Clinical trial results:
A randomized, subject and investigator blinded, placebo-controlled multicenter study to assess the efficacy and safety of CMK389 in patients with moderate to severe atopic dermatitis.

Summary

EudraCT number	2020-003406-31
Trial protocol	HU DE FR CZ ES
Global end of trial date	13 December 2022

Results information

Result version number	v1 (current)
This version publication date	21 December 2023
First version publication date	21 December 2023

Trial information

Trial identification

Sponsor protocol code	CCMK389B12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04836858
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	13 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 December 2022
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 CMK389 in participants with moderate to severe atopic dermatitis.

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 April 2021
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	Czechia: 15
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 38
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Spain: 3
Worldwide total number of subjects	71
EEA total number of subjects	71

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:

Participants took part in 18 investigative sites in 6 countries.

Pre-assignment

Screening details:

There was a screening period of up to 4 weeks to assess participants eligibility.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	CMK389 10mg/kg i.v.

Arm description:

CMK389 10 mg/kg monthly i.v. dose

Arm type	Experimental
Investigational medicinal product name	CMK389
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

CMK389 10mg/kg intravenously monthly

Arm title	CMK389 300mg s.c.

Arm description:

CMK389 300mg monthly s.c. dose

Arm type	Experimental
Investigational medicinal product name	CMK389
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

CMK389 300 mg subcutaneous monthly

Arm title	Placebo i.v.

Arm description:

Placebo monthly i.v. dose

Arm type	Placebo
Investigational medicinal product name	CMK389
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo intravenously monthly

Arm title	Placebo s.c.

Arm description:

Placebo monthly s.c. dose

Arm type	Placebo
Investigational medicinal product name	CMK389
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo subcutaneous monthly

Number of subjects in period 1[1]	CMK389 10mg/kg i.v.	CMK389 300mg s.c.	Placebo i.v.
Started	34	17	8
Completed	30	17	8
Not completed	4	0	0
Adverse events	-	-	-
Subject/Guardian decision	3	-	-
Lost to follow-up	1	-	-

Number of subjects in period 1[1]	Placebo s.c.
Started	8
Completed	6
Not completed	2
Adverse events	1
Subject/Guardian decision	1
Lost to follow-up	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: There were 4 participants who were randomized to the CMK389 10 mg/kg i.v. group but never received any dose of study treatment. They have not been included in the tables of Disposition and Baseline Characteristics.

Baseline characteristics

Reporting groups	
Reporting group title	CMK389 10mg/kg i.v.
Reporting group description: CMK389 10 mg/kg monthly i.v. dose	
Reporting group title	CMK389 300mg s.c.
Reporting group description: CMK389 300mg monthly s.c. dose	
Reporting group title	Placebo i.v.
Reporting group description: Placebo monthly i.v. dose	
Reporting group title	Placebo s.c.
Reporting group description: Placebo monthly s.c. dose	

Reporting group values	CMK389 10mg/kg i.v.	CMK389 300mg s.c.	Placebo i.v.
Number of subjects	34	17	8
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	34	17	8
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	33.7	34.1	35.3
standard deviation	± 9.86	± 11.35	± 8.86
Sex: Female, Male Units: participants			
Female	8	9	3
Male	26	8	5
Race/Ethnicity, Customized Units: Subjects			
Asian	0	1	0
White	34	16	8

Reporting group values	Placebo s.c.	Total	
Number of subjects	8	67	
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)	8	67	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	31.9		
standard deviation	± 8.53	-	
Sex: Female, Male			
Units: participants			
Female	2	22	
Male	6	45	
Race/Ethnicity, Customized			
Units: Subjects			
Asian	0	1	
White	8	66	

End points

End points reporting groups

Reporting group title	CMK389 10mg/kg i.v.
Reporting group description: CMK389 10 mg/kg monthly i.v. dose	
Reporting group title	CMK389 300mg s.c.
Reporting group description: CMK389 300mg monthly s.c. dose	
Reporting group title	Placebo i.v.
Reporting group description: Placebo monthly i.v. dose	
Reporting group title	Placebo s.c.
Reporting group description: Placebo monthly s.c. dose	

Primary: Number of participants with Investigator Global assessment (IGA) response

End point title	Number of participants with Investigator Global assessment (IGA) response[1]

End point description:

The Investigator Global assessment (IGA) scale used was vIGA-AD^TM (Validated Investigator Global Assessment scale for Atopic Dermatitis). The IGA rating scale was used to determine the severity of atopic dermatitis and clinical response to treatment. It reflected a participant's overall disease severity for the whole body based on a 5-point scale. The 5-point scale included: clear, almost clear, mild, moderate, and severe disease. IGA response is defined as clear or almost clear and at least a 2 point-reduction from baseline at week 16.

End point type	Primary

End point timeframe:

Baseline, Week 16

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 analyzed descriptively

End point values	CMK389 10mg/kg i.v.	CMK389 300mg s.c.	Placebo i.v.	Placebo s.c.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	17	8	8
Units: participants	5	2	0	0

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

End point timeframe:

AEs were reported from first dose until the end of the 12 weeks follow up period, up to a max. duration of approx. 197 days. For women of child-bearing potential, pregnancies were reported (if occurred) for up to approx. 268 days after first dose.

End point values	CMK389 10mg/kg i.v.	CMK389 300mg s.c.	Placebo i.v.	Placebo s.c.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	17	8	8
Units: participants				
Adverse Events	25	11	5	8
Serious Adverse Events	1	1	0	0
AEs leading to discontinuation of study treatment	0	0	0	0
SAEs leading to discontinuation of study treatment	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were reported from first dose until the end of the 12 weeks follow up period, up to a max. duration of approx. 197 days. For women of child-bearing potential, pregnancies were reported (if occurred) for up to approx. 268 days after first dose.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Pooled Placebo
Reporting group description:	
Pooled Placebo	
Reporting group title	Total
Reporting group description:	
Total	
Reporting group title	Placebo i.v.
Reporting group description:	
Placebo i.v.	
Reporting group title	Placebo s.c.
Reporting group description:	
Placebo s.c.	
Reporting group title	CMK389 10 mg/kg i.v.
Reporting group description:	
CMK389 10 mg/kg i.v.	
Reporting group title	CMK389 300 mg s.c.
Reporting group description:	
CMK389 300 mg s.c.	

Serious adverse events	Pooled Placebo	Total	Placebo i.v.
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	2 / 67 (2.99%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			

subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo s.c.	CMK389 10 mg/kg i.v.	CMK389 300 mg s.c.
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	1 / 17 (5.88%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Pooled Placebo	Total	Placebo i.v.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 16 (81.25%)	44 / 67 (65.67%)	5 / 8 (62.50%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	2 / 67 (2.99%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			

Injection site reaction			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Fatigue			
subjects affected / exposed	1 / 16 (6.25%)	1 / 67 (1.49%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dysphonia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	1 / 16 (6.25%)	1 / 67 (1.49%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	2 / 67 (2.99%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 16 (6.25%)	3 / 67 (4.48%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Blood creatine increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	2 / 67 (2.99%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Blood ketone body increased			

subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Urine analysis abnormal			
subjects affected / exposed	1 / 16 (6.25%)	1 / 67 (1.49%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Urinary sediment present			
subjects affected / exposed	1 / 16 (6.25%)	1 / 67 (1.49%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Lymphocyte count decreased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Glucose urine			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 67 (1.49%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	1 / 16 (6.25%)	5 / 67 (7.46%)	1 / 8 (12.50%)
occurrences (all)	0	8	2
Migraine			
subjects affected / exposed	2 / 16 (12.50%)	2 / 67 (2.99%)	2 / 8 (25.00%)
occurrences (all)	0	3	3
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Eye disorders			

Visual impairment			
subjects affected / exposed	1 / 16 (6.25%)	2 / 67 (2.99%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Eyelid oedema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	5 / 67 (7.46%)	0 / 8 (0.00%)
occurrences (all)	0	7	0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dermatitis atopic			
subjects affected / exposed	4 / 16 (25.00%)	8 / 67 (11.94%)	0 / 8 (0.00%)
occurrences (all)	0	8	0
Renal and urinary disorders			
Hypertonic bladder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 67 (2.99%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Muscle tightness			
subjects affected / exposed	1 / 16 (6.25%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

Asymptomatic bacteriuria			
subjects affected / exposed	1 / 16 (6.25%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	2 / 67 (2.99%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Rhinitis			
subjects affected / exposed	0 / 16 (0.00%)	2 / 67 (2.99%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Otitis externa			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	2 / 16 (12.50%)	13 / 67 (19.40%)	1 / 8 (12.50%)
occurrences (all)	0	13	1
COVID-19			
subjects affected / exposed	4 / 16 (25.00%)	19 / 67 (28.36%)	3 / 8 (37.50%)
occurrences (all)	0	21	3
Bacteriuria			
subjects affected / exposed	1 / 16 (6.25%)	1 / 67 (1.49%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 67 (1.49%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Placebo s.c.	CMK389 10 mg/kg i.v.	CMK389 300 mg s.c.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	20 / 34 (58.82%)	11 / 17 (64.71%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	3
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dysphonia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 34 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 8 (12.50%)	2 / 34 (5.88%)	0 / 17 (0.00%)
occurrences (all)	1	2	0
Blood creatine increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Aspartate aminotransferase			

increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 34 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Blood ketone body increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Urine analysis abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Urinary sediment present			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Glucose urine			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 8 (0.00%)	3 / 34 (8.82%)	1 / 17 (5.88%)
occurrences (all)	0	5	1
Migraine			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Eyelid oedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	3 / 34 (8.82%)	2 / 17 (11.76%)
occurrences (all)	0	5	2
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dermatitis atopic			
subjects affected / exposed	4 / 8 (50.00%)	2 / 34 (5.88%)	2 / 17 (11.76%)
occurrences (all)	4	2	2
Renal and urinary disorders			
Hypertonic bladder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 34 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Muscle tightness			

subjects affected / exposed	1 / 8 (12.50%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Asymptomatic bacteriuria			
subjects affected / exposed	1 / 8 (12.50%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Rhinitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Otitis externa			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 8 (12.50%)	7 / 34 (20.59%)	4 / 17 (23.53%)
occurrences (all)	1	7	4
COVID-19			
subjects affected / exposed	1 / 8 (12.50%)	10 / 34 (29.41%)	5 / 17 (29.41%)
occurrences (all)	1	10	7
Bacteriuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 34 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 34 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2021	The main purpose of this amendment is to address requests from Health Authorities (HA) and Ethics Committees (EC) received during review of the clinical trial application, which includes the creation of an independent Data Monitoring Committee (DMC) for this proof of concept study.
04 March 2022	The main purpose of this amendment is to address Health Authority (HA) request and to update and clarify language in selected sections of the protocol. In accordance with the HA request and to avoid ambiguity, a sentence in the rescue medication section stating that investigator should consult with sponsor's medical lead before study drug discontinuation has been deleted. Furthermore, in order to resolve previously detected issues in the protocol, the content of several sections have been updated with clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported