



Clinical trial results:

An open-label, single arm phase II study of DFV890 to assess the safety, tolerability and efficacy in participants with familial cold auto-inflammatory syndrome (FCAS)

Summary

EudraCT number	2020-005948-33
Trial protocol	DE IT FR
Global end of trial date	05 May 2023

Results information

Result version number	v1
This version publication date	27 March 2024
First version publication date	27 March 2024

Trial information

Trial identification

Sponsor protocol code	CDFV890A12201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04868968
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 May 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	05 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to assess the efficacy of DFV890 to reduce cold-induced inflammation in participants with Familial cold auto-inflammatory syndrome (FCAS).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 September 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 1
Worldwide total number of subjects	4
EEA total number of subjects	3

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)	4
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

Participants took part in 3 investigative sites in 3 countries.

Pre-assignment

Screening details:

During the screening period the participant's eligibility was assessed at a screening visit and a screening cold challenge was performed.

Period 1

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

Arms

Arm title	DFV890 100mg - Treatment
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Arm description:

DFV890 100mg oral dose, twice daily for 3 days and one last dose in the morning of Day 4 of the treatment period

Arm type	Experimental
Investigational medicinal product name	DFV890
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

DFV890 100 mg oral twice daily

Number of subjects in period 1	DFV890 100mg - Treatment
Started	4
Completed	3
Not completed	1
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	DFV890 100mg - Treatment
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Reporting group description:

DFV890 100mg oral dose, twice daily for 3 days and one last dose in the morning of Day 4 of the treatment period

Reporting group values	DFV890 100mg - Treatment	Total	
Number of subjects	4	4	
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)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	4	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	41.3		
standard deviation	± 15.48	-	
Sex: Female, Male			
Units: participants			
Female	1	1	
Male	3	3	
Race/Ethnicity, Customized			
Units: Subjects			
other	1	1	
white	3	3	

End points

End points reporting groups

Reporting group title	DFV890 100mg - Treatment
Reporting group description: DFV890 100mg oral dose, twice daily for 3 days and one last dose in the morning of Day 4 of the treatment period	
Subject analysis set title	Screening
Subject analysis set type	Per protocol
Subject analysis set description: Screening period	

Primary: Fold change from pre-challenge to the highest post-challenge value of white cell count (WCC)

End point title	Fold change from pre-challenge to the highest post-challenge value of white cell count (WCC) ^[1]
End point description: A cold challenge was performed during the screening period and on Day 4 of the treatment period. Fold change from pre-challenge to the highest post-challenge value of total WCC was the primary efficacy variable. The highest post-challenge value was based only on post-challenge measurements within the cold challenge visit (up to and including 8 hours post-challenge). Lower induction of total WCC was considered a favorable outcome. Fold change from pre-challenge to a post-challenge value of WCC was defined as the ratio of the post-challenge WCC value to the pre-challenge WCC value, i.e: post challenge WCC/pre challenge WCC. The unforeseen screen failure rate and recruitment challenges resulted in early closure of the study. As a result, only 4 out of planned 6 participants were enrolled in the study; thus, the results should be interpreted cautiously.	
End point type	Primary
End point timeframe: Screening period and treatment period (Day 4): pre cold challenge and up to 8 hours post cold challenge. The duration of the cold challenge was 45 minutes.	
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: only analysed descriptively	

End point values	DFV890 100mg - Treatment	Screening		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	4		
Units: ratio of fold changes				
number (not applicable)	1.33	1.62		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs)

End point title	Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs)
End point description: Number of participants with treatment emergent AEs (any AE regardless of seriousness), AEs led to	

study treatment discontinuation, SAEs and SAEs led to study treatment discontinuation.

End point type	Secondary
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End point timeframe:

Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of approximately 34 days

End point values	DFV890 100mg - Treatment			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: participants				
At least one AE	4			
At least one SAE	0			
AE leading to discontinuation	0			
SAE leading to discontinuation	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Physician global assessment of autoinflammatory disease activity

End point title	Physician global assessment of autoinflammatory disease activity
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End point description:

The Physician global assessment of autoinflammatory disease activity is a questionnaire completed by the Investigator. It uses a 5-point scale. Lower scores represent better outcomes.

0 = Absent

1 = Minimal

2 = Mild

3 = Moderate

4 = Severe

End point type	Secondary
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End point timeframe:

Screening and Treatment (Day 4): 1 hour pre and 2, 3, 5, 9 and 24 hours post. Scheduled time refers to the time post-meal (screening) and to the time post-dose (treatment). The start of the cold challenge is at 1 hour post and the duration is 45 minutes.

End point values	DFV890 100mg - Treatment	Screening		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	4		
Units: Participants				
1 hour pre Absent	2	0		
2 hours post Absent	2	0		
3 hours post Absent	2	0		
5 hours post Absent	2	0		
9 hours post Absent	1	0		

24 hours post Absent	2	0		
1 hour pre Minimal	2	3		
2 hours post Minimal	1	2		
3 hours post Minimal	1	1		
5 hours post Minimal	1	1		
9 hours post Minimal	2	1		
24 hours post Minimal	2	3		
1 hour pre Mild	0	1		
2 hours post Mild	1	2		
3 hours post Mild	1	3		
5 hours post Mild	1	3		
9 hours post Mild	1	0		
24 hours post Mild	0	1		
1 hour pre Moderate	0	0		
2 hours post Moderate	0	0		
3 hours post Moderate	0	0		
5 hours post Moderate	0	0		
9 hours post Moderate	0	3		
24 hours post Moderate	0	0		
1 hour pre Severe	0	0		
2 hours post Severe	0	0		
3 hours post Severe	0	0		
5 hours post Severe	0	0		
9 hours post Severe	0	0		
24 hours post Severe	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Physician's severity assessment of autoinflammatory disease signs and symptoms

End point title	Physician's severity assessment of autoinflammatory disease signs and symptoms
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End point description:

The Physician's severity assessment of autoinflammatory disease signs and symptoms is a questionnaire completed by the Investigator. It uses a 5-point scale. Lower scores represent better outcomes.

0 = Absent

1 = Minimal

2 = Mild

3 = Moderate

4 = Severe

The following items were assessed:

- Assessment of skin disease (urticarial skin rash)
- Assessment of arthralgia
- Assessment of myalgia
- Assessment of headache/migraine
- Assessment of conjunctivitis
- Assessment of fatigue/malaise

End point type	Secondary
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End point timeframe:

Screening and Treatment (Day 4): 1 hour pre and 2, 3, 5, 9 and 24 hours post. Scheduled time refers to the time post-meal (screening) and to the time post-dose (treatment). The start of the cold challenge is at 1 hour post and the duration is 45 minutes.

End point values	DFV890 100mg - Treatment	Screening		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	4		
Units: Participants				
Arthralgia 1 hour pre Absent	3	3		
Arthralgia 2 hours post Absent	4	4		
Arthralgia 3 hours post Absent	4	4		
Arthralgia 5 hours post Absent	4	3		
Arthralgia 9 hours post Absent	3	1		
Arthralgia 24 hours post Absent	3	4		
Conjunctivitis 1 hour pre Absent	3	3		
Conjunctivitis 2 hours post Absent	4	3		
Conjunctivitis 3 hours post Absent	4	3		
Conjunctivitis 5 hours post Absent	4	3		
Conjunctivitis 9 hours post Absent	4	2		
Conjunctivitis 24 hours post Absent	2	3		
Fatigue/Malaise 1 hour pre Absent	3	3		
Fatigue/Malaise 2 hours post Absent	3	3		
Fatigue/Malaise 3 hours post Absent	3	2		
Fatigue/Malaise 5 hours post Absent	3	2		
Fatigue/Malaise 9 hours post Absent	3	2		
Fatigue/Malaise 24 hours post Absent	3	3		
Headache/Migraine 1 hour pre Absent	4	4		
Headache/Migraine 2 hours post Absent	4	4		
Headache/Migraine 3 hours post Absent	4	4		
Headache/Migraine 5 hours post Absent	4	4		
Headache/Migraine 9 hours post Absent	4	3		
Headache/Migraine 24 hours post Absent	4	4		
Myalgia 1 hour pre Absent	4	3		
Myalgia 2 hours post Absent	3	4		
Myalgia 3 hours post Absent	4	3		
Myalgia 5 hours post Absent	4	3		
Myalgia 9 hours post Absent	4	3		
Myalgia 24 hours post Absent	4	4		
Skin disease 1 hour pre Absent	1	0		
Skin disease 2 hours post Absent	1	0		
Skin disease 3 hours post Absent	2	0		
Skin disease 5 hours post Absent	2	0		
Skin disease 9 hours post Absent	1	0		
Skin disease 24 hours post Absent	2	0		
Arthralgia 1 hour pre Minimal	1	1		
Arthralgia 2 hours post Minimal	0	0		
Arthralgia 3 hours post Minimal	0	0		
Arthralgia 5 hours post Minimal	0	0		
Arthralgia 9 hours post Minimal	1	3		
Arthralgia 24 hours post Minimal	1	0		
Conjunctivitis 1 hour pre Minimal	1	0		

Conjunctivitis 2 hours post Minimal	0	0		
Conjunctivitis 3 hours post Minimal	0	0		
Conjunctivitis 5 hours post Minimal	0	0		
Conjunctivitis 9 hours post Minimal	0	0		
Conjunctivitis 24 hours post Minimal	2	0		
Fatigue/Malaise 1 hour pre Minimal	0	0		
Fatigue/Malaise 2 hours post Minimal	0	0		
Fatigue/Malaise 3 hours post Minimal	0	1		
Fatigue/Malaise 5 hours post Minimal	0	0		
Fatigue/Malaise 9 hours post Minimal	0	0		
Fatigue/Malaise 24 hours post Minimal	1	1		
Headache/Migraine 1 hour pre Minimal	0	0		
Headache/Migraine 2 hours post Minimal	0	0		
Headache/Migraine 3 hours post Minimal	0	0		
Headache/Migraine 5 hours post Minimal	0	0		
Headache/Migraine 9 hours post Minimal	0	0		
Headache/Migraine 24 hours post Minimal	0	0		
Myalgia 1 hour pre Minimal	0	1		
Myalgia 2 hours post Minimal	1	0		
Myalgia 3 hours post Minimal	0	0		
Myalgia 5 hours post Minimal	0	0		
Myalgia 9 hours post Minimal	0	1		
Myalgia 24 hours post Minimal	0	0		
Skin disease 1 hour pre Minimal	3	3		
Skin disease 2 hours post Minimal	3	2		
Skin disease 3 hours post Minimal	2	1		
Skin disease 5 hours post Minimal	2	1		
Skin disease 9 hours post Minimal	3	1		
Skin disease 24 hours post Minimal	2	3		
Arthralgia 1 hour pre Mild	0	0		
Arthralgia 2 hours post Mild	0	0		
Arthralgia 3 hours post Mild	0	0		
Arthralgia 5 hours post Mild	0	1		
Arthralgia 9 hours post Mild	0	0		
Arthralgia 24 hours post Mild	0	0		
Conjunctivitis 1 hour pre Mild	0	1		
Conjunctivitis 2 hours post Mild	0	1		
Conjunctivitis 3 hours post Mild	0	1		
Conjunctivitis 5 hours post Mild	0	1		
Conjunctivitis 9 hours post Mild	0	1		
Conjunctivitis 24 hours post Mild	0	1		
Fatigue/Malaise 1 hour pre Mild	1	1		
Fatigue/Malaise 2 hours post Mild	0	1		
Fatigue/Malaise 3 hours post Mild	0	0		
Fatigue/Malaise 5 hours post Mild	0	2		
Fatigue/Malaise 9 hours post Mild	0	1		
Fatigue/Malaise 24 hours post Mild	0	0		
Headache/Migraine 1 hour pre Mild	0	0		

Headache/Migraine 2 hours post Mild	0	0		
Headache/Migraine 3 hours post Mild	0	0		
Headache/Migraine 5 hours post Mild	0	0		
Headache/Migraine 9 hours post Mild	0	1		
Headache/Migraine 24 hours post Mild	0	0		
Myalgia 1 hour pre Mild	0	0		
Myalgia 2 hours post Mild	0	0		
Myalgia 3 hours post Mild	0	1		
Myalgia 5 hours post Mild	0	1		
Myalgia 9 hours post Mild	0	0		
Myalgia 24 hours post Mild	0	0		
Skin disease 1 hour pre Mild	0	1		
Skin disease 2 hours post Mild	0	2		
Skin disease 3 hours post Mild	0	3		
Skin disease 5 hours post Mild	0	3		
Skin disease 9 hours post Mild	0	0		
Skin disease 24 hours post Mild	0	1		
Arthralgia 1 hour pre Moderate	0	0		
Arthralgia 2 hours post Moderate	0	0		
Arthralgia 3 hours post Moderate	0	0		
Arthralgia 5 hours post Moderate	0	0		
Arthralgia 9 hours post Moderate	0	0		
Arthralgia 24 hours post Moderate	0	0		
Conjunctivitis 1 hour pre Moderate	0	0		
Conjunctivitis 2 hours post Moderate	0	0		
Conjunctivitis 3 hours post Moderate	0	0		
Conjunctivitis 5 hours post Moderate	0	0		
Conjunctivitis 9 hours post Moderate	0	1		
Conjunctivitis 24 hours post Moderate	0	0		
Fatigue/Malaise 1 hour pre Moderate	0	0		
Fatigue/Malaise 2 hours post Moderate	1	0		
Fatigue/Malaise 3 hours post Moderate	1	1		
Fatigue/Malaise 5 hours post Moderate	1	0		
Fatigue/Malaise 9 hours post Moderate	1	1		
Fatigue/Malaise 24 hours post Moderate	0	0		
Headache/Migraine 1 hour pre Moderate	0	0		
Headache/Migraine 2 hours post Moderate	0	0		
Headache/Migraine 3 hours post Moderate	0	0		
Headache/Migraine 5 hours post Moderate	0	0		
Headache/Migraine 9 hours post Moderate	0	0		
Headache/Migraine 24 hours post Moderate	0	0		
Myalgia 1 hour pre Moderate	0	0		
Myalgia 2 hours post Moderate	0	0		
Myalgia 3 hours post Moderate	0	0		
Myalgia 5 hours post Moderate	0	0		
Myalgia 9 hours post Moderate	0	0		
Myalgia 24 hours post Moderate	0	0		
Skin disease 1 hour pre Moderate	0	0		

Skin disease 2 hours post Moderate	0	0		
Skin disease 3 hours post Moderate	0	0		
Skin disease 5 hours post Moderate	0	0		
Skin disease 9 hours post Moderate	0	3		
Skin disease 24 hours post Moderate	0	0		
Arthralgia 1 hour pre Severe	0	0		
Arthralgia 2 hours post Severe	0	0		
Arthralgia 3 hours post Severe	0	0		
Arthralgia 5 hours post Severe	0	0		
Arthralgia 9 hours post Severe	0	0		
Arthralgia 24 hours post Severe	0	0		
Conjunctivitis 1 hour pre Severe	0	0		
Conjunctivitis 2 hours post Severe	0	0		
Conjunctivitis 3 hours post Severe	0	0		
Conjunctivitis 5 hours post Severe	0	0		
Conjunctivitis 9 hours post Severe	0	0		
Conjunctivitis 24 hours post Severe	0	0		
Fatigue/Malaise 1 hour pre Severe	0	0		
Fatigue/Malaise 2 hours post Severe	0	0		
Fatigue/Malaise 3 hours post Severe	0	0		
Fatigue/Malaise 5 hours post Severe	0	0		
Fatigue/Malaise 9 hours post Severe	0	0		
Fatigue/Malaise 24 hours post Severe	0	0		
Headache/Migraine 1 hour pre Severe	0	0		
Headache/Migraine 2 hours post Severe	0	0		
Headache/Migraine 3 hours post Severe	0	0		
Headache/Migraine 5 hours post Severe	0	0		
Headache/Migraine 9 hours post Severe	0	0		
Headache/Migraine 24 hours post Severe	0	0		
Myalgia 1 hour pre Severe	0	0		
Myalgia 2 hours post Severe	0	0		
Myalgia 3 hours post Severe	0	0		
Myalgia 5 hours post Severe	0	0		
Myalgia 9 hours post Severe	0	0		
Myalgia 24 hours post Severe	0	0		
Skin disease 1 hour pre Severe	0	0		
Skin disease 2 hours post Severe	0	0		
Skin disease 3 hours post Severe	0	0		
Skin disease 5 hours post Severe	0	0		
Skin disease 9 hours post Severe	0	0		
Skin disease 24 hours post Severe	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's global assessment of disease activity

End point title	Patient's global assessment of disease activity
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End point description:

Patient's global assessment of disease activity is a questionnaire completed by the patient. It uses a 5-point scale. The patient selected a rating based on the patient's current disease activity at the time of the assessment. Lower scores represent better outcomes.

0 = Absent

1 = Minimal

2 = Mild

3 = Moderate

4 = Severe

End point type

Secondary

End point timeframe:

Screening and Treatment (Day 4): 1 hour pre and 2, 3, 5, 9 and 24 hours post. Scheduled time refers to the time post-meal (screening) and to the time post-dose (treatment). The start of the cold challenge is at 1 hour post and the duration is 45 minutes.

End point values	DFV890 100mg - Treatment	Screening		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	4		
Units: Participants				
1 hour pre Absent	3	2		
2 hours post Absent	3	0		
3 hours post Absent	3	0		
5 hours post Absent	2	0		
9 hours post Absent	2	0		
24 hours post Absent	2	1		
1 hour pre Minimal	1	2		
2 hours post Minimal	0	4		
3 hours post Minimal	0	2		
5 hours post Minimal	2	2		
9 hours post Minimal	2	1		
24 hours post Minimal	2	3		
1 hour pre Mild	0	0		
2 hours post Mild	1	0		
3 hours post Mild	1	2		
5 hours post Mild	0	2		
9 hours post Mild	0	2		
24 hours post Mild	0	0		
1 hour pre Moderate	0	0		
2 hours post Moderate	0	0		
3 hours post Moderate	0	0		
5 hours post Moderate	0	0		
9 hours post Moderate	0	1		
24 hours post Moderate	0	0		
1 hour pre Severe	0	0		
2 hours post Severe	0	0		
3 hours post Severe	0	0		
5 hours post Severe	0	0		
9 hours post Severe	0	0		
24 hours post Severe	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of approximately 34 days

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	DFV890 treatment
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Reporting group description:

DFV890 treatment

Serious adverse events	DFV890 treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	DFV890 treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Chills			

subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Cold urticaria			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Dermatitis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	3		
Myalgia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 March 2021	The primary purpose of this protocol amendment is to address comments raised by the Health Authorities during their review of the original protocol. Changes related to study stopping rules, the individual treatment stopping criteria and requirements for the cold challenge have been implemented. In addition, exclusion criterion 12 has been updated to exclude participants with a known history of renal disease including nephrolithiasis.
21 April 2021	The primary purpose of this protocol amendment is to address comments raised by Health Authorities and Institutional Review Board (IRBs)/Independent Ethics Committee (IECs) during their review of the original protocol. Changes related to the study stopping rules and requirements for the cold challenge has been implemented.
18 June 2021	The primary purpose of this protocol amendment is to address comments raised by Health Authorities and Institutional Review Boards (IRBs)/Independent Ethics Committees (IECs) during their review of the original protocol. Additional information has been added and changes have been implemented related to the distinction between familial cold autoinflammatory syndrome (FCAS) and cold urticaria, the design of the cold challenge procedure, risks and mitigation of any risks introduced by cold challenge, individual and study stopping rules and requirements for the cold challenge. In addition, exclusion criterion 23 has been updated to exclude participants with cold urticaria study stopping rules and requirements for the cold challenge have been implemented.
19 May 2022	The main purpose of this protocol amendment is to align inclusion and exclusion criteria defined in this study based on the observation from the screening cold challenge.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported