7 / 35 (20.00%)	8 / 36 (22.22%)	
occurrences (all)	8	8	
Acne pustular			
subjects affected / exposed	0 / 35 (0.00%)	4 / 36 (11.11%)	
occurrences (all)	0	5	
Nasopharyngitis			

subjects affected / exposed	3 / 35 (8.57%)	4 / 36 (11.11%)	
occurrences (all)	4	6	
Urinary tract infection			
subjects affected / exposed	3 / 35 (8.57%)	2 / 36 (5.56%)	
occurrences (all)	4	2	
Upper respiratory tract infection			
subjects affected / exposed	3 / 35 (8.57%)	3 / 36 (8.33%)	
occurrences (all)	4	3	
Tonsillitis			
subjects affected / exposed	0 / 35 (0.00%)	3 / 36 (8.33%)	
occurrences (all)	0	3	
Sinusitis			
subjects affected / exposed	2 / 35 (5.71%)	2 / 36 (5.56%)	
occurrences (all)	2	2	
Gastroenteritis			
subjects affected / exposed	0 / 35 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Pharyngitis			
subjects affected / exposed	0 / 35 (0.00%)	3 / 36 (8.33%)	
occurrences (all)	0	3	
Laryngitis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 36 (0.00%)	
occurrences (all)	2	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. 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 the data-cut on 19 May 2023, and will be updated after completion of the whole study.

Notes: