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.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28960

Source
Nationaal Trial Register

Brief title
HOVON 95 MM

Health condition

Multiple Myeloma (Kahler’s disease)

Sponsors and support

Primary sponsor: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)
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Source(s) of monetary or material Support: HOVON receives unrestricted grants and/or financial support from Amgen, Johnson&Johnson-Orthobiotech, Roche and Novartis for the execution of investigator sponsored trials.
In addition HOVON is supported by the Dutch Cancer Society.

Intervention

Outcome measures

Primary outcome

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.

Secondary outcome

1. Response (PR, VGPR, CR and stringent CR), and improvement of response during the various stages of the treatment;

2. Overall survival measured from the time of registration /randomization R1/ randomization R2. Patients still alive or lost to follow up are censored at the date they were last known to be alive;

3. Toxicity.

Study description

Background summary

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.

Study objective

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.

Study design

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

Intervention

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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Eligibility criteria

Inclusion criteria

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.

Exclusion criteria

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.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2010
Enrollment:	1500
Type:	Anticipated

Ethics review

Positive opinion

Date:	21-09-2010
Application type:	First submission

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
NTR-new	NL2420
NTR-old	NTR2528
Other	EudraCT : 2009-017903-28
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A