# A MULTICENTER, SINGLE-ARM, OPEN-LABEL STUDY WITH POMALIDOMIDE IN COMBINATION WITH LOW DOSE DEXAMETHASONE IN SUBJECTS WITH REFRACTORY OR RELAPSED AND REFRACTORY MULTIPLE MYELOMA

Published: 23-08-2012
Last updated: 26-04-2024

Primary Objective: Evaluate the safety of the combination of pomalidomide (POM) and low dose dexamethasone (LD-DEX) in a large cohort of subjects with refractory MM or relapsed and refractory MM.Secondary Objectives:- Analyze the population...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Plasma cell neoplasms |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON47798

**Source**
ToetsingOnline

**Brief title**
0451/0094: Pomalidomide in combination with low dose Dexamethasone

### Condition

- Plasma cell neoplasms

**Synonym**
a type of bone marrow cancer, multiple myeloma

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Celgene Corporation
**Source(s) of monetary or material Support:** Celgene Corporation

## Intervention

**Keyword:** Dexamethasone, Multiple myeloma, Pomalidomide

## Outcome measures

### Primary outcome

Primary Endpoint:

Adverse events (AEs) assessment (type, frequency, seriousness, severity,

relationship to POM and/or DEX and outcomes), including second primary

malignancies (SPM).

### Secondary outcome

Secondary Endpoints:

- POM exposure

- POM population pharmacokinetics and exposure-response

- Overall response rate (ORR)

- Time to response

- Duration of response (DoR)

- Progression-free survival (PFS)

- Time to progression (TTP)

- Overall survival (OS)

Exploratory Endpoints:

- Evaluation of markers that might predict response to POM

- Evaluation of markers that might predict resistance to POM

- Analysis of pharmacodynamic markers for POM

# Study description

**Background summary**

Multiple myeloma (MM) is a rare and incurable progressive disease that accounts for 10% of all hematological malignancies. MM is characterized by marrow plasmacytomas (plasma B cell tumors) and overproduction of monoclonal immunoglobulins (IgG, IgA, IgD or IgE) or Bence-Jones protein, while the production of normal immunoglobulin is impaired. The accumulation of plasmacytes within the bone marrow and overproduction of immunoglobulins and osteoclastic factors lead to increased risk of pathologic fractures, renal insufficiency, hypercalcemia, anemia, infection and bleeding.
The prognosis of subjects with MM depends on a variety of factors including subject*s age and the stage of MM. MM remains incurable using conventional treatments, with a median overall survival duration of less than 5 years. The disease follows a relapsing course in the majority of subjects, regardless of treatment regimen or initial response to treatment.

The treatment options for subjects with primary resistant or relapsed MM are varied and include combination therapies with glucocorticoids and cytotoxic chemotherapeutic agents more recently combined with autologous stem cell transplantation (ASCT) to allow higher doses that would otherwise destroy the bone marrow. Drugs targeting both myeloma and its microenvironment have been approved for clinical use in newly diagnosed and relapsed and refractory MM subjects. Determination of an appropriate salvage regimen is dependent on a number of factors, including initial therapy regimen used and duration of response to that therapy. Treatment options for relapsed disease include ASCT, a previous chemotherapy regimen, or a study of a new chemotherapy regimen. Many of the same chemotherapy regimens that are used as initial therapy may be used as salvage therapy.
Pomalidomide is a novel immunomodulatory drug under development for the treatment of MM. Pomalidomide (POM) shares a number of the beneficial pharmacologic properties of thalidomide and lenalidomide. The results of studies conducted thus far indicate that POM has activity in subjects with relapsed and/or refractory MM. Confirmed response rates range between 30% and 60% at POM doses between 2 mg and 4 mg/day. Notably, POM produces responses in subjects who are refractory to lenalidomide or thalidomide, aligning with the non-clinical results observed in lenalidomideresistant cells. Response rates in

this range are consistently seen in subjects who are refractory to both lenalidomide and bortezomib. The most common hematological toxicity experienced by these subjects is neutropenia (non-febrile), which can be managed by dose reductions or interruptions. The most common non-hematological toxicities are fatigue and pneumonia.
Furthermore, results show that the combination of POM plus dexamethasone (DEX) may be useful in the treatment of MM that is refractory to lenalidomide plus DEX. However, the clinical experience with POM alone or in combination with DEX in relapsed and/or refractory MM is limited. Therefore, this study investigates pomalidomide in combination with low dose dexamethasone in subjects with refractory or relapsed and refractory multiple myeloma.

**Study objective**

Primary Objective:
Evaluate the safety of the combination of pomalidomide (POM) and low dose dexamethasone (LD-DEX) in a large cohort of subjects with refractory MM or relapsed and refractory MM.

Secondary Objectives:
- Analyze the population pharmacokinetics of POM and assess POM exposure response relationships in subjects with refractory MM or relapsed and refractory MM administered POM and LD-DEX.
- Evaluate efficacy of the combination of POM and LD-DEX in subjects with refractory MM or relapsed and refractory MM.

**Study design**

This is an international, multicenter, single-arm, open-label study of POM in combination with LD-DEX in subjects with refractory MM or relapsed and refractory MM. This study consists of the following consecutive phases: Screening, Treatment and Follow-up.

Screening Phase
Study subjects will sign an informed consent document (ICD) prior to undergoing any studyrelated procedure. Subjects may have the choice to participate in an optional biomarker study conducted at selected clinical sites. If a subject chooses to participate in the biomarker study,
he/she must give consent for the optional biomarker study. Subjects will undergo screening for protocol eligibility within 28 days prior to Cycle 1 Day 1, as outlined in Table 1, Table of Events.
Subjects who meet all eligibility criteria will receive the study treatment and will be maintained on the pregnancy prevention program for the duration of the study.
The inclusion procedure will be accomplished by a validated interactive voice/web response system (IVRS/IWRS).

Treatment Phase
Study treatment administration should start within 72 hours after enrollment of the subject into the study, provided that the inclusion/exclusion criteria are still met. Otherwise, the subject will need to be re-screened. Each subject will receive the following study treatment until progressive disease (PD), or as long as they benefit from therapy according to the opinion of the responsible study Investigator and discussed with the Sponsor:
- POM administered orally at the starting dose of 4 mg on Days 1-21 of a 28-day cycle,
- LD-DEX administered orally at the starting dose of 40 mg/day (* 75 years old) or 20 mg/day (> 75 years old) on Days 1, 8, 15 and 22 of a 28-day cycle.
Pharmacokinetic (PK) blood samples for POM quantification will be collected at specified timepoints during the course of the study from all subjects from selected sites with PK capability. Bone marrow aspirate, bone marrow biopsy (if available) and blood samples will be collected for exploratory biomarker analysis from subjects at selected sites, who consent to participate in the optional biomarker study. The bone marrow aspirate and bone marrow biopsy (if available) willbe collected during screening when the procedure is performed for study entry and at response assessment or at disease progression, if clinically indicated.

Follow-up Phase
All study subjects will enter the follow-up phase within 28 days of last study treatment administration. During follow-up the following information will be collected from all subjects every 3 months for up to 5 years after last subject enrollment or longer if clinically indicated:
SPMs, survival, subsequent anti-myeloma treatments (type of treatment, start and stop dates, best response whenever possible) and date of progression.

## Intervention

All subjects will be treated with open label Pomalidomide (POM). POM will be supplied as Investigational Product by Celgene Corporation as 1 mg, 2 mg, 3 mg, and 4 mg capsules for oral administration.
Study drug will be packaged in bottles containing a 21-day supply of POM. The dosing schedule is as follows:
- POM is administered orally at the starting dose of 4 mg on Days 1-21 of a 28-day cycle,
- Low Dose-Dexamethasone is administered orally at the starting dose of 40 mg/day (* 75 years old) or 20 mg/day (> 75 years old) on Days 1, 8, 15 and 22 of a 28-day cycle.

## Study burden and risks

See section E9.

# 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. Must be * 18 years at the time of signing the informed consent document (ICD).;2. The subject must understand and voluntarily sign an ICD prior to any study related assessments/procedures being conducted.;3. Must be able to adhere to the study visit schedule and other protocol requirements.;4. 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).;5. Subjects must have undergone prior treatment with * 2 treatment lines of anti-myeloma therapy. Induction therapy followed by ASCT and consolidation/maintenance will be considered as one line. A new treatment line is always started after progressive disease.;6. Subjects must have either refractory or relapsed and refractory disease defined as documented disease progression during or within 60 days of completing their last myeloma therapy.
Primary refractory: Subjects who have never achieved any response better than PD to any

previous line of anti-myeloma therapy.
Relapsed and refractory: Subjects who have relapsed after having achieved at least stable disease for at least two cycles of treatment to at least one prior regimen and then developed PD on or within 60 days of completing their last myeloma therapy.;7. All subjects must have received at least 2 consecutive cycles of prior treatment that included lenalidomide and bortezomib, either alone or in combination regimens.
All subjects must have failed both lenalidomide and bortezomib and medical records must be available that provide documentation of the following criteria for refractoriness that make the subject eligible for the study.
-All subjects must have failed treatment with the last lenalidomide-containing regimen in one of the following ways:
* Documented PD during or within 60 days of completing last treatment with lenalidomide, regardless of the response achieved, or
* In case of prior response (* partial response - PR) to lenalidomide and PD > 60 days, subjects must have relapsed within 6 months after the last dose of treatment with lenalidomide-containing regimens.
-All subjects must have failed treatment with the last bortezomib-containing regimen in one of the following ways:
* Documented PD during or within 60 days of completing treatment with bortezomib, regardless of the response achieved, or
* In case of prior response (* PR) to bortezomib and PD > 60 days, subjects must have relapsed within 6 months after the last dose of treatment with bortezomib-containing regimens
Or for non-progressive subjects:
* Subjects who have less than MR response and have developed intolerance/toxicity after a minimum of two cycles of a bortezomib-containing regimen. Toxicity such as > grade 2 peripheral neuropathy or * grade 2 painful neuropathy. Peripheral neuropathy must resolve to grade 1 prior to study entry.;8. Subjects must have received adequate prior alkylator therapy in one of the following ways:
-As part of a stem cell transplant; or
-A minimum of 4 consecutive cycles of an alkylator based therapy; or
-Progression on treatment with an alkylator; provided that the subject received at least 2 cycles of an alkylator-containing therapy.;9. ECOG performance status score of 0, 1, or 2.;10. 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.;11. Females must agree to abstain from breastfeeding during study participation and 28 days after study drug discontinuation.;12. 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.;13. Males must also agree to refrain from donating semen or sperm while on POM and for 28 days after discontinuation from this study treatment.;14. All subjects must agree to refrain from donating blood while on study therapy and for 28 days after discontinuation from this study treatment.;15. All subjects must agree not to share medication.

## Exclusion criteria

1. Any of the following laboratory abnormalities:
-Absolute neutrophil count < 800/*L.
-Platelet count < 75,000/*L for subjects in whom < 50% of bone marrow nucleated cells are plasma cells; or a platelet count < 30,000/*L for subjects in whom * 50% of bone marrow nucleated cells are plasma cells. Platelet transfusion is not allowed within the previous 3 days before screening.
-Creatinine Clearance < 45 mL/min according to Cockcroft-Gault formula. If creatinine clearance calculated from the 24-hour urine sample is * 45 mL/min, subject will qualify for the study.
-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 *mol/L); or > 3.0 x ULN for subjects with hereditary benign hyperbilirubinemia.;2. 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 histological finding of prostate cancer (TNM stage of T1a or T1b).;3. Previous therapy with POM.;4. Hypersensitivity to thalidomide, lenalidomide, or DEX (this includes * Grade 3 rash during prior thalidomide or lenalidomide therapy).;5. Peripheral neuropathy * Grade 2.;6. 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.;7. Subjects who are planning for or who are eligible for stem cell transplant.;8. 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.;9. Subjects who received any of the following within the last 14 days of initiation of study treatment:
-Major surgery (kyphoplasty is not considered major surgery)
-Use of any anti-myeloma drug therapy.;10. Use of any investigational agents within 28 days or five half-lives (whichever is longer) of treatment, unless approved by the Sponsor.;11. Incidence of gastrointestinal disease that may significantly alter the absorption of POM.;12. Subjects unable or unwilling to undergo antithrombotic prophylactic treatment.;13. Any serious medical condition, laboratory abnormality, or psychiatric illness that would prevent the subjects from signing the ICD or participating in the study.;14. Pregnant or breastfeeding females.;15. Known human immunodeficiency virus (HIV) positivity, active infectious hepatitis A, B or C or chronic hepatitis B or C.

# Study design

## Design

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

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 23-05-2013 |
| Enrollment: | 40 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Dexamethasone |
| Generic name: | Dexamethasone |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | na |
| Generic name: | Pomalidomide |

# Ethics review

Approved WMO

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| Date: | 23-08-2012 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

Approved WMO

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|---|---|
| Date: | 22-03-2013 |

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|---|---|
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 02-08-2013 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 10-10-2013 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 18-12-2013 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 06-02-2014 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 16-05-2014 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 16-06-2014 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 20-06-2014 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

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|---|---|
| Approved WMO Date: | 29-08-2014 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 20-10-2014 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 26-06-2015 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 03-07-2015 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 26-10-2015 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 26-01-2016 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 25-03-2016 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 19-04-2016 |
| Application type: | Amendment |

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|---|---|
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 02-08-2016 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 26-08-2016 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 09-09-2016 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 21-07-2017 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 28-07-2017 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 19-02-2018 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 20-03-2018 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO | |

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|---|---|
| Date: | 20-02-2019 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 05-08-2019 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 16-09-2019 |
| 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 | EUCTR2012-001888-78-NL |
| CCMO | NL41584.078.12 |