Clinical trial results:
A Phase II, randomized, double-blind, placebo controlled, parallel-group, multicenter trial to evaluate the efficacy and safety of abituzumab in subjects with systemic sclerosis-associated interstitial lung disease (SSc-ILD)

Summary

EudraCT number	2015-005023-11
Trial protocol	GB PL ES IT
Global end of trial date	30 May 2018

Results information

Result version number	v1 (current)
This version publication date	14 June 2019
First version publication date	14 June 2019

Trial information

Trial identification

Sponsor protocol code	EMR 200017-014

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02745145
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck KGaA, Darmstadt, Germany
Sponsor organisation address	Frankfurter Strasse 250,, Darmstadt, Germany, 64293
Public contact	Communication Center, Merck KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.com
Scientific contact	Communication Center, Merck KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.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	30 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2018
Global end of trial reached?	Yes
Global end of trial date	30 May 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this trial was to compare two doses of abituzumab with placebo and determine whether abituzumab was more effective, safer, would be better tolerated and could provoke better immune response than placebo in the treatment of subjects with SSc-ILD who already receive constant doses of mycophenolate.

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 May 2016
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	Argentina: 3
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	United States: 14
Worldwide total number of subjects	24
EEA total number of subjects	4

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)	19
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study enrolled 24 subjects and was early terminated due to the difficulties experienced in identifying subjects who meet the eligibility criteria of the trial.

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	Investigator, Carer, Subject, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received Placebo matched to Abituzumab administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Placebo matched to Abituzumab administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.

Arm title	Abituzumab 500 milligrams (mg)

Arm description:

Subjects received Abituzumab 500 mg administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.

Arm type	Experimental
Investigational medicinal product name	Abituzumab 500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Abituzumab 500 mg administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.

Arm title	Abituzumab 1500 mg

Arm description:

Subjects received Abituzumab 1500 mg administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.

Arm type	Experimental

Investigational medicinal product name	Abituzumab 1500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Abituzumab 1500 mg administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.

Number of subjects in period 1	Placebo	Abituzumab 500 milligrams (mg)	Abituzumab 1500 mg
Started	10	5	9
Completed	0	0	0
Not completed	10	5	9
Adverse event, serious fatal	-	1	-
Study Termination	8	3	7
Adverse event, non-fatal	1	-	-
Withdrew consent	1	1	1
Progressive disease	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received Placebo matched to Abituzumab administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.	
Reporting group title	Abituzumab 500 milligrams (mg)
Reporting group description:	
Subjects received Abituzumab 500 mg administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.	
Reporting group title	Abituzumab 1500 mg
Reporting group description:	
Subjects received Abituzumab 1500 mg administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.	

Reporting group values	Placebo	Abituzumab 500 milligrams (mg)	Abituzumab 1500 mg
Number of subjects	10	5	9
Age categorical Units: Subjects			
Age Continuous Units: Years			
arithmetic mean	51	60	55
standard deviation	± 10.6	± 7.5	± 7.8
Sex: Female, Male Units: Subjects			
Female	8	4	7
Male	2	1	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	10	5	9
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	3
Not Hispanic or Latino	9	5	6
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	24		

Age categorical Units: Subjects			

Age Continuous Units: Years arithmetic mean standard deviation	- -		
Sex: Female, Male Units: Subjects			
Female	19		
Male	5		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	24		
More than one race	0		
Unknown or Not Reported	0		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4		
Not Hispanic or Latino	20		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received Placebo matched to Abituzumab administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.	
Reporting group title	Abituzumab 500 milligrams (mg)
Reporting group description:	
Subjects received Abituzumab 500 mg administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.	
Reporting group title	Abituzumab 1500 mg
Reporting group description:	
Subjects received Abituzumab 1500 mg administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.	

Primary: Change From Baseline in Absolute Forced Vital Capacity (FVC) at Week 52

End point title	Change From Baseline in Absolute Forced Vital Capacity (FVC) at Week 52[1]
End point description:	
FVC is the maximum amount of air exhaled from the lungs after taking the deepest breath possible. The FVC assessments were done using spirometry. Change from baseline in fvc at week 52 was reported. Modified intent-to-treat (mITT) population was defined as all randomized subjects who received at least 1 dose of study drug (including placebo). Here, "Number of Subjects Analyzed" signified subjects evaluable for the endpoint. Here, 99999 signified standard deviation was not estimable as there was only one subject evaluable for the arm.	
End point type	Primary
End point timeframe:	
Baseline, Week 52	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Placebo	Abituzumab 500 milligrams (mg)	Abituzumab 1500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	0[2]	1	
Units: milliliters				
arithmetic mean (standard deviation)	-130 (± 56.6)	()	-50 (± 99999)	

Notes:

[2] - All subjects for abituzumab 500 mg arm dropped out before the analysis was conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea as Measured by the Mahler's Transition Dyspnea Index (TDI) at Week 52

End point title	Change From Baseline in Dyspnea as Measured by the Mahler's Transition Dyspnea Index (TDI) at Week 52

End point description:

Mahler's TDI is an interview-administered instrument that allows subjects to assess their level of dyspnea which is assessed by functional impairment, magnitude of task and magnitude of effort. Scores for each subscale range from -3 to +3 so that the TDI focal score ranges from -9 (major deterioration) to +9 (major improvement). For all subscale scores and the TDI focal score a higher value indicates a better outcome.mITT population was defined as all randomized subjects who receive at least 1 dose of study drug (including placebo). Here,"number of subjects analyzed" signified subjects evaluable for the endpoint. Here, 99999 signified standard deviation was not estimable as there was only one subject evaluable for the arm.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	Abituzumab 500 milligrams (mg)	Abituzumab 1500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	0[3]	1	
Units: Score on a scale				
arithmetic mean (standard deviation)	3 (± 99999)	()	4 (± 99999)	

Notes:

[3] - All subjects for abituzumab 500 mg arm dropped out before the analysis was conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in St. George Respiratory Questionnaire (SGRQ) Total Score at Week 52

End point title	Absolute Change From Baseline in St. George Respiratory Questionnaire (SGRQ) Total Score at Week 52

End point description:

The SGRQ assesses health-related quality of life in subjects with chronic pulmonary disease by evaluating 3 health domains: symptoms (distress caused by respiratory symptoms); activity (effects of disturbances on mobility and physical activity); and impacts (the effect of disease on factors such as employment, personal control of one's health, and need for medication). A composite total score is derived as the weighted sum of domain scores for symptoms, activity, and impact (0=the best possible score and 100=the worst possible score). A reduction in score of 4 units is generally recognized as a clinically meaningful improvement in quality of life. mITT population was defined as all randomized subjects who receive at least 1 dose of study drug (including placebo). Here, "number of subjects analyzed" signified number of subjects evaluable for the endpoint. Here, 99999 signified standard deviation was not estimable as there was only one subject evaluable for the arm.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	Abituzumab 500 milligrams (mg)	Abituzumab 1500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	0[4]	1	
Units: Scores on a scale				
arithmetic mean (standard deviation)	6.4 (± 99999)	()	1.4 (± 99999)	

Notes:

[4] - All subjects for abituzumab 500 mg arm dropped out before the analysis was conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Modified Rodnan Skin Score (mRSS) at Week 52 in Subjects with Diffuse Cutaneous Skin Involvement at Baseline

End point title	Absolute Change From Baseline in Modified Rodnan Skin Score (mRSS) at Week 52 in Subjects with Diffuse Cutaneous Skin Involvement at Baseline

End point description:

mRSS measures dermal skin thickness through the examination of 17 body areas: fingers, hands, forearms, arms, feet, legs, and thighs (in pairs), and face, chest, and abdomen. The skin score is evaluated by manual palpation in each of these areas. The skin score is 0 for uninvolved skin, 1 for mild thickening, 2 for moderate thickening, and 3 for severe thickening (hidebound skin). The total skin score is the sum of the skin scores of the individual areas where the minimum score is 0 and the maximum score is 51. A higher score indicates greater severity of disease. mITT diffuse cutaneous systemic sclerosis population from mITT analysis set who had diffuse cutaneous skin involvement at baseline. Here, "number of subjects analyzed" signified number of subjects evaluable for the endpoint. Here, 99999 signified standard deviation was not estimable as there was only one subject evaluable for the arm.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	Abituzumab 500 milligrams (mg)	Abituzumab 1500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	0[5]	0[6]	
Units: Scores on a scale				
arithmetic mean (standard deviation)	0 (± 99999)	()	()	

Notes:

[5] - All subjects for abituzumab 500 mg arm dropped out before the analysis was conducted.

[6] - All subjects for abituzumab 1500 mg arm dropped out before the analysis was conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change from Baseline in Quantitative Lung Fibrosis (QLF) in the Region of Highest Baseline Severity at Week 52

End point title	Absolute Change from Baseline in Quantitative Lung Fibrosis (QLF) in the Region of Highest Baseline Severity at Week 52

End point description:

Absolute change from baseline in QLF score at week 52 was calculated as the difference of the QLF score at week 52 minus the QLF score at baseline divided in the region of highest baseline severity at Week 52 .The QLF score itself ranges from 0 to 100, where greater values represent a greater amount of lung fibrosis and are considered a worse health status. mITT population was defined as all randomized subjects who receive at least 1 dose of study drug (including placebo). Here, "number of subjects analyzed" signified number of subjects evaluable for the endpoint. Here, 99999 signified standard deviation was not estimable as there was only one subject evaluable for the arm.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	Abituzumab 500 milligrams (mg)	Abituzumab 1500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	0[7]	1	
Units: Scores on a scale				
arithmetic mean (standard deviation)	6.29 (± 2.638)	()	-2.27 (± 99999)	

Notes:

[7] - All subjects for abituzumab 500 mg arm dropped out before the analysis was conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival (OS) was defined as the time (in months) from randomization to death. Data has been presented in terms of number of subjects who died and number of censored subjects. mITT population was defined as all randomized subjects who receive at least 1 dose of study drug (including placebo).

End point type	Secondary

End point timeframe:

Time from date of randomization until death, assessed up to 2 years

End point values	Placebo	Abituzumab 500 milligrams (mg)	Abituzumab 1500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	5	9	
Units: subjects				
number (not applicable)				
Number of Deaths	0	1	0	
Number of censored	10	4	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Meaningful Progression of Systemic Sclerosis (SSc) by Meeting Criterion 1 (Interstitial Lung Disease [ILD])

End point title	Number of Subjects With Clinically Meaningful Progression of Systemic Sclerosis (SSc) by Meeting Criterion 1 (Interstitial Lung Disease [ILD])

End point description:

Clinically Meaningful Progression SSc-ILD was defined as one of the following (in the absence of causative intercurrent illness) on at least 2 occasions within approximately 4 weeks (per Outcome Measures in Rheumatology criteria): Relative decrease from baseline in forced vital capacity (FVC) % predicted greater than or equal to (>=)10%; Relative decrease from baseline in FVC % predicted of >=5% to less than (<) 10% and relative decrease from baseline in Diffusion capacity of the lung for carbon monoxide % predicted >=15%. mITT population was defined as all randomized subjects who receive at least 1 dose of study drug (including placebo).

End point type	Secondary

End point timeframe:

upto Week 52

End point values	Placebo	Abituzumab 500 milligrams (mg)	Abituzumab 1500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	5	9	
Units: subjects	0	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Meaningful Progression of Systemic sclerosis (SSc) by Meeting Criterion 2 (SSc Progression other than ILD)

End point title	Number of Subjects with Clinically Meaningful Progression of Systemic sclerosis (SSc) by Meeting Criterion 2 (SSc Progression other than ILD)

End point description:

Clinically Meaningful Progression SSc other than ILD was defined as new onset of one or more of the following: Scleroderma renal crisis; Left ventricular failure (defined as ejection fraction <=45%); Pulmonary arterial hypertension requiring treatment. mITT population was defined as all randomized subjects who receive at least 1 dose of study drug (including placebo).

End point type	Secondary

End point timeframe:

upto Week 52

End point values	Placebo	Abituzumab 500 milligrams (mg)	Abituzumab 1500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	5	9	
Units: subjects	0	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Meaningful Progression

End point title	Number of Subjects with Clinically Meaningful Progression

End point description:

Subjects meeting one or both of the below criteria was considered as having clinically meaningful disease progression. Clinically Meaningful SSc-ILD defined as one of the following (in the absence of causative intercurrent illness) on at least 2 occasions within approximately 4 weeks (per Outcome Measures in Rheumatology criteria): Relative decrease from baseline in forced vital capacity (FVC) % predicted greater than or equal to (>=)10%; Relative decrease from baseline in FVC % predicted of >=5% to less than (<) 10% and relative decrease from baseline in Diffusion capacity of the lung for carbon monoxide % predicted >=15%. Clinically Meaningful SSc progression other than ILD defined as new onset of one or more of the following: Scleroderma renal crisis; Left ventricular failure (defined as ejection fraction <=45%); Pulmonary arterial hypertension requiring treatment. mITT population was defined as all randomized subjects who receive at least 1 dose of study drug (including placebo).

End point type	Secondary

End point timeframe:

upto Week 52

End point values	Placebo	Abituzumab 500 milligrams (mg)	Abituzumab 1500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	5	9	
Units: subjects	0	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Absolute Decrease From Baseline of FVC Percentage (%) Predicted Greater than or Equal to (>=) 10% on 2 or more Consecutive Occasions at Least 4 Weeks Apart

End point title	Number of Subjects With Absolute Decrease From Baseline of FVC Percentage (%) Predicted Greater than or Equal to (>=) 10% on 2 or more Consecutive Occasions at Least 4 Weeks Apart

End point description:

FVC is the maximum amount of air exhaled from the lungs after taking the deepest breath possible. The FVC assessments were done using spirometry. mITT population was defined as all randomized subjects

who receive at least 1 dose of study drug (including placebo).

End point type	Secondary

End point timeframe:

upto Week 52

End point values	Placebo	Abituzumab 500 milligrams (mg)	Abituzumab 1500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	5	9	
Units: subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of study drug administration up to 2 years	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0
Reporting groups	
Reporting group title	Abituzumab 500 milligrams (mg)
Reporting group description:	
Subjects received Abituzumab 500 mg administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.	
Reporting group title	Placebo
Reporting group description:	
Subjects received Placebo matched to Abituzumab administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.	
Reporting group title	Abituzumab 1500 mg
Reporting group description:	
Subjects received Abituzumab 1500 mg administered as an intravenous infusion for 1 hour every 4 weeks up to Week 64.	

Serious adverse events	Abituzumab 500 milligrams (mg)	Placebo	Abituzumab 1500 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	1 / 10 (10.00%)	2 / 9 (22.22%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Neutrophil count increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Small fibre neuropathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			

subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

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

Non-serious adverse events	Abituzumab 500 milligrams (mg)	Placebo	Abituzumab 1500 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	9 / 10 (90.00%)	8 / 9 (88.89%)
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	1 / 5 (20.00%)	1 / 10 (10.00%)	2 / 9 (22.22%)
occurrences (all)	1	1	2
Generalised oedema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Impaired healing			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Multiple allergies			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 5 (0.00%)	3 / 10 (30.00%)	3 / 9 (33.33%)
occurrences (all)	0	3	3
Dyspnoea			
subjects affected / exposed	1 / 5 (20.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
Dyspnoea exertional			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2

Interstitial lung disease			
subjects affected / exposed	1 / 5 (20.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
Nasal dryness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Pulmonary hypertension			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Pulmonary mass			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Sinus congestion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood urine present			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Glycosylated haemoglobin increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Neutrophil count increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Platelet count increased			

subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Protein urine present			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
White blood cell count increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 5 (20.00%)	1 / 10 (10.00%)	2 / 9 (22.22%)
occurrences (all)	1	1	2
Hypoaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Lethargy			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Migraine			

subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Sciatica			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	3 / 10 (30.00%)	3 / 9 (33.33%)
occurrences (all)	1	3	3
Dry mouth			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Frequent bowel movements			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 5 (20.00%)	1 / 10 (10.00%)	2 / 9 (22.22%)
occurrences (all)	1	1	2
Stomatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Vomiting			

subjects affected / exposed	1 / 5 (20.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Dermal cyst			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Intertrigo			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Rosacea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Skin exfoliation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Skin hypertrophy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Skin ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2

Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Eye pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 10 (10.00%)	2 / 9 (22.22%)
occurrences (all)	1	1	2
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Bursitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Fibromyalgia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Synovial cyst			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	4 / 10 (40.00%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
Gastrointestinal bacterial overgrowth			
subjects affected / exposed	0 / 5 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Onychomycosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2016	To remove the Dyspnea-12 index assessment; To decrease the frequency of select quality of life assessments; To specify the required visits following discontinuation of Investigational Medicinal Product (IMP); To update the number of planned sites; To include criteria for the classification of systemic sclerosis to the protocol appendices; To include minor corrections and clarifications to the clinical trial protocol.

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.

The analysis of outcome measures at Week 104 wasn't conducted as the study was terminated due to the difficulties experienced in identifying subjects who meet the eligibility criteria of the trial.

Notes: