Clinical trial results:
A Phase 1b Randomized, Double-Blind, Placebo-Controlled, Multiple-Ascending Dose Study to Evaluate the Safety, Pharmacokinetics, and Pharmacodynamics of ACE-1334 Plus Standard of Care in Participants with Systemic Sclerosis

Summary

EudraCT number	2021-001004-15
Trial protocol	IT
Global end of trial date	18 October 2023

Results information

Result version number	v1 (current)
This version publication date	23 October 2024
First version publication date	23 October 2024

Trial information

Trial identification

Sponsor protocol code	MK-2225-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04948554
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.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	18 October 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 October 2023
Global end of trial reached?	Yes
Global end of trial date	18 October 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of the MK-2225-002 (A1334-02) study is to evaluate the safety and tolerability of MK-2225 (ACE-1334) plus standard of care (SOC) in participants with Systemic Sclerosis (SSc) following multiple doses.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 March 2023
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	Canada: 2
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	5
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study enrolled male and female participants at least 18 years of age.

Pre-assignment

Screening details:

A total of 5 participants were randomized in this study.

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	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	MK-2225

Arm description:

Participants received MK-2225 plus standard of care (SOC) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	MK-2225
Investigational medicinal product code	
Other name	ACE-1334
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered subcutaneously (SC) for 12 weeks

Arm title	Placebo

Arm description:

Participants received placebo plus SOC for 12 weeks.

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

Dosage and administration details:

Placebo administered SC for 12 weeks

Number of subjects in period 1	MK-2225	Placebo
Started	4	1
Completed	3	0
Not completed	1	1
Adverse event, non-fatal	-	1
site closure	1	-

Baseline characteristics

Reporting groups	
Reporting group title	MK-2225
Reporting group description:	
Participants received MK-2225 plus standard of care (SOC) for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo plus SOC for 12 weeks.	

Reporting group values	MK-2225	Placebo	Total
Number of subjects	4	1	5
Age Categorical Units: Participants			
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)	4	1	5
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender Categorical Units: Participants			
Female	4	1	5
Male	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	2
Not Hispanic or Latino	3	0	3
Race Units: Subjects			
Black or African American	1	0	1
Other	1	0	1
White	2	1	3

End points

End points reporting groups

Reporting group title	MK-2225
Reporting group description:	
Participants received MK-2225 plus standard of care (SOC) for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo plus SOC for 12 weeks.	
Subject analysis set title	MK-2225 or Placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received MK-2225 or Placebo.	

Primary: Number of Participants Discontinuing from Study Therapy Due to AE

End point title	Number of Participants Discontinuing from Study Therapy Due to AE[1]

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. The number of participants who discontinued study treatment due to an AE is reported. Study participants who received at least one dose of study treatment were analyzed.

End point type	Primary

End point timeframe:

Up to 12 Weeks

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: No between-group statistical analyses were performed for this endpoint, because the study ended early with only 5 participants enrolled.

End point values	MK-2225 or Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: Number of Participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with ≥1 Adverse Event (AE)

End point title	Number of Participants with ≥1 Adverse Event (AE)[2]

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. The number of participants who experienced an AE is reported. Study participants who received at least one dose of study treatment were analyzed.

End point type	Primary

End point timeframe:

Up to 20 Weeks

Notes:

[2] - 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: No between-group statistical analyses were performed for this endpoint, because the study ended early with only 5 participants enrolled.

End point values	MK-2225 or Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: Number of Participants	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve (AUC0-tau) of MK-2225

End point title	Area Under the Concentration-Time Curve (AUC0-tau) of MK-2225

End point description:

AUC0-tau is the area under the concentration-time curve for one dose cycle of 14 days (336 hours). Blood samples were collected at designated timepoints to determine AUC0-tau of MK-2225. The analysis population included the participants who completed the study without dosing anomalies.

End point type	Secondary

End point timeframe:

Up to 12 Weeks

End point values	MK-2225 or Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	3[3]			
Units: hr*ug/mL				
geometric mean (confidence interval 95%)	585 (398 to 860)			

Notes:

[3] - Analysis population included the 3 participants who completed the study without dosing anomalies.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Apparent Terminal Half-Life (t1/2) of MK-2225

End point title	Serum Apparent Terminal Half-Life (t1/2) of MK-2225

End point description:

t1/2 is the time required for 50% of drug to be cleared from serum. A value of 9999 indicates t1/2 could not be calculated, due to the insufficient availability of data beyond post Tmax time points.

End point type	Secondary

End point timeframe:

Up to 12 Weeks

End point values	MK-2225 or Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	3[4]			
Units: hr				
geometric mean (confidence interval 95%)	9999 (9999 to 9999)			

Notes:

[4] - t1/2 could not be calculated, due to insufficient availability of data beyond post Tmax time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to peak Serum Concentration (Tmax) of MK-2225

End point title	Time to peak Serum Concentration (Tmax) of MK-2225

End point description:

Tmax is the amount of time required to reach Cmax. Blood samples were collected at designated timepoints to determine Tmax of MK-2225. The analysis population included the participants who completed the study without dosing anomalies.

End point type	Secondary

End point timeframe:

Up to 12 Weeks

End point values	MK-2225 or Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	3[5]			
Units: hr				
geometric mean (confidence interval 95%)	161.82 (115.50 to 167.20)			

Notes:

[5] - Analysis population included the 3 participants who completed the study without dosing anomalies.

Statistical analyses

No statistical analyses for this end point

Secondary: Accumulation Ratio for AUC0-tau (RAUC) of MK-2225

End point title	Accumulation Ratio for AUC0-tau (RAUC) of MK-2225

End point description:

RAUC is the accumulation ratio of AUC0-336 from time 0 to 336 hours. The accumulation ratio (Day 57:

Day 1) for AUC0-336 is presented. The analysis population included the participants who completed the study without dosing anomalies.

End point type	Secondary

End point timeframe:

Up to 12 Weeks

End point values	MK-2225 or Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	3[6]			
Units: hr*ug/mL				
geometric mean (confidence interval 95%)	2.61 (1.77 to 3.84)			

Notes:

[6] - Analysis population included the 3 participants who completed the study without dosing anomalies.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Maximum Concentration (Cmax) of MK-2225

End point title	Serum Maximum Concentration (Cmax) of MK-2225

End point description:

Cmax is the maximum concentration of the drug observed in plasma. Blood samples were collected at designated timepoints to determine Cmax of MK-2225. The analysis population included the participants who completed the study without dosing anomalies.

End point type	Secondary

End point timeframe:

Up to 12 Weeks

End point values	MK-2225 or Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	3[7]			
Units: ug/mL				
geometric mean (confidence interval 95%)	2.08 (1.29 to 3.37)			

Notes:

[7] - Analysis population included the 3 participants who completed the study without dosing anomalies.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 20 Weeks

Adverse event reporting additional description:

The analysis population for deaths (all-causes) included all randomized participants. The analysis population for AEs included all randomized participants who received at least one dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	MK-2225 or Placebo

Reporting group description:

Participants received MK-2225 or Placebo plus SOC for 12 weeks.

Serious adverse events	MK-2225 or Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	MK-2225 or Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Blood urine present			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	2		
Occult blood positive			

subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Post procedural erythema			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	3		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
Injection site swelling			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	6		
Reproductive system and breast disorders			
Genital ulceration			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Polymenorrhoea			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Keloid scar			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue			

disorders Neck pain subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Infected skin ulcer subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1		
Metabolism and nutrition disorders Vitamin D deficiency subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2021	Amendment 01: Primary reason for amendment was to incorporate revisions to objectives, endpoints, exclusion criteria, and schedule of assessments.
10 September 2021	Amendment 02: Primary reason for amendment was to incorporate revisions to objectives and endpoints.
07 February 2022	Amendment 03: Primary reason for amendment was to incorporate revisions to schedule of assessments.
24 August 2022	Amendment 04: Primary reason for amendment was to incorporate revisions to study design and objectives.
20 September 2022	Amendment 05: Primary reason for amendment was to incorporate revisions to exclusion criteria and clinical laboratory assessments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported