Clinical trial results:
An Interventional PK, PD, Phase 1, Open-Label Study to Investigate PK and PD of Multiple-Dose Ritlecitinib in Children 6 to Less Than 12 Years of Age With Severe Alopecia Areata

Summary

EudraCT number	2023-000824-12
Trial protocol	Outside EU/EEA
Global end of trial date	11 August 2023

Results information

Result version number	v1 (current)
This version publication date	28 January 2024
First version publication date	28 January 2024

Trial information

Trial identification

Sponsor protocol code	B7981031

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05650333
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 Centre, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Centre, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002451-PIP01-18
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 December 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to characterise the pharmacokinetics (PK) of Ritlectinib in subjects with alopecia areata (AA) 6 to less than (<) 12 years of age.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 March 2023
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	United States: 15
Worldwide total number of subjects	15
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	15
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 15 subjects were enrolled at 6 sites in the United States. Study started from 02 March 2023 and completed on 11 August 2023.

Period 1

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

Arms

Arm title	Ritlecitinib 20 mg

Arm description:

Subjects received Ritlecitinib 20 milligram (mg) orally once daily (QD), for 7 consecutive days.

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

Dosage and administration details:

Subjects received Ritlecitinib 20 mg, orally QD, for 7 consecutive days.

Number of subjects in period 1	Ritlecitinib 20 mg
Started	15
Completed	14
Not completed	1
Adverse event, non-fatal	1

Period 2

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

Arms

Arm title	Ritlecitinib 20 mg
Arm description:	
Subjects received Ritlecitinib 20 mg, orally QD, for 7 consecutive days.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Ritlecitinib 20 mg
Started	14
Completed	15

Joined	1
For follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Ritlecitinib 20 mg
Reporting group description:	
Subjects received Ritlecitinib 20 milligram (mg) orally once daily (QD), for 7 consecutive days.	

Reporting group values	Ritlecitinib 20 mg	Total	
Number of subjects	15	15	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	15	15	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	8.5		
standard deviation	± 1.60	-	
Gender Categorical Units: Subjects			
Female	12	12	
Male	3	3	
Race Units: Subjects			
White	13	13	
Black or African American	2	2	
Ethnicity Units: Subjects			
Hispanic or Latino	8	8	
Not Hispanic or Latino	7	7	

End points

End points reporting groups

Reporting group title	Ritlecitinib 20 mg
Reporting group description:	
Subjects received Ritlecitinib 20 milligram (mg) orally once daily (QD), for 7 consecutive days.	
Reporting group title	Ritlecitinib 20 mg
Reporting group description:	
Subjects received Ritlecitinib 20 mg, orally QD, for 7 consecutive days.	

Primary: Area Under the Plasma Concentration-Time Profile Over the Dosing Interval of 24 Hours, at Steady State (AUC24) of Ritlecitinib on Day 7

End point title	Area Under the Plasma Concentration-Time Profile Over the Dosing Interval of 24 Hours, at Steady State (AUC24) of Ritlecitinib on Day 7[1]
End point description:	
Linear-log trapezoidal method was used for evaluation. The pharmacokinetic (PK) parameter analysis population included all subjects treated who had at least 1 of the PK parameters of primary interest. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint. Two subjects were not included in analysis because they did not have evaluable PK data.	
End point type	Primary
End point timeframe:	
0 (pre-dose), 0.5, 1, 3, 8 and 24 hours post-dose on Day 7 [Pre-dose concentration was used as an estimate for the concentration of 24 hours post-dose]	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Statistical analysis was not planned for this endpoint.	

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Nanogram*hours per millilitre (ng*hr/mL)				
geometric mean (geometric coefficient of variation)	437.5 (± 30)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Ritlecitinib

End point title	Maximum Observed Plasma Concentration (Cmax) of Ritlecitinib
End point description:	
The PK parameter analysis population included all subjects treated who had at least 1 of the PK parameters of primary interest. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint. Two subjects were not included in analysis because they did not have evaluable PK data.	

End point type	Secondary

End point timeframe:

0 (pre-dose), 0.5, 1, 3 and 8 hours post-dose on Day 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Nanogram per millilitre (ng/mL)				
geometric mean (geometric coefficient of variation)	208.7 (± 38)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentration (Tmax) of Ritlecitinib

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) of Ritlecitinib

End point description:

The PK parameter analysis population included all subjects treated who had at least 1 of the PK parameters of primary interest. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint. Two subjects were not included in analysis because they did not have evaluable PK data.

End point type	Secondary

End point timeframe:

0 (pre-dose), 0.5, 1, 3 and 8 hours post-dose on Day 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Hours				
median (full range (min-max))	0.500 (0.450 to 1.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Interferon Gamma Induced Protein 10 (IP-10) on Day 7

End point title	Change From Baseline in Interferon Gamma Induced Protein 10

	(IP-10) on Day 7

End point description:

The pharmacodynamic (PD) parameter analysis population included all subjects treated who had at least 1 of the PD parameters of primary interest. Here, "n" signifies number of subjects evaluable for specified rows.

End point type	Secondary

End point timeframe:

Baseline and Day 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Picogram per millilitre (pg/mL)				
median (full range (min-max))				
Baseline (n =15) Change at Day 7 (n =12)	121.0 (74.7 to 888.0) -9.9 (-555.0 to 104.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Half-Life (t1/2) of Ritlecitinib

End point title	Terminal Elimination Half-Life (t1/2) of Ritlecitinib

End point description:

The PK parameter analysis population included all subjects treated who had at least 1 of the PK parameters of primary interest. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint. Two subjects were not included in analysis because they did not have evaluable PK data.

End point type	Secondary

End point timeframe:

0 (pre-dose), 0.5, 1, 3 and 8 hours post-dose on Day 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Hours				
arithmetic mean (standard deviation)	1.191 (± 0.10776)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution (Vz/F) of Ritlecitinib

End point title	Apparent Volume of Distribution (Vz/F) of Ritlecitinib

End point description:

Volume of distribution is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired plasma concentration of a drug. Vz/F is influenced by the fraction absorbed. The PK parameter analysis population included all subjects treated who had at least 1 of the PK parameters of primary interest. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint. Two subjects were not included in analysis because they did not have evaluable PK data.

End point type	Secondary

End point timeframe:

0 (pre-dose), 0.5, 1, 3 and 8 hours post-dose on Day 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Litre				
geometric mean (geometric coefficient of variation)	74.92 (± 23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Oral Clearance (CL/F) of Ritlecitinib

End point title	Apparent Oral Clearance (CL/F) of Ritlecitinib

End point description:

Clearance of a drug is a measure of the rate at which a drug is metabolized or eliminated by normal biological process. Clearance obtained after oral dose (apparent oral clearance) is influenced by the fraction of the dose absorbed. The PK parameter analysis population included all subjects treated who had at least 1 of the PK parameters of primary interest. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint. Two subjects were not included in analysis because they did not have evaluable PK data.

End point type	Secondary

End point timeframe:

0 (pre-dose), 0.5, 1, 3 and 8 hours post-dose on Day 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Litre per hour (L/hr)				
geometric mean (geometric coefficient of variation)	45.70 (± 30)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in T Lymphocytes on Day 7

End point title	Change From Baseline in T Lymphocytes on Day 7

End point description:

The PD parameter analysis population included all subjects treated who had at least 1 of the PD parameters of primary interest. T lymphocytes included CD3 cells, CD4 T helper lymphocytes and CD8 T cytotoxic lymphocytes. Here, "n" signifies number of subjects evaluable for specified rows.

End point type	Secondary

End point timeframe:

Baseline and Day 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: 10^9 Cells per litre				
median (full range (min-max))				
CD3 cells: Baseline (n=15)	1.8 (0.8 to 3.4)			
CD3 cells: Change at Day 7(n=12)	-0.0 (-1.3 to 2.0)			
CD4 T helper lymphocytes: Baseline (n=15)	1.0 (0.6 to 1.6)			
CD4 T helper lymphocytes: Change at Day 7(n=12)	-0.1 (-0.6 to 1.1)			
CD8 T cytotoxic lymphocytes: Baseline (n=15)	0.6 (0.2 to 1.5)			
CD8 T cytotoxic lymphocytes: Change at Day 7(n=12)	0.0 (-0.6 to 0.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in B Lymphocytes on Day 7

End point title	Change From Baseline in B Lymphocytes on Day 7

End point description:

The PD parameter analysis population included all subjects treated who had at least 1 of the PD parameters of primary interest. B lymphocytes included CD19 cells. Here, "n" signifies number of subjects evaluable for specified rows.

End point type	Secondary

End point timeframe:

Baseline and Day 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: 10^6 Cells per litre				
median (full range (min-max))				
Baseline (n =15) Change at Day 7 (n =12)	439.0 (191.0 to 881.0) -19.0 (-116.0 to 766.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Natural Killer (NK) Cells on Day 7

End point title	Change From Baseline in Natural Killer (NK) Cells on Day 7

End point description:

The PD parameter analysis population included all subjects treated who had at least 1 of the PD parameters of primary interest. NK cells included CD3 (-), CD16 (+), CD56 (+) cells. Here, "n" signifies number of subjects evaluable for specified rows.

End point type	Secondary

End point timeframe:

Baseline and Day 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: 10^6 Cells per litre				
median (full range (min-max))				
Baseline (n =15) Change at Day 7 (n =12)	254.0 (85.0 to 729.0) -25.5 (-318.0 to 627.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point description:

An AE is any untoward medical occurrence in a subject or clinical study subject, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Treatment-emergent were events between first dose to 35 days after last dose, that were absent before treatment or that worsened relative to pretreatment state. Safety analysis set included all subjects assigned to study intervention and who received at least 1 dose of study intervention. Subjects were analysed according to the product they actually received.

End point type	Secondary

End point timeframe:

Day 1 of dosing up to 35 days after the last dose (Day 42)

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Subjects	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Related AEs

End point title	Number of Subjects With Treatment Related AEs

End point description:

Treatment-related AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. Safety analysis set included all subjects assigned to study intervention and who received at least 1 dose of study intervention. Subjects were analysed according to the product they actually received.

End point type	Secondary

End point timeframe:

Day 1 of dosing up to 35 days after the last dose (Day 42)

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Subjects	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With AEs Leading to Treatment Discontinuation

End point title	Number of Subjects With AEs Leading to Treatment Discontinuation

End point description:

Safety analysis set included all subjects assigned to study intervention and who received at least 1 dose of study intervention. Subjects were analysed according to the product they actually received.

End point type	Secondary

End point timeframe:

Day 1 up to Day 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Subjects	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious AEs (SAEs)

End point title	Number of Subjects With Serious AEs (SAEs)

End point description:

SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Safety analysis set included all subjects assigned to study intervention and who received at least 1 dose of study intervention. Subjects were analysed according to the product they actually received.

End point type	Secondary

End point timeframe:

Day 1 of dosing up to 35 days after the last dose (Day 42)

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Subjects	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:

Vital Signs evaluation included blood pressure and heart rate measurements. Clinical significance was judged by investigator. Safety analysis set included all subjects assigned to study intervention and who received at least 1 dose of study intervention. Subjects were analysed according to the product they actually received.

End point type	Secondary

End point timeframe:

Day 1 up to Day 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Subjects	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:

Clinical laboratory parameters included haematology: haemoglobin, haematocrit, red blood cells count, platelet count, white blood cells count, total absolute: neutrophils, eosinophils, monocytes, basophils, lymphocytes; chemistry: urea and creatinine estimated creatinine clearance, glucose (fasting), sodium, potassium, chloride, aspartate aminotransferase (AT), alanine AT, total bilirubin, alkaline phosphatase, albumin, total protein; urinalysis: local dipstick: pH, qualitative: glucose, protein, albuminuria, blood, ketones, nitrites, leukocyte esterase and others. Clinical significance was judged by investigator. Safety analysis set was evaluated.

End point type	Secondary

End point timeframe:

Day 1 up to Day 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects as per Score for Paediatric Taste Assessment Questionnaire

End point title	Number of Subjects as per Score for Paediatric Taste Assessment Questionnaire

End point description:

The paediatric taste questionnaire included 3 questions regarding: 1) Overall Taste, 2) Overall Mouthfeel and 3) Overall Volume of Medicine. Each question ranged from 1 (most favourable) to 5 (least favourable). Safety analysis set included all subjects assigned to study intervention and who received at least 1 dose of study intervention. Subjects were analysed according to the product they actually received. Here, "Number of Subjects Analyzed" signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Day 1 and 7

End point values	Ritlecitinib 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Subjects				
Day 1: Taste, Score 1	1			
Day 1: Taste, Score 2	0			
Day 1: Taste, Score 3	3			
Day 1: Taste, Score 4	3			
Day 1: Taste, Score 5	7			
Day 1: Mouthfeel, Score 1	0			
Day 1: Mouthfeel, Score 2	5			
Day 1: Mouthfeel, Score 3	3			
Day 1: Mouthfeel, Score 4	4			
Day 1: Mouthfeel, Score 5	2			
Day 1: Volume, Score 1	2			
Day 1: Volume, Score 2	5			
Day 1: Volume, Score 3	2			
Day 1: Volume, Score 4	2			
Day 1: Volume, Score 5	3			
Day 7: Taste, Score 1	0			

Day 7: Taste, Score 2	1			
Day 7: Taste, Score 3	4			
Day 7: Taste, Score 4	2			
Day 7: Taste, Score 5	7			
Day 7: Mouthfeel, Score 1	0			
Day 7: Mouthfeel, Score 2	5			
Day 7: Mouthfeel, Score 3	3			
Day 7: Mouthfeel, Score 4	5			
Day 7: Mouthfeel, Score 5	1			
Day 7: Volume, Score 1	1			
Day 7: Volume, Score 2	6			
Day 7: Volume, Score 3	2			
Day 7: Volume, Score 4	1			
Day 7: Volume, Score 5	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Day 1 up to 35 days after last dose (Day 42)	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0
Reporting groups	
Reporting group title	Ritlecitinib 20 mg QD
Reporting group description: Subjects received Ritlecitinib 20 mg, orally QD, for 7 consecutive days.	

Serious adverse events	Ritlecitinib 20 mg QD		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Ritlecitinib 20 mg QD		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 15 (20.00%)		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			

Myalgia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported