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

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

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 investiational 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 (± 0.85)	-1.6 (± 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

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 stud 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 stud 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

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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	GLPG1690 600 mg
Reporting group description:	
Participants received GLPG1690 600 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.	

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

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

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

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	

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

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	

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

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

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