# 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<br>Units: Subjects | | | |
| Adults (18-64 years) | 33 | 33 | |
| From 65-84 years | 40 | 40 | |
| 85 years and over | 1 | 1 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 64.9 | | |
| standard deviation | ± 9.25 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 32 | 32 | |
| Male | 42 | 42 | |
| Race<br>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<br>Units: Subjects | | | |
| Hispanic or Latino | 6 | 6 | |
| Not Hispanic or Latino | 49 | 49 | |
| Not Collected | 19 | 19 | |
| Participants with Prior Anti-Myeloma (MM) Therapies<br>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<br>occurrences (all) | 5 / 73 (6.85%)<br>6 | | |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all) | <br><br>9 / 73 (12.33%)<br>11<br><br>15 / 73 (20.55%)<br>15 | | |
| Skin and subcutaneous tissue disorders<br>Hyperhidrosis<br>subjects affected / exposed<br>occurrences (all) | <br><br>6 / 73 (8.22%)<br>6 | | |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all) | <br><br>4 / 73 (5.48%)<br>4 | | |
| Renal and urinary disorders<br>Renal Failure<br>subjects affected / exposed<br>occurrences (all) | <br><br>4 / 73 (5.48%)<br>4 | | |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all)<br>Back Pain<br>subjects affected / exposed<br>occurrences (all)<br>Bone Pain<br>subjects affected / exposed<br>occurrences (all)<br>Muscle Spasms<br>subjects affected / exposed<br>occurrences (all) | <br><br>5 / 73 (6.85%)<br>5<br><br>13 / 73 (17.81%)<br>18<br><br>12 / 73 (16.44%)<br>12<br><br>5 / 73 (6.85%)<br>6 | | |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Bronchitis<br>subjects affected / exposed<br>occurrences (all) | 6 / 73 (8.22%)<br>8 | | |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all) | 5 / 73 (6.85%)<br>5 | | |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 4 / 73 (5.48%)<br>4 | | |
| Upper Respiratory Tract Infection<br>subjects affected / exposed<br>occurrences (all) | 5 / 73 (6.85%)<br>10 | | |
| Urinary Tract Infection<br>subjects affected / exposed<br>occurrences (all) | 5 / 73 (6.85%)<br>7 | | |
| Metabolism and nutrition disorders<br>Decreased Appetite<br>subjects affected / exposed<br>occurrences (all) | 7 / 73 (9.59%)<br>8 | | |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all) | 11 / 73 (15.07%)<br>14 | | |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all) | 13 / 73 (17.81%)<br>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:<br>1. Required that Secondary Primary Malignancy (SPMs) be treated as SAEs and reported throughout the study duration, including long-term follow-up.<br>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.<br>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.<br>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.<br>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.<br>6. Clarified pomalidomide dose modification instructions for neutropenia and thrombocytopenia. |
| 04 November 2011 | The global amendment consisted of the following changes:<br>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.<br>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.<br>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.<br>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.<br>5. Subjects were no longer required to have 14-day wash-out of steroids for entry into the study.<br>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.<br>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:<br>1. Clarified that Low-dose dexamethasone (LD-dex) was a permitted concomitant medication.<br>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