

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 TRIALCC-4047-MM-003.

Published: 19-05-2011

Last updated: 28-04-2024

The primary objective is: To evaluate the efficacy of pomalidomide (CC-4047) monotherapy in subjects with refractory or relapsed and refractory multiple myeloma who discontinued treatment after being treated with dexamethasone alone (Treatment Arm B)...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skeletal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON39077

Source

ToetsingOnline

Brief title

CC-4047-MM-003/C

Condition

- Skeletal neoplasms malignant and unspecified

Synonym

multiple myeloma, type of bone marrow cancer

Research involving

Human

Sponsors and support

Primary sponsor: Celgene Corporation

Source(s) of monetary or material Support: Sponsor

Intervention

Keyword: multiple myeloma, pomalidomide

Outcome measures

Primary outcome

The primary endpoint is overall response rate (ORR) using the new International Myeloma

Working Group Uniform (IMWG) response criteria. An analysis comparing the results of

response assessments judged by the EMBT criteria (Blade, 1998) to those of the IMWG criteria

will also be performed.

Secondary outcome

- Safety (type, frequency, and severity of adverse events [AEs], and relationship of AEs to study drug)

- Progression-free survival (PFS)

- Time to progression (TTP)
- Duration of response
- Overall survival (OS)

Study description

Background summary

The phase 1 segment of the Celgene sponsored Study CC-4047-MM-002 determined the maximum tolerated dose (MTD) of pomalidomide in this subject population to be 4 mg/day. In

Study CC-4047-MM-002, responses were seen in both the 2 and 4-mg dose levels; however, the best response rate and duration of response was associated with a dose of 4 mg/day of pomalidomide (the starting dose in the present trial) in a cyclic 21 out of 28-day dosing schedule.

This regimen will allow a one-week rest period per every 28-day cycle for bone marrow

recovery to minimize the occurrence of neutropenia, which were the DLTs during the phase 1 segment of the study. The Phase 2 segment of the study CC-4047-

MM-002 was started in November 2009 and as of September 22, 2010 enrolment has been completed and 221 subjects have been enrolled.

The results of a number of investigator-initiated studies conducted thus far indicate that

pomalidomide produces responses in subjects who are refractory to lenalidomide, another

IMiDs® compound, aligning with the non-clinical results observed in lenalidomide-resistant cells

(Adams, 2009). The phase 2 study using pomalidomide plus low-dose dexamethasone for

relapsed multiple myeloma (Lacy, 2009; 2010) showed a response rate of 40% in lenalidomide-refractory

patients. These results imply a non-cross resistance for pomalidomide and suggesting

a special role for this drug in the treatment of refractor/relapsed patients.

Pomalidomide, to date,

has an acceptable safety profile, and the most common hematological toxicity experienced by

subjects is neutropenia (non-febrile), which can be managed by dose reductions or interruptions and growth factors.

The most common non-hematological toxicities are fatigue and pneumonia.

Based on these published data, pomalidomide would be expected to provide clinical benefit to

such subjects with high unmet medical need who have very limited available treatment options.

This companion study will provide more information about the safety and efficacy of singleagent

pomalidomide in patients who are refractory or relapse after multiple lines of therapy

Study objective

The primary objective is:

To evaluate the efficacy of pomalidomide (CC-4047) monotherapy in subjects with refractory or

relapsed and refractory multiple myeloma who discontinued treatment after being treated with

dexamethasone alone (Treatment Arm B) in Study CC-4047-MM-003 due to the development of

documented disease progression during treatment.

The secondary objective is:

To evaluate the safety of pomalidomide monotherapy in subjects with refractory or relapsed and

refractory multiple myeloma who discontinued treatment after being treated with dexamethasone

alone (Treatment Arm B) in Study CC-4047-MM-003 due to the development of documented

disease progression during treatment.

Study design

Study CC-4047-MM003/C is the companion study for clinical trial CC-4047-MM-003.

This is a

multi-center, open-label, single-arm study to evaluate the safety and efficacy of pomalidomide

monotherapy in subjects with refractory or relapsed and refractory multiple myeloma. This

companion study will enroll subjects who have discontinued study treatment with dexamethasone alone (Treatment Arm B) in the CC-4047-MM-003 trial due to disease progression. Subjects who have discontinued study treatment with pomalidomide plus

dexamethasone (Treatment Arm A) will not be eligible to participate in the

companion study.

The key inclusion criteria in the CC-4047-MM-003/C trial limits the enrollment to all evaluable subjects in the CC-4047-MM-003 study who discontinue therapy after at least starting the second cycle of dexamethasone alone (Treatment Arm B) due to development of documented disease progression according to the IMWG criteria and as decided by an IRAC. Subjects who discontinue therapy with dexamethasone alone (Treatment Arm B) due to toxicity or intolerance to dexamethasone and not due to development of confirmed progressive disease will not be eligible to enroll in the companion trial.

It is estimated that 30% to 60% of subjects in the control arm of Study CC-4047-MM-003 (dexamethasone alone; n = 142) could be enrolled in the companion study. Thus the estimated number of subjects in Study CC-4047-MM-003/C will be in the range of 42-85. Enrollment of subjects will be opened to all investigator sites that participated in Study CC-4047-MM-003 (EU, Switzerland, Russia, Australia and Canada.

Figure 1 summarizes the flow and the transition between both CC-4047-MM-003 and CC-4047-

MM-003/C. For subjects with treatment discontinuation visit assessments for Study CC-4047-MM-003 performed within ≤ 28 days of screening for Study CC-4047-MM-003/C, any overlapping assessments do not have to be repeated for screening in this study if approved by the Study Team. If the assessments were done > 28 days from screening, these assessments need to be repeated at the screening phase.

Subjects will not be eligible to enroll in the companion study if 120 days or more have passed since their discontinuation from CC-4047-MM-003 study. No other anti-myeloma therapies are allowed from the time of disease progression on CC-4047-MM-003 to the time of treatment initiation in the companion study.

The oral pomalidomide starting dose is 4 mg daily on Days 1-21 every 28 days.

Dosing

interruptions and reductions are permitted throughout the study. All subjects participating in the trial will continue treatment until they stop taking the study medication because of disease progression or another reason. For all subjects who enroll into this study, study visits and serial measurements of safety and

efficacy will be performed as outlined in Table 1 Table of Events.

Intervention

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Study burden and risks

The patient needs to visit the hospital as described in E2. The following study procedures will be done as described in the schedule on page 31 of the protocol:

- bone marrow biopsy or aspirate
- ECG
- Physical examination
- Pregnancy test
- Blood drawing
- Completion of questionnaires

Risks of the study are described in the appendix of the informed consent.

Contacts

Public

Celgene Corporation

Morris Avenue 86
Summit NJ 07901
US

Scientific

Celgene Corporation

Morris Avenue 86
Summit NJ 07901
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

1. Subjects with refractory or relapsed and refractory multiple myeloma who were enrolled in Study CC-4047-MM-003 and discontinued study therapy with dexamethasone alone (Treatment Arm B) after at least starting the second cycle of dexamethasone treatment and due to development of documented disease progression according to the IMWG criteria and as decided by an IRAC.
2. Must be ≥ 18 years at the time of signing the informed consent form.
3. The subject must understand and voluntarily sign an informed consent document prior to any study related assessments/procedures being conducted. The only exception is if a skeletal survey was performed within 90 days prior to the start of Cycle 1, then a new survey will not be required.
4. Must be able to adhere to the study visit schedule and other protocol requirements.
5. Subjects must have documented diagnosis of multiple myeloma and have measurable disease (serum M-protein ≥ 0.5 g/dL or urine M-protein ≥ 200 mg/24 hours).
6. Eastern Cooperative Oncology Group (ECOG) performance status score of 0, 1, or 2.
7. Females of childbearing potential (FCBP*) must agree to utilize two reliable forms of contraception simultaneously or practice complete abstinence from heterosexual contact for at least 28 days before starting study drug, while participating in the study (including dose interruptions), and for at least 28 days after study treatment discontinuation and must agree to regular pregnancy testing during this timeframe.
8. Females must agree to abstain from breastfeeding during study participation and 28 days after study discontinuation.
9. Males must agree to use a latex condom during any sexual contact with FCBP while participating in the study and for 28 days following discontinuation from this study, even if he has undergone a successful vasectomy.
10. Males must also agree to refrain from donating semen or sperm while on pomalidomide and for 28 days after discontinuation from this study treatment.
11. All subjects must agree to refrain from donating blood while on study drug and for 28 days after discontinuation from this study treatment.
12. All subjects must agree not to share study medication.

Exclusion criteria

1. Subjects with multiple myeloma who were not treated as a part of Study CC-4047-MM-003 (Arm B).

2. Subjects who received any anti-myeloma or anti-cancer therapies within the last 14 days of wash-out period before initiation of study treatment.
3. Subjects who discontinued CC-4047-MM-003 study ≥ 120 days.
4. Subjects who initiate another anti-myeloma therapy from the time of disease progression on study CC-4047-MM-003 to the time of treatment initiation in the companion study.
5. Any of the following laboratory abnormalities:
 - Absolute neutrophil count (ANC) $< 1,000/\mu\text{L}$.
 - Platelet count $< 75,000/\mu\text{L}$ for subjects in whom $< 50\%$ of bone marrow nucleated cells are plasma cells; or a platelet count $< 30,000/\mu\text{L}$ for subjects in whom $\geq 50\%$ of bone marrow nucleated cells are plasma cells
 - Creatinine Clearance < 45 mL/min according to Cockcroft-Gault formula (If creatinine clearance calculated from the 24-hour urine sample is ≥ 45 ml/min, patient will qualify for the trial)
 - Corrected serum calcium > 14 mg/dL (> 3.5 mmol/L)
 - Hemoglobin < 8 g/dL (< 4.9 mmol/L; prior RBC transfusion or recombinant human erythropoietin use is permitted)
 - Serum SGOT/AST or SGPT/ALT > 3.0 x upper limit of normal (ULN)
 - Serum total bilirubin > 2.0 mg/dL ($34.2 \mu\text{mol/L}$); or > 3.0 x ULN for subjects with hereditary benign hyperbilirubineamia
6. Prior history of malignancies, other than MM, unless the subject has been free of the disease for ≥ 5 years. Exceptions include the following:
 - Basal or Squamous cell carcinoma of the skin
 - Carcinoma in situ of the cervix or breast
 - Incidental histologic finding of prostate cancer (TNM stage of T1a or T1b)
7. Hypersensitivity to thalidomide or lenalidomide. (This includes \geq Grade 3 rash during prior thalidomide or lenalidomide therapy).
8. Peripheral neuropathy \geq Grade 2.
9. Subjects who received an allogeneic bone marrow or allogeneic peripheral blood stem cell transplant less than 12 months prior to initiation of study treatment and who have not discontinued immunosuppressive treatment for at least 4 weeks prior to initiation of study treatment and are currently dependent on such treatment.
10. Subjects who are planning for or who are eligible for stem cell transplant.
11. Subjects with any one of the following:
 - Congestive heart failure (NY Heart Association Class III or IV)
 - Myocardial infarction within 12 months prior to starting study treatment
 - Unstable or poorly controlled angina pectoris, including Prinzmetal variant angina pectoris
12. Subjects who received any of the following within the last 14 days of initiation of study treatment:
 - Plasmapheresis
 - Major surgery (kyphoplasty is not considered major surgery)
 - Radiation therapy
13. Use of any investigational agents within 28 days or 5 half-lives (whichever is longer) of treatment.
14. Subjects with chronic conditions such as rheumatoid arthritis, multiple sclerosis and lupus, which likely need additional steroid or immunosuppressive treatments in addition to the study treatment.

15. Any condition including the presence of laboratory abnormalities, which places the subject at unacceptable risk if he/she were to participate in the study.
16. Incidence of gastrointestinal disease that may significantly alter the absorption of pomalidomide.
17. Subjects unable or unwilling to undergo antithrombotic prophylactic treatment.
18. Any serious medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from signing the informed consent form.
19. Pregnant or breastfeeding females.
20. Known HIV positivity or active infectious hepatitis A, B or C.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	15-11-2012
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	Pomalidomide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

9 - OPEN-LABEL, MULTI-CENTER, SINGLE-ARM STUDY FOR THE SAFETY AND EFFICACY OF POMAL ...
25-05-2025

Date:	19-05-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	
Date:	13-10-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	
Date:	12-01-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	
Date:	08-02-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	
Date:	02-11-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	
Date:	06-11-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	
Date:	01-03-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	
Date:	16-04-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

10 - OPEN-LABEL, MULTI-CENTER, SINGLE-ARM STUDY FOR THE SAFETY AND EFFICACY OF POMAL ...

25-05-2025

(Rotterdam)

Approved WMO

Date: 10-06-2013

Application type: Amendment

Review commission: METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date: 01-11-2013

Application type: Amendment

Review commission: METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date: 17-12-2013

Application type: Amendment

Review commission: METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date: 08-04-2014

Application type: Amendment

Review commission: METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date: 10-04-2014

Application type: Amendment

Review commission: METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2010-023343-16-NL
ClinicalTrials.gov	NCT01324947
CCMO	NL36039.078.11