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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Not applicable

Trial Indication(s)

Familial cold auto-inflammatory syndrome (FCAS)

Protocol Number

CDFV890A12201

Protocol Title

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)

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase 2

Study Start/End Dates

Study Start Date: September 20, 2021 (Actual)

Primary Completion Date: December 13, 2022 (Actual)
Study Completion Date: May 05, 2023 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was an open-label, single-arm, multiple dose, phase II study to assess safety, tolerability and efficacy of DFV890 in participants with FCAS who showed evidence of inflammatory activity after the cold challenge performed during screening.

The study consisted of three periods:

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

Treatment period: Eligible participants (defined as those participants who respond to the screening cold challenge) entered the treatment period where they were administered with oral DFV890 100 mg twice daily (b.i.d.) for 3 days, last dose was administered in the morning of Day 4 followed by a treatment cold challenge.

Follow-up period: The study completion visit was conducted approximately 10 days after last dose and a post study safety contact occurred 30 days after last dose. The total study duration from screening until study completion was expected to be up to 7 months (and up to 13 months for participants with a historical screening cold challenge prior to protocol amendment 04).

Centers

3 centers in 3 countries: United States(1), Germany(1), France(1)

Objectives:

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).

The secondary objectives of the trial were:

- To assess safety and tolerability of DFV890.
- To assess the efficacy of DFV890 to improve the signs and symptoms of FCAS.
- To assess the effect of DFV890 on patient reported outcomes.

Test Product (s), Dose(s), and Mode(s) of Administration

Participants received 100 mg of DFV890 film coated tablets twice daily for 3 days starting in the morning of Day 1 and 100 mg of DFV890 in the morning on the fourth day. At each administration, 4 tablets of 25 mg DFV890 each were taken orally.

Statistical Methods

The primary objective would be achieved and DFV890 would be considered efficacious in treating cold-induced inflammation in participants with FCAS if the estimated ratio of fold change from pre-challenge to highest post challenge white cell count (WCC) between treatment and screening period were statistically significant ($p<0.10$) and less than 80%.

The fold change from pre-challenge to the highest post-challenge WCC was analyzed by a log-linear model, including logarithm of pre-challenge values as covariates and modeling period effect, taking into account the intra-participant correlation.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Written informed consent must be obtained before any study-specific assessment is performed
- Body mass index within the range of 18-35 kg/m2
- Patients with a genetic diagnosis of FCAS

- Patients with a clinical history and investigations consistent with FCAS

Exclusion Criteria:

- Anti-rejection and/or immunomodulatory drugs must be discontinued (please, see protocol for further details)
- Clinically significant, suspected active or chronic bacterial (including Mycobacterium tuberculosis), viral or fungal infection within 30 days prior to Day 1.
- Patients with innate (e.g. TLR immunodeficiencies, defects in IFN-γ signaling) or acquired immune deficiencies (e.g. AIDS).
- Presence of human immunodeficiency virus (HIV) infection, hepatitis B surface antigen (HBsAg) or hepatitis B core antibody (anti-HBc), or hepatitis C antibodies at screening.
- Live vaccines within 4 weeks of Day 1
- Pregnant or nursing (lactating) women.
- Women of child-bearing potential unless they are using highly effective methods of contraception.

Other protocol-defined inclusion/exclusion criteria may apply.

Participant Flow Table

Overall Study

	DFV890 100mg	Total
Arm/Group Description	DFV890 100mg oral dose, twice daily	
Started	4	4
Completed	3	3
Not Completed	1	1
Lost to Follow-up	1	1

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Baseline Characteristics

	DFV890 100mg	Total
Arm/Group Description	DFV890 100mg oral dose, twice daily	
Number of Participants [units: participants]	4	4
Baseline Analysis Population Description		
Age Continuous (units: years) Analysis Population Type: Mean ± Standard Deviation		
	41.3±15.48	
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)		
Female	1	1
Male	3	3
Race/Ethnicity, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)		
other	1	1
white	3	3

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Primary Outcome Result(s)

Ratio of fold change from pre-challenge to the highest post-challenge value of white cell count (WCC) between treatment and screening period

Description	A cold challenge was performed during the screening period and on Day 4 of the treatment period. Fold change from pre-challenge to highest post-challenge value of WCC was defined as the ratio of the highest post-challenge WCC value to the pre-challenge WCC value. The ratio of fold change was defined as treatment fold change divided by the screen fold change. A value of less than 1 for the ratio of fold change indicates a lower relative increase of WCC in the treatment than in the screening period, which is a favorable outcome. The log-transformed fold change from pre-challenge to the highest post challenge WCC was analyzed using a log-linear mixed effect model. The analysis was carried out considering the data from -2 to 8 hrs post challenge. The unforeseen screen failure rate and recruitment challenges resulted in early closure of the study. Only 4 out of planned 6 participants were enrolled in the study; thus, the results should be interpreted cautiously.
Time Frame	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.
Analysis Population Description	The Pharmacodynamic (PD) analysis set included all participants with no protocol deviations with relevant impact on PD data.

	DFV890 100mg - Treatment	
Arm/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	
Number of Participants Analyzed [units: participants]	4	
Ratio of fold change from pre-challenge to the highest post-challenge value of white cell count (WCC) between treatment and screening period (units: ratio of fold change)	Geometric Least Squares Mean	90% Confidence Interval
	0.82	0.56 to 1.21

Secondary Outcome Result(s)

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

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.
Time Frame	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
Analysis Population Description	The safety analysis set included all participants that received any study drug.

	DFV890 100mg
Arm/Group Description	DFV890 100mg oral dose, twice daily
Number of Participants Analyzed [units: participants]	4
Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs) (units: participants)	**Count of Participants (Not Applicable)**
At least one AE	4 (100%)
At least one SAE	0 (%)
AE leading to discontinuation	0 (%)
SAE leading to discontinuation	0 (%)

Physician global assessment of autoinflammatory disease activity

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

Time Frame	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.
Analysis Population Description	The Pharmacodynamic (PD) analysis set included all participants with no protocol deviations with relevant impact on PD data.

	Screening	**DFV890 100mg - Treatment**
Arm/Group Description	Screening period	DFV890 100mg oral dose, twice daily for 3 days and one last dose in the morning of Day 4 of the treatment period
Number of Participants Analyzed [units: participants]	4	4
Physician global assessment of autoinflammatory disease activity (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
1 hour pre : Absent	0 (%)	2 (50%)
1 hour pre : Minimal	3 (75%)	2 (50%)
1 hour pre : Mild	1 (25%)	0 (%)
1 hour pre : Moderate	0 (%)	0 (%)
1 hour pre : Severe	0 (%)	0 (%)
2 hours post : Absent	0 (%)	2 (50%)
2 hours post : Minimal	2 (50%)	1 (25%)
2 hours post : Mild	2 (50%)	1 (25%)
2 hours post : Moderate	0 (%)	0 (%)

2 hours post : Severe	0 (%)	0 (%)
3 hours post : Absent	0 (%)	2 (50%)
3 hours post : Minimal	1 (25%)	1 (25%)
3 hours post : Mild	3 (75%)	1 (25%)
3 hours post : Moderate	0 (%)	0 (%)
3 hours post : Severe	0 (%)	0 (%)
5 hours post : Absent	0 (%)	2 (50%)
5 hours post : Minimal	1 (25%)	1 (25%)
5 hours post : Mild	3 (75%)	1 (25%)
5 hours post : Moderate	0 (%)	0 (%)
5 hours post : Severe	0 (%)	0 (%)
9 hours post : Absent	0 (%)	1 (25%)
9 hours post : Minimal	1 (25%)	2 (50%)
9 hours post : Mild	0 (%)	1 (25%)
9 hours post : Moderate	3 (75%)	0 (%)
9 hours post : Severe	0 (%)	0 (%)

24 hours post : Absent	0 (%)	2 (50%)
24 hours post : Minimal	3 (75%)	2 (50%)
24 hours post : Mild	1 (25%)	0 (%)
24 hours post : Moderate	0 (%)	0 (%)
24 hours post : Severe	0 (%)	0 (%)

Physician's severity assessment of autoinflammatory disease signs and symptoms

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
Time Frame	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.
Analysis Population Description	The Pharmacodynamic (PD) analysis set included all participants with no protocol deviations with relevant impact on PD data.

	Screening	**DFV890 100mg**
Arm/Group Description	Screening period	DFV890 100mg oral dose, twice daily for 3 days and one last dose in the morning of Day 4 of the treatment period
Number of Participants Analyzed [units: participants]	4	4
Physician's severity assessment of autoinflammatory disease signs and symptoms (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**

Arthralgia 1 hour pre : Absent	3 (75%)	3 (75%)
Arthralgia 1 hour pre : Minimal	1 (25%)	1 (25%)
Arthralgia 1 hour pre : Mild	0 (%)	0 (%)
Arthralgia 1 hour pre : Moderate	0 (%)	0 (%)
Arthralgia 1 hour pre : Severe	0 (%)	0 (%)
Arthralgia 2 hours post : Absent	4 (100%)	4 (100%)
Arthralgia 2 hours post : Minimal	0 (%)	0 (%)
Arthralgia 2 hours post : Mild	0 (%)	0 (%)
Arthralgia 2 hours post : Moderate	0 (%)	0 (%)
Arthralgia 2 hours post : Severe	0 (%)	0 (%)
Arthralgia 3 hours post : Absent	4 (100%)	4 (100%)
Arthralgia 3 hours post : Minimal	0 (%)	0 (%)
Arthralgia 3 hours post : Mild	0 (%)	0 (%)
Arthralgia 3 hours post : Moderate	0 (%)	0 (%)
Arthralgia 3 hours post : Severe	0 (%)	0 (%)
Arthralgia 5 hours post : Absent	3 (75%)	4 (100%)

Arthralgia 5 hours post : Minimal	0 (%)	0 (%)
Arthralgia 5 hours post : Mild	1 (25%)	0 (%)
Arthralgia 5 hours post : Moderate	0 (%)	0 (%)
Arthralgia 5 hours post : Severe	0 (%)	0 (%)
Arthralgia 9 hours post : Absent	1 (25%)	3 (75%)
Arthralgia 9 hours post : Minimal	3 (75%)	1 (25%)
Arthralgia 9 hours post : Mild	0 (%)	0 (%)
Arthralgia 9 hours post : Moderate	0 (%)	0 (%)
Arthralgia 9 hours post : Severe	0 (%)	0 (%)
Arthralgia 24 hours post : Absent	4 (100%)	3 (75%)
Arthralgia 24 hours post : Minimal	0 (%)	1 (25%)
Arthralgia 24 hours post : Mild	0 (%)	0 (%)
Arthralgia 24 hours post : Moderate	0 (%)	0 (%)
Arthralgia 24 hours post : Severe	0 (%)	0 (%)
Conjunctivitis 1 hour pre : Absent	3 (75%)	3 (75%)
Conjunctivitis 1 hour pre : Minimal	0 (%)	1 (25%)

Conjunctivitis 1 hour pre : Mild	1 (25%)	0 (%)
Conjunctivitis 1 hour pre : Moderate	0 (%)	0 (%)
Conjunctivitis 1 hour pre : Severe	0 (%)	0 (%)
Conjunctivitis 2 hours post : Absent	3 (75%)	4 (100%)
Conjunctivitis 2 hours post : Minimal	0 (%)	0 (%)
Conjunctivitis 2 hours post : Mild	1 (25%)	0 (%)
Conjunctivitis 2 hours post : Moderate	0 (%)	0 (%)
Conjunctivitis 2 hours post : Severe	0 (%)	0 (%)
Conjunctivitis 3 hours post : Absent	3 (75%)	4 (100%)
Conjunctivitis 3 hours post : Minimal	0 (%)	0 (%)
Conjunctivitis 3 hours post : Mild	1 (25%)	0 (%)
Conjunctivitis 3 hours post : Moderate	0 (%)	0 (%)
Conjunctivitis 3 hours post : Severe	0 (%)	0 (%)
Conjunctivitis 5 hours post : Absent	3 (75%)	4 (100%)
Conjunctivitis 5 hours post : Minimal	0 (%)	0 (%)
Conjunctivitis 5 hours post : Mild	1 (25%)	0 (%)

Conjunctivitis 5 hours post : Moderate	0 (%)	0 (%)
Conjunctivitis 5 hours post : Severe	0 (%)	0 (%)
Conjunctivitis 9 hours post : Absent	2 (50%)	4 (100%)
Conjunctivitis 9 hours post : Minimal	0 (%)	0 (%)
Conjunctivitis 9 hours post : Mild	1 (25%)	0 (%)
Conjunctivitis 9 hours post : Moderate	1 (25%)	0 (%)
Conjunctivitis 9 hours post : Severe	0 (%)	0 (%)
Conjunctivitis 24 hours post : Absent	3 (75%)	2 (50%)
Conjunctivitis 24 hours post : Minimal	0 (%)	2 (50%)
Conjunctivitis 24 hours post : Mild	1 (25%)	0 (%)
Conjunctivitis 24 hours post : Moderate	0 (%)	0 (%)
Conjunctivitis 24 hours post : Severe	0 (%)	0 (%)
Fatigue/Malaise 1 hour pre : Absent	3 (75%)	3 (75%)
Fatigue/Malaise 1 hour pre : Minimal	0 (%)	0 (%)
Fatigue/Malaise 1 hour pre : Mild	1 (25%)	1 (25%)
Fatigue/Malaise 1 hour pre : Moderate	0 (%)	0 (%)

Fatigue/Malaise 1 hour pre : Severe	0 (%)	0 (%)
Fatigue/Malaise 2 hours post : Absent	3 (75%)	3 (75%)
Fatigue/Malaise 2 hours post : Minimal	0 (%)	0 (%)
Fatigue/Malaise 2 hours post : Mild	1 (25%)	0 (%)
Fatigue/Malaise 2 hours post : Moderate	0 (%)	1 (25%)
Fatigue/Malaise 2 hours post : Severe	0 (%)	0 (%)
Fatigue/Malaise 3 hours post : Absent	2 (50%)	3 (75%)
Fatigue/Malaise 3 hours post : Minimal	1 (25%)	0 (%)
Fatigue/Malaise 3 hours post : Mild	0 (%)	0 (%)
Fatigue/Malaise 3 hours post : Moderate	1 (25%)	1 (25%)
Fatigue/Malaise 3 hours post : Severe	0 (%)	0 (%)
Fatigue/Malaise 5 hours post : Absent	2 (50%)	3 (75%)
Fatigue/Malaise 5 hours post : Minimal	0 (%)	0 (%)
Fatigue/Malaise 5 hours post : Mild	2 (50%)	0 (%)
Fatigue/Malaise 5 hours post : Moderate	0 (%)	1 (25%)
Fatigue/Malaise 5 hours post : Severe	0 (%)	0 (%)

Fatigue/Malaise 9 hours post : Absent	2 (50%)	3 (75%)
Fatigue/Malaise 9 hours post : Minimal	0 (%)	0 (%)
Fatigue/Malaise 9 hours post : Mild	1 (25%)	0 (%)
Fatigue/Malaise 9 hours post : Moderate	1 (25%)	1 (25%)
Fatigue/Malaise 9 hours post : Severe	0 (%)	0 (%)
Fatigue/Malaise 24 hours post : Absent	3 (75%)	3 (75%)
Fatigue/Malaise 24 hours post : Minimal	1 (25%)	1 (25%)
Fatigue/Malaise 24 hours post : Mild	0 (%)	0 (%)
Fatigue/Malaise 24 hours post : Moderate	0 (%)	0 (%)
Fatigue/Malaise 24 hours post : Severe	0 (%)	0 (%)
Headache/Migraine 1 hour pre : Absent	4 (100%)	4 (100%)
Headache/Migraine 1 hour pre : Minimal	0 (%)	0 (%)
Headache/Migraine 1 hour pre : Mild	0 (%)	0 (%)
Headache/Migraine 1 hour pre : Moderate	0 (%)	0 (%)
Headache/Migraine 1 hour pre : Severe	0 (%)	0 (%)
Headache/Migraine 2 hours post : Absent	4 (100%)	4 (100%)

Headache/Migraine 2 hours post : Minimal	0 (%)	0 (%)
Headache/Migraine 2 hours post : Mild	0 (%)	0 (%)
Headache/Migraine 2 hours post : Moderate	0 (%)	0 (%)
Headache/Migraine 2 hours post : Severe	0 (%)	0 (%)
Headache/Migraine 3 hours post : Absent	4 (100%)	4 (100%)
Headache/Migraine 3 hours post : Minimal	0 (%)	0 (%)
Headache/Migraine 3 hours post : Mild	0 (%)	0 (%)
Headache/Migraine 3 hours post : Moderate	0 (%)	0 (%)
Headache/Migraine 3 hours post : Severe	0 (%)	0 (%)
Headache/Migraine 5 hours post : Absent	4 (100%)	4 (100%)
Headache/Migraine 5 hours post : Minimal	0 (%)	0 (%)
Headache/Migraine 5 hours post : Mild	0 (%)	0 (%)
Headache/Migraine 5 hours post : Moderate	0 (%)	0 (%)
Headache/Migraine 5 hours post : Severe	0 (%)	0 (%)
Headache/Migraine 9 hours post : Absent	3 (75%)	4 (100%)
Headache/Migraine 9 hours post : Minimal	0 (%)	0 (%)

Headache/Migraine 9 hours post : Mild	1 (25%)	0 (%)
Headache/Migraine 9 hours post : Moderate	0 (%)	0 (%)
Headache/Migraine 9 hours post : Severe	0 (%)	0 (%)
Headache/Migraine 24 hours post : Absent	4 (100%)	4 (100%)
Headache/Migraine 24 hours post : Minimal	0 (%)	0 (%)
Headache/Migraine 24 hours post : Mild	0 (%)	0 (%)
Headache/Migraine 24 hours post : Moderate	0 (%)	0 (%)
Headache/Migraine 24 hours post : Severe	0 (%)	0 (%)
Myalgia 1 hour pre : Absent	3 (75%)	4 (100%)
Myalgia 1 hour pre : Minimal	1 (25%)	0 (%)
Myalgia 1 hour pre : Mild	0 (%)	0 (%)
Myalgia 1 hour pre : Moderate	0 (%)	0 (%)
Myalgia 1 hour pre : Severe	0 (%)	0 (%)
Myalgia 2 hours post : Absent	4 (100%)	3 (75%)
Myalgia 2 hours post : Minimal	0 (%)	1 (25%)
Myalgia 2 hours post : Mild	0 (%)	0 (%)

Myalgia 2 hours post : Moderate	0 (%)	0 (%)
Myalgia 2 hours post : Severe	0 (%)	0 (%)
Myalgia 3 hours post : Absent	3 (75%)	4 (100%)
Myalgia 3 hours post : Minimal	0 (%)	0 (%)
Myalgia 3 hours post : Mild	1 (25%)	0 (%)
Myalgia 3 hours post : Moderate	0 (%)	0 (%)
Myalgia 3 hours post : Severe	0 (%)	0 (%)
Myalgia 5 hours post : Absent	3 (75%)	4 (100%)
Myalgia 5 hours post : Minimal	0 (%)	0 (%)
Myalgia 5 hours post : Mild	1 (25%)	0 (%)
Myalgia 5 hours post : Moderate	0 (%)	0 (%)
Myalgia 5 hours post : Severe	0 (%)	0 (%)
Myalgia 9 hours post : Absent	3 (75%)	4 (100%)
Myalgia 9 hours post : Minimal	1 (25%)	0 (%)
Myalgia 9 hours post : Mild	0 (%)	0 (%)
Myalgia 9 hours post : Moderate	0 (%)	0 (%)

Myalgia 9 hours post : Severe	0 (%)	0 (%)
Myalgia 24 hours post : Absent	4 (100%)	4 (100%)
Myalgia 24 hours post : Minimal	0 (%)	0 (%)
Myalgia 24 hours post : Mild	0 (%)	0 (%)
Myalgia 24 hours post : Moderate	0 (%)	0 (%)
Myalgia 24 hours post : Severe	0 (%)	0 (%)
Skin disease 1 hour pre : Absent	0 (%)	1 (25%)
Skin disease 1 hour pre : Minimal	3 (75%)	3 (75%)
Skin disease 1 hour pre : Mild	1 (25%)	0 (%)
Skin disease 1 hour pre : Moderate	0 (%)	0 (%)
Skin disease 1 hour pre : Severe	0 (%)	0 (%)
Skin disease 2 hours post : Absent	0 (%)	1 (25%)
Skin disease 2 hours post : Minimal	2 (50%)	3 (75%)
Skin disease 2 hours post : Mild	2 (50%)	0 (%)
Skin disease 2 hours post : Moderate	0 (%)	0 (%)
Skin disease 2 hours post : Severe	0 (%)	0 (%)

Skin disease 3 hours post : Absent	0 (%)	2 (50%)
Skin disease 3 hours post : Minimal	1 (25%)	2 (50%)
Skin disease 3 hours post : Mild	3 (75%)	0 (%)
Skin disease 3 hours post : Moderate	0 (%)	0 (%)
Skin disease 3 hours post : Severe	0 (%)	0 (%)
Skin disease 5 hours post : Absent	0 (%)	2 (50%)
Skin disease 5 hours post : Minimal	1 (25%)	2 (50%)
Skin disease 5 hours post : Mild	3 (75%)	0 (%)
Skin disease 5 hours post : Moderate	0 (%)	0 (%)
Skin disease 5 hours post : Severe	0 (%)	0 (%)
Skin disease 9 hours post : Absent	0 (%)	1 (25%)
Skin disease 9 hours post : Minimal	1 (25%)	3 (75%)
Skin disease 9 hours post : Mild	0 (%)	0 (%)
Skin disease 9 hours post : Moderate	3 (75%)	0 (%)
Skin disease 9 hours post : Severe	0 (%)	0 (%)
Skin disease 24 hours post : Absent	0 (%)	2 (50%)

Skin disease 24 hours post : Minimal	3 (75%)	2 (50%)
Skin disease 24 hours post : Mild	1 (25%)	0 (%)
Skin disease 24 hours post : Moderate	0 (%)	0 (%)
Skin disease 24 hours post : Severe	0 (%)	0 (%)

Patient's global assessment of disease activity

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
Time Frame	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.
Analysis Population Description	The Pharmacodynamic (PD) analysis set included all participants with no protocol deviations with relevant impact on PD data.

	Screening	**DFV890 100mg**
Arm/Group Description	Screening period	DFV890 100mg oral dose, twice daily for 3 days and one last dose in the morning of Day 4 of the treatment period
Number of Participants Analyzed [units: participants]	4	4
Patient's global assessment of disease activity (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
1 hour pre : Absent	2 (50%)	3 (75%)
1 hour pre : Minimal	2 (50%)	1 (25%)

1 hour pre : Mild	0 (%)	0 (%)
1 hour pre : Moderate	0 (%)	0 (%)
1 hour pre : Severe	0 (%)	0 (%)
2 hours post : Absent	0 (%)	3 (75%)
2 hours post : Minimal	4 (100%)	0 (%)
2 hours post : Mild	0 (%)	1 (25%)
2 hours post : Moderate	0 (%)	0 (%)
2 hours post : Severe	0 (%)	0 (%)
3 hours post : Absent	0 (%)	3 (75%)
3 hours post : Minimal	2 (50%)	0 (%)
3 hours post : Mild	2 (50%)	1 (25%)
3 hours post : Moderate	0 (%)	0 (%)
3 hours post : Severe	0 (%)	0 (%)
5 hours post : Absent	0 (%)	2 (50%)
5 hours post : Minimal	2 (50%)	2 (50%)
5 hours post : Mild	2 (50%)	0 (%)

5 hours post : Moderate	0 (%)	0 (%)
5 hours post : Severe	0 (%)	0 (%)
9 hours post : Absent	0 (%)	2 (50%)
9 hours post : Minimal	1 (25%)	2 (50%)
9 hours post : Mild	2 (50%)	0 (%)
9 hours post : Moderate	1 (25%)	0 (%)
9 hours post : Severe	0 (%)	0 (%)
24 hours post : Absent	1 (25%)	2 (50%)
24 hours post : Minimal	3 (75%)	2 (50%)
24 hours post : Mild	0 (%)	0 (%)
24 hours post : Moderate	0 (%)	0 (%)
24 hours post : Severe	0 (%)	0 (%)

Safety Results

Time Frame	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

Source Vocabulary for Table Default	MedDRA (26.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	DFV890 100 mg N = 4
Arm/Group Description	DFV890 100mg oral dose, twice daily
Total Number Affected	0
Total Number At Risk	4

Serious Adverse Events

There were no serious adverse events reported.

Other (Not Including Serious) Adverse Events

Frequent Event Reporting Threshold	5%

	DFV890 100 mg N = 4
Arm/Group Description	DFV890 100mg oral dose, twice daily
Total # Affected by any Other Adverse Event	4
Total # at Risk by any Other Adverse Event	4
General disorders and administration site conditions	
Asthenia	1 (25.00%)
Chills	1 (25.00%)
Fatigue	2 (50.00%)
Infections and infestations	
Conjunctivitis	1 (25.00%)
Musculoskeletal and connective tissue disorders	
Arthralgia	3 (75.00%)
Myalgia	1 (25.00%)
Nervous system disorders	
Headache	1 (25.00%)
Skin and subcutaneous tissue disorders	
Cold urticaria	2 (50.00%)
Dermatitis	1 (25.00%)
Erythema	1 (25.00%)
Rash	1 (25.00%)
Urticaria	2 (50.00%)

Conclusion:

DFV890 was safe and well tolerated in this study.

Improvements in the treatment period as compared to the screening period were observed across multiple clinical endpoints (WCC count and clinical outcome assessments). This potentially indicates signs of efficacy of DFV890. However, as the study enrolled a limited number of participants in the primary analysis the interpretation should be made cautiously.

Date of Clinical Trial Report

02-February-2024