A randomized phase III study to compare Bortezomib, Melphalan, Prednisone (VMP) with High Dose Melphalan followed by Bortezomib, Lenalidomide, Dexamethasone (VRD) consolidation and Lenalidomide maintenance in patients with newly diagnosed multiple myeloma.

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1st randomization: The hypothesis to be tested is that the outcome in the HDM arm is better than in the VMP arm. 2nd randomization: The hypothesis to be tested is that the outcome in the arm with VRD consolidation followed by lenalidomide...

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

Samenvatting

ID

NL-OMON28960

Bron
Nationaal Trial Register

Verkorte titel
HOVON 95 MM

Aandoening

Multiple Myeloma (Kahler’s disease)

Ondersteuning

Primaire sponsor: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)
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Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1. For all registered patients: progression free survival (PFS) as defined by time from registration to progression or death from any cause (whichever occurs first);
2. For all patients included in R1; PFS as defined by time from randomization R1 to progression or death from any cause whichever comes first;
3. For all patients included in R2; PFS as defined by time from randomization R2 to progression or death from any cause whichever comes first.

Toelichting onderzoek

Achtergrond van het onderzoek

Study phase: Phase III.

Study objective:

1. Comparison of Bortezomib, Melphalan, Prednisone (VMP) with High Dose Melphalan followed autologous stem cell transplantation (ASCT);

2. Comparison of Bortezomib, Lenalidomide, Dexamethasone (VRD) as consolidation versus no consolidation;

3. Comparison of single versus tandem high dose Melphalan with ASCT.

Patient population:

Patients with symptomatic multiple myeloma, previously untreated, ISS stages 1-3, age 18-65 years inclusive.

Study design:

Prospective, multicenter, intergroup, randomized.

Duration of treatment:

Expected duration of induction, stem cell collection and intensification is 6 - 9 months. Consolidation with VRD will last 2 months. Maintenance therapy with Lenalidomide will be given until relapse. All patients will be followed until 10 years after registration.

Doel van het onderzoek

1st randomization:

The hypothesis to be tested is that the outcome in the HDM arm is better than in the VMP arm.

2nd randomization:

The hypothesis to be tested is that the outcome in the arm with VRD consolidation followed by lenalidomide maintenance is better than in the arm with lenalidomide maintenance alone.

Onderzoeksopzet

1. At entry: Before start of treatment (results from diagnostic tests may be used, provided that they are no older than 4 weeks prior to randomization);

2. After VCD III: 4 weeks after end of the 3rd VCD cycle;

3. After VMP: After the 2nd VMP and 4 weeks after end of the 4th VMP cycle;

4. After HDM: 8 weeks after each course of HDM;

5. After VRD: 4 weeks after end of the 2nd VRD cycle;

6. During maintenance/follow up: Every 2 months

Onderzoeksproduct en/of interventie

Patients with multiple myeloma, meeting all eligibility criteria will be registered on entry and treated with 3 induction cycles with VCD, followed by Cyclophosphamide for stem cell mobilization and collection.

After induction patients will be randomized to compare two intensification regimens VMP vs. HDM (R1), except if a patient will proceed to allogenic SCT. In hospitals with a policy of double intensification, all patients will be randomized at R1 between VMP, 1 HDM and 2 HDM, in order also to evaluate 1 HDM vs. 2 HDM.

After intensification treatment there will be a 2nd randomization to compare VRD consolidation vs. no consolidation (R2), followed by Lenalidomide maintenance in both arms.

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Patients with a confirmed diagnosis of symptomatic multiple myeloma stage I to III according to the International Staging System ISS, i.e. at least one of the CRAB criteria should be present;

2. Measurable disease as defined by the presence of M-protein in serum or urine (serum Mprotein > 10 g/l or urine M-protein > 200 mg/24 hours), or abnormal free light chain ratio;

3. Age 18-65 years inclusive;

4. WHO performance status 0-3 (WHO=3 is allowed only when caused by MM and not by comorbid conditions);

5. Negative pregnancy test at inclusion if applicable;

6. Written informed consent.

Inclusion for randomisation 1:

1. WHO performance 0-2;

2. Bilirubin and transaminases < 2.5 times the upper limit of normal values;

3. A suitable stem cell graft containing at least 4 x 106 CD34+ cells/kg (or according to national guidelines).

Inclusion for randomisation 2:

1. Bilirubin and transaminases < 2.5 times the upper limit of normal values;

2. ANC >= 0.5 x 109/l and platelets > 20 x 10^9/l;

3. Patient is able to adhere to the requirements of the Lenalidomide Pregnancy Prevention Risk Management Plan.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Known intolerance of Boron;

2. Systemic AL amyloidosis;

3. Primary Plasmacell Leukemia;

4. Non-secretory MM;

5. Previous chemotherapy or radiotherapy except local radiotherapy in case of local myeloma progression or corticosteroids maximum 5 days for symptom control;

6. Severe cardiac dysfunction (NYHA classification II-IV, see appendix E);

7. Significant hepatic dysfunction, unless related to myeloma;

8. Patients with GFR <15 ml/min;

9. Patients known to be HIV-positive;

10. Patients with active, uncontrolled infections;

11. Patients with neuropathy, CTC grade 2 or higher;

12. Patients with a history of active malignancy during the past 5 years with the exception of basal carcinoma of the skin or stage 0 cervical carcinoma;

13. Patients who are not willing or capable to use adequate contraception during the therapy (all men, all pre-menopausal women);

14. Lactating women.

Exclusion for randomisation 1:

1. Severe pulmonary, neurologic, or psychiatric disease;

2. CTCAE grade 3-4 polyneuropathy during Bortezomib treatment;

3. Allogeneic Stem Cell Transplantation (Allo SCT) planned;

4. Progressive disease.

Exclusion for randomisation 2:

1. Progressive disease;

2. Neuropathy, except CTCAE grade 1;

3. CTCAE grade 3-4 polyneuropathy during Bortezomib treatment.

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-10-2010
Aantal proefpersonen:	1500
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	21-09-2010
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	NL2420
NTR-old	NTR2528
Ander register	EudraCT : 2009-017903-28
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A