Pomalidomide combined with Carfilzomib and Dexamethasone (PCd) for induction and consolidation followed by Pomalidomide combined with Dexamethason vs Pomalidomide maintenance for patients with Multiple Myeloma in progression after prior 1st line treatment with Lenalidomide and Bortezomib.

Gepubliceerd: 04-08-2015 Laatst bijgewerkt: 18-08-2022

This study aims to assess the efficacy and safety of induction and consolidation therapy with Carfilzomib, Pomalidomide and Dexamethasone in subjects with relapsed or refractory multiple myeloma (MM) after prior first-line treatment in the EMN02/…

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24039

Bron
NTR

Verkorte titel
HOVON 114 MM

Aandoening

Multiple Myeloma
Multiple Myeloom

ziekte van Kahler

Ondersteuning

Primaire sponsor: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)
Overige ondersteuning: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON), Dutch Cancer Society, Onyx Pharmaceuticals, Celgene Corporation

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

- Progression free survival (PFS) from randomization, defined as time from randomization to progression or death from any cause which ever occur first. Patient still alive at the date of last contact will be censored.
- Response rate (sCR, CR, VGPR, PR) after induction and consolidation treatment

Toelichting onderzoek

Achtergrond van het onderzoek

This trial will try to evaluate the efficacy of the combination of Pomalidomide, Carfilzomib and low dose Dexamethasone
for induction and consolidation in subjects with relapsed or refractory multiple myeloma after prior first-line treatment in the
EMN02/HO95 trial and who are refractory to Lenalidomide and Bortezomib.
Despite the use of high-dose chemotherapy and autologous stem cell transplantation, Multiple Myeloma remains
incurable. The 5-year survival rate for patients with multiple myeloma among patients treated with conventional
chemotherapy is 25%, while with intensified therapy this may increase to more than 50 %. In the majority of subjects the
disease follows a relapsing course, regardless of treatment regimen or initial response to treatment. Novel agents are
urgently needed to improve the treatment results of this disease.

Doel van het onderzoek

This study aims to assess the efficacy and safety of induction and consolidation therapy with Carfilzomib, Pomalidomide and Dexamethasone in subjects with relapsed or refractory

multiple myeloma (MM)
after prior first-line treatment in the EMN02/HO95 trial who are refractory to Lenalidomide and/or Bortezomib.

Furthermore, the efficacy of maintenance therapy with Pomalidomide versus Pomalidomide plus Dexamethasone will be determined.

Onderzoeksopzet

- At entry

− After induction treatment cycle 2 and 4

− After High-dose Melphalan and autologous stem cell transplantation (if applicable)

− After consolidation treatment cycle 2 and 4

− After every 2nd maintenance cycle until progression

− During follow up every 2 months until progression/relapse. Thereafter every 6 months until 8 years after registration.

Onderzoeksproduct en/of interventie

The following treatments will apply:

Patients who progess from EMN02/HO95, who were treated with standard dose melphalan (VCD, followed by VMP, followed by yes/no VRD consolidation, followed by lenalidomide maintenance) will be treated with 4 cycles of PCd induction (Pomalidomide Carfilzomib dexamethasone).

After induction they will receive HighDose Melphalan and autologous stem cell reinfusion (autoSCT) of cells already stored during initial treatment, if possible. Following hematologic recovery, these patients will receive 4 cycles of consolidation treatment with PCd.

Patients who progress from EMN02/HO95, who were treated with High Dose Melphalan (VCD, followed by HDM+autoSCT followed by yes/no VRD consolidation, followed by lenalidomide maintenance) will be treated with 4 cycles of PCd induction, followed by 4 cycles of consolidation treatment with PCd.

All patients who have completed the re-induction and consolidation treatment will be randomized for maintenance

treatment with pomalidomide alone or pomalidomide plus dexamethasone until progression of disease.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Included in EMN02/HO95 trial

- The subject must understand and voluntarily sign an informed consent document prior to any study related assessments/procedures.

- Age ¡Ý 18 years at the time of signing the informed consent form.

- Able to adhere to the study visit schedule and other protocol requirements.

- Documented diagnosis of multiple myeloma and measurable disease

(serum M-protein ¡Ý 10 g/L or urine M-protein ¡Ý 200 mg/24 hours or abnormal FLC ratio with involved free light chain (FLC) > 100 mg/L) or proven plasmacytoma by biopsy);

- At least prior anti-myeloma regimen according to the EMN02/HO95 trial and documented progression or refractory multiple myeloma as per the IMWG uniform response criteria (Durie, 2006) during or after the last anti-myeloma regimen. Induction therapy followed by autologous stem cell transplant (AutoSCT) and consolidation/ maintenance will be considered as one regimen.

- Patients who have never achieved a response better than PD after at least 2 cycles of lenalidomide containing therapy or who progressed whilst on treatment.

- Normal renal function with a Creatinine Clearance > 45mL/min according to the Modification of Diet in Renal Disease (MDRD) equation for estimation of Glomerular Filtration Rate (GFR)

- WHO performance status score of 0, 1 or 2.

- Patients must be willing and capable to use adequate contraception during the therapy (all men, all pre-menopausal women). Patients must be able to adhere to the requirements of the Pregnancy Prevention Risk Management Plan.

- All subjects must agree to refrain from donating blood while on study drug and for 28 days after discontinuation from this study treatment.

- All subjects must agree not to share medication.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Absolute neutrophil count (ANC) <1.0 x 109/L, unless related to MM.

- Platelet count < 75 x 109/L, unless related to MM.

- 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).

- Significant hepatic dysfunction (Serum SGOT/AST or SGPT/ALT > 3.0 x

upper limit of normal (ULN) or serum total bilirubin > 3.0 x ULN)

- Prior history of malignancies, other than MM, unless the subject has been free of the disease for ¡Ý 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).

- Previous therapy with pomalidomide or carfilzomib.
- Hypersensitivity to thalidomide, lenalidomide, bortezomib or dexamethasone (this includes ¡Ý Grade 3 rash during prior thalidomide or lenalidomide or bortezomib therapy).

- Peripheral neuropathy ¡Ý Grade 2.

- Subjects who received an allogeneic bone marrow or allogeneic peripheral blood stem cell transplant less than 12 months prior to initiation of study treatment

- LVEF ¡Ü 40%.

- QTc > 450 msec.

- History of torsade de pointe.

- History of ventricular tachycardia, ventricular fibrillation.
- Uncontrolled atrial fibrillation/flatter.

- 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.

- History of pulmonary hypertension.

- Uncontrolled infection.

- 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.

- Use of any investigational agents (with the exception of lenalidomide)

within 28 days or five half-lives (whichever is longer) of treatment.

- Incidence of gastrointestinal disease that may significantly alter the absorption of pomalidomide.

- Subjects unable or unwilling to undergo antithrombotic prophylactic treatment.

- Any serious medical condition, laboratory abnormality, or psychiatric illness that would prevent the subjects from signing the informed consent form.

- Pregnant or breastfeeding females.

- Known human immunodeficiency virus (HIV) positivity, active infectious hepatitis A, B or C or chronic hepatitis B or C.

- Pre-existing pulmonary, cardiac or renal impairement that prevents hydration measures as described at section 9.5.

- Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	30-07-2015
Aantal proefpersonen:	222
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	04-08-2015
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL5201
NTR-old	NTR5349
Ander register	MEC/CCMO : 2014-664/NL 45339.078.14.

Resultaten