Clinical trial results:
Open-label, multi-center, single-arm study for the safety and efficacy of pomalidomide (CC-4047) monotherapy for subjects with refractory or relapsed and refractory multiple myeloma: a companion study for clinical trial CC-4047-MM-003

Summary

EudraCT number	2010-023343-16
Trial protocol	BE GB DE ES GR IT CZ NL SE DK
Global end of trial date	31 July 2014

Results information

Result version number	v1 (current)
This version publication date	14 July 2016
First version publication date	16 August 2015

Trial information

Trial identification

Sponsor protocol code	CC-4047-MM-003/C

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01324947
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Celgene Corporation
Sponsor organisation address	86 Morris Avenue, Summit, United States, 07901
Public contact	ClinicalTrialDisclosure, Celgene Corporation, 888 260-1599,
Scientific contact	Lars Sternas, Celgene Corporation, ClinicalTrialDisclosure@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	31 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2014
Global end of trial reached?	Yes
Global end of trial date	31 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of pomalidomide (CC-4047) monotherapy in subjects with refractory or relapsed and refractory multiple myeloma who discontinued from Treatment Arm B (dexamethasone alone) of Study CC-4047-MM-003 due to the development of documented disease progression during treatment. Upon discontinuing this study, participants will be followed in the long term follow-up phase of CC-4047-MM-003 study.

Protection of trial subjects:

Protection of trial subjects through Ethics Committees and Institutional Review Boards
Protection patient confidentiality

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 May 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Greece: 5
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	Russian Federation: 3
Worldwide total number of subjects	74
EEA total number of subjects	54

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)	33
From 65 to 84 years	40
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

CC-4047-MM003C is a companion study for the trial CC-4047-MM-003. CC-4047-MM-003C enrolled participants who had discontinued treatment with dexamethasone alone (Treatment Arm B) in the CC-4047-MM-003 trial due to disease progression; those who had discontinued treatment with pomalidomide plus dexamethasone (Arm A) were not eligible to participate.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Pomalidomide

Arm description:

Oral pomalidomide 4 mg capsule on Days 1-21 of each 28-day cycle until progressive disease (PD) or unacceptable toxicity

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

Dosage and administration details:

Oral Pomalidomide 4mg capsules by mouth (PO) on Days 1 through 21 of each 28 day cycle.

Number of subjects in period 1	Pomalidomide
Started	74
Safety Population	73
Efficacy Evaluable Population (EEP)	64
Completed	0
Not completed	74
Consent withdrawn by subject	3
'1 discontinued before starting drug '	1
Adverse event, non-fatal	7
Death	10
Progressive Disease	50
Unspecified	3

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	74	74	
Age categorical Units: Subjects			
Adults (18-64 years)	33	33	
From 65-84 years	40	40	
85 years and over	1	1	
Age continuous Units: years			
arithmetic mean	64.9		
standard deviation	± 9.25	-	
Gender categorical Units: Subjects			
Female	32	32	
Male	42	42	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Black or African American	1	1	
Native Hawaiian or Other Pacific Islanders	0	0	
White	52	52	
Other -Unspecified	2	2	
Not Collected	19	19	
Ethnicity Units: Subjects			
Hispanic or Latino	6	6	
Not Hispanic or Latino	49	49	
Not Collected	19	19	
Participants with Prior Anti-Myeloma (MM) Therapies Units: Subjects			
Participants with Prior Anti-Myeloma (MM) Therapie	74	74	
Durie-Salmon Multiple Myeloma Stage before Study Entry			

Stages are:
Stage I: Hemoglobulin > 10 g/dL; serum calcium normal on roentgenogram; normal bone structure or solitary bone plasmacytoma only; Low M-component production rates (IgG value < 5 g/dL, IgA value < 3 g/dL; Bence Jones protein < 4 g/24h)
Stage II: Overall data as minimally abnormal for stage I, and no single value as abnormal as defined for stage III
Stage III: 1 or more of below:
Hemoglobin < 8.5 g/dL; serum calcium > 12 mg/dL; Advanced lytic bone lesions (scale 3); High-M-component production rates (IgG value > 7 g/dL, IgA value > 5 g/dL; Bence Jones protein > 12 g/24h)

Units: Subjects			
Stage I	8	8	
Stage II	15	15	
Stage III	50	50	
Missing	1	1	
Time From First Pathologic Diagnosis			
Units: Years			
arithmetic mean	7.6		
standard deviation	± 3.72	-	

End points

End points reporting groups

Reporting group title	Pomalidomide

Reporting group description:

Oral pomalidomide 4 mg capsule on Days 1-21 of each 28-day cycle until progressive disease (PD) or unacceptable toxicity

Primary: Percentage of Participants With an Objective Response According to International Myeloma Working Group (IMWG) Uniform Response Criteria Based on Investigator Assessment

End point title	Percentage of Participants With an Objective Response According to International Myeloma Working Group (IMWG) Uniform Response Criteria Based on Investigator Assessment[1]

End point description:

Objective response defined as a best overall response of stringent complete response (SCR), complete response (CR), very good partial response (VGPR) or partial response (PR) based on Investigator Assessment.
SCR: CR and normal free light chain (FLC) ratio and no clonal cells in bone marrow; CR: Negative serum and urine on immunofixation, disappearance of any soft tissue plasmacytomas and ≤5% plasma cells in bone marrow; VGPR: Serum and urine M-protein detectable by immunofixation but not on electrophoresis or ≥90% reduction in serum M-protein and urine M-protein level <100 mg/24 hours; PR: ≥50% reduction of serum M-Protein and reduction in urinary M-protein by ≥90% or to <200 mg/24 hours. A ≥50% decrease in the difference between involved and uninvolved FLC levels in place of the M-protein criteria or a ≥50% reduction in plasma cells in place of M-protein if baseline was ≥30%. If present at baseline a ≥50% reduction in size of soft tissue plasmacytomas

End point type	Primary

End point timeframe:

From randomization through the study follow-up phase; up to the data cut-off of 31 July 2014; Maximum time on follow-up was 141.1 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: The study is a single-armed trial, no statistical analysis was done due to lack of a comparator.

End point values	Pomalidomide			
Subject group type	Reporting group			
Number of subjects analysed	74[2]			
Units: Percentage of Participants				
number (not applicable)	23			

Notes:

[2] - Intent to Treat Population was defined as all enrolled participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Objective Response According to European Group for Blood and Marrow Transplantation (EBMT) Criteria Based on Investigator Assessment

End point title	Percentage of Participants With Objective Response According to European Group for Blood and Marrow Transplantation

	(EBMT) Criteria Based on Investigator Assessment

End point description:

Objective response defined as a best overall response of complete response (CR) or partial response (PR) based on the CR and requires all of the following:
- Absence of original monoclonal paraprotein in serum and urine by immunofixation maintained at least 42 days.
- <5% plasma cell in bone marrow aspirate and on bone marrow biopsy, if performed.
- No increase in size or number of lytic bone lesions.
- Disappearance of soft tissue plasmacytomas.

PR requires all of the following:
- ≥50% reduction in level of serum monoclonal paraprotein, maintained at least 42 days.
- Reduction in 24-hour urinary light chain extraction by ≥90% or to <200 mg, maintained at least 42 days.
- For patients with non-secretory myeloma, ≥50% reduction in plasma cells in bone marrow aspirate and on biopsy, if performed, for at least 42 days.

End point type	Secondary

End point timeframe:

From randomization through the study follow-up phase; up to the data cut-off of 31 July 2014; Maximum time on follow-up was 141.1 weeks.

End point values	Pomalidomide			
Subject group type	Reporting group			
Number of subjects analysed	74[3]			
Units: Percentage of participants				
number (not applicable)	20.3			

Notes:

[3] - Intent to treat population includes all participants enrolled.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events (AEs) and Type of Adverse Events

End point title	Number of Participants With Adverse Events (AEs) and Type of Adverse Events

End point description:

An AE is any noxious, unintended, or untoward medical occurrence that may appear or worsen in a participant during the course of a study. A serious AE is any AE occurring at any dose that:
- Results in death;
- Is life-threatening;
- Requires or prolongs existing inpatient hospitalization;
- Results in persistent or significant disability/incapacity;
- Is a congenital anomaly/birth defect;
- Constitutes an important medical event.

The Investigator assessed the relationship of each AE to study drug and graded the severity according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE, Version 4.0): Grade 1 = Mild (no limitation in activity or intervention required); Grade 2 = Moderate (some limitation in activity; no/minimal medical intervention required); Grade 3 = Severe (marked limitation in activity); medical intervention needed, hospitalization possible); Grade 4 = Life-threatening; Grade 5 = Death

End point type	Secondary

End point timeframe:

From first dose of study drug through to 30 days after the last dose, until the data cut-off date of 31 July 2014. Maximum time on treatment was 94.1 weeks.

End point values	Pomalidomide			
Subject group type	Reporting group			
Number of subjects analysed	73[4]			
Units: Number of Participants				
number (not applicable)				
Any adverse event	73			
Grade 3-4 adverse event	64			
AE related to pomalidomide	51			
Grade 3-4 AE related to pomalidomide	33			
Grade 5 AE	19			
≥1 Serious AE (SAE)	52			
≥1 SAE related to pomalidomide	15			
≥1 SAE leading to stopping pomalidomide	6			
≥AE leading to discontinuation of pomalidomide	8			
≥1 study drug related AE leading to stopping POM	1			
≥1 AE leading to reduction of pomalidomide	11			
≥1 study drug related AE leading to reducing POM	9			
≥1 AE leading to interruption of pomalidomide	41			
≥ 1 study drug related interruption of POM	25			

Notes:

[4] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan Meier Estimates for Progression Free Survival (PFS) by Investigator Based on IMWG

End point title	Kaplan Meier Estimates for Progression Free Survival (PFS) by Investigator Based on IMWG

End point description:

Progression-free survival was calculated as the time from randomization to disease progression as determined by the Investigator based on the International Myeloma Working Group Uniform Response criteria (IMWG), or death on study, whichever occurred earlier.

Progressive disease requires 1 of the following:
- Increase of ≥ 25% from nadir in:
  - Serum M-component (absolute increase ≥ 0.5 g/dl)
  - Urine M-component (absolute increase ≥ 200 mg/24 hours)
  - In patients without measurable serum and urine M-protein levels the difference between involved and uninvolved free light chain (FLC) levels (absolute increase > 100 mg/dl)
  - Bone marrow plasma cell percentage (absolute % ≥ 10%)
- Development of new or increase in the size of existing bone lesions or soft tissue plasmacytomas

Intent to Treat included all participants enrolled

End point type	Secondary

End point timeframe:

From randomization through the follow-up phase; Maximum duration of follow-up for PFS was 90.3 weeks.

End point values	Pomalidomide			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: Weeks				
median (confidence interval 95%)	16 (11.6 to 19.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate for Time to Progression (TTP) Based on Investigator Assessment Using IMWG Criteria

End point title	Kaplan-Meier Estimate for Time to Progression (TTP) Based on Investigator Assessment Using IMWG Criteria

End point description:

Time to progression (TTP) was calculated as the time from randomization to the first documented progression confirmed by the investigator and based on the International Myeloma Working Group Uniform Response criteria (IMWG).
Progressive disease requires 1 of the following:
o Increase of ≥ 25% from nadir in:
o Serum M-component (absolute increase ≥ 0.5 g/dl)
o Urine M-component (absolute increase ≥ 200 mg/24 hours)
o In patients without measurable serum and urine M-protein levels the difference between involved and uninvolved free light chain (FLC) levels (absolute increase > 100 mg/dl)
o Bone marrow plasma cell percentage (absolute % ≥ 10%)
o Development of new or increase in the size of existing bone lesions or soft tissue plasmacytomas.
o Development of hypercalcemia (corrected serum calcium > 11.5 mg/dl) attributed solely to plasma cell proliferative disease.

End point type	Secondary

End point timeframe:

From randomization through the follow-up phase; up to the data-cut off of 31 July 2014; Maximum time to progression follow-up was 90.3 weeks.

End point values	Pomalidomide			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: weeks				
median (confidence interval 95%)	19 (14.1 to 27.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Duration of Response Based on Investigator Assessment Using IMWG Criteria

End point title	Kaplan-Meier Estimate of Duration of Response Based on Investigator Assessment Using IMWG Criteria

End point description:

Duration of Response (calculated for responders only) is defined as the time from the initial documented response (partial response or better) to confirmed disease progression by the investigator based on IMWG criteria.

End point type	Secondary

End point timeframe:

From randomization through the study follow-up phase; up to the data cut-off of 31 July 2014; Maximum duration of response follow-up was 90.3 weeks.

End point values	Pomalidomide			
Subject group type	Reporting group			
Number of subjects analysed	17[5]			
Units: weeks				
median (confidence interval 95%)	28.3 (8.1 to 53.4)			

Notes:

[5] - Includes those who had a partial response or better

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate for Overall Survival

End point title	Kaplan-Meier Estimate for Overall Survival

End point description:

Overall survival was calculated as the time from randomization to death from any cause. Overall survival was censored at the last date that the participant was known to be alive for participants who were alive at the time of analysis and for participants who were lost to follow-up before death was documented.

End point type	Secondary

End point timeframe:

From randomization through the follow-up phase; Maximum time on follow-up was 141.1 weeks.

End point values	Pomalidomide			
Subject group type	Reporting group			
Number of subjects analysed	74[6]			
Units: weeks				
median (confidence interval 95%)	33.6 (26.4 to 66.3)			

Notes:

[6] - Intent to Treat population included all participants enrolled into the study

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response Based on IMWG and Assessed by the Investigator

End point title	Time to Response Based on IMWG and Assessed by the Investigator

End point description:

Time to Response was calculated only for participants with a PR or better based on IMWG and assessed by the investigator.

End point type	Secondary

End point timeframe:

Randomization through the follow-up phase; up to the data-cut off: 31 July 2014; Maximum time to response was 23.1 weeks

End point values	Pomalidomide			
Subject group type	Reporting group			
Number of subjects analysed	17[7]			
Units: weeks				
median (confidence interval 95%)	8.3 (4.1 to 23.1)			

Notes:

[7] - Includes those who had at least a partial response or better; Intent to Treat

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug through to 30 days after the last dose, until the data cut-off date of 31 July 2014. Maximum time on treatment was 94.1 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14

Reporting groups

Reporting group title	Pomalidomide

Reporting group description:

Oral pomalidomide 4 mg on Days 1-21 of each 28-day cycle until progressive disease (PD) or unacceptable toxicity

Serious adverse events	Pomalidomide		
Total subjects affected by serious adverse events			
subjects affected / exposed	52 / 73 (71.23%)		
number of deaths (all causes)	19		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign Neoplasm Of Bladder			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple Myeloma			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Prostate Cancer			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			

subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
General Physical Health Deterioration			
subjects affected / exposed	8 / 73 (10.96%)		
occurrences causally related to treatment / all	0 / 11		
deaths causally related to treatment / all	0 / 7		
Pyrexia			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung Disorder			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pleural Effusion			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pulmonary Embolism				
subjects affected / exposed	4 / 73 (5.48%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	1 / 1			
Pulmonary Oedema				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional State				
subjects affected / exposed	2 / 73 (2.74%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Injury, poisoning and procedural complications				
Hip Fracture				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac disorders				
Atrial Fibrillation				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac Failure				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac Failure Congestive				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sinus Tachycardia				

subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Spinal Cord Compression			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 73 (13.70%)		
occurrences causally related to treatment / all	3 / 10		
deaths causally related to treatment / all	0 / 0		
Febrile Neutropenia			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		

Dysphagia				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal Haemorrhage				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal infarction				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Vomiting				
subjects affected / exposed	1 / 73 (1.37%)			
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	3 / 73 (4.11%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Renal Failure Acute				
subjects affected / exposed	4 / 73 (5.48%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back Pain				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Osteolysis			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium Difficile Colitis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enterocolitis Infectious			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			

subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Meningitis Cryptococcal			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenic Sepsis			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Otitis Media			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	11 / 73 (15.07%)		
occurrences causally related to treatment / all	3 / 12		
deaths causally related to treatment / all	0 / 1		
Pneumonia Streptococcal			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory Tract Infection			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			

subjects affected / exposed	2 / 73 (2.74%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Septic Shock				
subjects affected / exposed	2 / 73 (2.74%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 2			
Subcutaneous Abscess				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Cachexia				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Decreased Appetite				
subjects affected / exposed	2 / 73 (2.74%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	4 / 73 (5.48%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemic Hyperosmolar Nonketotic Syndrome				

subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hyperproteinaemia			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hypomagnesaemia			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pomalidomide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 73 (93.15%)		
Investigations			
Blood Creatinine Increased			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	5		
Weight Decreased			
subjects affected / exposed	6 / 73 (8.22%)		
occurrences (all)	6		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 73 (9.59%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	36 / 73 (49.32%)		
occurrences (all)	104		
Leukopenia			
subjects affected / exposed	9 / 73 (12.33%)		
occurrences (all)	18		
Thrombocytopenia			
subjects affected / exposed	16 / 73 (21.92%)		
occurrences (all)	51		
Neutropenia			
subjects affected / exposed	35 / 73 (47.95%)		
occurrences (all)	106		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	7 / 73 (9.59%)		
occurrences (all)	11		
Fatigue			
subjects affected / exposed	16 / 73 (21.92%)		
occurrences (all)	21		
Oedema peripheral			
subjects affected / exposed	6 / 73 (8.22%)		
occurrences (all)	8		
Pyrexia			
subjects affected / exposed	13 / 73 (17.81%)		
occurrences (all)	17		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	16 / 73 (21.92%)		
occurrences (all)	21		
Diarrhoea			
subjects affected / exposed	11 / 73 (15.07%)		
occurrences (all)	20		
Nausea			
subjects affected / exposed	9 / 73 (12.33%)		
occurrences (all)	11		
Vomiting			

subjects affected / exposed occurrences (all)	5 / 73 (6.85%) 6		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	 9 / 73 (12.33%) 11 15 / 73 (20.55%) 15		
Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all)	 6 / 73 (8.22%) 6		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 4 / 73 (5.48%) 4		
Renal and urinary disorders Renal Failure subjects affected / exposed occurrences (all)	 4 / 73 (5.48%) 4		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back Pain subjects affected / exposed occurrences (all) Bone Pain subjects affected / exposed occurrences (all) Muscle Spasms subjects affected / exposed occurrences (all)	 5 / 73 (6.85%) 5 13 / 73 (17.81%) 18 12 / 73 (16.44%) 12 5 / 73 (6.85%) 6		
Infections and infestations			

Bronchitis subjects affected / exposed occurrences (all)	6 / 73 (8.22%) 8		
Gastroenteritis subjects affected / exposed occurrences (all)	5 / 73 (6.85%) 5		
Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 73 (5.48%) 4		
Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	5 / 73 (6.85%) 10		
Urinary Tract Infection subjects affected / exposed occurrences (all)	5 / 73 (6.85%) 7		
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	7 / 73 (9.59%) 8		
Hypercalcaemia subjects affected / exposed occurrences (all)	11 / 73 (15.07%) 14		
Hypokalaemia subjects affected / exposed occurrences (all)	13 / 73 (17.81%) 15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 June 2011	The global amendment consisted of the following: 1. Required that Secondary Primary Malignancy (SPMs) be treated as SAEs and reported throughout the study duration, including long-term follow-up. 2. Lowered the eligibility requirement for measurable level of serum M-protein from 1.0 g/dL to 0.5 g/dL, since this patient population was heavily pre-treated. 3. Updated exclusion criterion for serum total bilirubin to allow for higher level at study entry for subjects with hereditary enzymatic disorders such as Gilbert syndrome, glucose-6-phosphate dehydrogenase deficiency, etc., who had a mild increase in total bilirubin primarily due to increase of indirect bilirubin. 4. For exclusion criterion related to hypersensitivity to thalidomide or lenalidomide, specified that ≥ Grade 3 rash during prior thalidomide or lenalidomide treatment was considered hypersensitivity. 5. Eligibility for subjects with prior allogeneic bone marrow or allogeneic peripheral blood stem cell transplant was revised so that subjects could enter the study if at least 12 months had elapsed since their transplant or if they were not receiving concomitant immunosuppressive medications related to the transplant at the time of study entry. 6. Clarified pomalidomide dose modification instructions for neutropenia and thrombocytopenia.
04 November 2011	The global amendment consisted of the following changes: 1. Required that subjects with a prior history of malignancies, other than MM, be free of the disease for ≥ 5 years rather than ≥ 3 years. 2. Updated inclusion criterion to allow subjects to become eligible for the companion study after starting the second cycle of High-Dose dexamethasone (HD-dex) in the core Study CC-4047-MM-003, rather than completing the second cycle of HD-dex. 3. Updated screening requirements to reflect that, in addition to the use of growth factors, the use of platelet and/or RBC transfusions were allowed throughout the study, including the screening period, at the discretion of the investigator. However, subjects who failed screening as a result of neutropenia, thrombocytopenia, or anemia were not permitted to use growth factors, platelet or RBC transfusions to become eligible. 4. Updated to reflect that subjects who had a creatinine clearance less than 45 mL/min by the Cockcroft-Gault method at screening and/or Cycle 1 Day 1, an evaluation of creatinine clearance would be performed using the 24-hour urine sample from the urine M-protein collection. The Cockcroft-Gault method was used for the remainder of the study. 5. Subjects were no longer required to have 14-day wash-out of steroids for entry into the study. 6. Updated exclusion criterion # 9 to reflect that subjects who had not discontinued immunosuppressive treatment for at least 4 weeks prior to initiation of study treatment (rather than 12 months) and were currently dependent on such treatment would not be eligible for the study. 7. Updated the dose modification instructions for hematologic toxicities based on CTCAE version 4.0 for febrile neutropenia: ANC < 1,000/µL with a single temperature of > 38.3°C or a sustained temperature of ≥ 38°C for more than 1 hour.
12 December 2012	The global amendment consisted of the following: 1. Clarified that Low-dose dexamethasone (LD-dex) was a permitted concomitant medication. 2. Revised the language explaining abstinence as a method of contraception to ensure consistency across all Immunomodulatory (IMiD) studies.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported