



Clinical trial results:

A Phase 2a Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study to Evaluate the Efficacy, Safety, and Tolerability of Orally Administered GLPG1690 for 24 Weeks in Subjects with Systemic Sclerosis

Summary

EudraCT number	2018-001817-33
Trial protocol	GB DE BE IT
Global end of trial date	22 June 2020

Results information

Result version number	v1 (current)
This version publication date	25 April 2021
First version publication date	25 April 2021

Trial information

Trial identification

Sponsor protocol code	GLPG1690-CL-204
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03798366
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galapagos NV
Sponsor organisation address	Generaal De Wittelaan L11 A3, Mechelen, Belgium, 2800
Public contact	Galapagos Medical Information, Galapagos NV, medicalinfo@glpg.com
Scientific contact	Galapagos Medical Information, Galapagos NV, medicalinfo@glpg.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 February 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	22 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of GLPG1690 as evaluated by modified Rodnan Skin Score (mRSS) compared to placebo over 24 weeks for the treatment of participants with systemic sclerosis

Protection of trial subjects:

The study was performed in accordance with the ethical principles that have their origin in the "Declaration of Helsinki" and its amendments in force at the time of the study (2013 version). It was also carried out in conformity with the protocol, the International Council for Harmonisation Guideline for Good Clinical Practice (ICH-GCP) E6 (R2), and local ethical and legal requirements.

The investigator informed the subjects of the risks and benefits of the study. The subjects were informed that they could withdraw from the study at any time for any reason. Consent was obtained in writing prior to any study-related activities; the investigator retained a copy of the ICFs, which are available to the sponsor for inspection.

The subjects were covered by the sponsor's insurance according to local legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 January 2019
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	Italy: 2
Country: Number of subjects enrolled	United States: 10
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Belgium: 12
Worldwide total number of subjects	33
EEA total number of subjects	23

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)	28
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Belgium, the United States, United Kingdom, Spain, and Italy. The first participant was screened on 14 Jan 2019. The last study visit occurred on 22 Jun 2020.

Pre-assignment

Screening details:

A total of 40 participants were screened, of whom 33 participants were randomized and treated.

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, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	GLPG1690 600 mg

Arm description:

Participants received GLPG1690 600 milligrams (mg), orally once daily for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	GLPG1690
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GLPG1690 was administered per dose and schedule specified in the arm description.

Arm title	Placebo
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Arm description:

Participants received GLPG1690 matching placebo, orally once daily for 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo was administered per the schedule specified in the arm description.

Number of subjects in period 1	GLPG1690 600 mg	Placebo
Started	21	12
Completed	21	11
Not completed	0	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	GLPG1690 600 mg
Reporting group description:	
Participants received GLPG1690 600 milligrams (mg), orally once daily for 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received GLPG1690 matching placebo, orally once daily for 24 weeks.	

Reporting group values	GLPG1690 600 mg	Placebo	Total
Number of subjects	21	12	33
Age categorical			
Units: Subjects			
Less than or equal to 45 years	7	5	12
Greater than 45 years	14	7	21
Age continuous			
Units: years			
arithmetic mean	50.4	47.3	-
standard deviation	± 13.58	± 17.99	-
Gender categorical			
Units: Subjects			
Female	15	8	23
Male	6	4	10
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	1	2
Not Hispanic or Latino	20	10	30
Unknown or Not Reported	0	1	1
Race			
Units: Subjects			
Asian	0	1	1
White	21	11	32
Modified Rodnan Skin Score (mRSS)			
The mRSS is a validated physical examination method for estimating skin thickness. The 17 body site mRSS was used, with each body site assessed on a scale of 0 (uninvolved) to 3 (severe thickening) with a total score range from 0 (best) to 51 (worst), with higher scores indicating greater severity of skin thickening.			
Units: units on a scale			
arithmetic mean	27.0	22.5	-
standard deviation	± 8.84	± 6.24	-

End points

End points reporting groups

Reporting group title	GLPG1690 600 mg
Reporting group description:	
Participants received GLPG1690 600 milligrams (mg), orally once daily for 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received GLPG1690 matching placebo, orally once daily for 24 weeks.	

Primary: Change From Baseline in mRSS at Week 4

End point title	Change From Baseline in mRSS at Week 4
End point description:	
The mRSS is a validated physical examination method for estimating skin thickness. The 17 body site mRSS was used, with each body site assessed on a scale of 0 (uninvolved) to 3 (severe thickening) with a total score range from 0 (best) to 51 (worst), with higher scores indicating greater severity of skin thickening. Full analysis set (FAS) consisted of all randomized participants who received at least 1 dose of investigational product.	
End point type	Primary
End point timeframe:	
Baseline, Week 4	

End point values	GLPG1690 600 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	12		
Units: units on a scale				
least squares mean (standard error)	-2.2 (\pm 0.85)	-1.6 (\pm 1.04)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Results were estimated using a mixed-effect model repeated measure using treatment and visit as fixed effects, baseline mRSS score and country as covariates, treatment-visit as interaction terms, and participant as a random effect. The variance-covariance matrix used in the model was compound symmetric. A negative difference indicates a greater improvement in the GLPG1690 treatment group.	
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6757
Method	Mixed models analysis
Parameter estimate	Least square (LS) mean difference
Point estimate	-0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	1.29

Primary: Change From Baseline in mRSS at Week 8

End point title	Change From Baseline in mRSS at Week 8
End point description:	
The mRSS is a validated physical examination method for estimating skin thickness. The 17 body site mRSS was used, with each body site assessed on a scale of 0 (uninvolved) to 3 (severe thickening) with a total score range from 0 (best) to 51 (worst), with higher scores indicating greater severity of skin thickening. Participants in the FAS were analyzed.	
End point type	Primary
End point timeframe:	
Baseline, Week 8	

End point values	GLPG1690 600 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	12		
Units: units on a scale				
least squares mean (standard error)	-3.2 (± 0.85)	-2.5 (± 1.07)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Results were estimated using a mixed-effect model repeated measure using treatment and visit as fixed effects, baseline mRSS score and country as covariates, treatment-visit as interaction terms, and participant as a random effect. The variance-covariance matrix used in the model was compound symmetric. A negative difference indicates a greater improvement in the GLPG1690 treatment group.	
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6079
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	-0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	1.31

Primary: Change From Baseline in mRSS at Week 16

End point title	Change From Baseline in mRSS at Week 16
End point description:	
The mRSS is a validated physical examination method for estimating skin thickness. The 17 body site mRSS was used, with each body site assessed on a scale of 0 (uninvolved) to 3 (severe thickening) with a total score range from 0 (best) to 51 (worst), with higher scores indicating greater severity of skin thickening. Participants in the FAS were analyzed.	
End point type	Primary
End point timeframe:	
Baseline, Week 16	

End point values	GLPG1690 600 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	12		
Units: units on a scale				
least squares mean (standard error)	-6.8 (± 0.85)	-4.8 (± 1.12)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Results were estimated using a mixed-effect model repeated measure using treatment and visit as fixed effects, baseline mRSS score and country as covariates, treatment-visit as interaction terms, and participant as a random effect. The variance-covariance matrix used in the model was compound symmetric. A negative difference indicates a greater improvement in the GLPG1690 treatment group.	
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1298
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	-2.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	1.35

Primary: Change From Baseline in mRSS at Week 24

End point title	Change From Baseline in mRSS at Week 24
End point description:	
The mRSS is a validated physical examination method for estimating skin thickness. The 17 body site mRSS was used, with each body site assessed on a scale of 0 (uninvolved) to 3 (severe thickening) with a total score range from 0 (best) to 51 (worst), with higher scores indicating greater severity of skin thickening. Participants in the FAS were analyzed.	
End point type	Primary
End point timeframe:	
Baseline, Week 24	

End point values	GLPG1690 600 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	12		
Units: units on a scale				
least squares mean (standard error)	-8.9 (± 0.87)	-6.0 (± 1.11)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Results were estimated using a mixed-effect model repeated measure using treatment and visit as fixed effects, baseline mRSS score and country as covariates, treatment-visit as interaction terms, and participant as a random effect. The variance-covariance matrix used in the model was compound symmetric. A negative difference indicates a greater improvement in the GLPG1690 treatment group.	
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0411
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	-2.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	1.36

Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Serious TEAEs
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End point description:

An adverse event (AE) was any untoward medical occurrence in a participant administered study drug and which did not necessarily have a causal relationship with study drug. A treatment-emergent adverse event (TEAE) is any AE with an onset date on or after the start of study drug intake and no later than 30 days after last dose of study drug, or any worsening of any AE on or after the start of study drug intake. A serious AE was defined as an AE that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was medically significant. Safety analysis set consisted of all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary
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End point timeframe:

Baseline up to end of the study (36 weeks)

End point values	GLPG1690 600 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	12		
Units: participants				
TEAEs	20	11		
Serious TEAEs	2	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to end of the study (36 weeks)

Adverse event reporting additional description:

Participants in the safety analysis set were analyzed.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	GLPG1690 600 mg
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Reporting group description:

Participants received GLPG1690 600 mg, orally once daily for 24 weeks.

Reporting group title	Placebo
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Reporting group description:

Participants received GLPG1690 matching placebo, orally once daily for 24 weeks.

Serious adverse events	GLPG1690 600 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 21 (9.52%)	1 / 12 (8.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Foreign body in gastrointestinal tract			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device related infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 21 (9.52%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GLPG1690 600 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 21 (95.24%)	11 / 12 (91.67%)	
Vascular disorders			
Hot flush			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Raynaud's phenomenon			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Discomfort			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Peripheral swelling			
alternative assessment type: Systematic			

subjects affected / exposed	3 / 21 (14.29%)	0 / 12 (0.00%)	
occurrences (all)	4	0	
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 21 (14.29%)	1 / 12 (8.33%)	
occurrences (all)	3	1	
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Interstitial lung disease			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Sinus congestion			
alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 12 (0.00%) 0	
Psychiatric disorders Anger alternative assessment type: Systematic subjects affected / exposed occurrences (all) Insomnia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1 0 / 21 (0.00%) 0	0 / 12 (0.00%) 0 2 / 12 (16.67%) 2	
Investigations Alanine aminotransferase increased alternative assessment type: Systematic subjects affected / exposed occurrences (all) Aspartate aminotransferase increased alternative assessment type: Systematic subjects affected / exposed occurrences (all) Blood lactate dehydrogenase increased alternative assessment type: Systematic subjects affected / exposed occurrences (all) Weight increased alternative assessment type: Systematic subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2 1 / 21 (4.76%) 1 1 / 21 (4.76%) 1 2 / 21 (9.52%) 2	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	
Injury, poisoning and procedural complications Ligament sprain alternative assessment type: Systematic subjects affected / exposed occurrences (all) Limb injury	1 / 21 (4.76%) 1	0 / 12 (0.00%) 0	

<p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Procedural pain</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Skin abrasion</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Tendon injury</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Vascular injury</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Cardiac disorders</p> <p>Bundle branch block left</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Palpitations</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 21 (0.00%)</p> <p>0</p> <p>2 / 21 (9.52%)</p> <p>2</p>	<p>1 / 12 (8.33%)</p> <p>1</p> <p>1 / 12 (8.33%)</p> <p>1</p>	
<p>Nervous system disorders</p> <p>Dizziness</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyskinesia</p> <p>alternative assessment type: Systematic</p>	<p>3 / 21 (14.29%)</p> <p>3</p>	<p>1 / 12 (8.33%)</p> <p>1</p>	

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Headache</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Memory impairment</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Migraine</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p> <p>5 / 21 (23.81%)</p> <p>5</p> <p>1 / 21 (4.76%)</p> <p>1</p> <p>1 / 21 (4.76%)</p> <p>2</p>	<p>0 / 12 (0.00%)</p> <p>0</p> <p>2 / 12 (16.67%)</p> <p>3</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Blood and lymphatic system disorders</p> <p>Anaemia</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Ear and labyrinth disorders</p> <p>Vertigo</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Eye disorders</p> <p>Vision blurred</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Gastrointestinal disorders</p> <p>Abdominal distension</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Abdominal pain</p> <p>alternative assessment type: Systematic</p>	<p>2 / 21 (9.52%)</p> <p>2</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	

subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)
occurrences (all)	1	0
Aphthous ulcer		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)
occurrences (all)	1	0
Constipation		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)
occurrences (all)	1	0
Diarrhoea		
alternative assessment type: Systematic		
subjects affected / exposed	7 / 21 (33.33%)	2 / 12 (16.67%)
occurrences (all)	7	5
Dyspepsia		
alternative assessment type: Systematic		
subjects affected / exposed	2 / 21 (9.52%)	0 / 12 (0.00%)
occurrences (all)	2	0
Eructation		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Gastric antral vascular ectasia		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Gastrointestinal inflammation		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)
occurrences (all)	1	0
Gastrooesophageal reflux disease		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 21 (4.76%)	1 / 12 (8.33%)
occurrences (all)	1	1

<p>Gingival recession</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Nausea</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Oesophagitis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>1 / 12 (8.33%)</p> <p>1</p>	
<p>Skin and subcutaneous tissue disorders</p> <p>Acne</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Digital pitting scar</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hair growth abnormal</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hyperhidrosis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypertrichosis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Night sweats</p> <p>alternative assessment type: Systematic</p>	<p>1 / 21 (4.76%)</p> <p>1</p> <p>1 / 21 (4.76%)</p> <p>1</p> <p>0 / 21 (0.00%)</p> <p>0</p> <p>1 / 21 (4.76%)</p> <p>1</p> <p>1 / 21 (4.76%)</p> <p>1</p> <p>0 / 12 (0.00%)</p> <p>0</p>	<p>0 / 12 (0.00%)</p> <p>0</p> <p>1 / 12 (8.33%)</p> <p>1</p> <p>1 / 12 (8.33%)</p> <p>1</p> <p>1 / 12 (8.33%)</p> <p>0 / 12 (0.00%)</p> <p>0</p>	

subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Rash erythematous			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Rash macular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin lesion			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 21 (19.05%)	0 / 12 (0.00%)	
occurrences (all)	4	0	
Skin ulcer			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	1 / 12 (8.33%)	
occurrences (all)	1	2	
Renal and urinary disorders			
Pollakiuria			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 21 (9.52%)	0 / 12 (0.00%)
occurrences (all)	3	0
Back pain		
alternative assessment type: Systematic		
subjects affected / exposed	2 / 21 (9.52%)	0 / 12 (0.00%)
occurrences (all)	2	0
Bone disorder		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)
occurrences (all)	1	0
Fibromyalgia		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Muscular weakness		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Musculoskeletal pain		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)
occurrences (all)	2	0
Myalgia		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Osteolysis		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)
occurrences (all)	1	0
Pain in extremity		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1

<p>Scleroderma</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Synovitis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Tendonitis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>2</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Tenosynovitis stenosans</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 21 (4.76%)</p> <p>1</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	
<p>Infections and infestations</p> <p>Bronchitis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cellulitis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Conjunctivitis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Gastroenteritis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Gastroenteritis viral</p> <p>alternative assessment type: Systematic</p>	<p>0 / 21 (0.00%)</p> <p>0</p> <p>2 / 21 (9.52%)</p> <p>2</p> <p>1 / 21 (4.76%)</p> <p>1</p> <p>1 / 21 (4.76%)</p> <p>1</p>	<p>1 / 12 (8.33%)</p> <p>1</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p>	

subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)
occurrences (all)	1	0
Herpes zoster		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)
occurrences (all)	1	0
Hordeolum		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)
occurrences (all)	1	0
Influenza		
alternative assessment type: Systematic		
subjects affected / exposed	2 / 21 (9.52%)	0 / 12 (0.00%)
occurrences (all)	2	0
Nasopharyngitis		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Oral herpes		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Otitis media		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)
occurrences (all)	1	0
Pharyngitis		
alternative assessment type: Systematic		
subjects affected / exposed	2 / 21 (9.52%)	0 / 12 (0.00%)
occurrences (all)	2	0
Rhinitis		
alternative assessment type: Systematic		
subjects affected / exposed	2 / 21 (9.52%)	1 / 12 (8.33%)
occurrences (all)	2	1

Sinusitis alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 12 (0.00%) 0	
Suspected COVID-19 alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 12 (8.33%) 1	
Upper respiratory tract infection alternative assessment type: Systematic subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2	2 / 12 (16.67%) 3	
Urinary tract infection alternative assessment type: Systematic subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 4	0 / 12 (0.00%) 0	
Metabolism and nutrition disorders Decreased appetite alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 12 (8.33%) 1	
Dyslipidaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 12 (0.00%) 0	
Iron deficiency alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 12 (0.00%) 0	
Lactose intolerance alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 12 (8.33%) 1	
Vitamin D deficiency alternative assessment type: Systematic			

subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 November 2018	The protocol was amended to revise the participant exclusion criteria.
31 July 2019	The protocol was amended to update the information based on Investigator Brochure Edition 6 (28 Jun 2019), for corrections of errors, and for revision of participant exclusion criteria.
28 April 2020	The protocol was amended to implement urgent safety measures (USM) to mitigate the impact of the coronavirus disease-2019 (COVID-19) pandemic for the systemic sclerosis participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This was a proof-of-concept study not sized or powered to confirm any treatment effect.

Notes: