A PHASE 3, MULTICENTER, RANDOMIZED, OPEN-LABEL STUDY TO COMPARE THE EFFICACY AND SAFETY OF POMALIDOMIDE, BORTEZOMIB AND LOW-DOSE DEXAMETHASONE VERSUS BORTEZOMIB AND LOW-DOSE DEXAMETHASONE IN SUBJECTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA

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Study ObjectivesTo compare the efficacy of POM + BTZ + LD-DEX with BTZ + LD-DEX in subjects with relapsed or refractory MM Secondary Objectives:To evaluate the safety and additional efficacy of POM + BTZ + LD-DEX versus BTZ + LD-DEX in subjects with...

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

Summary

ID

NL-OMON44661

Source
ToetsingOnline

Brief title
POM-CC-4047-MM-007

Condition

- Plasma cell neoplasms

Synonym
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: BORTEZOMIB, DEXAMETHASONE, MULTIPLE MYELOMA, POMALIDOMIDE

Outcome measures

Primary outcome

Primary Endpoint

• Progression-Free Survival (PFS)

Secondary outcome

Secondary Endpoints

• Overall Survival (OS)

• Safety (type, frequency, seriousness and severity of AEs, and relationship of

AEs to study drug or comparator)

• Overall response rate (ORR) (using the International Myeloma Working Group

Uniform [IMWG] response criteria)

• Duration of response

Exploratory Endpoints

• ORR (using the European Group for Blood and Marrow Transplantation [EBMT]

criteria)

• Time to response

• Time to progression (TTP)

• Efficacy analysis in subgroups

• Progression-free survival after next-line therapy (PFS2)

• POM concentrations in plasma

• Clinical benefits (improvement in hemoglobin value, improvement in renal function, improvement of ECOG performance status, improvement in hypercalcaemia, improvement in non-myeloma immunoglobulins)

• The European Organization for Research and Treatment of Cancer QoL Questionnaire for Patients with Multiple Myeloma (EORTC QLQ-MY20) Module, the Cancer QoL Questionnaire for Patients with Cancer (EORTC QLQ-C30) Module, and the descriptive system of the EQ-5D

• Minimal Residual Disease (MRD), genomic, molecular/mechanistic and immune biomarkers for only those subjects who give their consent (Optional)

Study description

Background summary

Multiple myeloma (MM) is a rare and incurable progressive neoplastic disease that accounts for 10% of all hematological malignancies. It was estimated in 2010 that 20,180 new cases and 10,650 deaths from the disease occurred in the United States (US) (Jemal, 2010).
Significant progress has been made in the treatment of newly diagnosed MM with different combinations of melphalan, prednisone, dexamethasone, doxorubicin, thalidomide, lenalidomide and proteasome inhibitors (bortezomib) or autologous stem cell transplant following high-dose chemotherapy in appropriate patients (National Comprehensive Cancer Network [NCCN] Clinical Practice Guidelines in Oncology for MM, 2012; Child, 2003; Fermand, 2005). In recent years, innovative

therapies such as proteasome inhibitors and immunomodulators have improved the prognosis for previously treated MM subjects (Kumar, 2008). However, the disease follows a relapsing course in the majority of patients, regardless of treatment regimen or initial response to treatment. MM remains incurable using conventional treatments, with median survival duration of approximately 5 years (Richardson, 2007a). Therefore, there is a need for more effective therapeutic options for the treatment of relapsed or refractory multiple myeloma.

Study objective

Study Objectives
To compare the efficacy of POM + BTZ + LD-DEX with BTZ + LD-DEX in subjects with relapsed or refractory MM
Secondary Objectives:
To evaluate the safety and additional efficacy of POM + BTZ + LD-DEX versus BTZ + LD-DEX in subjects with relapsed or refractory MM.
Exploratory Objectives:
• To explore the pharmacokinetics of pomalidomide and the relationship between drug exposure and response (pharmacodynamic effects, safety and/or efficacy as appropriate) in subjects with relapsed or refractory MM treated with pomalidomide
• To evaluate the differences in pharmacoeconomics of POM + BTZ + LD-DEX versus BTZ + LD-DEX in subjects with relapsed or refractory MM
• To evaluate the differences in clinical benefits of POM + BTZ + LD-DEX versus BTZ + LD-DEX in subjects with relapsed or refractory MM
• To evaluate the differences in key efficacy variables of POM + BTZ + LD-DEX versus BTZ + LD-DEX within defined subgroups
• To evaluate the differences in health-related quality of life of POM + BTZ + LD-DEX versus BTZ + LD-DEX in subjects with relapsed or refractory MM
• To evaluate Minimal Residual Disease (MRD), genomic, molecular/mechanistic and immune biomarkers and their correlation to clinical outcome measures for only those subjects who give their consent (Optional)

Study design

This study is a multicenter, randomized, open-label, phase 3 study comparing the efficacy and safety of POM + BTZ + LD-DEX (Treatment Arm A) versus BTZ + LD-DEX (Treatment Arm B) in subjects with relapsed or refractory MM.

Intervention

There are two different treatments that will be compared in this study.
The first study treatment (treatment A) will be a combination of pomalidomide, bortezomib, and dexamethasone and the second (treatment B) a combination of bortezomib and dexamethasone.
Subjects will receive the study treatment in cycles; each cycle will be 21 days

long. The first cycle will start when subjects take their first dose of study treatment (Cycle 1 Day 1).
The study will last for 5 years.

Study burden and risks

1. POTENTIAL BENEFITS
This is a Phase 3, Multicenter, Randomized, Open-label Study to Compare the Efficacy and Safety of Pomalidomide (POM), Bortezomib (BTZ) and Low-Dose Dexamethasone (LD-DEX) (Treatment Arm A) versus Bortezomib and Low-Dose Dexamethasone (Treatment Arm B) in Subjects with Relapsed or Refractory Multiple Myeloma (MM).
The objectives for this study are as follows: To compare the efficacy of POM + BTZ + LD-DEX with BTZ + LD-DEX in subjects with relapsed or refractory MM and To evaluate the safety and additional efficacy of POM + BTZ + LD-DEX versus BTZ + LD-DEX in subjects with relapsed or refractory MM.
For Treatment Arm A (POM + BTZ + DEX), the dose was based on the results from the CC-4047-MM-005 (MM-005) Phase 1 dose escalation MTD study in which bortezomib was administered via IV infusion. In the MM-005 study, the maximum planned dose (MPD), POM (4 mg) + IV BTZ (1.3 mg /m2) and DEX (20 mg subjects <= 75 years old/10 mg subjects > 75 years old) was reached without any DLTs. Considering an early POM single agent MTD study (Richardson, 2013) as well as the findings in MM-005, the MPD was determined to be the optimal dose for the triple combination therapy. With the optimal dose determined, MM-007 was initiated using the MPD dose for the combination of POM + BTZ + LD-DEX (with IV BTZ).
During the conduct of the MM-005 study, subcutaneous (SQ) BTZ was approved as an alternative administration method for BTZ (23 Jan 2013). The SQ BTZ was reported to have a decreased incidence of neurotoxicity versus the IV BTZ (Velcade® Prescribing Information, 2014). To explore the SQ route of BTZ administration in combination with POM and DEX, the MM-005 protocol was amended to add a cohort of 6 subjects at the MPD/optimal dose for the combination of POM + BTZ + LD-DEX with BTZ administered via SQ injection. Based on the safety, efficacy and PK data for this SQ BTZ cohort and general adoption in medical practice of SQ BTZ as standard of care due to decreased neurotoxicity, BTZ administration is now to be SQ for both arms in the MM-007 study (Treatment Arm A and B). Subjects consented to the original MM-007 protocol can continue with IV BTZ or switch to SQ BTZ at the discretion of the treating physician.
Subjects randomized into MM-007 under IV BTZ treatment will not be replaced.
Multiple myeloma (MM) is a rare and incurable progressive neoplastic disease that accounts for 10% of all hematological malignancies. It was estimated in 2010 that 20,180 new cases and 10,650 deaths from the disease occurred in the United States (US) (Jemal, 2010).
Significant progress has been made in the treatment of newly diagnosed MM with different combinations of melphalan, prednisone, dexamethasone, doxorubicin, thalidomide, lenalidomide and proteasome inhibitors (bortezomib) or autologous stem cell transplant following high-dose chemotherapy in appropriate patients

(National Comprehensive Cancer Network [NCCN] Clinical Practice Guidelines in Oncology for MM, 2012; Child, 2003; Fermand, 2005). In recent years, innovative therapies such as proteasome inhibitors and immunomodulators have improved the prognosis for previously treated MM subjects (Kumar, 2008). However, the disease follows a relapsing course in the majority of patients, regardless of treatment regimen or initial response to treatment. MM remains incurable using conventional treatments, with median survival duration of approximately 5 years (Richardson, 2007a). Therefore, there is a need for more effective therapeutic options for the treatment of relapsed or refractory multiple myeloma.

The treatment options approved for use in relapsed and/or refractory MM currently include: Lenalidomide in combination with dexamethasone for the treatment of patients with MM who have received at least one prior therapy (Bortezomib monotherapy for the treatment of patients with relapsed MM, Pegylated liposomal doxorubicin (PLD) in combination with bortezomib for the treatment of patients with MM who have not previously received bortezomib and have received at least one prior therapy. Carfilzomib for the treatment of multiple myeloma in patients who have received at least 2 prior therapies including bortezomib and an immunomodulatory agent and have demonstrated disease progression on or within 60 days of completion of the last therapy. Pomalidomide for the treatment of multiple myeloma in patients who have received at least 2 prior therapies including lenalidomide and bortezomib and have demonstrated disease progression on or within 60 days of completion of the last therapy. Other options that may be considered for salvage therapy in MM patients include thalidomide alone or in combination with dexamethasone or other agents, lenalidomide monotherapy, lenalidomide in combination with bortezomib and dexamethasone, or lenalidomide or bortezomib in combination with cyclophosphamide and dexamethasone (NCCN Clinical Practice Guidelines in Oncology for Multiple Myeloma, 2012).

Bortezomib (Velcade®) was approved for the treatment of relapsed or refractory MM based on the results of a Phase 3 trial (APEX Trial) comparing bortezomib to high dose dexamethasone as salvage therapy. In an updated efficacy analysis of the APEX trial, the response rate was 43% with bortezomib vs. 18% for dexamethasone and the overall survival (OS) was 30 months with bortezomib vs. 23.7 months with dexamethasone (Richardson, 2007c).

The benefits of the adding dexamethasone to bortezomib therapy were shown in the SUMMIT trial in which 202 relapsed or refractory MM subjects were enrolled (Richardson, 2003). In this phase 2 study, patients received 1.3 mg/m2 of bortezomib for up to eight cycles. In patients with a suboptimal response, oral dexamethasone (20 mg daily, on the day of and the day after bortezomib administration) was added to the regimen. Seventy-eight patients who had either stable or progressive disease (PD) while receiving bortezomib alone subsequently received dexamethasone in combination with bortezomib. Of these 76, a total of 74 patients could be evaluated for a response to this combination, and 13 of these patients (18 percent) had a minimal or partial response. In 6 of these 13 patients, the disease had previously been refractory to corticosteroid therapy. Bortezomib in combination with dexamethasone is therefore included in the NCCN clinical practice guidelines as a category 2A

recommendation for salvage therapy in MM patients (NCCN Clinical Practice Guidelines in Oncology for MM, 2012).

The most recent approval of Doxil® (doxorubicin HCl) in combination with bortezomib has led to more treatment options for relapsed or refractory MM. The approval of this regimen was based on a Phase 3 study in 646 patients showing a significant increase in median time to disease progression in Doxil plus bortezomib arm compared to bortezomib monotherapy arm (9.3 vs. 6.5 months, respectively). Starting from the 2010 NCCN clinical practice guidelines for Multiple Myeloma, this combination was recommended as superior over bortezomib monotherapy for relapsed / refractory MM. However, no data were submitted in support of the conventional treatments, with median survival duration of approximately 5 years (

Richardson, 2007a). Therefore, there is a need for more effective therapeutic options for the treatment of relapsed or refractory multiple myeloma.

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Pomalidomide, [4-amino-2-(2, 6-dioxopiperidin-3-yl) isoindoline-1], 3-dione, is a novel drug in the class of immunomodulatory drugs (IMiDs®), which include thalidomide and lenalidomide. IMiDs may affect the immune system in several ways, such as inducing immune responses, enhancing activity of immune cells, altering and modulating the induction of pro- and anti-inflammatory cytokines, and inhibiting inflammation. Pomalidomide binds to its molecular target cereblon, a protein that is part of an E3 ubiquitin ligase complex, which is responsible for the polyubiquitination of substrate proteins, targeting them for subcellular redistribution and destruction by the proteasome. IMiDs are also anti-angiogenic. Although their precise mechanism of action is currently under investigation, these agents offer promise for their anticancer and anti-inflammatory activities. In addition to its anti-tumor, immunomodulatory and anti-fibrotic properties, pomalidomide also affects the regulation of fetal hemoglobin expression by erythroid precursors in healthy adults as well as adults with sickle cell disease (SCD), making it a potential therapeutic agent for the treatment of nonmalignant hematologic disorders such as SCD and β-thalassemia. The pharmacologic properties of pomalidomide are of potential therapeutic benefit in the treatment of hematologic neoplasms, such as multiple myeloma (MM) and myelofibrosis (MF), non-oncologic hematologic disorders, such as SCD, non-neoplastic non-hematologic disorders, such as systemic sclerosis (SSC), as well as solid tumor neoplasms, such as soft tissue sarcoma and lung cancer.

Pomalidomide was first approved for marketing in the US under the trade name Pomalyst® on 08 Feb 2013, for the treatment of patients with MM who have received at least two prior therapies including lenalidomide and bortezomib and have demonstrated disease progression on or within 60 days of completion of the last therapy. Pomalidomide was approved within the EU (Imnovid®, originally Pomalidomide Celgene®) on 05 Aug 2013 in combination with dexamethasone for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including both

lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy. Most recently, pomalidomide was approved in Canada (Pomalyst*) on 20 Jan 2014 in combination with dexamethasone for patients with MM for whom both bortezomib and lenalidomide have failed and who have received at least two prior treatment regimens and have demonstrated disease progression on the last regimen.
Pomalidomide is formulated for oral administration in clinical studies as 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg and 5 mg gelatin capsules. In ongoing Celgene-sponsored studies, pomalidomide has been administered in doses ranging from 0.5 to 4 mg once daily generally on a cyclical regimen (eg, days 1-21 of a 28-day cycle) in hematology/oncology clinical studies.

2. POTENTIAL RISKS AND PRECAUTIONS
The safety profile of pomalidomide appears to have some similarity to that of thalidomide and lenalidomide. However, with Pomalidomide*s human exposure to date, true similarities and differences have not been fully elucidated, therefore, due vigilance must be exercised in monitoring subjects for safety. Individual subject care should be optimized, and every precaution undertaken to ensure careful medical monitoring. To this end, it is expected that centers participating in studies will be able to provide a high standard of clinical care as well as conduct clinical research in accordance with Good Clinical Practice (GCP).
As expected, based on the preclinical experience of pomalidomide, the common adverse events associated with the use of pomalidomide were related to the blood and lymphatic system, namely, neutropenia and thrombocytopenia. These AEs can be dose limiting toxicities that should be managed through dose adjustments, clinical and laboratory monitoring, and the use of hematopoietic growth factors as required. Other adverse events observed with pomalidomide and also associated with other immunomodulatory agents (ie, IMiDs compounds) have included infection, fatigue, renal failure, neuropathy, venous thromboembolic events, and constipation.
In the 9-month toxicity study in monkeys (Report CC-4047-TOX-006), pomalidomide was administered at doses of 0.05, 0.1, and 1 mg/kg/day.
Pomalidomide-associated morbidity and early euthanasia (3/sex) were observed in the 1 mg/kg/day group, and were attributed to immunomodulation/ immunosuppression (decreased peripheral lymphocytes, histologic lymphoid depletion, and hypocellularity of bone marrow), effects associated with the pharmacology of pomalidomide. These immunosuppressive effects were associated with staphylococcal infection and chronic inflammation of the large intestine. Villous atrophy of the small intestine and minimal and mild bile duct proliferation were also present. In addition, findings consistent with AML were observed in 1 of these females that was terminated early. Clinical observations and clinical pathology and/or bone marrow alterations were also consistent with immunosuppression. In the surviving animals, there were no treatment-related changes in body weight, electrocardiography, blood pressure measurements, ophthalmology, and urinalysis. Evaluation of recovery animals indicated that all treatment related findings were reversible after 8 weeks of dosing

cessation, except for proliferation of intrahepatic bile ducts observed in 1 animal in the 1.0 mg/kg/day group.
The NOAEL was 0.1 mg/kg/day, corresponding to Day 272 pomalidomide AUC24hr of 227, and 211 ng•h/mL for male and female monkeys, respectively (approximately 0.5-fold exposure ratio relative to a 4 mg clinical dose).
Cardiovascular assessment (vital signs, electrocardiogram [ECG], respiration, and heart rate) conducted in the 3 and 9 months monkey studies (Reports CC-4047-TOX-002; CC-4047-TOX-006), indicated no test article-related cardiovascular changes at doses up to 2 mg/kg/day for 3 months, and up to 1 mg/kg/day for 9 months (Cmax = 1249 and 653 ng/mL, both sexes combined, at 2 and 1 mg/kg/day respectively).
Second primary malignancies have also been reported, and to date, the incidence rate appears to be below what would be expected in similar populations independent of any treatment. As of 07 Feb 2014, 29 subjects have experienced a total of 34 SPMs across all programs, including ongoing Celgene-sponsored studies (Study CC-4047-MM-002 Phase 1 [2 subjects, including 1 subject with 2 SPMs); Study CC-4047-MM-002 Phase 2 [4 subjects]; Study CC-4047-MM-003/C [7 subjects, including 1 subjects with 5 SPMs]; Study CC-4047-MM-005 [2 subjects]; Study CC-4047-MM-010 [7 subjects], Study CC-4047-MF-002 [6 subjects], and Study CC-4047-SCLC-002 [1 subject]).
Events of AML have also been reported, primarily from studies in subjects where the natural course of the disease being treated, MPN-associated MF, includes a risk of disease progression to AML (leukemic transformation or transformation to blastic phase), and therefore were reported as disease progression and not SPMs.
The important identified risks with pomalidomide continue to be those previously identified, including teratogenicity, neutropenia, thromboembolic events, and thrombocytopenia.
Tumor lysis syndrome (TLS) may occur in subjects treated with pomalidomide. Subjects at risk for TLS are those with high tumor burden prior to treatment. These subjects should be monitored closely and appropriate precautions taken.
Subjects with a prior history of serious allergic reactions associated with thalidomide or lenalidomide were excluded from clinical studies, may be at higher risk of hypersensitivity and should not receive pomalidomide.

3. ADDITIONAL PRECAUTIONS
No data are available on administration of pomalidomide to pediatric or adolescent subjects (< 18 years of age).
No dosage adjustment is required for pomalidomide in the elderly. For subjects >= 75 years of age, the starting dose of dexamethasone is 20 mg/day on Days 1, 8, 15 and 22 of each 28-day treatment cycle.
A study in subjects with renal impairment has not been conducted with pomalidomide. Subjects with serum creatinine > 3.0 mg/dL were excluded from study CC-4047-MM-002. Subjects with creatinine clearance < 45 mL/minute were excluded from study CC-4047-MM-003.
A study in subjects with hepatic impairment has not been conducted with pomalidomide. Subjects with serum bilirubin > 2.0 mg/dL were excluded from the

efficacy studies.
Pomalidomide tested negative for mutagenicity and genotoxicity, however, tests to evaluate the carcinogenic potential of pomalidomide have not been performed..
Fertility and Early Embryonic Development
In a fertility and early embryonic development non-clinical study in rats, pomalidomide treatment of males and females resulted in a decrease mean number of viable embryos and an increase in postimplantation loss at dosages of 25 mg/kg/day or higher. These effects were not observed when treated males were mated with untreated females. The NOAEL was < 25 mg/kg/day. Pomalidomide was found to be teratogenic in both rats and rabbits when administered during the period of major organogenesis. The NOAELs for developmental toxicity were < 25 mg/kg/day for rat and < 10 mg/kg/day for rabbit.
The effect of pomalidomide on human fertility and early embryonic development is currently unknown, therefore proactive precautionary family planning options and/or alternatives should be thoroughly discussed with female study subjects, as appropriate.
Use in Pregnancy
Pomalidomide was found to be teratogenic in embryo-fetal development toxicity studies in rats and rabbits. Pomalidomide crossed the placenta and was detected in fetal blood following administration to pregnant rabbits.
A teratogenic effect of pomalidomide in humans cannot be ruled out. All patients and investigators must follow the Global Pregnancy Prevention Program.
Use During Lactation
It is not known if pomalidomide is excreted in human milk. Pomalidomide was detected in milk of lactating rats following administration to the mother. Because of the potential for adverse reactions in nursing infants from pomalidomide, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
Effects on Ability To Drive Vehicles and Operate Machinery
No studies on effects of pomalidomide on the ability to drive or use machines have been performed. Confusion, fatigue, depressed level of consciousness and dizziness have been reported with the use of pomalidomide. Therefore, caution is recommended when driving or operating machines in persons receiving pomalidomide.
Interactions and Overdose
Pomalidomide is not anticipated to cause clinically relevant pharmacokinetic drug-drug interactions due to enzyme inhibition or induction or transporter inhibition when co-administered with substrates of these enzymes or transporters. The potential for such drug-drug interactions, including the potential impact of pomalidomide on exposure of oral contraceptives, has not been evaluated clinically.
If strong inhibitors of CYP1A2 are co-administered with pomalidomide, subjects should be closely monitored for the occurrrence of side effects.
Dexamethasone is a weak to moderate enzyme inducer and its effect on warfarin is unknown. Close monitoring of warfarin concentration is advised during treatment.

No drug/laboratory test Interactions interactions identified.
Pomalidomide can be administered without regard to food intake.
Doses of pomalidomide explored in clinical trials are between 0.5 and 4 mg/day, pomalidomide doses as high as 50 mg as a single dose in healthy volunteers and 10 mg as once-daily multiple doses in MM patients have been studied without reported serious AEs related to overdose. No specific information is available on the treatment of overdose with pomalidomide, and it is currently unknown whether pomalidomide or its metabolites are dialyzable.

4. CONCLUSIONS
Currently available information supports an acceptable investigational benefit-risk balance for pomalidomide when used in accordance with the precautions, risk mitigation/management, dosing and safety monitoring outlined in the study protocol, and routine trial safety surveillance practices.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

Subjects must satisfy the following criteria to be enrolled in the study:
1. Must be >= 18 years at the time of signing the informed consent form.
2. The subject must understand and voluntarily sign an informed consent document prior to any study-related assessments/procedures.
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 by serum or urine protein electrophoresis (sPEP or uPEP): sPEP >= 0.5 g/dL or uPEP >= 200 mg/24 hours.
5. All subjects must have had at least 1 but no greater than 3 prior anti-myeloma regimens. (note: induction with or without bone marrow transplant and with or without maintenance therapy is considered one regimen.)
6. All subjects must have documented disease progression during or after their last anti-myeloma therapy.
7. All subjects must have received prior treatment with a lenalidomide-containing regimen for at least 2 consecutive cycles.
8. Eastern Cooperative Oncology Group (ECOG) performance status score of 0, 1, or 2.
9. 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 4 weeks before starting study treatment, while participating in the study treatment phase (including dose interruptions), and for at least 4 weeks after the last dose of POM or 3 months after the last dose of BTZ, whichever is longer, and must agree to regular pregnancy testing during this timeframe.
10. Females must agree to abstain from breastfeeding during study treatment and for at least 4 weeks after study treatment discontinuation.
11. Males must agree to use a latex or synthetic condom during any sexual contact with FCBP while participating in the study treatment phase and for at least 4 weeks after the last dose of POM or 3 months after the last dose of BTZ, whichever is longer, even if he has undergone a successful vasectomy.
12. Males must also agree to refrain from donating sperm while on pomalidomide and for 4 weeks after discontinuation from this study treatment.
13. All subjects must agree to refrain from donating blood while on study treatment and for 4 weeks after discontinuation from this study treatment.
14. All subjects must agree not to share medication.

Exclusion criteria

The presence of any of the following will exclude a subject from enrollment:
1. Subjects who had documented progressive disease during therapy or within 60 days of the last dose of a bortezomib-containing therapy under the 1.3 mg/m2 dose twice weekly dosing schedule
2. Peripheral neuropathy Grade 3, Grade 4 or Grade 2 with pain within 14 days prior to

randomization
3. Non-secretory multiple myeloma
4. Any of the following laboratory abnormalities:
• Absolute neutrophil count (ANC) < 1,000/µL
• Hemoglobin < 8 g/dL (< 4.9 mmol/L)
• Platelet count < 75,000/µL for subjects in whom < 50% of bone marrow nucleated cells are plasma cells; or a platelet count < 30,000/ µL for subjects in whom >= 50% of bone marrow nucleated cells are plasma cells
• Corrected serum calcium > 13.5 mg/dL (> 3.4 mmol/L)
• Serum SGOT/AST or SGPT/ALT > 3.0 x upper limit of normal (ULN)
• Serum total bilirubin > 1.5 x ULN
5. Subjects with severe renal impairment (Creatinine Clearance [CrCl] <30 mL/min) requiring dialysis
6. Subjects with prior history of malignancies, other than MM, unless the subject has been free of the disease for >= 5 years with the exception of the following non-invasive malignancies:
• Basal cell carcinoma of the skin
• Squamous cell carcinoma of the skin
• Carcinoma in situ of the cervix
• Carcinoma in situ of the breast
• Incidental histologic finding of prostate cancer (T1a or T1b using the TNM [tumor, nodes, metastasis] clinical staging system) or prostate cancer that is curative.
7. Previous therapy with pomalidomide
8. History of anaphylaxis or hypersensitivity to thalidomide, lenalidomide, bortezomib, boron, mannitol, or dexamethasone
9. >= Grade 3 rash during prior thalidomide or lenalidomide therapy
10. Incidence of gastrointestinal disease that may significantly alter the absorption of pomalidomide
11. Subjects with any one of the following:
• Clinically significant abnormal ECG finding at screening
• Congestive heart failure (New York 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 other than local therapy for myeloma associated bone lesions
• Use of any systemic anti-myeloma drug therapy
13. Use of any investigational agents within 28 days or 5 half-lives (whichever is longer) of treatment
14. Subjects with conditions requiring chronic steroid or immunosuppressive treatment, such as rheumatoid arthritis, multiple sclerosis, and lupus, which likely need additional steroid or immunosuppressive treatments in addition to the study treatment. Includes subjects receiving corticosteroids (> 10 mg/day of prednisone or equivalent) within 3 weeks prior to enrollment.
15. Subjects unable or unwilling to undergo protocol required thromboembolism prophylaxis

or herpes zoster prophylaxis will not be eligible to participate in this study
16. Any condition, including the presence of laboratory abnormalities, which places the subject at unacceptable risk if he/she were to participate in the study
17. Any serious medical condition, laboratory abnormality, or psychiatric illness that would prevent the subjects from signing the informed consent form
18. Pregnant or breastfeeding females
19. Known seropositive for or active viral infection with human immunodeficiency virus (HIV)
20. Known active viral infection with hepatitis A virus (HAV).
21. Known seropositive for or active viral infection with hepatitis B virus (HBV):
• Subjects who are HBsAg negative and viral DNA negative are eligible.
• Subjects who had hepatitis B but have received an antiviral treatment and show non-detectable viral DNA for 6 months are eligible.
• Subjects who are seropositive because of hepatitis B virus vaccine are eligible.
22. Known seropositive for or active viral infection with hepatitis C virus (HCV):
• Subjects who had hepatitis C but have received an antiviral treatment and show no detectable viral RNA for 6 months are eligible.

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):	15-01-2013
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dexamethasone Tablets BP 2.0 mg
Generic name:	DEXAMETHASONE

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Dexamethason-ratiopharm® 4 mg tablets
Generic name:	DEXAMETHASONE
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Imnovid 3 mg hard capsules
Generic name:	Pomalidomide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Imnovid 4 mg hard capsules
Generic name:	Pomalidomide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Velcade
Generic name:	BORTEZOMIB
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	15-04-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-09-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-06-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	02-08-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-01-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-08-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-08-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-11-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-04-2021
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-09-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-12-2021
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	EUCTR2014-000268-17-NL
CCMO	NL52758.078.15

Study results

Date completed:	01-01-1900
Results posted:	22-11-2023
Actual enrolment:	2

First publication
01-01-1900