



Clinical trial results:

A Phase 2, Proof-of-Concept, Multicenter, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Efficacy of Pomalidomide (CC-4047) In Subjects with Systemic Sclerosis with Interstitial Lung Disease

Summary

EudraCT number	2010-023047-15
Trial protocol	DE GB IT ES PL
Global end of trial date	03 November 2016

Results information

Result version number	v1 (current)
This version publication date	19 November 2017
First version publication date	19 November 2017

Trial information

Trial identification

Sponsor protocol code	CC-4047-SSC-001
-----------------------	-----------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01559129
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Celgene Corporation
Sponsor organisation address	86 Morris Avenue, Summit, NJ, United States, 07901
Public contact	ClinicalTrialDisclosure, Celgene Corporation, +1 8882601599, ClinicalTrialDisclosure@celgene.com
Scientific contact	Shimon Korish, MD, Celgene Corporation, +1 908-897-6350, Skorish@Celgene.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	17 September 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	03 November 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the safety, tolerability, and efficacy of pomalidomide in the treatment of patients with systemic sclerosis with interstitial lung disease.

Protection of trial subjects:

This study was conducted in accordance with the guidelines of current Good Clinical Practice including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 August 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Russian Federation: 6
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	23
EEA total number of subjects	6

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)	20
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were randomized in a 1:1 ratio to receive either pomalidomide 1 mg daily or matching placebo. Randomization was stratified based on type of systemic sclerosis (limited [lSSc] versus diffuse [dSSc]).

Period 1

Period 1 title	Treatment Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo orally once a day for 52 weeks during the treatment phase.

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

Dosage and administration details:

Placebo capsules taken orally once a day

Arm title	Pomalidomide
------------------	--------------

Arm description:

Participants received 1 mg pomalidomide orally once a day for 52 weeks during the treatment phase.

Arm type	Experimental
Investigational medicinal product name	Pomalidomide
Investigational medicinal product code	CC-4047
Other name	POMALYST®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Pomalidomide capsules taken orally once a day

Number of subjects in period 1	Placebo	Pomalidomide
Started	12	11
Received Treatment	12	10
Completed	7	4
Not completed	5	7
Protocol exclusion criteria	1	-
Study terminated by sponsor	3	2
Adverse event	-	2
Did not receive study drug	-	1
Progressive disease	1	1
Lack of efficacy	-	1

Period 2

Period 2 title	Open-label Extension Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Pomalidomide

Arm description:

Participants who received placebo orally once a day for 52 weeks during the treatment phase transitioned to receive 1 mg pomalidomide orally once a day for up to 2 years during the open-label extension period.

Arm type	Experimental
Investigational medicinal product name	Pomalidomide
Investigational medicinal product code	CC-4047
Other name	POMALYST®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Pomalidomide capsules taken orally once a day

Arm title	Pomalidomide/Pomalidomide
------------------	---------------------------

Arm description:

Participants who received 1 mg pomalidomide orally once a day for 52 weeks during the treatment phase continued to receive the same treatment for up to 2 years during the open-label extension phase.

Arm type	Experimental
Investigational medicinal product name	Pomalidomide
Investigational medicinal product code	CC-4047
Other name	POMALYST®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Pomalidomide capsules taken orally once a day

Number of subjects in period 2^[1]	Placebo/Pomalidomide	Pomalidomide/Pomalidomide
Started	6	2
Completed	0	0
Not completed	6	2
Adverse event	1	-
Study terminated by sponsor	5	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Three participants who completed the treatment phase elected not to enter the open-label extension phase.

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo orally once a day for 52 weeks during the treatment phase.	
Reporting group title	Pomalidomide
Reporting group description:	
Participants received 1 mg pomalidomide orally once a day for 52 weeks during the treatment phase.	

Reporting group values	Placebo	Pomalidomide	Total
Number of subjects	12	11	23
Age categorical			
Units: Subjects			
Adults (18-64 years)	10	10	20
From 65-84 years	2	1	3
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	44.8	48.9	-
standard deviation	± 13.77	± 9.84	-
Gender categorical			
Units: Subjects			
Female	10	10	20
Male	2	1	3
Race			
Units: Subjects			
Asian	0	2	2
Black or African American	0	1	1
Native Hawaiian or Other Pacific Islanders	1	0	1
White	10	8	18
Other	1	0	1
Body Mass Index (BMI)			
Units: kg/m ²			
arithmetic mean	30.64	27.61	-
standard deviation	± 5.392	± 9.4	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Participants received placebo orally once a day for 52 weeks during the treatment phase.	
Reporting group title	Pomalidomide
Reporting group description: Participants received 1 mg pomalidomide orally once a day for 52 weeks during the treatment phase.	
Reporting group title	Placebo/Pomalidomide
Reporting group description: Participants who received placebo orally once a day for 52 weeks during the treatment phase transitioned to receive 1 mg pomalidomide orally once a day for up to 2 years during the open-label extension period.	
Reporting group title	Pomalidomide/Pomalidomide
Reporting group description: Participants who received 1 mg pomalidomide orally once a day for 52 weeks during the treatment phase continued to receive the same treatment for up to 2 years during the open-label extension phase.	

Primary: Number of Participants With Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs) ^[1]
End point description: An adverse event (AE) is any noxious, unintended, or untoward medical occurrence that may appear or worsen during the course of a study. A TEAE is any AE that began or worsened on or after the start of study drug through 28 days after the last dose. A treatment-related TEAE is a TEAE which was considered by the investigator to be related to study drug. The severity/intensity of AEs was assessed by the investigator as Mild (asymptomatic or mild symptoms; intervention not indicated), Moderate (symptoms cause moderate discomfort, intervention may be required), or Severe (symptoms cause severe discomfort/pain, requiring medical intervention, inability to perform daily activities). A serious AE is any AE that: • Resulted in death; • Was life-threatening; • Required inpatient hospitalization or prolongation of existing hospitalization • Resulted in persistent or significant disability/incapacity; • Was a congenital anomaly/birth defect; • Constituted an important medical event	
End point type	Primary
End point timeframe: From the start of study drug to 28 days after last dose; Treatment Phase median duration of treatment was 358 for Placebo and 320 days for Pomalidomide; Extension phase median duration of treatment was 161 days for Placebo and 194 days for pomalidomide.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were performed due to the low number of subjects enrolled.

End point values	Placebo	Placebo/Pomali- domide	Pomalidomide	Pomalidomide/ Pomalidomide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	6	10	2
Units: participants				
Any TEAE	12	5	9	2
Drug-related TEAE	8	3	6	1
Severe TEAE	1	0	4	0
Serious TEAE	1	0	4	1
Serious Drug-related TEAE	0	0	1	0

TEAE Leading to Drug Interruption	2	0	1	0
TEAE Leading to Drug Withdrawal	0	0	4	0
TEAE Leading to Death	0	0	0	0

Statistical analyses

No statistical analyses for this end point

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

End point title	Change From Baseline in Percent Predicted Forced Vital Capacity (FVC) at Week 52 ^[2]
-----------------	---

End point description:

Forced vital capacity (FVC) is a pulmonary function test and is the volume of air in the lungs that can forcibly be blown out after a full inhalation. Percent predicted values are based comparison between the participant's measured value with expected FVC for someone of the same sex, age and height (reference value). For the analysis of FVC, the baseline value was defined as the average of all values between Screening and Baseline (inclusive), and the average of Weeks 48 and 52 was treated as the Week 52 value, to reduce the total data variability at the key time points. The Full Analysis Set (FAS) consisted of all randomized participants who received at least one dose of study drug. Participants with a Baseline value and a Week 52 were included in the analysis.

End point type	Primary
----------------	---------

End point timeframe:

Baseline (defined as the average of all values between Screening and Baseline) and Weeks 48 and 52

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were performed due to the low number of subjects enrolled.

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	8		
Units: percent predicted				
arithmetic mean (standard deviation)	-2.8 (± 4.02)	-5.2 (± 5.29)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in the Modified Rodnan Skin Score (mRSS) at Week 52/Early Termination

End point title	Change From Baseline in the Modified Rodnan Skin Score (mRSS) at Week 52/Early Termination ^[3]
-----------------	---

End point description:

Improvement in skin thickening is associated with improved survival and may be useful as a surrogate measurement in clinical studies. The mRSS is an assessment tool which is used to evaluate the extent and severity of the skin thickening associated with systemic sclerosis (SSc). Seventeen body areas were evaluated on a 4-point scale (0 [normal], 1 [mild], 2 [moderate]), or 3 [severe]). The total score, which is the sum of the 17 individual body assessments, can range from 0 to 51.

End point type	Primary
----------------	---------

End point timeframe:

Baseline and Week 52 (or the Treatment Phase Early Termination visit)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were performed due to the low number of subjects enrolled.

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11 ^[4]	10 ^[5]		
Units: units on a scale				
arithmetic mean (standard deviation)	-3.7 (± 6.99)	-2.7 (± 5.66)		

Notes:

[4] - FAS participants with a Baseline value and a post-baseline value at Week 52 or Early Termination

[5] - FAS participants with a Baseline value and a post-baseline value at Week 52 or Early Termination

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in University of California, Los Angeles, Scleroderma Clinical Trial Consortium Gastrointestinal Tract (UCLA SCTC GIT 2.0) Total Score at Week 52/Early Termination

End point title	Change From Baseline in University of California, Los Angeles, Scleroderma Clinical Trial Consortium Gastrointestinal Tract (UCLA SCTC GIT 2.0) Total Score at Week 52/Early Termination ^[6]
-----------------	---

End point description:

The UCLA SCTC GIT 2.0 is a 34-item, health-related quality of life self-administered evaluation tool, which targets GI activity and severity in patients with SSc. Individual scales include reflux, distention/bloating, fecal soilage, diarrhea, social functioning, emotional well-being and constipation. The items are scored on a scale from 0 to 3, where 0 indicates better health and 3 indicates worse health (except for Questions 15 and 31 which are scored as 0 (better health) or 1 (worse health)). The total score is calculated as the average of the first 6 scale scores (excluding constipation) which captures overall burden (severity) of SSc-associated GIT. The overall score ranges from 0 to 3, where higher scores indicate more severe symptoms.

End point type	Primary
----------------	---------

End point timeframe:

Baseline and Week 52 (or Treatment Phase Early Termination visit)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were performed due to the low number of subjects enrolled.

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[7]	10 ^[8]		
Units: units on a scale				
arithmetic mean (standard deviation)	0.0 (± 0.18)	0.1 (± 0.29)		

Notes:

[7] - FAS participants with a Baseline value and a post-baseline value at Week 52 or Early Termination

[8] - FAS participants with a Baseline value and a post-baseline value at Week 52 or Early Termination

Statistical analyses

Secondary: Change From Baseline in Percent Predicted Forced Vital Capacity Over Time

End point title	Change From Baseline in Percent Predicted Forced Vital Capacity Over Time
End point description: Forced vital capacity (FVC) is a pulmonary function test and is the volume of air in the lungs that can forcibly be blown out after a full inhalation. Percent predicted values are based comparison between the participant's measured value with expected FVC for someone of the same sex, age and height (reference value). "99999" indicates a value that could not be calculated.	
End point type	Secondary
End point timeframe: Baseline (defined as the average of all values between Screening and Baseline) and Weeks 12, 24, 36, 64, 76, and 156	

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[9]	10 ^[10]		
Units: percent predicted				
arithmetic mean (standard deviation)				
Week 12 (n = 10, 8)	-2.4 (± 3.07)	-1.8 (± 3.39)		
Week 24 (n = 10, 8)	-1.3 (± 3.33)	2.3 (± 12.58)		
Week 36 (n = 9, 6)	-2.6 (± 2.48)	-4.4 (± 3.97)		
Week 64 (n = 6, 2)	-7.0 (± 4.29)	-6.4 (± 4.49)		
Week 76 (n = 2, 1)	-8.7 (± 10.34)	-5.2 (± 99999)		
Week 156 (n = 4, 2)	-6.7 (± 6.19)	-5.9 (± 2.31)		

Notes:

[9] - FAS participants with a Baseline value and post-baseline value at the time point.

[10] - FAS participants with a Baseline value and post-baseline value at the time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Modified Rodnan Skin Score Over Time

End point title	Change From Baseline in Modified Rodnan Skin Score Over Time
End point description: Improvement in skin thickening is associated with improved survival and may be useful as a surrogate measurement in clinical studies. The mRSS is an assessment tool which is used to evaluate the extent and severity of the skin thickening associated with systemic sclerosis (SSc). Seventeen body areas were evaluated on a 4-point scale (0 [normal], 1 [mild], 2 [moderate], or 3 [severe]). The total score, which is the sum of the 17 individual body assessments, can range from 0 to 51. "99999" indicates values that could not be calculated.	
End point type	Secondary
End point timeframe: Baseline and Weeks 12, 24, 64, 76, and 156 (or the Extension Phase Early Termination visit).	

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11 ^[11]	10 ^[12]		
Units: unit's on a scale				
arithmetic mean (standard deviation)				
Week 12 (n = 10, 8)	-1.8 (± 3.94)	-0.3 (± 1.83)		
Week 24 (n = 10, 8)	-3.6 (± 5.68)	-2.0 (± 3.38)		
Week 64 (n = 6, 2)	-4.3 (± 8.36)	-4.0 (± 2.83)		
Week 76 (n = 2, 1)	-8.5 (± 7.78)	-7.0 (± 99999)		
Week 156/Early Termination (n = 6, 2)	-3.7 (± 8.52)	-4.5 (± 3.54)		

Notes:

[11] - FAS participants with a Baseline value and a post-baseline value at each time point.

[12] - FAS participants with a Baseline value and a post-baseline value at each time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in UCLA SCTC GIT 2.0 Total Score Over Time

End point title	Change From Baseline in UCLA SCTC GIT 2.0 Total Score Over Time
-----------------	---

End point description:

The UCLA SCTC GIT 2.0 is a 34-item, health-related quality of life self-administered evaluation tool, which targets GI activity and severity in patients with SSc. Individual scales include reflux, distention/bloating, fecal soilage, diarrhea, social functioning, emotional well-being and constipation. The items are scored on a scale from 0 to 3, where 0 indicates better health and 3 indicates worse health (except for Questions 15 and 31 which are scored as 0 (better health) or 1 (worse health). The total score is calculated as the average of the first 6 scale scores (excluding constipation) which captures overall burden (severity) of SSc-associated GIT. The overall score ranges from 0 to 3, where higher scores indicate more severe symptoms. "99999" indicates values that could not be calculated.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Weeks 12, 24, 64, 76, and 156 (or the Extension Phase Early Termination visit).

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[13]	10 ^[14]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n = 10, 8)	0.2 (± 0.36)	-0.1 (± 0.30)		
Week 24 (n = 10, 8)	0.1 (± 0.23)	-0.1 (± 0.20)		
Week 64 (n = 6, 2)	0.0 (± 0.20)	0.4 (± 0.01)		
Week 76 (n = 2, 1)	-0.1 (± 0.01)	0.5 (± 99999)		
Week 156/Early Termination (n = 6, 2)	0.0 (± 0.14)	0.0 (± 0.14)		

Notes:

[13] - FAS participants with a Baseline value and post-baseline value at each time point.

[14] - FAS participants with a Baseline value and post-baseline value at each time point.

Statistical analyses

Secondary: Change From Baseline in UCLA SCTC GIT 2.0 Reflux Subscale Score Over Time

End point title	Change From Baseline in UCLA SCTC GIT 2.0 Reflux Subscale Score Over Time
-----------------	---

End point description:

The UCLA SCTC GIT 2.0 is a 34-item, health-related quality of life self-administered evaluation tool, which targets GI activity and severity in patients with SSc. Individual scales include reflux, distention/bloating, fecal soilage, diarrhea, social functioning, emotional well-being and constipation. The items are scored on a scale from 0 to 3, where 0 indicates better health and 3 indicates worse health. The reflux subscale score is calculated as the average of eight reflux-related questions; the score ranges from 0 to 3, where higher scores indicate more frequent symptoms. "99999" indicates values that could not be calculated.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Weeks 12, 24, 52 (or at the Treatment Phase Early Termination visit), 64, 76, and 156 (or the Extension Phase Early Termination visit).

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[15]	10 ^[16]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n = 10, 8)	0.1 (± 0.36)	-0.1 (± 0.51)		
Week 24 (n = 10, 8)	-0.1 (± 0.27)	0.0 (± 0.47)		
Week 52/Early Termination (n = 12, 10)	-0.1 (± 0.54)	0.1 (± 0.38)		
Week 64 (n = 6, 2)	-0.2 (± 0.14)	0.2 (± 0.46)		
Week 76 (n = 2, 1)	-0.5 (± 0.18)	-0.2 (± 99999)		
Week 156/Early Termination (n = 6, 2)	0.0 (± 0.44)	0.1 (± 0.28)		

Notes:

[15] - FAS participants with a Baseline value and post-baseline value at each time point.

[16] - FAS participants with a Baseline value and post-baseline value at each time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in UCLA SCTC GIT 2.0 Distension/Bloating Subscale Score Over Time

End point title	Change From Baseline in UCLA SCTC GIT 2.0 Distension/Bloating Subscale Score Over Time
-----------------	--

End point description:

The UCLA SCTC GIT 2.0 is a 34-item, health-related quality of life self-administered evaluation tool, which targets GI activity and severity in patients with SSc. Individual scales include reflux, distention/bloating, fecal soilage, diarrhea, social functioning, emotional well-being and constipation. The items are scored on a scale from 0 to 3, where 0 indicates better health and 3 indicates worse health. The distension/bloating subscale score is calculated as the average of four distension/bloating-related questions; the score ranges from 0 to 3, where higher scores indicate more frequent symptoms. "99999" indicates values that could not be calculated.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Weeks 12, 24, 52 (or at the Treatment Phase Early Termination visit), 64, 76, and 156 (or

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[17]	10 ^[18]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n = 10, 8)	0.4 (± 0.56)	0.2 (± 1.21)		
Week 24 (n = 10, 8)	0.0 (± 0.53)	0.3 (± 0.80)		
Week 52/Early Termination (n = 12, 10)	0.0 (± 0.55)	0.2 (± 1.07)		
Week 64 (n = 6, 2)	-0.2 (± 0.70)	1.0 (± 1.41)		
Week 76 (n = 2, 1)	0.0 (± 0.00)	3.0 (± 99999)		
Week 156/Early Termination (n = 6, 2)	-0.3 (± 0.30)	0.9 (± 1.24)		

Notes:

[17] - FAS participants with a Baseline value and post-baseline value at each time point.

[18] - FAS participants with a Baseline value and post-baseline value at each time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in UCLA SCTC GIT 2.0 Fecal Soilage Subscale Score Over Time

End point title	Change From Baseline in UCLA SCTC GIT 2.0 Fecal Soilage Subscale Score Over Time
-----------------	--

End point description:

The UCLA SCTC GIT 2.0 is a 34-item, health-related quality of life self-administered evaluation tool, which targets GI activity and severity in patients with SSc. Individual scales include reflux, distention/bloating, fecal soilage, diarrhea, social functioning, emotional well-being and constipation. The items are scored on a scale from 0 to 3, where 0 indicates better health and 3 indicates worse health. The fecal soilage subscale score is calculated from one soilage question; the score ranges from 0 to 3, where higher scores indicate more frequent symptoms. "99999" indicates values that could not be calculated.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Weeks 12, 24, 52 (or at the Treatment Phase Early Termination visit), 64, 76, and 156 (or the Extension Phase Early Termination visit).

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[19]	10 ^[20]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n = 10, 8)	0.0 (± 0.00)	0.0 (± 0.00)		
Week 24 (n = 10, 8)	0.2 (± 0.42)	0.0 (± 0.00)		
Week 52/Early Termination (n = 12, 9)	0.0 (± 0.00)	0.1 (± 0.33)		
Week 64 (n = 6, 2)	0.2 (± 0.41)	0.0 (± 0.00)		
Week 76 (n = 2, 1)	0.0 (± 0.00)	0.0 (± 99999)		

Week 156/Early Termination (n = 6, 2)	0.2 (± 0.41)	0.0 (± 0.00)		
---------------------------------------	--------------	--------------	--	--

Notes:

[19] - FAS participants with a Baseline value and post-baseline value at each time point.

[20] - FAS participants with a Baseline value and post-baseline value at each time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in UCLA SCTC GIT 2.0 Diarrhea Subscale Score Over Time

End point title	Change From Baseline in UCLA SCTC GIT 2.0 Diarrhea Subscale Score Over Time
-----------------	---

End point description:

The UCLA SCTC GIT 2.0 is a 34-item, health-related quality of life self-administered evaluation tool, which targets GI activity and severity in patients with SSc. Individual scales include reflux, distention/bloating, fecal soilage, diarrhea, social functioning, emotional well-being and constipation. The diarrhea subscale score is calculated as the average of one diarrhea question about the frequency of loose stools (on a scale from 0 [none] to 3 [5-7 days/week] and one question about the presence of watery stools (scored as 0 [No] or 1 [Yes]); the score ranges from 0 to 2, where a higher score indicates more frequent symptoms. "99999" indicates values that could not be calculated.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Weeks 12, 24, 52 (or at the Treatment Phase Early Termination visit), 64, 76, and 156 (or the Extension Phase Early Termination visit).

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[21]	10 ^[22]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n = 10, 8)	0.4 (± 0.57)	-0.2 (± 0.65)		
Week 24 (n = 10, 8)	0.1 (± 0.21)	-0.3 (± 0.46)		
Week 52/Early Termination (n = 12, 10)	0.3 (± 0.34)	0.0 (± 0.75)		
Week 64 (n = 6, 2)	0.1 (± 0.38)	0.5 (± 0.71)		
Week 76 (n = 2, 1)	0.0 (± 0.00)	-0.5 (± 99999)		
Week 156/Early Termination (n = 6, 2)	0.3 (± 0.42)	-0.8 (± 0.35)		

Notes:

[21] - FAS participants with a Baseline value and post-baseline value at each time point.

[22] - FAS participants with a Baseline value and post-baseline value at each time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in UCLA SCTC GIT 2.0 Social Functioning Subscale Score Over Time

End point title	Change From Baseline in UCLA SCTC GIT 2.0 Social Functioning Subscale Score Over Time
-----------------	---

End point description:

The UCLA SCTC GIT 2.0 is a 34-item, health-related quality of life self-administered evaluation tool, which targets GI activity and severity in patients with SSc. Individual scales include reflux, distention/bloating, fecal soilage, diarrhea, social functioning, emotional well-being and constipation. The items are scored on a scale from 0 to 3, where 0 indicates better health and 3 indicates worse health. The social functioning subscale score is calculated as the average of six questions about how often symptoms interfered with social activities; the score ranges from 0 to 3, where higher scores indicate more frequent symptoms. "99999" indicates values that could not be calculated.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Weeks 12, 24, 52 (or at the Treatment Phase Early Termination visit), 64, 76, and 156 (or the Extension Phase Early Termination visit).

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11 ^[23]	10 ^[24]		
Units: unites on a scale				
arithmetic mean (standard deviation)				
Week 12 (n = 9, 8)	0.3 (± 0.49)	0.0 (± 0.28)		
Week 24 (n = 9, 8)	0.1 (± 0.30)	-0.1 (± 0.20)		
Week 52/Early Termination (n = 11, 10)	0.0 (± 0.25)	0.2 (± 0.45)		
Week 64 (n = 5, 2)	0.0 (± 0.18)	0.3 (± 0.35)		
Week 76 (n = 1, 1)	0.2 (± 99999)	0.0 (± 99999)		
Week 156/Early Termination (n = 5, 2)	0.0 (± 0.25)	-0.2 (± 0.23)		

Notes:

[23] - FAS participants with a Baseline value and post-baseline value at each time point.

[24] - FAS participants with a Baseline value and post-baseline value at each time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in UCLA SCTC GIT 2.0 Emotional Well Being Subscale Score Over Time

End point title	Change From Baseline in UCLA SCTC GIT 2.0 Emotional Well Being Subscale Score Over Time
-----------------	---

End point description:

The UCLA SCTC GIT 2.0 is a 34-item, health-related quality of life self-administered evaluation tool, which targets GI activity and severity in patients with SSc. Individual scales include reflux, distention/bloating, fecal soilage, diarrhea, social functioning, emotional well-being and constipation. The items are scored on a scale from 0 to 3, where 0 indicates better health and 3 indicates worse health. The emotional well-being subscale score is calculated as the average of nine questions regarding the impact of bowel problems on emotional status; the score ranges from 0 to 3, where higher scores indicate more frequent problems. "99999" indicates values that could not be calculated.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Weeks 12, 24, 52 (or at the Treatment Phase Early Termination visit), 64, 76, and 156 (or the Extension Phase Early Termination visit).

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[25]	10 ^[26]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n = 10, 8)	0.2 (± 0.40)	-0.4 (± 0.80)		
Week 24 (n = 10, 8)	0.1 (± 0.16)	-0.3 (± 0.56)		
Week 52/Early Termination (n = 12, 10)	0.1 (± 0.25)	-0.1 (± 0.42)		
Week 64 (n = 6, 2)	0.0 (± 0.36)	0.2 (± 0.00)		
Week 76 (n = 2, 1)	0.0 (± 0.00)	0.3 (± 99999)		
Week 156/Early Termination (n = 6, 2)	-0.1 (± 0.15)	0.0 (± 0.00)		

Notes:

[25] - FAS participants with a Baseline value and post-baseline value at each time point.

[26] - FAS participants with a Baseline value and post-baseline value at each time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in UCLA SCTC GIT 2.0 Constipation Subscale Score Over Time

End point title	Change From Baseline in UCLA SCTC GIT 2.0 Constipation Subscale Score Over Time
-----------------	---

End point description:

The UCLA SCTC GIT 2.0 is a 34-item, health-related quality of life self-administered evaluation tool, which targets GI activity and severity in patients with SSc. Individual scales include reflux, distention/bloating, fecal soilage, diarrhea, social functioning, emotional well-being and constipation. The items are scored on a scale from 0 to 3, where 0 indicates better health and 3 indicates worse health. The constipation subscale score is calculated as the average of three questions regarding the frequency of constipation (scored from 0 [no days] to 3 [5-7 days/week] and one question about the presence of stools becoming harder (scored as 0 [No] or 1 [Yes]); the score ranges from 0 to 2.5, where higher scores indicate more frequent symptoms. "99999" indicates values that could not be calculated.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Weeks 12, 24, 52 (or at the Treatment Phase Early Termination visit), 64, 76, and 156 (or the Extension Phase Early Termination visit).

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[27]	10 ^[28]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 12 (n = 10, 8)	-0.1 (± 0.36)	0.2 (± 0.98)		
Week 24 (n = 10, 8)	-0.2 (± 0.31)	0.3 (± 0.81)		
Week 52/Early Termination (n = 12, 10)	0.0 (± 0.25)	0.3 (± 0.51)		
Week 64 (n = 6, 2)	0.0 (± 0.60)	0.1 (± 0.18)		
Week 76 (n = 2, 1)	0.0 (± 0.00)	0.0 (± 99999)		
Week 156/Early Termination (n = 6, 2)	-0.2 (± 0.20)	0.1 (± 0.18)		

Notes:

[27] - FAS participants with a Baseline value and post-baseline value at each time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Functional Impairment at Week 12

End point title	Change From Baseline in Dyspnea Functional Impairment at Week 12
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. Changes in dyspnea functional impairment were assessed on a scale from Major Deterioration (formerly working but had to stop working and abandoned usual activities due to shortness of breath) to Major Improvement (able to return to work at former pace and return to full activities with only mild restriction due to improvement of shortness of breath). Further impairment for other reasons includes participants who gave up or reduced work or other activities for reasons other than shortness of breath.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 12

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10 ^[29]	7 ^[30]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	1	1		
Minor deterioration	0	1		
No change	7	3		
Minor improvement	2	1		
Moderate improvement	0	0		
Major improvement	0	0		
Further impairment for other reasons	0	1		

Notes:

[29] - FAS participants with available data

[30] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Functional Impairment at Week 24

End point title	Change From Baseline in Dyspnea Functional Impairment at Week 24
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. Changes in dyspnea functional impairment were assessed on a scale from Major Deterioration (formerly working but had to stop working and abandoned usual activities due to shortness of breath) to Major Improvement (able to return to work at former pace and return to full activities with only mild restriction due to improvement of shortness of breath). Further impairment for other reasons includes participants who gave up or reduced work or other activities for reasons other than shortness of breath.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 24

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10 ^[31]	7 ^[32]		
Units: participants				
Major deterioration	1	0		
Moderate deterioration	0	2		
Minor deterioration	1	1		
No change	4	2		
Minor improvement	3	1		
Moderate improvement	1	0		
Major improvement	0	0		
Further impairment for other reasons	0	1		

Notes:

[31] - FAS participants with available data

[32] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Functional Impairment at Week 52/Early Termination

End point title	Change From Baseline in Dyspnea Functional Impairment at Week 52/Early Termination
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. Changes in dyspnea functional impairment were assessed on a scale from Major Deterioration (formerly working but had to stop working and abandoned usual activities due to shortness of breath) to Major Improvement (able to return to work at former pace and return to full activities with only mild restriction due to improvement of shortness of breath). Further impairment for other reasons includes participants who gave up or reduced work or other activities for reasons other than shortness of breath.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 52 or at the Treatment Phase Early Termination visit

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[33]	10 ^[34]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	0	4		
Minor deterioration	1	1		
No change	8	4		
Minor improvement	3	1		
Moderate improvement	0	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[33] - FAS participants with available data

[34] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Functional Impairment at Week 64

End point title	Change From Baseline in Dyspnea Functional Impairment at Week 64
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. Changes in dyspnea functional impairment were assessed on a scale from Major Deterioration (formerly working but had to stop working and abandoned usual activities due to shortness of breath) to Major Improvement (able to return to work at former pace and return to full activities with only mild restriction due to improvement of shortness of breath). Further impairment for other reasons includes participants who gave up or reduced work or other activities for reasons other than shortness of breath.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 64

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6 ^[35]	2 ^[36]		
Units: participants				
Major deterioration	0	1		
Moderate deterioration	0	1		
Minor deterioration	1	0		
No change	4	0		
Minor improvement	1	0		
Moderate improvement	0	0		

Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[35] - FAS participants with available data

[36] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Functional Impairment at Week 76

End point title	Change From Baseline in Dyspnea Functional Impairment at Week 76
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. Changes in dyspnea functional impairment were assessed on a scale from Major Deterioration (formerly working but had to stop working and abandoned usual activities due to shortness of breath) to Major Improvement (able to return to work at former pace and return to full activities with only mild restriction due to improvement of shortness of breath). Further impairment for other reasons includes participants who gave up or reduced work or other activities for reasons other than shortness of breath.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 76

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2 ^[37]	1 ^[38]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	0	1		
Minor deterioration	1	0		
No change	0	0		
Minor improvement	1	0		
Moderate improvement	0	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[37] - FAS participants with available data

[38] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Functional Impairment at Week 156/Early Termination

End point title	Change From Baseline in Dyspnea Functional Impairment at Week 156/Early Termination
-----------------	---

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. Changes in dyspnea functional impairment were assessed on a scale from Major Deterioration (formerly working but had to stop working and abandoned usual activities due to shortness of breath) to Major Improvement (able to return to work at former pace and return to full activities with only mild restriction due to improvement of shortness of breath). Further impairment for other reasons includes participants who gave up or reduced work or other activities for reasons other than shortness of breath.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 156 or the Extension Phase Early Termination visit

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6 ^[39]	2 ^[40]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	0	1		
Minor deterioration	2	1		
No change	2	0		
Minor improvement	1	0		
Moderate improvement	1	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[39] - FAS participants with available data

[40] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Magnitude of Task at Week 12

End point title	Change From Baseline in Dyspnea Magnitude of Task at Week 12
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. At Baseline magnitude of task was assessed on a scale from Grade 0 (becomes short of breath at rest, while sitting or lying) to Grade 4 (becomes short of breath only with extraordinary activity such as running or carrying very heavy loads). Changes in dyspnea magnitude of task were assessed on a scale from Major Deterioration (deteriorated ≥ 2 grades from Baseline) to Major Improvement (Improved ≥ 2 grades from Baseline). Further impairment for other reasons includes participants with reduced exertion capacity for reasons other than shortness of breath, for example musculoskeletal problems or chest pain.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 12

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10 ^[41]	7 ^[42]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	0	0		
Minor deterioration	2	1		
No change	5	5		
Minor improvement	3	1		
Moderate improvement	0	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[41] - FAS participants with available data

[42] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Magnitude of Task at Week 24

End point title	Change From Baseline in Dyspnea Magnitude of Task at Week 24
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. At Baseline magnitude of task was assessed on a scale from Grade 0 (becomes short of breath at rest, while sitting or lying) to Grade 4 (becomes short of breath only with extraordinary activity such as running or carrying very heavy loads). Changes in dyspnea magnitude of task were assessed on a scale from Major Deterioration (deteriorated ≥ 2 grades from Baseline) to Major Improvement (Improved ≥ 2 grades from Baseline). Further impairment for other reasons includes participants with reduced exertion capacity for reasons other than shortness of breath, for example musculoskeletal problems or chest pain.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 24

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10 ^[43]	7 ^[44]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	1	1		
Minor deterioration	2	1		
No change	5	2		
Minor improvement	2	3		

Moderate improvement	0	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[43] - FAS participants with available data

[44] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Magnitude of Task at Week 52/Early Termination

End point title	Change From Baseline in Dyspnea Magnitude of Task at Week 52/Early Termination
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. At Baseline magnitude of task was assessed on a scale from Grade 0 (becomes short of breath at rest, while sitting or lying) to Grade 4 (becomes short of breath only with extraordinary activity such as running or carrying very heavy loads). Changes in dyspnea magnitude of task were assessed on a scale from Major Deterioration (deteriorated ≥ 2 grades from Baseline) to Major Improvement (Improved ≥ 2 grades from Baseline). Further impairment for other reasons includes participants with reduced exertion capacity for reasons other than shortness of breath, for example musculoskeletal problems or chest pain.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 52 or at the Treatment Phase Early Termination visit

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[45]	10 ^[46]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	0	3		
Minor deterioration	1	1		
No change	8	6		
Minor improvement	2	0		
Moderate improvement	0	0		
Major improvement	1	0		
Further impairment for other reasons	0	0		

Notes:

[45] - FAS participants with available data

[46] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Magnitude of Task at Week 64

End point title	Change From Baseline in Dyspnea Magnitude of Task at Week
-----------------	---

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. At Baseline magnitude of task was assessed on a scale from Grade 0 (becomes short of breath at rest, while sitting or lying) to Grade 4 (becomes short of breath only with extraordinary activity such as running or carrying very heavy loads). Changes in dyspnea magnitude of task were assessed on a scale from Major Deterioration (deteriorated ≥ 2 grades from Baseline) to Major Improvement (Improved ≥ 2 grades from Baseline). Further impairment for other reasons includes participants with reduced exertion capacity for reasons other than shortness of breath, for example musculoskeletal problems or chest pain.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 64

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6 ^[47]	2 ^[48]		
Units: participants				
Major deterioration	0	1		
Moderate deterioration	0	0		
Minor deterioration	2	0		
No change	3	0		
Minor improvement	1	1		
Moderate improvement	0	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[47] - FAS participants with available data

[48] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Magnitude of Task at Week 76

End point title	Change From Baseline in Dyspnea Magnitude of Task at Week 76
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. At Baseline magnitude of task was assessed on a scale from Grade 0 (becomes short of breath at rest, while sitting or lying) to Grade 4 (becomes short of breath only with extraordinary activity such as running or carrying very heavy loads). Changes in dyspnea magnitude of task were assessed on a scale from Major Deterioration (deteriorated ≥ 2 grades from Baseline) to Major Improvement (Improved ≥ 2 grades from Baseline). Further impairment for other reasons includes participants with reduced exertion capacity for reasons other than shortness of breath, for example musculoskeletal problems or chest pain.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 76

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2 ^[49]	1 ^[50]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	0	0		
Minor deterioration	1	0		
No change	1	0		
Minor improvement	0	1		
Moderate improvement	0	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[49] - FAS participants with available data

[50] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Magnitude of Task at Week 156/Early Termination

End point title	Change From Baseline in Dyspnea Magnitude of Task at Week 156/Early Termination
-----------------	---

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. At Baseline magnitude of task was assessed on a scale from Grade 0 (becomes short of breath at rest, while sitting or lying) to Grade 4 (becomes short of breath only with extraordinary activity such as running or carry very heavy loads). Changes in dyspnea magnitude of task were assessed on a scale from Major Deterioration (deteriorated ≥ 2 grades from Baseline) to Major Improvement (Improved ≥ 2 grades from Baseline). Further impairment for other reasons includes participants with reduced exertion capacity for reasons other than shortness of breath, for example musculoskeletal problems or chest pain.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 156 or the Extension Phase Early Termination visit

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6 ^[51]	2 ^[52]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	1	0		
Minor deterioration	1	1		
No change	2	0		
Minor improvement	2	1		

Moderate improvement	0	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[51] - FAS participants with available data

[52] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Magnitude of Effort at Week 12

End point title	Change From Baseline in Dyspnea Magnitude of Effort at Week 12
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. At Baseline magnitude of task was assessed on a scale from Grade 0 (becomes short of breath at rest, while sitting or lying) to Grade 4 (becomes short of breath only with greatest imaginable effort). Changes in dyspnea magnitude of task were assessed on a scale from Major Deterioration (severe decrease in effort from Baseline to avoid shortness of breath, activities take 50-100% longer to complete) to Major Improvement (able to do things with much greater effort than previously with few, if any, pauses). Further impairment for other reasons includes participants with reduced exertion capacity for reasons other than shortness of breath.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 12

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10 ^[53]	7 ^[54]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	1	0		
Minor deterioration	2	2		
No change	4	4		
Minor improvement	2	1		
Moderate improvement	1	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[53] - FAS participants with available data

[54] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Magnitude of Effort at Week 24

End point title	Change From Baseline in Dyspnea Magnitude of Effort at Week 24
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. At Baseline magnitude of task was assessed on a scale from Grade 0 (becomes short of breath at rest, while sitting or lying) to Grade 4 (becomes short of breath only with greatest imaginable effort). Changes in dyspnea magnitude of task were assessed on a scale from Major Deterioration (severe decrease in effort from Baseline to avoid shortness of breath, activities take 50-100% longer to complete) to Major Improvement (able to do things with much greater effort than previously with few, if any, pauses). Further impairment for other reasons includes participants with reduced exertion capacity for reasons other than shortness of breath.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 24

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10 ^[55]	7 ^[56]		
Units: participants				
Major deterioration	1	1		
Moderate deterioration	0	1		
Minor deterioration	1	0		
No change	4	3		
Minor improvement	3	2		
Moderate improvement	1	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[55] - FAS participants with available data

[56] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Magnitude of Effort at Week 52/Early Termination

End point title	Change From Baseline in Dyspnea Magnitude of Effort at Week 52/Early Termination
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. At Baseline magnitude of task was assessed on a scale from Grade 0 (becomes short of breath at rest, while sitting or lying) to Grade 4 (becomes short of breath only with greatest imaginable effort). Changes in dyspnea magnitude of task were assessed on a scale from Major Deterioration (severe decrease in effort from Baseline to avoid shortness of breath, activities take 50-100% longer to complete) to Major Improvement (able to do things with much greater effort than previously with few, if any, pauses). Further impairment for other reasons includes participants with reduced exertion capacity for reasons other than shortness of breath.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 52 or at the Treatment Phase Early Termination visit

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[57]	10 ^[58]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	0	3		
Minor deterioration	1	1		
No change	7	6		
Minor improvement	3	0		
Moderate improvement	1	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[57] - FAS participants with available data

[58] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Magnitude of Effort at Week 64

End point title	Change From Baseline in Dyspnea Magnitude of Effort at Week 64
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. At Baseline magnitude of task was assessed on a scale from Grade 0 (becomes short of breath at rest, while sitting or lying) to Grade 4 (becomes short of breath only with greatest imaginable effort). Changes in dyspnea magnitude of task were assessed on a scale from Major Deterioration (severe decrease in effort from Baseline to avoid shortness of breath, activities take 50-100% longer to complete) to Major Improvement (able to do things with much greater effort than previously with few, if any, pauses). Further impairment for other reasons includes participants with reduced exertion capacity for reasons other than shortness of breath.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 64

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6 ^[59]	2 ^[60]		
Units: participants				
Major deterioration	0	1		
Moderate deterioration	0	0		
Minor deterioration	3	0		
No change	2	1		
Minor improvement	1	0		

Moderate improvement	0	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[59] - FAS participants with available data

[60] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Magnitude of Effort at Week 76

End point title	Change From Baseline in Dyspnea Magnitude of Effort at Week 76
-----------------	--

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. At Baseline magnitude of task was assessed on a scale from Grade 0 (becomes short of breath at rest, while sitting or lying) to Grade 4 (becomes short of breath only with greatest imaginable effort). Changes in dyspnea magnitude of task were assessed on a scale from Major Deterioration (severe decrease in effort from Baseline to avoid shortness of breath, activities take 50-100% longer to complete) to Major Improvement (able to do things with much greater effort than previously with few, if any, pauses). Further impairment for other reasons includes participants with reduced exertion capacity for reasons other than shortness of breath.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 76

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2 ^[61]	1 ^[62]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	0	0		
Minor deterioration	1	0		
No change	0	1		
Minor improvement	1	0		
Moderate improvement	0	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[61] - FAS participants with available data

[62] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dyspnea Magnitude of Effort at Week 156/Early Termination

End point title	Change From Baseline in Dyspnea Magnitude of Effort at Week
-----------------	---

End point description:

The Transition Dyspnea Index (TDI) provides interview-based measurements of breathlessness related to activities of daily living. The TDI is an evaluative instrument that includes specific criteria for each of three components (functional impairment, magnitude of task and magnitude of effort) to measure changes from a baseline state. At Baseline magnitude of task was assessed on a scale from Grade 0 (becomes short of breath at rest, while sitting or lying) to Grade 4 (becomes short of breath only with greatest imaginable effort). Changes in dyspnea magnitude of task were assessed on a scale from Major Deterioration (severe decrease in effort from Baseline to avoid shortness of breath, activities take 50-100% longer to complete) to Major Improvement (able to do things with much greater effort than previously with few, if any, pauses). Further impairment for other reasons includes participants with reduced exertion capacity for reasons other than shortness of breath.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 156 or at the Extension Phase Early Termination visit

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6 ^[63]	2 ^[64]		
Units: participants				
Major deterioration	0	0		
Moderate deterioration	1	0		
Minor deterioration	2	1		
No change	2	1		
Minor improvement	1	0		
Moderate improvement	0	0		
Major improvement	0	0		
Further impairment for other reasons	0	0		

Notes:

[63] - FAS participants with available data

[64] - FAS participants with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Oxygen Saturation Over Time

End point title	Oxygen Saturation Over Time
-----------------	-----------------------------

End point description:

Oxygen saturation was measured by pulse oximetry. "99999" indicates values that could not be calculated.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Weeks 12, 24, 52 (or at the Treatment Phase Early Termination visit), 64, 76, and 156 (or the Extension Phase Early Termination visit).

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[65]	9 ^[66]		
Units: percent saturation				
arithmetic mean (standard deviation)				
Baseline (n = 12, 9)	97.5 (± 2.07)	96.8 (± 1.92)		
Week 12 (n = 10, 8)	97.1 (± 2.18)	97.4 (± 1.51)		
Week 24 (n = 10, 8)	97.6 (± 1.65)	96.5 (± 4.31)		
Week 52/Early Termination (n = 12, 9)	96.8 (± 2.18)	96.8 (± 1.86)		
Week 64 (n = 6, 2)	96.3 (± 2.94)	94.0 (± 2.83)		
Week 76 (n = 2, 1)	98.5 (± 0.71)	97.0 (± 99999)		
Week 156/Early Termination (n = 6, 2)	95.8 (± 5.12)	97.5 (± 0.71)		

Notes:

[65] - FAS participants with a value at each time point.

[66] - FAS participants with a value at each time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameters of Pomalidomide in Plasma

End point title	Pharmacokinetic Parameters of Pomalidomide in Plasma
End point description: Pharmacokinetic analyses were not conducted as there were too few participants with available data.	
End point type	Secondary
End point timeframe: Day 1 and week 4 pre-dose and up to 24 hours post-dose.	

End point values	Placebo	Pomalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[67]	0 ^[68]		
Units: ng/mL				
arithmetic mean (standard deviation)	()	()		

Notes:

[67] - Pharmacokinetic analyses were not conducted as there were too few participants with available data

[68] - Pharmacokinetic analyses were not conducted as there were too few participants with available data

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of study drug to 28 days after last dose; Treatment Phase median duration of treatment was 358 and 320 days for Placebo and Pomalidomide; Extension phase median duration of treatment was 161 days and 194 days for Placebo and Pomalidomide.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Treatment Phase: Placebo
-----------------------	--------------------------

Reporting group description:

Participants received placebo orally once a day for 52 weeks during the treatment phase.

Reporting group title	Treatment Phase: Pomalidomide
-----------------------	-------------------------------

Reporting group description:

Participants received 1 mg pomalidomide orally once a day for 52 weeks during the treatment phase.

Reporting group title	Extension Phase: Placebo/Pomalidomide
-----------------------	---------------------------------------

Reporting group description:

In the open-label extension phase participants received 1 mg pomalidomide orally once a day for up to 2 years.

Reporting group title	Extension Phase: Pomalidomide/Pomalidomide
-----------------------	--

Reporting group description:

Participants received 1 mg pomalidomide orally once a day for up to 2 years during the open-label extension phase.

Serious adverse events	Treatment Phase: Placebo	Treatment Phase: Pomalidomide	Extension Phase: Placebo/Pomalidomide
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)	4 / 10 (40.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic respiratory failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary embolism			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Extension Phase: Pomalidomide/Pomalidomide		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic respiratory failure			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Treatment Phase: Placebo	Treatment Phase: Pomalidomide	Extension Phase: Placebo/Pomalidomide
Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 12 (100.00%)	9 / 10 (90.00%)	5 / 6 (83.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Seborrhoeic keratosis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	1 / 6 (16.67%) 1
Hypertension subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	0 / 6 (0.00%) 0
Raynaud's phenomenon subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	0 / 6 (0.00%) 0
General disorders and administration site conditions Chills subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Device breakage subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	0 / 6 (0.00%) 0
Influenza like illness subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Non-cardiac chest pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Oedema subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0

Oedema peripheral subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 10 (10.00%) 2	0 / 6 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	1 / 6 (16.67%) 1
Pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 10 (10.00%) 1	0 / 6 (0.00%) 0
Immune system disorders Contrast media allergy subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	0 / 6 (0.00%) 0
Seasonal allergy subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Social circumstances Menopause subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Reproductive system and breast disorders Amenorrhoea subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	1 / 6 (16.67%) 1
Nipple pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	0 / 6 (0.00%) 0
Ovarian cyst ruptured subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 10 (10.00%) 1	1 / 6 (16.67%) 1
Dysphonia			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Productive cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Pulmonary hypertension			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Rhinorrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Sinus congestion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Blood creatinine increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood iron decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Heart rate increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Procedural pain			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0	1 / 6 (16.67%) 1
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	0 / 6 (0.00%) 0
Nervous system disorders Ageusia subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Hypoaesthesia subjects affected / exposed occurrences (all) Migraine subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 3 / 12 (25.00%) 3 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1	1 / 10 (10.00%) 1 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Splenomegaly subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1 1 / 12 (8.33%) 1	1 / 10 (10.00%) 1 0 / 10 (0.00%) 0	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0

Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Barrett's oesophagus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Colonic polyp			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	1 / 12 (8.33%)	3 / 10 (30.00%)	0 / 6 (0.00%)
occurrences (all)	1	3	0
Diarrhoea			
subjects affected / exposed	3 / 12 (25.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	5	1	0
Dry mouth			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastric polyps			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hiatus hernia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Mucous stools			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cholecystitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cholelithiasis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatic steatosis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Butterfly rash			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dermatitis acneiform			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Digital ulcer			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Dry skin			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Eczema			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Macule			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Papule			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 12 (8.33%)	2 / 10 (20.00%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Rash maculo-papular			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rash papular			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rosacea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin ulcer			

subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 3	0 / 10 (0.00%) 0	2 / 6 (33.33%) 2
Toxic skin eruption subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	0 / 6 (0.00%) 0
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Glycosuria subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Renal failure subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 2	0 / 6 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 4	4 / 10 (40.00%) 5	0 / 6 (0.00%) 0
Joint swelling subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Muscle spasms subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 2	0 / 6 (0.00%) 0
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	0 / 6 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 10 (10.00%) 1	0 / 6 (0.00%) 0
Pain in jaw subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Synovitis			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tendon disorder			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Tendon pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Diverticulitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infected skin ulcer			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	2 / 6 (33.33%)
occurrences (all)	2	0	2
Laryngitis viral			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Localised infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Tooth abscess subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 3	1 / 10 (10.00%) 2	0 / 6 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 10 (0.00%) 0	2 / 6 (33.33%) 2
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 2	0 / 6 (0.00%) 0
Metabolism and nutrition disorders			
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 10 (10.00%) 1	0 / 6 (0.00%) 0
Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Iron deficiency subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	0 / 6 (0.00%) 0
Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0	1 / 6 (16.67%) 1

Non-serious adverse events	Extension Phase: Pomalidomide/Pomalidomide		
Total subjects affected by non-serious adverse events subjects affected / exposed	2 / 2 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Seborrhoeic keratosis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		

Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Raynaud's phenomenon			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Device breakage			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Immune system disorders			

Contrast media allergy subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Seasonal allergy subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Social circumstances Menopause subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Reproductive system and breast disorders Amenorrhoea subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Nipple pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Ovarian cyst ruptured subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Dysphonia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Dyspnoea subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Productive cough subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		

Pulmonary hypertension subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 2		
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Sinus congestion subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Depressed mood subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Insomnia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Blood iron decreased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
C-reactive protein increased			

subjects affected / exposed occurrences (all) Heart rate increased subjects affected / exposed occurrences (all) Hepatic enzyme increased subjects affected / exposed occurrences (all) White blood cell count increased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all) Ligament sprain subjects affected / exposed occurrences (all) Procedural pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Nervous system disorders Ageusia subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Headache	0 / 2 (0.00%) 0 1 / 2 (50.00%) 1		

subjects affected / exposed occurrences (all) Hypoaesthesia subjects affected / exposed occurrences (all) Migraine subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Splenomegaly subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Barrett's oesophagus subjects affected / exposed occurrences (all) Colonic polyp subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gastric polyps			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Hiatus hernia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Mucous stools			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Mouth ulceration			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cholecystitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cholelithiasis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Hepatic steatosis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Butterfly rash			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dermatitis acneiform			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Digital ulcer			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hyperkeratosis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Macule			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Papule			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Rash papular			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Rosacea			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Skin ulcer			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Toxic skin eruption			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Glycosuria			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Renal failure			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pain in jaw			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Synovitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tendon disorder			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tendon pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Diverticulitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Folliculitis			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Infected skin ulcer			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Laryngitis viral			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Localised infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tooth abscess			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		

Hypomagnesaemia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Iron deficiency			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 November 2011	Significant changes included in this amendment are summarized below: - Increase the daily dose of pomalidomide from 0.5 mg to 1 mg. The amendment also included several other minor clarifications and corrections: - Deletion of calculated creatinine clearance as a serum chemistry assessment performed by the central lab. - Clarification of requirement to take study drug at the investigative site on the days of study visits. - Update of Figure 1 – “Overall Study Design” to reflect new dosage information. - Update of UCLA SCTC GIT 2.0 instrument (Appendix D) and SHAQ (Appendix E) scales.
20 March 2012	Significant changes included in this amendment are summarized below: - Clarification of the duration of the Long-term Follow-up Phase. - Deletion of DLco as an efficacy assessment and secondary endpoint. - Specification of required timeframes for discontinuation of short- and long-acting beta agonists and inhaled steroids prior to spirometry testing. - Inclusion of the definition of true abstinence. - Increase of heart rate entry exclusion criteria from < 45 beats per minute to < 50 beats per minute. - Modification of FEV1/FVC ratio definition of obstructive lung disease. - Lower threshold of heart rate-related stopping rule increased from < 40 beats per minute to < 45 beats per minute based on modification to protocol entrance criteria. - Modification of wording related to renal inclusion criteria and stopping rule requirements from serum creatinine to the MDRD eGFR reported in mL/min. Other changes included in this amendment are summarized below: - Modification of protocol wording to provide clarity and consistency throughout the document. - Inclusion of wording indicating experimental treatments are acceptable during the Long-term Follow-up Phase. - Modification of the footnote wording on the Overall Study Design Figure to clarify length of time of Long-term Follow-up Phase and to note that experimental treatments are permissible during this phase of the study. - Inclusion of wording regarding acceptable timeframe for DLco assessment required for study entry. - Clarification of protocol language regarding FVC study entry criteria. - Revision of footnote language in the Table of Events to reflect the deletion of DLco as a required assessment (beyond Screening). - Clarification of the timing of the first Long-term Follow-up Phase visit. - Correction of the total number of study visits.
14 December 2012	Significant changes included: - Addition of SSc-related cough status as an exploratory endpoint, and a cough visual analogue scale as a new assessment. - Modification of the inclusion criteria to permit up to 50% of enrolled subjects to have ISSc (limited cutaneous form systemic sclerosis). - Deletion of specific references to dSSc. - Modification of onset of the first non-Raynaud's manifestation of SSc from 5 years to within 7 years of Screening. - Expansion of pulmonary-related inclusion criteria. - Deletion of history of hypercoagulable state exclusion criteria. - Clarification of terminology regarding HRCT findings consistent with SSc-ILD. - Lower threshold of DLco decreased to 35%. - Clarification of hepatitis test results inclusion/exclusion. - Modification of the list of acceptable concomitant medications to include: - Endothelin-1 inhibitors and prostaglandin analogues for digital ulcers if taken for at least 28 days prior to Screening. - Use of anti-thrombotic/anti coagulant medications if a subject is hospitalized and use is in the best interest of the subject. - Continued use/addition of certain concomitant medications which may promote QT/QTc prolongation, if there is a positive risk/benefit ratio and ECGs are closely monitored. - Cough medications. - Deletion of the requirement that subjects must be on oral statins for hyperlipidemia for ≥ 84 days prior to Screening. - Modification of the list of excluded prior treatments to include: - Use of bosentan, ambrisentan, iloprost, trepostinil, epoprostenol, sildenafil, tadalafil for PAH within 28 days. - Deletion of misoprostol as an unacceptable concomitant medication. - Addition of medications generally accepted to have a risk of causing torsades de pointes - Change of required concomitant medication washout periods for: - Cytotoxic/immunosuppressive agents from 84 days to within 28 days of Screening. - Clarification of the definitions of I

27 March 2014	Significant changes included: - Specification of target enrollment completion date. - Addition of Open-Label Extension Phase with inclusion of relevant information (eg, study duration, objectives, endpoints, rationale, etc.). - Clarification of timing of the Long-term Follow-up Phase. Other less significant revisions included: - Clarification of the timing of entry into the Observation Phase. - Modification of timeframe for evaluation of exploratory QoL endpoints. - Clarification of concomitant medication use during the course of the study. - Clarification of timeframe for IDMC involvement and monitoring responsibilities following dissolution of the IDMC. - Inclusion of assessment of quantitative serum beta-HCG if warranted. - Treatment Phase safety endpoints updated to include SAEs. - Clarification of unblinding procedures. - Update of the last visit on the Treatment Phase Table of Events to include assessments for Investigational Product Dispensing and Urine Pregnancy Testing. - Clarification of pregnancy testing requirements for non-menstruating FCBP. - Correction of UCLA SCTC GIT 2.0 instrument scoring information. - Clarification of timing of ECGs in both phases. - Clarification of Exclusion 9 to indicate acceptability of subjects having Sjogren's syndrome secondary to systemic sclerosis. - Clarification of Exclusions 17 & 19 to indicate that specified abnormalities must be present on 2 of 3 Screening/Baseline ECGs - Update of Exclusion 33 to include macitentan as a treatment for PAH. - Addition of information regarding assignment of subject numbers for rescreened subjects. - Clarification of the use of anti-thrombotic medications vs subject discontinuation requirements. - Clarification of wording related to FVC analyses - Modification of "end-of-trial" definition and timing of analyses - Clarification regarding interim analyses. - Clarification of time frame for reporting SAEs
23 September 2015	The significant change included in this amendment is: - Termination of the Long-term Follow-up Phase intended to monitor for the occurrence of primary malignancies. Another, less significant revision is: - Updated information for Medical Monitor.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported