Clinical trial results:
A Phase-3, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study To Compare Efficacy and Safety of Pomalidomide in subjects With Myeloproliferative Neoplasm-Associated Myelofibrosis and Red Blood Cell-Transfusion-Dependence

Summary

EudraCT number	2010-018965-42
Trial protocol	GB DE NL AT IT ES BE SE PL
Global end of trial date	14 May 2018

Results information

Result version number	v2 (current)
This version publication date	13 July 2019
First version publication date	31 May 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CC-4047-MF-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01178281
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Celgene Corporation
Sponsor organisation address	87 Morris Avenue, Summit, United States, 07901
Public contact	Clinical Trial Disclosure, Celgene Corporation, 01 888-260-1599, ClinicalTrialDisclosure@Celgene.com
Scientific contact	Robert Peter Gale, MD, PhD, Celgene Corporation, 01 908 656 0484, RGale@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	14 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to determine whether pomalidomide is safe and effective in reversing red blood cell (RBC)-transfusion-dependence in persons with myeloproliferative neoplasm (MPN)-associated myelofibrosis (global study) and in reversing anemia in Chinese with MPN-associated myelofibrosis and severe anemia not receiving RBC-transfusions (China extension study only).

Protection of trial subjects:

Protection of Patient Confidentiality, Archiving of Essential Documents

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 September 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Austria: 9
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	China: 36
Country: Number of subjects enrolled	France: 21
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Italy: 36
Country: Number of subjects enrolled	Japan: 9
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Russian Federation: 13
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Sweden: 6
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	United States: 75
Worldwide total number of subjects	267
EEA total number of subjects	123

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)	91
From 65 to 84 years	172
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Participants in the global study were enrolled at 72 clinical centers in 15 countries. In addition, the China-specific extension study enrolled participants with myeloproliferative neoplasm (MPN)-associated myelofibrosis and severe anemia not receiving red blood cell (RBC)-transfusions at 5 sites in China.

Pre-assignment

Screening details:

Participants in the global study were randomized 2:1 to receive blinded pomalidomide or placebo. All participants in the China extension received open-label pomalidomide. Randomization was stratified by age (≤vs >65 years), white blood cells (< or ≥25 × 10/L), and baseline transfusion requirement (≤vs >4units RBC/28 days over the prior 84 days).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Pomalidomide 0.5 mg

Arm description:

Participants received pomalidomide 0.5 mg/day by mouth for at least 168 days unless there were unacceptable side effects or disease progression. Participants who were RBC-transfusion independent or experienced clinical benefit (defined as a reduction from Baseline of ≥ 50% in RBC-transfusion frequency during the prior 84-day interval) could continue to receive pomalidomide until loss of RBC-transfusion independence response or clinical benefit, or other criteria for treatment discontinuation applied.

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

Dosage and administration details:

Pomalidomide 0.5 mg by mouth once daily

Arm title	Placebo

Arm description:

Participants received placebo taken by mouth once daily for at least 168 days unless there were unacceptable side effects or disease progression. Participants who were RBC-transfusion independent or experienced clinical benefit could continue to receive placebo until loss of RBC-transfusion independence response or clinical benefit, or other criteria for treatment discontinuation applied.

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 by mouth once daily

Arm title	China Extension: Pomalidomide 0.5 mg

Arm description:

Participants received pomalidomide 0.5 mg/day by mouth for at least 168 days unless there were unacceptable side effects, disease progression, or they received a RBC-transfusion. Participants who experienced anemia response could continue treatment until the response was lost or other criteria for treatment discontinuation applied. Participants enrolled in the China extension study were not blinded.

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

Dosage and administration details:

Pomalidomide 0.5 mg by mouth once daily

Number of subjects in period 1	Pomalidomide 0.5 mg	Placebo	China Extension: Pomalidomide 0.5 mg
Started	168	84	15
Received Study Drug	167 [1]	83 [2]	15
Completed	168	84	15

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Completed indicates participants no longer on-study

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Completed indicates participants no longer on-study

Baseline characteristics

Reporting groups	
Reporting group title	Pomalidomide 0.5 mg
Reporting group description:	
Participants received pomalidomide 0.5 mg/day by mouth for at least 168 days unless there were unacceptable side effects or disease progression. Participants who were RBC-transfusion independent or experienced clinical benefit (defined as a reduction from Baseline of ≥ 50% in RBC-transfusion frequency during the prior 84-day interval) could continue to receive pomalidomide until loss of RBC-transfusion independence response or clinical benefit, or other criteria for treatment discontinuation applied.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo taken by mouth once daily for at least 168 days unless there were unacceptable side effects or disease progression. Participants who were RBC-transfusion independent or experienced clinical benefit could continue to receive placebo until loss of RBC-transfusion independence response or clinical benefit, or other criteria for treatment discontinuation applied.	
Reporting group title	China Extension: Pomalidomide 0.5 mg
Reporting group description:	
Participants received pomalidomide 0.5 mg/day by mouth for at least 168 days unless there were unacceptable side effects, disease progression, or they received a RBC-transfusion. Participants who experienced anemia response could continue treatment until the response was lost or other criteria for treatment discontinuation applied. Participants enrolled in the China extension study were not blinded.	

Reporting group values	Pomalidomide 0.5 mg	Placebo	China Extension: Pomalidomide 0.5 mg
Number of subjects	168	84	15
Age categorical			
Units: Subjects			
Adults (18-64 years)	55	26	10

White	122	66	0
Other	3	0	0
Missing	19	4	0
Eastern Cooperative Oncology Group (ECOG) Performance Status			
ECOG performance status is used to describe a patient's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability (walking, working, etc.). The scale ranges from 0 to 5: 0 = Fully active, no restrictions; 1= Restricted activity but ambulatory, able to carry out work of a light nature; 2= Ambulatory and capable of all self-care but unable to carry out work activities; 3= Limited self-care, confined to bed or chair more than 50% of waking hours; 4= Completely disabled, no self-care, confined to bed or chair; 5= Dead			
Units: Subjects			
0 (Fully active)	53	22	5
1 (Restrictive but ambulatory)	85	47	9
2 (Ambulatory but unable to work)	30	15	1
3 (Limited self care)	0	0	0
4 (Completely disabled)	0	0	0
Disease sub-type			
Units: Subjects			
Primary myelofibrosis	127	65	10
Post-polycythemia vera myelofibrosis	17	8	2
Post-essential thrombocythemia myelofibrosis	23	11	3
Missing	1	0	0
Baseline RBC Transfusion Burden			
Defined as the average number of RBC-transfusion-units per 28 days over the 84 days immediately prior to randomization.			
Units: units per 28 days			
median	2.7	2.8	0.0
full range (min-max)	1.3 to 13.3	1.3 to 10.0	0.0 to 0.0

Reporting group values	Total		
Number of subjects	267		
Age categorical			
Units: Subjects			
Adults (18-64 years)	91		
From 65-84 years	172		
85 years and over	4		
Age Continuous			
Units: years			
median			
full range (min-max)	-		
Gender, Male/Female			
Units: Subjects			
Female	75		
Male	192		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	4		
Not Hispanic or Latino	238		
Unknown or Not Reported	25		
Race/Ethnicity, Customized			
Units: Subjects			

American Indian or Alaskan Native	1		
Asian	46		
Black or African American	5		
Native Hawaiian or Other Pacific Islanders	1		
White	188		
Other	3		
Missing	23		
Eastern Cooperative Oncology Group (ECOG) Performance Status			
ECOG performance status is used to describe a patient's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability (walking, working, etc.). The scale ranges from 0 to 5: 0 = Fully active, no restrictions; 1= Restricted activity but ambulatory, able to carry out work of a light nature; 2= Ambulatory and capable of all self-care but unable to carry out work activities; 3= Limited self-care, confined to bed or chair more than 50% of waking hours; 4= Completely disabled, no self-care, confined to bed or chair; 5= Dead			
Units: Subjects			
0 (Fully active)	80		
1 (Restrictive but ambulatory)	141		
2 (Ambulatory but unable to work)	46		
3 (Limited self care)	0		
4 (Completely disabled)	0		
Disease sub-type Units: Subjects			
Primary myelofibrosis	202		
Post-polycythemia vera myelofibrosis	27		
Post-essential thrombocythemia myelofibrosis	37		
Missing	1		
Baseline RBC Transfusion Burden			
Defined as the average number of RBC-transfusion-units per 28 days over the 84 days immediately prior to randomization.			
Units: units per 28 days			
median			
full range (min-max)	-		

End points

End points reporting groups

Reporting group title	Pomalidomide 0.5 mg

Reporting group description:

Participants received pomalidomide 0.5 mg/day by mouth for at least 168 days unless there were unacceptable side effects or disease progression. Participants who were RBC-transfusion independent or experienced clinical benefit (defined as a reduction from Baseline of ≥ 50% in RBC-transfusion frequency during the prior 84-day interval) could continue to receive pomalidomide until loss of RBC-transfusion independence response or clinical benefit, or other criteria for treatment discontinuation applied.

Reporting group title	Placebo

Reporting group description:

Participants received placebo taken by mouth once daily for at least 168 days unless there were unacceptable side effects or disease progression. Participants who were RBC-transfusion independent or experienced clinical benefit could continue to receive placebo until loss of RBC-transfusion independence response or clinical benefit, or other criteria for treatment discontinuation applied.

Reporting group title	China Extension: Pomalidomide 0.5 mg

Reporting group description:

Participants received pomalidomide 0.5 mg/day by mouth for at least 168 days unless there were unacceptable side effects, disease progression, or they received a RBC-transfusion. Participants who experienced anemia response could continue treatment until the response was lost or other criteria for treatment discontinuation applied. Participants enrolled in the China extension study were not blinded.

Primary: China Extension: Number of Participants Achieving a Hemoglobin Increase of ≥ 15 g/L Compared to Baseline for ≥ 84 Consecutive Days

End point title	China Extension: Number of Participants Achieving a Hemoglobin Increase of ≥ 15 g/L Compared to Baseline for ≥ 84 Consecutive Days[1][2]

End point description:

A response in the China extension study was defined as an increase in hemoglobin ≥ 15 g/L above baseline value (in the absence of RBC transfusion) for ≥ 84 consecutive days. The analysis was conducted in the China extension intent-to-treat (ITT) population which included all participants enrolled in the China extension study.

End point type	Primary

End point timeframe:

From the first dose of study drug until treatment discontinuation; median treatment duration was 24.0 weeks.

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: Endpoint was analyzed in the global study population only

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was analyzed in the global study population only

End point values	China Extension: Pomalidomide 0.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants who Achieved RBC-Transfusion Independence

End point title	Percentage of Participants who Achieved RBC-Transfusion Independence[3]

End point description:

RBC-transfusion independence was defined as the absence of RBC transfusions for any consecutive 84-day interval. The analysis was conducted in the global study intent-to-treat (ITT) population which included all randomized participants.

End point type	Primary

End point timeframe:

168 days

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoint was analyzed in the global study population only

End point values	Pomalidomide 0.5 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	84		
Units: percentage of participants				
number (confidence interval 95%)	17.3 (11.88 to 23.84)	16.7 (9.42 to 26.38)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Pomalidomide 0.5 mg v Placebo
Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Overall Survival

End point title	Overall Survival[4]

End point description:

The time from randomization to the death or to the latest date when participants were known to be alive. Overall survival was analyzed in the global study intent-to-treat population using the Kaplan-Meier method; participants who were alive or lost to follow-up were censored at the latest date they were

known to be alive.

End point type	Secondary

End point timeframe:

From first dose of study drug up to end of study; median follow-up time was 19.1 months in the pomalidomide 0.5 mg arm and 17.6 months in the placebo arm.

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was analyzed in the global study population only

End point values	Pomalidomide 0.5 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	84		
Units: months				
median (confidence interval 95%)	24.2 (19.5 to 33.5)	26.2 (18.0 to 32.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Pomalidomide 0.5 mg v Placebo
Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.929
Method	Logrank

Secondary: Duration of RBC-Transfusion Independence

End point title	Duration of RBC-Transfusion Independence[5]

End point description:

The duration of RBC-transfusion independence is the time from the date at which the first RBC-transfusion independence started to the date of another RBC-transfusion given at least 84 days after the time the transfusion independence started. The duration of RBC-transfusion independence was analyzed in the global study intent-to-treat population who had an RBC-transfusion independence response using the Kaplan-Meier method. Data were censored at the end of the treatment phase for participants who had not received another RBC-transfusion after the start of transfusion independence by the end of treatment phase. "99999" indicates data that were not estimable.

End point type	Secondary

End point timeframe:

From first dose of study drug up to 28 days after last dose, as of the data cut-off date of 16 Jan 2013; Median treatment duration was 23.6 weeks in the pomalidomide arm and 23.9 weeks in the placebo arm.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was analyzed in the global study population only

End point values	Pomalidomide 0.5 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[6]	14[7]		
Units: months				
median (confidence interval 95%)	99999 (4.8 to 99999)	5.8 (3.0 to 99999)		

Notes:

[6] - Participants with an RBC-transfusion independence response

[7] - Participants with an RBC-transfusion independence response

Statistical analyses

No statistical analyses for this end point

Secondary: Time to RBC-Transfusion Independence

End point title	Time to RBC-Transfusion Independence[8]

End point description:

Time to response was measured from first dose of study drug to the start of the first response. The start date of the response was defined as one day after the last date of an RBC-transfusion for participants who received a transfusion after the first dose, and as the date of the first dose of study drug for participants who received no transfusions during the 84 days after the first dose of study drug.

End point type	Secondary

End point timeframe:

From first dose of study drug up to 28 days after last dose, as of the data cut-off date of 16 Jan 2013; median treatment duration was 23.6 weeks in the pomalidomide arm and 23.9 weeks in the placebo arm.

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoint was analyzed in the global study population only

End point values	Pomalidomide 0.5 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[9]	14[10]		
Units: weeks				
median (full range (min-max))	6.9 (0.1 to 20.1)	2.4 (0.1 to 15.4)		

Notes:

[9] - Participants with an RBC-transfusion independence response

[10] - Participants with an RBC-transfusion independence response

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-emergent Adverse Events

End point title	Number of Participants with Treatment-emergent Adverse Events

End point description:

A TEAE is an adverse event (AE) that starts on or after the first dose of study drug. The severity of each AE was graded according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE),Version 4.0 and according to the following scale: Grade 1 = Mild (transient or mild discomfort; no limitation in activity; no medical intervention/therapy required); Grade 2 = Moderate (mild to moderate limitation in activity, some assistance may be needed; minimal medical intervention/therapy required); Grade 3 = Severe (marked limitation in activity, assistance usually

required; medical intervention/therapy required, hospitalization possible); Grade 4 = Life-threatening (extreme limitation in activity, significant assistance or medical intervention/therapy required, hospitalization or hospice care probable); Grade 5 = Death Drug-related (related) AEs are those suspected by the Investigator as being related to administration of study drug.

End point type	Secondary

End point timeframe:

From the first dose of study drug until 28 days after last dose; median treatment duration was 23.7 weeks in the pomalidomide arm, 23.9 weeks in the placebo arm, and 24.0 weeks in the China extension pomalidomide arm.

End point values	Pomalidomide 0.5 mg	Placebo	China Extension: Pomalidomide 0.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	167	83	15	
Units: Participants				
Any adverse event (AE)	164	81	12	
Adverse event suspected as related to study drug	90	32	3	
Adverse event leading to dose interruption	48	17	2	
Drug-related AE leading to dose interruption	26	6	1	
AE leading to discontinuation of study drug	53	14	0	
Related AE leading to study drug discontinuation	21	8	0	
Grade 3/4 adverse event	100	44	4	
Grade 3/4 AE related to study drug	45	13	0	
Grade 3/4 AE leading to study drug discontinuation	33	9	0	
Grade 3/4 AE leading to dose interruption	36	14	1	
Grade 5 adverse event	17	10	0	
Grade 5 AE related to study drug	1	3	0	
Serious adverse event (SAE)	76	29	0	
SAE related to study drug	24	7	0	
SAE leading to discontinuation of study drug	31	8	0	
SAE leading to dose interruption	22	7	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Healthcare Resource Utilization

End point title	Healthcare Resource Utilization[11]

End point description:

Characterization of medical resource utilization among participants treated with pomalidomide as compared to participants receiving placebo treatment.

End point type	Secondary

End point timeframe:

From first dose of study drug up to 28 days after last dose, as of the data cut-off date of 16 Jan 2013; Median treatment duration was 23.6 weeks in the pomalidomide arm and 23.9 weeks in the placebo arm.

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There was no data collected for healthcare resource utilization

End point values	Pomalidomide 0.5 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: Participants				

Notes:

[12] - Healthcare resource utilization data were not collected during the study.

[13] - Healthcare resource utilization data were not collected during the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EuroQoL-5D (EQ-5D) Health Index Score

End point title	Change From Baseline in EuroQoL-5D (EQ-5D) Health Index Score[14]

End point description:

EQ-5D is a standardized, participant-rated questionnaire to assess health-related quality of life. The EQ-5D includes 2 components: the EQ-5D health state profile (descriptive system) and the EQ-5D visual analog scale (VAS). For the health state profile participants rate their perceived health state today on 5 dimensions: mobility, selfcare, usual activities, pain/discomfort, and anxiety/depression on a Likert-type scale from 1 to 3, where 1 = “no problems,” 2 = “some problems,” and 3 = “extreme problems.” The EQ-5D Health Utility Index (HUI) was generated from the five health state domain scores, and ranges from -0.594 (worst) and 1 (best) imaginable health state, with -0.594 representing an “unconscious” health state.

End point type	Secondary

End point timeframe:

Baseline and Days 85 and 169

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was analyzed in the global study population only

End point values	Pomalidomide 0.5 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162[15]	82[16]		
Units: score on a scale				
arithmetic mean (standard deviation)				
Day 85	-0.0385 (± 0.2480)	-0.0298 (± 0.2129)		
Day 169	-0.0202 (± 0.1666)	0.0766 (± 0.1546)		

Notes:

[15] - Day 85 N = 112
Day 169 N = 41

[16] - Day 85, N = 56
Day 169 N = 13

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EuroQoL-5D (EQ-5D) Visual Analog Scale

End point title	Change From Baseline in EuroQoL-5D (EQ-5D) Visual Analog Scale[17]

End point description:

EQ-5D is a standardized, participant-rated questionnaire to assess health-related quality of life. The EQ-5D includes 2 components: the EQ-5D health state profile (descriptive system) and the EQ-5D visual analog scale (VAS). On the VAS the participant rates his/her health state on a line from 0 (worst imaginable health) to 100 (best imaginable health).

End point type	Secondary

End point timeframe:

Baseline and Days 85 and 169

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was analyzed in the global study population only

End point values	Pomalidomide 0.5 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161[18]	81[19]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 85	2.0 (± 20.78)	-1.4 (± 14.07)		
Day 169	2.9 (± 22.85)	0.3 (± 24.25)		

Notes:

[18] - Day 85 N = 111
Day 169 N = 41
[19] - Day 85 N = 55
Day 169 N = 13

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Functional Assessment of Cancer Therapy-Anemia (FACT-An) Total Score

End point title	Change From Baseline in Functional Assessment of Cancer Therapy-Anemia (FACT-An) Total Score[20]

End point description:

The FACT-An is a 47-item, cancer-specific questionnaire consisting of a core 27-item general questionnaire measuring the four general domains of QoL (physical, social/family, emotional and functional well-being), and an additional 20-item anemia questionnaire (FACT-An Anemia subscale) that measures 13 fatigue-associated items (FACT-F Fatigue subscale) and seven non-fatigue-related items. Each item is scored using a 5-point Likert rating scale (0 = Not at all; 1 = A little bit; 2 = Somewhat; 3 = Quite a bit; and 4 = Very much). FACT-An total score is calculated by adding all the FACT-An

subscales together. The total score ranges from 0-188 with higher scores representing better QOL.

End point type	Secondary

End point timeframe:

Baseline and Days 85 and 169

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was analyzed in the global study population only

End point values	Pomalidomide 0.5 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159[21]	81[22]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 85	-2.1 (± 20.32)	4.3 (± 18.73)		
Day 169	6.2 (± 20.49)	11.9 (± 18.60)		

Notes:

[21] - Day 85 N = 109
Day 169 N = 41
[22] - Day 85 N = 56
Day 169 N = 13

Statistical analyses

No statistical analyses for this end point

SKIN ULCER			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
Renal and urinary disorders			
CALCULUS BLADDER			
subjects affected / exposed	0 / 167 (0.00%)	1 / 83 (1.20%)	0 / 15 (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
CALCULUS URETERIC			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEPHROLITHIASIS			
subjects affected / exposed	0 / 167 (0.00%)	1 / 83 (1.20%)	0 / 15 (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
NEPHROTIC SYNDROME			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
RENAL COLIC			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
RENAL FAILURE			
subjects affected / exposed	3 / 167 (1.80%)	0 / 83 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
RENAL FAILURE ACUTE			
subjects affected / exposed	1 / 167 (0.60%)	1 / 83 (1.20%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
RENAL FAILURE CHRONIC			

subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
URINARY RETENTION			
subjects affected / exposed	0 / 167 (0.00%)	1 / 83 (1.20%)	0 / 15 (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
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (0.00%)
		0 / 0	

CELLULITIS			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED INFECTION			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
ENTEROCOLITIS INFECTIOUS			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
ERYSIPELAS			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL CANDIDIASIS			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
INFECTIOUS PLEURAL EFFUSION			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
LUNG INFECTION			
subjects affected / exposed	3 / 167 (1.80%)	1 / 83 (1.20%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHADENITIS BACTERIAL			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
NECROTISING FASCIITIS			

subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARONYCHIA			
subjects affected / exposed	0 / 167 (0.00%)	1 / 83 (1.20%)	0 / 15 (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
PNEUMOCYSTIS JIROVECI PNEUMONIA			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	6 / 167 (3.59%)	4 / 83 (4.82%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 7	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	1 / 167 (0.60%)	1 / 83 (1.20%)	0 / 15 (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
SEPTIC SHOCK			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
SIALOADENITIS			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	2 / 167 (1.20%)	0 / 83 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			

subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
UROSEPSIS			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
WOUND INFECTION			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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
DEHYDRATION			
subjects affected / exposed	0 / 167 (0.00%)	1 / 83 (1.20%)	0 / 15 (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
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 167 (0.00%)	1 / 83 (1.20%)	0 / 15 (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
HYPOGLYCAEMIA			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	0 / 15 (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

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

Non-serious adverse events	Global Study: Pomalidomide 0.5 mg	Global Study: Placebo	China Extension: Pomalidomide 0.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	155 / 167 (92.81%)	76 / 83 (91.57%)	12 / 15 (80.00%)
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	23 / 167 (13.77%)	8 / 83 (9.64%)	0 / 15 (0.00%)
occurrences (all)	31	9	0
FATIGUE			
subjects affected / exposed	35 / 167 (20.96%)	17 / 83 (20.48%)	3 / 15 (20.00%)
occurrences (all)	51	23	4
OEDEMA PERIPHERAL			
subjects affected / exposed	53 / 167 (31.74%)	14 / 83 (16.87%)	1 / 15 (6.67%)
occurrences (all)	83	18	1
PYREXIA			
subjects affected / exposed	30 / 167 (17.96%)	9 / 83 (10.84%)	2 / 15 (13.33%)
occurrences (all)	51	13	2
CHEST PAIN			
subjects affected / exposed	2 / 167 (1.20%)	0 / 83 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	2
OEDEMA			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	24 / 167 (14.37%)	9 / 83 (10.84%)	1 / 15 (6.67%)
occurrences (all)	31	10	1
DYSPNOEA			
subjects affected / exposed	28 / 167 (16.77%)	8 / 83 (9.64%)	1 / 15 (6.67%)
occurrences (all)	44	8	1
DYSPNOEA EXERTIONAL			
subjects affected / exposed	10 / 167 (5.99%)	3 / 83 (3.61%)	0 / 15 (0.00%)
occurrences (all)	12	5	0
EPISTAXIS			
subjects affected / exposed	8 / 167 (4.79%)	5 / 83 (6.02%)	0 / 15 (0.00%)
occurrences (all)	15	10	0

PLEURAL EFFUSION			
subjects affected / exposed	5 / 167 (2.99%)	2 / 83 (2.41%)	1 / 15 (6.67%)
occurrences (all)	5	2	1
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	11 / 167 (6.59%)	3 / 83 (3.61%)	1 / 15 (6.67%)
occurrences (all)	12	3	1
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	2 / 167 (1.20%)	0 / 83 (0.00%)	1 / 15 (6.67%)
occurrences (all)	5	0	2
WHITE BLOOD CELL COUNT INCREASED			
subjects affected / exposed	0 / 167 (0.00%)	1 / 83 (1.20%)	1 / 15 (6.67%)
occurrences (all)	0	1	2
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	7 / 167 (4.19%)	5 / 83 (6.02%)	0 / 15 (0.00%)
occurrences (all)	9	7	0
LIGAMENT SPRAIN			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Cardiac disorders			
ARRHYTHMIA			
subjects affected / exposed	2 / 167 (1.20%)	1 / 83 (1.20%)	1 / 15 (6.67%)
occurrences (all)	4	1	1
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	17 / 167 (10.18%)	12 / 83 (14.46%)	0 / 15 (0.00%)
occurrences (all)	25	16	0
SOMNOLENCE			
subjects affected / exposed	5 / 167 (2.99%)	5 / 83 (6.02%)	0 / 15 (0.00%)
occurrences (all)	5	7	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	12 / 167 (7.19%)	5 / 83 (6.02%)	2 / 15 (13.33%)
occurrences (all)	16	9	2
NEUTROPENIA			

subjects affected / exposed	25 / 167 (14.97%)	4 / 83 (4.82%)	0 / 15 (0.00%)
occurrences (all)	73	9	0
THROMBOCYTOPENIA			
subjects affected / exposed	21 / 167 (12.57%)	12 / 83 (14.46%)	1 / 15 (6.67%)
occurrences (all)	41	22	1
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	11 / 167 (6.59%)	1 / 83 (1.20%)	0 / 15 (0.00%)
occurrences (all)	12	1	0
ABDOMINAL PAIN			
subjects affected / exposed	22 / 167 (13.17%)	11 / 83 (13.25%)	0 / 15 (0.00%)
occurrences (all)	27	11	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	10 / 167 (5.99%)	3 / 83 (3.61%)	0 / 15 (0.00%)
occurrences (all)	12	3	0
CONSTIPATION			
subjects affected / exposed	24 / 167 (14.37%)	9 / 83 (10.84%)	0 / 15 (0.00%)
occurrences (all)	28	9	0
DIARRHOEA			
subjects affected / exposed	35 / 167 (20.96%)	17 / 83 (20.48%)	2 / 15 (13.33%)
occurrences (all)	53	20	3
NAUSEA			
subjects affected / exposed	21 / 167 (12.57%)	16 / 83 (19.28%)	0 / 15 (0.00%)
occurrences (all)	25	17	0
VOMITING			
subjects affected / exposed	12 / 167 (7.19%)	7 / 83 (8.43%)	0 / 15 (0.00%)
occurrences (all)	18	9	0
Hepatobiliary disorders			
HEPATIC CYST			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
HEPATIC FUNCTION ABNORMAL			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Skin and subcutaneous tissue disorders			

NIGHT SWEATS			
subjects affected / exposed	10 / 167 (5.99%)	3 / 83 (3.61%)	0 / 15 (0.00%)
occurrences (all)	12	3	0
PRURITUS			
subjects affected / exposed	12 / 167 (7.19%)	5 / 83 (6.02%)	0 / 15 (0.00%)
occurrences (all)	14	6	0
RASH			
subjects affected / exposed	11 / 167 (6.59%)	2 / 83 (2.41%)	0 / 15 (0.00%)
occurrences (all)	19	2	0
Renal and urinary disorders			
CALCULUS URETERIC			
subjects affected / exposed	1 / 167 (0.60%)	0 / 83 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
NEPHROLITHIASIS			
subjects affected / exposed	3 / 167 (1.80%)	0 / 83 (0.00%)	1 / 15 (6.67%)
occurrences (all)	4	0	1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	6 / 167 (3.59%)	8 / 83 (9.64%)	0 / 15 (0.00%)
occurrences (all)	9	10	0
MUSCLE SPASMS			
subjects affected / exposed	9 / 167 (5.39%)	5 / 83 (6.02%)	0 / 15 (0.00%)
occurrences (all)	12	6	0
PAIN IN EXTREMITY			
subjects affected / exposed	11 / 167 (6.59%)	6 / 83 (7.23%)	0 / 15 (0.00%)
occurrences (all)	13	9	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	9 / 167 (5.39%)	4 / 83 (4.82%)	2 / 15 (13.33%)
occurrences (all)	13	5	2
NASOPHARYNGITIS			
subjects affected / exposed	13 / 167 (7.78%)	0 / 83 (0.00%)	0 / 15 (0.00%)
occurrences (all)	22	0	0
PNEUMONIA			
subjects affected / exposed	10 / 167 (5.99%)	2 / 83 (2.41%)	1 / 15 (6.67%)
occurrences (all)	10	2	1

UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	10 / 167 (5.99%)	5 / 83 (6.02%)	1 / 15 (6.67%)
occurrences (all)	11	5	2
URINARY TRACT INFECTION			
subjects affected / exposed	12 / 167 (7.19%)	2 / 83 (2.41%)	0 / 15 (0.00%)
occurrences (all)	15	3	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	20 / 167 (11.98%)	7 / 83 (8.43%)	0 / 15 (0.00%)
occurrences (all)	22	7	0
HYPERURICAEMIA			
subjects affected / exposed	7 / 167 (4.19%)	5 / 83 (6.02%)	0 / 15 (0.00%)
occurrences (all)	8	5	0
HYPERGLYCAEMIA			
subjects affected / exposed	3 / 167 (1.80%)	2 / 83 (2.41%)	1 / 15 (6.67%)
occurrences (all)	3	2	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 September 2010	Significant changes included: - The concept of Clinical Benefit was introduced to enable subjects with a 50% decrease in RBC-transfusion frequency to continue receiving study-medication even if RBC-transfusion independence was not achieved. This applied to subjects achieving RBC-transfusion independence if RBC transfusion independence ended due to an unrelated event. - Blood sampling was done in a subset of subjects to explore the pharmacokinetics of pomalidomide in this population. - RBC transfusions used to determine eligibility required a pre RBC-transfusion hemoglobin level ≤ 90 g/L. In subjects where a hemoglobin level < 90 g/L is dangerous, entry into the study with pre RBC-transfusion hemoglobin level > 90 g/L was allowed as long as a 6-month RBC-transfusion history was available to confirm eligibility. - If a subject could not be randomized within 28 days of signing Informed Consent due to logistical reasons, the medical monitor could approve randomization as soon as possible thereafter to eliminate the need to repeat screening procedures when not otherwise necessary. - A hemoglobin level measured > 72 hours before a RBC-transfusion could be used to determine eligibility if there were no intervening RBC-transfusions. - The medical monitor could approve the inclusion of a subject based on a bone marrow biopsy done > 6 months pre-screening. - In North America and the European Union a unit of RBC is approximately 240 mL and the average weight of a 50-year-old male is 90 kg. The protocol definition of ≥ 2 U RBC/28 days is equivalent to 5 mL/kg/28 days. In Japan and China a unit of RBCs is about 125 mL and the average weight of a 50-year-old male is 60 kg. The equivalent RBC-transfusion dose is 2.5 U/28 days. - Subjects receiving anti-coagulants other than low-dose aspirin were not excluded - Criteria for determination of blastic transformation based on blasts in blood was clarified. - 5-year follow-up for collection of new cancers was added

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported