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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Not Applicable

Trial Indication(s)

Chronic pulmonary sarcoidosis

Protocol Number

CCMK389X2201

Protocol Title

A subject and investigator blinded, randomized, placebo-controlled, repeat-dose, multicenter study to investigate efficacy, safety, and tolerability of CMK389 in patients with chronic pulmonary sarcoidosis

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase 2

Study Start/End Dates

Study Start Date: September 23, 2020 (Actual)
Primary Completion Date: September 19, 2023 (Actual)
Study Completion Date: December 12, 2023 (Actual)

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Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was a participant and investigator blinded, randomized, placebo-controlled, parallel-group, repeat-dose, multicenter, nonconfirmatory study of the safety and efficacy of CMK389 administered intravenously every 4 weeks for a total of 4 doses in chronic pulmonary sarcoidosis patients. Sixty-two patients were randomized in a 1:1 ratio to receive either CMK389 or placebo. The total duration of participation for men and women of non-childbearing potential was approximately 38 weeks. For women of childbearing potential, the duration of participation was approximately 46 weeks.

Centers

22 centers in 6 countries: Germany(5), Denmark(3), Poland(3), Czech Republic(2), United States(7), United Kingdom(2)

Objectives:

The primary objective of the trial was to assess the efficacy of CMK389 in participants with chronic pulmonary sarcoidosis.
The secondary objectives of the trial were:

- To assess the impact of CMK389 on steroid use (mg days)
- To assess the impact of CMK389 on a composite index of pulmonary physiology and exercise capacity
- To explore the impact of CMK389 observed with [18F]-fluorodeoxyglucose positron emission tomography/computed tomography ([18F]-FDG-PET/CT) imaging
- To assess the pharmacokinetics of CMK389
- To assess the safety and tolerability of CMK389
- To assess the impact of CMK389 on pulmonary physiology
- To assess the impact of CMK389 on exercise capacity

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

Participants were assigned to one of the following 2 treatment groups in a ratio of 1:1.

- CMK389: four doses of 10 mg/kg i.v. every 4 weeks
- Placebo: four doses of matching placebo i.v. every 4 weeks

Statistical Methods

The primary aim of the study was to assess efficacy of CMK389 in participants with chronic pulmonary sarcoidosis. This was evaluated by assessing the change from baseline in percent predicted FVC at week 16. The model investigated effects for treatment by time (included as a class variable) interaction, baseline percent predicted FVC by time interaction and included the covariates prior sarcoidosis immunosuppressant therapy (stratification factor) and baseline prednisone dose. Uninformative priors for all the parameters were utilized to obtain the posterior estimates. The correlation among the repeated measures collected on the same patient were assessed via an unstructured covariance matrix. Baseline FVC and prednisone were centered and standardized before used in the model.

Secondary variables for this study were:

- Steroid use: Change from baseline in steroid usage.
- Composite index of pulmonary physiology (CIPP) and exercise capacity: a patient who deteriorated from baseline to each visit was defined as a patient with:
    - relative reduction if FVC ≥ 10%, or
    - relative reduction if FEV1 ≥ 10%, or
    - relative reduction of DLCO ≥ 15%, or
    - relative reduction of 6MWD ≥ 50 m.

- [18F]FDG-PET/CT: [18F]FDG focal uptake was assessed from the measurements of SUVmax (value for the single voxel with the highest activity in the focal region volume) and SUVmean (mean value for activity in the focal region volume) in up to 10 regions in three main categories: lung parenchyma, lymph nodes and extrathoracic areas. For the statistical analysis, the mean SUVmax and SUVmean values over the different uptake regions were derived for each category at baseline and Week 16.

- Pulmonary function tests: Change from baseline in FEV1 (L), and DLCO (absolute values).

- 6MWD: Change from baseline in distance walked and for the distance saturation product. The latter was derived as the product between the distance walked and lowest oxygen saturation (SpO2%) value observed during the test; that is, the lowest of the values taken after 1, 2, 3, 4, 5, and 6 minutes from the start of the test.

All participants within the safety analysis set were included in the safety data analysis.

Adverse events collected before the start of the study drug and during the pregnancy testing epoch were listed separately, while treatment emergent adverse events (events with an onset day ≥ date of the first dosing and ≤ date of the end of the follow-up phase) were listed and summarized as described below.

All information obtained on adverse events was displayed by treatment and patient. The number and percentage of patients with adverse events was tabulated by body system and preferred term with a breakdown by treatment. A patient with multiple adverse events within a body system was only counted once towards the total of this body system and treatment.

All participants within the PK analysis set were included in the PK data analysis. CMK389 plasma concentration data was listed by patient and visit/sampling time point. Descriptive summary statistics were provided by visit/sampling time point. Summary statistics included mean (arithmetic and geometric), SD, CV (arithmetic and geometric), median, minimum and maximum.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Subjects must have a body mass index (BMI) at screening within the range of 18 - 46 kg/m2. BMI = Body weight (kg) / [Height (m)]2
- Biopsy proven pulmonary sarcoidosis diagnosed > 1 year prior to screening

- Scadding stage II, III or IV as determined by the most recent chest x-ray obtained within 12 months prior to screening or at screening (confirmed by the Investigator)
- HRCT extent of fibrosis <20% (confirmed by the central imaging reader) at screening
- Treatment with 5-15 mg/day prednisone (or prednisone oral equivalents) for ≥ 6 months prior to screening.
- Co-medication with methotrexate or azathioprine for ≥ 6 months prior to screening (Note: hydroxychloroquine is allowed as background therapy but not required)
- Able to perform reliable, reproducible pulmonary function test maneuvers per American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines

Exclusion Criteria:

- Diagnosis of significant pulmonary hypertension (WHO group 5) requiring pharmacological treatment
- Active cardiac sarcoidosis requiring treatment. Inactive cardiac sarcoidosis or stable cardiac sarcoidosis not requiring treatment are permissible.
- A known diagnosis of neurosarcoidosis
- Forced vital capacity (FVC) <50% of predicted at screening (central read)
- Modified British Medical Research Council (mMRC) dyspnea scale ≥ 3 at screening
- Concomitant treatment with leflunomide, cyclophosphamide, mycophenolate, infliximab, etanercept, adalimumab, golimumab, ustekinumab, roflumilast, pentoxifylline, and abatacept within 12 weeks of screening
- Prior treatment with rituximab, canakinumab, anakinra, and tocilizumab
- Current use of any inhaled substance, including but not limited to tobacco, marijuana products and use of electronic cigarette or vaping device, and excluding inhalers or nebulizers prescribed for pulmonary sarcoidosis
- Any conditions or significant medical problems which in the opinion of the investigator and in consultation with the sponsor,

immunocompromises the patient and/or places the patient at unacceptable risk for immunomodulatory therapy

- Contraindication to FDG-PET scan investigations such as severe claustrophobia or uncontrolled diabetes

- History or current diagnosis of ECG abnormalities not due to Cardiac Sarcoidosis and indicating significant risk of safety for patients participating in the study

- A diagnosis of Lofgren's syndrome

- A history of pancreatitis

Participant Flow Table

Overall Study

	CMK389 10 mg/kg i.v.	Placebo i.v.	Total
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses	Placebo i.v. every 4 weeks for a total of 4 doses	
Started	31	31	62
Completed	31	31	62
Not Completed	0	0	0

Baseline Characteristics

	CMK389 10 mg/kg i.v.	Placebo i.v.	Total
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses	Placebo i.v. every 4 weeks for a total of 4 doses	
Number of Participants [units: participants]	31	31	62

Baseline Analysis Population Description			
Age Continuous (units: years) Analysis Population Type: Mean ± Standard Deviation			
	51.5±8.69	50.7±9.36	51.1±8.96
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
Female	7	13	20
Male	24	18	42
Race/Ethnicity, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
Black Or African American	3	2	5
Unknown	0	1	1
White	28	28	56

Primary Outcome Result(s)

Change in percent predicted FVC from baseline to 16 weeks of treatment

Description	To assess the effect of CMK389 compared to placebo after 16 weeks of treatment on spirometry (Forced Vital Capacity). Forced Vital Capacity (FVC) is the amount of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. Percent predicted FVC is the percentage of the age, height and gender adjusted predicted value.
Time Frame	Baseline, Week 16
Analysis Population Description	The Pharmacodynamic (PD) analysis set included all patients with available PD data and no protocol deviations with relevant impact on PD data. Data collected after a change of the steroid dose not based on the clinical status evaluation (CSE) algorithm were excluded from the analysis set if assessed as having a potentially relevant impact on PD data.

	CMK389 10 mg/kg i.v.	Placebo i.v.
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses	Placebo i.v. every 4 weeks for a total of 4 doses
Number of Participants Analyzed [units: participants]	26	27
Change in percent predicted FVC from baseline to 16 weeks of treatment (units: Percent predicted)	**Mean** **± Standard Deviation**	**Mean** **± Standard Deviation**
	-0.48 ± 1.17	1.02 ± 1.13

Statistical Analysis

Groups	CMK389 10 mg/kg i.v., Placebo i.v.	
Type of Statistical Test	Other	
Non-Inferiority/Equivalence Test	A Bayesian model for repeated measurements including data collected at Weeks 4, 8, 12 and 16 was applied to compare FVC between CMK389 and placebo groups.	
P Value	0.1804	
Method	Other Bayesian analysis	Posterior probability that treatment is better than placebo.
Other Posterior estimate treatment difference	-1.49	80% credible intervals are reported on the treatment difference
Standard Deviation	1.62	
80 % Confidence Interval 2-Sided	-3.56 to 0.60	

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Secondary Outcome Result(s)

Number of participants who had an increase in steroid usage from baseline to 16 weeks of treatment

Description	The Clinical Status Evaluation (CSE) served as a safety evaluation and served to establish the patient's clinical status (Clinical Status Determination [CSD]). CSE was performed prior to the titration of steroids, and the CSD guided selection of the next dose of steroids. Participants with CSD of "improved" or "stable" decreased steroid dose by 1 step on the dosing scale. Participants with CSD of "deteriorating" were ineligible to continue the study (if found during the run-in epoch or at study Day 1); or they increased steroid dose by 1 step (if found during the treatment epoch).
Time Frame	Baseline, Week 16
Analysis Population Description	The PD analysis set included all patients with available PD data and no protocol deviations with relevant impact on PD data. Data collected after a change of the steroid dose not based on the CSE algorithm were excluded from the analysis set if assessed as having a potentially relevant impact on PD data.

	CMK389 10 mg/kg i.v.	**Placebo i.v.**
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses	Placebo i.v. every 4 weeks for a total of 4 doses
Number of Participants Analyzed [units: participants]	29	31
Number of participants who had an increase in steroid usage from baseline to 16 weeks of treatment (units: participants)	**Count of Participants**	**Count of Participants**
	5 (17.24%)	4 (12.9%)

Number of participants who deteriorate from baseline to 16 weeks of treatment

Description	Composite index of pulmonary physiology (CIPP) and exercise capacity: a participant who deteriorated from baseline to each visit was defined as a patient with: relative reduction if FVC ≥ 10%, or relative reduction if FEV1 ≥ 10%, or relative reduction of DLCO ≥ 15%, or relative reduction of 6MWD ≥ 50 m.
Time Frame	Baseline, Week 16
Analysis Population Description	The PD analysis set included all patients with available PD data and no protocol deviations with relevant impact on PD data. Data collected after a change of the steroid dose not based on the CSE algorithm were excluded from the analysis set if assessed as having a potentially relevant impact on PD data.

	CMK389 10 mg/kg i.v.	Placebo i.v.
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses	Placebo i.v. every 4 weeks for a total of 4 doses
Number of Participants Analyzed [units: participants]	29	31
Number of participants who deteriorate from baseline to 16 weeks of treatment (units: participants)	**Count of Participants**	**Count of Participants**
	9 (31.03%)	10 (32.26%)

Percent change in [18F]-FDG-PET/CT (SUVmax and SUVmean) from baseline to 16 weeks of treatment

Description	[18F]-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) maximum standardized uptake value and mean standardized uptake value (SUVmax and SUVmean) imaging was used to assess potential anti-inflammatory effects by CMK389 on the sarcoidosis process. All participants underwent whole-body head to mid-thigh [18F]FDG-PET/CT imaging state-of-the-art, 3D PET/CT scanners with a reconstructed resolution of ≤5 mm. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.
Time Frame	Baseline, Week 16
Analysis Population Description	The PD analysis set included all patients with available PD data and no protocol deviations with relevant impact on PD data. Data collected after a change of the steroid dose not based on the CSE algorithm were excluded from the analysis set if assessed as having a potentially relevant impact on PD data. This analysis included only participants with a baseline positron emission tomography (PET) signal in the corresponding region.

	CMK389 10 mg/kg i.v.	Placebo i.v.
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses	Placebo i.v. every 4 weeks for a total of 4 doses
Number of Participants Analyzed [units: participants]	29	31

Percent change in [18F]-FDG-PET/CT (SUVmax and SUVmean) from baseline to 16 weeks of treatment (units: percent change from Baseline)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Lung Parenchyma SUVmax (n=12,18)	-29.23 ± 31.128	26.78 ± 24.461
Lymph Nodes SUVmax (n=11,9)	-23.40 ± 9.083	-16.48 ± 9.759
Extrathoracic SUVmax (n=4,13)	-12.89 ± 14.361	-19.07 ± 6.908
Lung Parenchyma SUVmean (n=12,18)	-34.06 ± 28.626	20.74 ± 22.443
Lymph Nodes SUVmean (n=11,9)	-30.83 ± 8.157	-22.75 ± 9.101
Extrathoracic SUVmean (n=4,13)	-11.23 ± 13.020	-23.99 ± 6.440

The observed serum concentration following CMK389 administration at end of infusion

Description	Pharmacokinetic parameters were directly derived from the PK concentration data using non-compartmental analysis. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.
Time Frame	Post 1 hour: Day 1, Day 29, Day 57, Day 85
Analysis Population Description	The Pharmacokinetics (PK) analysis set included all patients with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received CMK389 and with no protocol deviations with relevant impact on PK data.

	CMK389 10 mg/kg i.v.
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses
Number of Participants Analyzed [units: participants]	31
The observed serum concentration following CMK389 administration at end of infusion (units: ng/mL)	**Median (Full Range)**
Day 1 (n=30)	453000 (236000 to 1230000)
Day 29 (n=31)	533000 (58100 to 2460000)

Day 57 (n=29)	571000 (77600 to 3070000)
Day 85 (n=28)	541000 (78300 to 893000)

Pre-dose trough concentration (Ctrough) of CMK389

Description	Pharmacokinetic parameters were directly derived from the PK concentration data using non-compartmental analysis. Ctrough is the observed plasma concentration that is just prior to the beginning of a dosing interval. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.
Time Frame	Pre-dose: Day 1, Day 29, Day 57, Day 85
Analysis Population Description	The PK analysis set included all patients with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received CMK389 and with no protocol deviations with relevant impact on PK data.

	CMK389 10 mg/kg i.v.
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses
Number of Participants Analyzed [units: participants]	31
Pre-dose trough concentration (Ctrough) of CMK389 (units: ng/mL)	**Median** **(Full Range)**
Day 1 (n=15)	0.00 (0.00 to 619000)
Day 29 (n=31)	83500 (43300 to 176000)
Day 57 (n=30)	105000 (41700 to 182000)
Day 85 (n=30)	125000 (27900 to 444000)

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Change in FEV1 from baseline to 16 weeks of treatment

Description	FEV1 (forced expiratory volume in one second) is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation, measured through spirometry testing. The least-squares means for change from baseline in FEV1 to assess the effect of CMK389 compared to placebo after 16 weeks were obtained from a mixed effects model for repeated measures (MMRM). A positive change from baseline in pre-dose FEV1 is considered a favourable outcome.
Time Frame	Baseline, Week 16
Analysis Population Description	The PD analysis set included all patients with available PD data and no protocol deviations with relevant impact on PD data. Data collected after a change of the steroid dose not based on the CSE algorithm were excluded from the analysis set if assessed as having a potentially relevant impact on PD data.

	CMK389 10 mg/kg i.v.	**Placebo i.v.**
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses	Placebo i.v. every 4 weeks for a total of 4 doses
Number of Participants Analyzed [units: participants]	26	27
Change in FEV1 from baseline to 16 weeks of treatment (units: liters (L))	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	-0.03 ± 0.033	0.00 ± 0.032

Statistical Analysis

Groups	CMK389 10 mg/kg i.v., Placebo i.v.	
Type of Statistical Test	Superiority	
P Value	0.783	
Method	Other Mixed effects Model for Repeated Measure	
Median Difference (Net)	-0.04	Treatment difference (CMK389-placebo)
Standard Error of the mean	0.045	

80 % Confidence Interval 2-Sided	-0.09 to 0.02

Change in diffusion capacity of the lung for carbon monoxide (DLCO) from baseline to 16 weeks of treatment

Description	DLCO is a measurement to assess the lungs' ability to transfer gas from inspired air to the bloodstream. The least squares means for change from baseline in DLCO to assess the effect of CMK389 compared to placebo after 16 weeks were obtained from a mixed effects model for repeated measures (MMRM). A positive change from baseline in DLCO is considered a favourable outcome.
Time Frame	Baseline, Week 16
Analysis Population Description	The PD analysis set included all patients with available PD data and no protocol deviations with relevant impact on PD data. Data collected after a change of the steroid dose not based on the CSE algorithm were excluded from the analysis set if assessed as having a potentially relevant impact on PD data.

	CMK389 10 mg/kg i.v.	**Placebo i.v.**
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses	Placebo i.v. every 4 weeks for a total of 4 doses
Number of Participants Analyzed [units: participants]	20	25
Change in diffusion capacity of the lung for carbon monoxide (DLCO) from baseline to 16 weeks of treatment (units: mL/min/mmHg)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	-0.58 ± 0.493	-0.40 ± 0.448

Statistical Analysis

Groups	CMK389 10 mg/kg i.v., Placebo i.v.
Type of Statistical Test	Superiority
P Value	0.608

Method	Other Mixed effects Model for Repeated Measure	
Mean Difference (Net)	-0.18	Treatment difference (CMK389-placebo)
Standard Error of the mean	0.664	
80 % Confidence Interval 2-Sided	-1.05 to 0.68	

Change in 6-minute walk distance (6MWD) from baseline to 16 weeks of treatment

Description	The 6MWD test is self-paced, with standardized instructions and encouragement being given as participants walk as far as possible over 6 minutes through a flat corridor. The final distance is recorded in meters. The least squares means for change from baseline in 6MWD to assess the effect of CMK389 compared to placebo after 16 weeks were obtained from a mixed effects model for repeated measures (MMRM). A positive change from baseline in 6MWD is considered a favourable outcome.
Time Frame	Baseline, Week 16
Analysis Population Description	The PD analysis set included all patients with available PD data and no protocol deviations with relevant impact on PD data. Data collected after a change of the steroid dose not based on the CSE algorithm were excluded from the analysis set if assessed as having a potentially relevant impact on PD data.

	CMK389 10 mg/kg i.v.	**Placebo i.v.**
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses	Placebo i.v. every 4 weeks for a total of 4 doses
Number of Participants Analyzed [units: participants]	26	26
Change in 6-minute walk distance (6MWD) from baseline to 16 weeks of treatment (units: meters)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	11.21 ± 9.470	10.50 ± 9.223

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Statistical Analysis

Groups	CMK389 10 mg/kg i.v., Placebo i.v.	
Type of Statistical Test	Superiority	
P Value	0.479	
Method	Other Mixed effects Model for Repeated Measure	
Median Difference (Net)	0.71	Treatment difference (CMK389-placebo)
Standard Error of the mean	13.126	
80 % Confidence Interval 2-Sided	-16.35 to 17.76	

Safety Results

Time Frame	Adverse events were reported from first dose of study treatment until end of study treatment plus follow up period, up to a maximum duration of approximately 197 days..
Source Vocabulary for Table Default	MedDRA (22.0)
Collection Approach for Table Default	Systematic Assessment

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All-Cause Mortality

	CMK389 10 mg/kg i.v N = 31	Placebo i.v N = 31	Total N = 62
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses	Placebo i.v. every 4 weeks for a total of 4 doses	Total
Total Number Affected	0	0	0
Total Number At Risk	31	31	62

Serious Adverse Events

	CMK389 10 mg/kg i.v N = 31	Placebo i.v N = 31	Total N = 62
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses	Placebo i.v. every 4 weeks for a total of 4 doses	Total
Total # Affected by any Serious Adverse Event	2	0	2
Total # at Risk by any Serious Adverse Event	31	31	62
Injury, poisoning and procedural complications			
Head injury	1 (3.23%)	0 (0.00%)	1 (1.61%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin	1 (3.23%)	0 (0.00%)	1 (1.61%)

Other (Not Including Serious) Adverse Events

Frequent Event Reporting Threshold 5%

	CMK389 10 mg/kg i.v N = 31	Placebo i.v N = 31	Total N = 62
Arm/Group Description	CMK389 10 mg/kg i.v. every 4 weeks for a total of 4 doses	Placebo i.v. every 4 weeks for a total of 4 doses	Total
Total # Affected by any Other Adverse Event	21	19	40
Total # at Risk by any Other Adverse Event	31	31	62
Gastrointestinal disorders			
Diarrhoea	1 (3.23%)	2 (6.45%)	3 (4.84%)
Nausea	3 (9.68%)	1 (3.23%)	4 (6.45%)
General disorders and administration site conditions			
Chest pain	3 (9.68%)	1 (3.23%)	4 (6.45%)
Fatigue	4 (12.90%)	4 (12.90%)	8 (12.90%)
Infections and infestations			
COVID-19	3 (9.68%)	4 (12.90%)	7 (11.29%)
Nasopharyngitis	2 (6.45%)	2 (6.45%)	4 (6.45%)
Upper respiratory tract infection	4 (12.90%)	2 (6.45%)	6 (9.68%)
Urinary tract infection	1 (3.23%)	3 (9.68%)	4 (6.45%)
Injury, poisoning and procedural complications			
Ligament sprain	0 (0.00%)	2 (6.45%)	2 (3.23%)

Investigations			
Blood alkaline phosphatase increased	0 (0.00%)	2 (6.45%)	2 (3.23%)
Blood creatinine increased	2 (6.45%)	0 (0.00%)	2 (3.23%)
Lipase increased	2 (6.45%)	0 (0.00%)	2 (3.23%)
Musculoskeletal and connective tissue disorders			
Arthralgia	4 (12.90%)	4 (12.90%)	8 (12.90%)
Back pain	3 (9.68%)	1 (3.23%)	4 (6.45%)
Myalgia	1 (3.23%)	2 (6.45%)	3 (4.84%)
Nervous system disorders			
Dizziness	3 (9.68%)	1 (3.23%)	4 (6.45%)
Headache	2 (6.45%)	4 (12.90%)	6 (9.68%)
Renal and urinary disorders			
Haematuria	0 (0.00%)	2 (6.45%)	2 (3.23%)
Respiratory, thoracic and mediastinal disorders			
Cough	2 (6.45%)	4 (12.90%)	6 (9.68%)
Dyspnoea	4 (12.90%)	3 (9.68%)	7 (11.29%)
Pulmonary sarcoidosis	2 (6.45%)	1 (3.23%)	3 (4.84%)
Skin and subcutaneous tissue disorders			
Cutaneous sarcoidosis	2 (6.45%)	0 (0.00%)	2 (3.23%)
Vascular disorders			
Hypertension	2 (6.45%)	1 (3.23%)	3 (4.84%)

Conclusion:

- CMK389 does not demonstrate improvement over placebo for the following endpoints: Change from baseline at week 16 in percent predicted Forced Vital Capacity (FVC), 6MWD, FEV1, DLCO.

- Positron emission tomography (PET) data ([18F]-FDG-PET SUVmax and SUVmean) showed decrease in the inflammatory burden in lung parenchyma for CMK389-treated participants when compared to placebo. The study had a small number of PET-positive patients at baseline; thus, this finding would need confirmation with a larger population.

- Steroid reduction was not superior in CMK389-treated participants when compared to placebo.

- Pharmacokinetic profiles were as expected.

- CMK389 was safe and well-tolerated at repeat doses up to 10 mg/kg in patients with sarcoidosis. No SAEs were attributed to study drug. No deaths or discontinuations occurred in treated patients.

Date of Clinical Trial Report

5-September-2024