



Clinical trial results:

A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate Efficacy, Safety, and Tolerability of MT-7117 in Subjects with Diffuse Cutaneous Systemic Sclerosis

Summary

EudraCT number	2020-000134-17
Trial protocol	GB DE BE IT PL
Global end of trial date	14 February 2024

Results information

Result version number	v1 (current)
This version publication date	22 December 2024
First version publication date	22 December 2024

Trial information

Trial identification

Sponsor protocol code	MT-7117-G02
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04440592
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Mitsubishi Tanabe Pharma America, Inc.
Sponsor organisation address	525 Washington Boulevard, Suite 1100, Jersey City , United States, 07310
Public contact	Mitsubishi Tanabe Pharma Europe Ltd (MTPE), General Information, +44 2070655000, regulatory@mt-pharma-eu.com
Scientific contact	Mitsubishi Tanabe Pharma Europe Ltd (MTPE), General Information, +44 2070655000, regulatory@mt-pharma-eu.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	14 February 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	14 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of MT-7117 treatment in participants with diffuse cutaneous systemic sclerosis (dcSSc) using the American College of Rheumatology Composite Response Index in Diffuse Systemic Sclerosis (ACR CRISS) at Week 52.

Protection of trial subjects:

The study was conducted in accordance with the 2013 (Fortaleza) revision of the 1964 Declaration of Helsinki, Good Clinical Practice (GCP) as required by the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines, applicable regional and local legislation, and standard operating procedures (SOPs) in place at Mitsubishi Tanabe Pharma America Inc. (MTPA).

Prior to undergoing any study-specific procedure, all legally competent participants were required to provide consent in writing to participate in the study. An Informed Consent Form (ICF) was given to each participants, which contained all regulatory, ICH and data protection requirements, as applicable, in language understandable to the participant. If a participant was legally incompetent, the enrollment of such a participant was required to be in accordance with all applicable laws, and consent sought by the Investigator from the participant's legally authorized representative. Either the Investigator or a designated person, qualified to meet any applicable local regulations, who was equally knowledgeable about the study explained the aims, methods, anticipated benefits and potential hazards of the study and any discomfort it could entail. A corresponding written explanation was also provided, and the subject allowed sufficient time to consider the study information.

Clinical monitoring was conducted to confirm the ethical conduct of the study at the investigational site(s).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 February 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	Canada: 1
Country: Number of subjects enrolled	United States: 18
Country: Number of subjects enrolled	Poland: 26
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 2

Worldwide total number of subjects	76
EEA total number of subjects	52

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)	63
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 76 participants were enrolled in North America and Europe, between 05 February 2021 and 14 February 2024.

Pre-assignment

Screening details:

After providing informed consent, male and female participants were eligible to participate if aged 18 or older, with documented diagnosis of systemic sclerosis (SSc), as defined using the 2013 ACR/European League Against Rheumatism (EULAR) criteria and with disease duration \leq 5 years.

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
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Arm title	MT-7117
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Arm description:

Participants with dcSSc took oral tablets of 300mg MT-7117 once daily for the duration of the study. If the participant continuously presented significant intolerable AEs at the following scheduled or unscheduled visit and the Investigator deemed it necessary, the daily dose of study drug could have been reduced.

Arm type	Experimental
Investigational medicinal product name	MT-7117
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral administration once daily in the morning with or without food.

Arm title	Placebo
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Arm description:

Participants with dcSSc took oral tablets of placebo to match MT-7117 once daily for the duration of the study.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral administration once daily in the morning with or without food.

Number of subjects in period 1	MT-7117	Placebo
Started	38	38
Completed	28	36
Not completed	10	2
Consent withdrawn by subject	1	1
Adverse event, non-fatal	8	-
Other	-	1
Lost to follow-up	1	-

Baseline characteristics

Reporting groups

Reporting group title	MT-7117
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Reporting group description:

Participants with dcSSc took oral tablets of 300mg MT-7117 once daily for the duration of the study. If the participant continuously presented significant intolerable AEs at the following scheduled or unscheduled visit and the Investigator deemed it necessary, the daily dose of study drug could have been reduced.

Reporting group title	Placebo
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Reporting group description:

Participants with dcSSc took oral tablets of placebo to match MT-7117 once daily for the duration of the study.

Reporting group values	MT-7117	Placebo	Total
Number of subjects	38	38	76
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	29	63
From 65-84 years	4	9	13
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	49.2	54.2	
standard deviation	± 12.5	± 12.4	-
Gender categorical Units: Subjects			
Female	26	30	56
Male	12	8	20
Race Units: Subjects			
White	33	32	65
Black or African American	2	1	3
Asian	0	1	1
American Indian or Alaska Native	0	1	1
Native Hawaiian or Pacific Islander	1	0	1
Other	2	3	5
Ethnicity Units: Subjects			
Hispanic or Latino	7	7	14
Non-Hispanic or Latino	31	29	60
Other	0	2	2

End points

End points reporting groups

Reporting group title	MT-7117
Reporting group description: Participants with dcSSc took oral tablets of 300mg MT-7117 once daily for the duration of the study. If the participant continuously presented significant intolerable AEs at the following scheduled or unscheduled visit and the Investigator deemed it necessary, the daily dose of study drug could have been reduced.	
Reporting group title	Placebo
Reporting group description: Participants with dcSSc took oral tablets of placebo to match MT-7117 once daily for the duration of the study.	

Primary: ACR CRISS Composite Score at Week 52

End point title	ACR CRISS Composite Score at Week 52
End point description: The ACR CRISS is a composite endpoint that calculates probability of improvement from baseline, incorporating change in modified Rodnan Skin Score (mRSS), percentage predicted forced vital capacity (%pFVC), physician and patient global assessments, and Health Assessment Questionnaire Disability Index (HAQ-DI). The outcome was a continuous variable between 0.0 and 1.0 with higher score indicating improvement in symptoms. A higher score indicated greater improvement. An ACR CRISS score of 0.60 or greater indicated that a participant improved on treatment and a score of less than 0.60 suggested that a participant had not improved. Intent-to-treat (ITT) population: Included all randomized participants who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe: Week 52	

End point values	MT-7117	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	38		
Units: ACR CRISS score				
median (full range (min-max))				
ACR CRISS score	0.8537 (0.000 to 1.000)	0.8502 (0.000 to 1.000)		

Statistical analyses

Statistical analysis title	MT-7117 versus (vs) placebo
Comparison groups	MT-7117 v Placebo

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9514
Method	Hodges-Lehman
Parameter estimate	Location shift
Point estimate	-0.0038
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1243
upper limit	0.1168

Secondary: Change in HAQ-DI from Baseline at Weeks 16, 26, 39, and 52

End point title	Change in HAQ-DI from Baseline at Weeks 16, 26, 39, and 52
End point description:	
<p>The HAQ-DI is a self-administered instrument consists of 20 questions referring to eight component sets consisting of dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities. Each item was scored on a 4-point scale from 0 to 3: 0 = Without any difficulty; 1 = With some difficulty; 2 = With much difficulty; 3 = Unable to do. Overall score, ranging from 0 to 3, was calculated as the sum of component set scores and divided by the number of component sets answered. A negative change from baseline indicated improvement.</p> <p>ITT population: Included all randomized participants who received at least 1 dose of study drug.</p>	
End point type	Secondary
End point timeframe:	
From Baseline, Week 16, Week 26, Week 39, and Week 52	

End point values	MT-7117	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	38		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change from baseline (BL) at Week 16	-0.1439 (± 0.3803)	-0.0395 (± 0.3900)		
Change from BL at Week 26	-0.0847 (± 0.3360)	-0.0691 (± 0.4481)		
Change from BL at Week 39	-0.0927 (± 0.3178)	-0.0439 (± 0.5147)		
Change from BL at Week 52	-0.1111 (± 0.4265)	-0.0208 (± 0.5102)		

Statistical analyses

Statistical analysis title	MT-7117 vs Placebo Week 16
Comparison groups	MT-7117 v Placebo

Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1908
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.1185
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2976
upper limit	0.0605

Statistical analysis title	MT-7117 vs Placebo Week 26
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7757
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.027
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2154
upper limit	0.1614

Statistical analysis title	MT-7117 vs Placebo Week 39
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5994
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.0549
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2625
upper limit	0.1527

Statistical analysis title	MT-7117 vs Placebo Week 52
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Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1739
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.1508
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3699
upper limit	0.0683

Secondary: Change in Patient Global Assessment (PtGA) from Baseline at Weeks 16, 26, 39, and 52

End point title	Change in Patient Global Assessment (PtGA) from Baseline at Weeks 16, 26, 39, and 52
End point description:	The PtGA was used to assess the participants' rating of their overall disease activity. Participants rated their perceived health on an 11 point scale from 0 (excellent) to 10 (extremely poor). A negative change from baseline indicated improvement in symptoms. ITT population: Included all randomized participants who received at least 1 dose of study drug.
End point type	Secondary
End point timeframe:	From Baseline, Week 16, Week 26, Week 39, and Week 52

End point values	MT-7117	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	38		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change from BL at Week 16	-0.8 (± 1.8)	-0.3 (± 1.9)		
Change from BL at Week 26	0.0 (± 2.5)	-0.4 (± 2.6)		
Change from BL at Week 39	-0.7 (± 2.2)	-0.5 (± 2.3)		
Change from BL at Week 52	-0.5 (± 2.3)	-0.3 (± 2.5)		

Statistical analyses

Statistical analysis title	MT-7117 vs Placebo Week 16
Comparison groups	MT-7117 v Placebo

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1902
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.24

Statistical analysis title	MT-7117 vs Placebo Week 26
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5075
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	1.32

Statistical analysis title	MT-7117 vs Placebo Week 39
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.799
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.85

Statistical analysis title	MT-7117 vs Placebo Week 52
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Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.606
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	0.79

Secondary: Change in %pFVC from Baseline at Weeks 16, 26, 39, and 52

End point title	Change in %pFVC from Baseline at Weeks 16, 26, 39, and 52
End point description:	
%pFVC was measured to assess pulmonary function.	
ITT population: Included all randomized participants who received at least 1 dose of study drug.	
End point type	Secondary
End point timeframe:	
From Baseline, Week 16, Week 26, Week 39, and Week 52	

End point values	MT-7117	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	38		
Units: %pFVC				
arithmetic mean (standard deviation)				
Change from BL at Week 16	0.754 (± 4.938)	-1.058 (± 5.749)		
Change from BL at Week 26	0.904 (± 5.669)	-0.691 (± 5.847)		
Change from BL at Week 39	-1.201 (± 6.293)	-1.457 (± 5.600)		
Change from BL at Week 52	0.048 (± 6.917)	-2.906 (± 5.101)		

Statistical analyses

Statistical analysis title	MT-7117 vs Placebo Week 16
Comparison groups	MT-7117 v Placebo

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1441
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	1.968
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.691
upper limit	4.627

Statistical analysis title	MT-7117 vs Placebo Week 26
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2261
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	1.708
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.084
upper limit	4.5

Statistical analysis title	MT-7117 vs Placebo Week 39
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5901
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	0.763
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.053
upper limit	3.578

Statistical analysis title	MT-7117 vs Placebo Week 52
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Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1071
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	2.556
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.571
upper limit	5.683

Secondary: Change in Physician Global Assessment (PhGA) from Baseline at Weeks 16, 26, 39, and 52

End point title	Change in Physician Global Assessment (PhGA) from Baseline at Weeks 16, 26, 39, and 52
End point description:	The PhGA was used to assess the physician's rating of overall health of the participant. Physicians rated the perceived health of the participant on an 11-point scale from 0 (excellent) to 10 (extremely poor). A negative change from baseline indicated improvement in symptoms. ITT population: Included all randomized participants who received at least 1 dose of study drug.
End point type	Secondary
End point timeframe:	From Baseline, Week 16, Week 26, Week 39, and Week 52

End point values	MT-7117	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	38		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change from BL at Week 16	-1.6 (± 1.9)	-1.7 (± 1.8)		
Change from BL at Week 26	-1.6 (± 2.1)	-1.7 (± 2.1)		
Change from BL at Week 39	-2.1 (± 2.5)	-2.2 (± 2.3)		
Change from BL at Week 52	-2.0 (± 2.9)	-1.7 (± 2.2)		

Statistical analyses

Statistical analysis title	MT-7117 vs Placebo Week 16
Comparison groups	MT-7117 v Placebo

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5319
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	0.51

Statistical analysis title	MT-7117 vs Placebo Week 26
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8085
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.97
upper limit	0.76

Statistical analysis title	MT-7117 vs Placebo Week 39
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5004
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	0.62

Statistical analysis title	MT-7117 vs Placebo Week 52
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Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3485
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.57
upper limit	0.56

Secondary: Change in mRSS from Baseline at Weeks 16, 26, 39, and 52

End point title	Change in mRSS from Baseline at Weeks 16, 26, 39, and 52
End point description:	mRSS evaluated a participant's skin thickness which was assessed by palpation and rated on a scale ranged from 0 (normal) to 3 (severe skin thickening) across 17 different body sites. The total score was the sum of the individual skin scores from all of these sites and ranged from 0 to 51 units. A negative change from baseline indicated improvement in skin symptoms. ITT population: Included all randomized participants who received at least 1 dose of study drug.
End point type	Secondary
End point timeframe:	From Baseline, Week 16, Week 26, Week 39, and Week 52

End point values	MT-7117	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	38		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change from BL at Week 16	-3.2 (± 4.7)	-3.6 (± 3.9)		
Change from BL at Week 26	-4.9 (± 5.5)	-5.3 (± 6.9)		
Change from BL at Week 39	-6.4 (± 7.0)	-6.2 (± 7.5)		
Change from BL at Week 52	-6.6 (± 8.2)	-6.5 (± 7.9)		

Statistical analyses

Statistical analysis title	MT-7117 vs Placebo Week 16
Comparison groups	MT-7117 v Placebo

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7639
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	2.3

Statistical analysis title	MT-7117 vs Placebo Week 26
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8134
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	3.2

Statistical analysis title	MT-7117 vs Placebo Week 39
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8556
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	3

Statistical analysis title	MT-7117 vs Placebo Week 52
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Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7776
Method	Mixed models analysis
Parameter estimate	Least square mean difference vs Placebo
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	3.2

Secondary: ACR CRISS Score at Weeks 16, 26, and 39

End point title	ACR CRISS Score at Weeks 16, 26, and 39
End point description:	
<p>The ACR CRISS is a composite endpoint that calculates probability of improvement from baseline, incorporating change in modified Rodnan Skin Score (mRSS), percentage predicted forced vital capacity (%pFVC), physician and patient global assessments, and Health Assessment Questionnaire Disability Index (HAQ-DI). The outcome was a continuous variable between 0.0 and 1.0 with higher score indicating improvement in symptoms. A higher score indicated greater improvement. An ACR CRISS score of 0.60 or greater indicated that a participant improved on treatment and a score of less than 0.60 suggested that a participant had not improved.</p> <p>Intent-to-treat (ITT) population: Included all randomized participants who received at least 1 dose of study drug.</p>	
End point type	Secondary
End point timeframe:	
Week 16, Week 26, and Week 39	

End point values	MT-7117	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	38		
Units: ACR CRISS Score				
median (full range (min-max))				
Week 16	0.0349 (0.000 to 1.000)	0.1236 (0.000 to 1.000)		
Week 26	0.2626 (0.000 to 1.000)	0.6232 (0.000 to 1.000)		
Week 39	0.3890 (0.000 to 1.000)	0.5289 (0.000 to 1.000)		

Statistical analyses

Statistical analysis title	MT-7117 vs Placebo Week 16
Comparison groups	MT-7117 v Placebo

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.939
Method	Hodges-Lehman
Parameter estimate	Location shift
Point estimate	0.0047
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1156
upper limit	0.125

Statistical analysis title	MT-7117 vs Placebo Week 26
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.616
Method	Hodges-Lehman
Parameter estimate	Location shift
Point estimate	-0.0446
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2191
upper limit	0.1298

Statistical analysis title	MT-7117 vs Placebo Week 39
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6589
Method	Hodges-Lehman
Parameter estimate	Location shift
Point estimate	-0.0308
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1677
upper limit	0.106

Secondary: ACR CRISS Score Responders (CRISS \geq 0.6) at Weeks 16, 26, 39, and 52

End point title	ACR CRISS Score Responders (CRISS \geq 0.6) at Weeks 16, 26, 39, and 52
End point description:	
The ACR CRISS is a composite endpoint that calculates probability of improvement from baseline, incorporating change in modified Rodnan Skin Score (mRSS), percentage predicted forced vital capacity (%pFVC), physician and patient global assessments, and Health Assessment Questionnaire Disability Index (HAQ-DI). The outcome was a continuous variable between 0.0 and 1.0 with higher score indicating improvement in symptoms. A higher score indicated greater improvement. An ACR CRISS score of 0.60 or greater indicated that a participant improved on treatment and a score of less than 0.60 suggested that a participant had not improved. Participants experiencing a response are reported. Intent-to-treat (ITT) population: Included all randomized participants who received at least 1 dose of study drug.	
End point type	Secondary
End point timeframe:	
Week 16, Week 26, Week 39 and Week 52	

End point values	MT-7117	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	38		
Units: Responders				
number (not applicable)				
Week 16	10	8		
Week 26	10	18		
Week 39	11	15		
Week 52	14	18		

Statistical analyses

Statistical analysis title	MT-7117 vs Placebo Week 16
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.295
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	1.826
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.589
upper limit	5.664

Statistical analysis title	MT-7117 vs Placebo Week 26
Comparison groups	MT-7117 v Placebo

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.181
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	0.487
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.169
upper limit	1.402

Statistical analysis title	MT-7117 vs Placebo Week 39
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.601
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	0.758
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.267
upper limit	2.154

Statistical analysis title	MT-7117 vs Placebo Week 52
Comparison groups	MT-7117 v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.913
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	1.061
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.363
upper limit	3.096

Adverse events

Adverse events information

Timeframe for reporting adverse events:

60 weeks

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	MT-7117
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Reporting group description:

Participants with dcSSc took 300mg of MT-7117 daily for the duration of the study. If the participant continuously presented significant intolerable AEs at the following scheduled or unscheduled visit and the Investigator deemed it necessary, the daily dose of study drug could have been reduced.

Reporting group title	Placebo
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Reporting group description:

Participants with dcSSc took oral tablets of placebo to match MT-7117 once daily for the duration of the study.

Serious adverse events	MT-7117	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 38 (10.53%)	2 / 38 (5.26%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma in situ			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Organising pneumonia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Systemic sclerosis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	MT-7117	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 38 (92.11%)	28 / 38 (73.68%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			

subjects affected / exposed occurrences (all)	12 / 38 (31.58%) 18	2 / 38 (5.26%) 2	
Dysplastic naevus subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 3	1 / 38 (2.63%) 1	
Seborrhoeic keratosis subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	0 / 38 (0.00%) 0	
Investigations Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 38 (5.26%) 2	
Injury, poisoning and procedural complications Accidental overdose subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	4 / 38 (10.53%) 4	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	2 / 38 (5.26%) 2	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	4 / 38 (10.53%) 4	3 / 38 (7.89%) 4	
Eye disorders Cataract subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 38 (5.26%) 3	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting	10 / 38 (26.32%) 13 7 / 38 (18.42%) 7	5 / 38 (13.16%) 8 2 / 38 (5.26%) 2	

subjects affected / exposed occurrences (all)	6 / 38 (15.79%) 6	2 / 38 (5.26%) 2	
Dysphagia subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	1 / 38 (2.63%) 1	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	3 / 38 (7.89%) 3	
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 38 (5.26%) 2	
Skin and subcutaneous tissue disorders Skin discolouration subjects affected / exposed occurrences (all)	8 / 38 (21.05%) 10	0 / 38 (0.00%) 0	
Pruritus subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3	2 / 38 (5.26%) 2	
Skin ulcer subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	2 / 38 (5.26%) 2	
Solar lentigo subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	1 / 38 (2.63%) 1	
Nail pigmentation subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	0 / 38 (0.00%) 0	
Skin hyperpigmentation subjects affected / exposed occurrences (all)	16 / 38 (42.11%) 17	1 / 38 (2.63%) 1	
Erythema subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 38 (5.26%) 2	
Musculoskeletal and connective tissue disorders			

Muscle spasms subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	0 / 38 (0.00%) 0	
Systemic scleroderma subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 38 (5.26%) 2	
Infections and infestations			
COVID-19 subjects affected / exposed occurrences (all)	4 / 38 (10.53%) 4	5 / 38 (13.16%) 5	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	2 / 38 (5.26%) 5	
Bronchitis subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	1 / 38 (2.63%) 1	
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3	5 / 38 (13.16%) 7	
Gastroenteritis subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	2 / 38 (5.26%) 2	
Lower respiratory tract infection subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 38 (5.26%) 2	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	1 / 38 (2.63%) 1	
Hypercholesterolaemia subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	0 / 38 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 September 2020	<p>Amendment 1:</p> <ol style="list-style-type: none">1. Study exclusion criteria were amended, including prohibited medications.2. Text of assessments were modified.3. Reverse translational study objective, endpoint, and analysis of this endpoint were added.4. ACR CRIS improvement score (secondary endpoint) was modified.5. COVID-19 pandemic language was added.6. Language was added to clarify allowed medication during study treatment.7. Text about rescue medication was clarified.8. Language was added to clarify treatments for SSc complications.9. Drug-drug interaction text was added.10. Role of the dual assessor and melanin assessor were clarified.11. AESI definition was updated.12. Contraception language was updated.13. Composite Response Index for dcSSc language was updated.14. Schedule of Activities (SoA) was revised.
02 December 2020	<p>Amendment 2:</p> <ol style="list-style-type: none">1. Study entry criteria was updated to select a more homogeneous population.2. Exclusion criteria was updated to ensure subject safety.3. Text was updated to exclude use of nintedanib and language was added for vaccine use.4. Dual assessor approach language was updated.
28 January 2021	<p>Amendment 3:</p> <ol style="list-style-type: none">1. Exploratory objective/endpoint was updated.2. Exclusion criteria was modified.3. Urine dipstick pregnancy test was added and methodology for dosing in the case of positive results was clarified.4. Risk/benefit statement was updated to include new findings in the non-clinical pre-and postnatal development study in rats and the COVID-19 pandemic.5. Rescue therapy was clarified.6. Composite response index for dcSSc section was updated.7. PFT test section was updated.8. Dual assessor approach was clarified.9. Modified Rodnan skin score section was updated.10. Pharmacogenomics sampling section was updated.11. Clinical laboratory abnormalities and other abnormal assessments section was updated.12. Recording and reporting of SAEs or hepatic AESIs section was updated.13. Pregnancy section was updated.14. Impact of COVID-19 section was updated.15. Analysis of exploratory endpoints section was updated.16. SoA was amended to reflect new additional pregnancy test.

20 December 2021	Amendment 4: 1. Eligibility criteria were updated. 2. New exploratory endpoint for the revised ACR-CRISS was added. 3. Withdrawal of individual subjects section was updated. 4. Dose reduction criteria section was updated, and dose interruption section was added. 5. Permitted immunosuppressant therapy section was updated. 6. PFT was updated. 7. Vital signs section was updated. 8. AESI section was updated. 9. Management and evaluation of hepatic AESI section was updated. 10. Analysis of ACR CRISS score improvement proportion was updated. 11. SoA was revised.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported