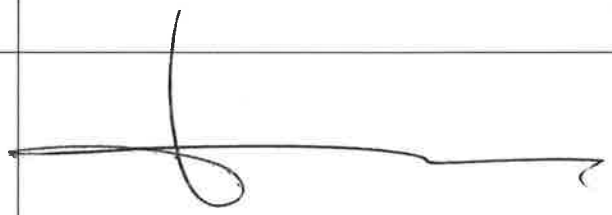
End of trial report

Sponsor:	HOVON foundation
Trial:	HOVON 108 MM
EudraCT:	2010-018494-37
Title of study:	A phase II study for the evaluation of T cell repleted allogeneic stem cell transplantation followed by early consolidation with bortezomib and subsequent DLI for patients with multiple myeloma in progression or relapse following first line therapy
Report date:	09-OCT-14

Signature	
Name:	Dr. H. Lokhorst
Function:	Principal Investigator
Date:	11 november 2014
Signature:	

Publications:

No publications yet

Studied period:

Date of inclusion of first patient: 15SEP11

date end of trial (last FU received): 31JUL14

Phase of development:

Phase 2

Objectives:

Primary objective:

Assessment of feasibility and toxicity of T cell depleted NMA Allo-SCT followed by lenalidomide or Lenalidomide combined with bortezomib, and subsequent DLI; as

treatment of relapsed multiple myeloma.

Secondary objectives:

To investigate the efficacy of this regimen in terms of complete remission rate, overall and progression free survival.

To evaluate quality of life with these regimens.

Methodology:

Randomized phase II trial for patients 18 - 65 years, with high risk multiple myeloma in relapse or progression following first line therapy and achieving at least PR after reinduction with an HLA-identical sibling or unrelated donor.

T cell depleted NMA Allo-SCT followed by 3 cycles of lenalidomide 10 mg/daily or lenalidomide 10 mg/daily combined with weekly bortezomib 1.3 mg/m2, and preemptive DLI. The conditioning of NMA Allo-SCT is performed with melphalan/fludarabine and in vitro and in vivo T cell depletion with Alemtuzumab in combination with ciclosporin.

Number of patients:

Planned: 110

Enrolled: 31

Analyzed: 0

Enrolled but not analyzed, including reason:

Based on unexpected toxicity of the allo-sct procedure the study was prematurely stopped. Unexpected toxicity was not related to the IMP bortezomib. Due to the low number of patients included in the study no valuable results can be obtained from the analysis of the study except that this scheme of transplantation is not feasible for a multicentre trial

Diagnosis and main criteria for inclusion:

Eligibility for registration/randomization

All patients must be registered and randomized before start of Allo-SCT treatment and must meet all of the following eligibility criteria.

Inclusion criteria

- Patients with multiple myeloma with a first relapse or progression after first line therapy;
- Relapsed or progressive patients have received reinduction therapy before entering this trial;
- At least a PR after reinduction treatment;
- 18-65 years,inclusive;
- HLA-identical sibling or unrelated donor completely matched (10/10) (excluding identical twins);
- WHO-performance status 0-2;
- Written informed consent.

Exclusion criteria

- Previous Allo-SCT;
- Severe pulmonary dysfunction (CTCAE grade III-IV, see appendix D);
- Severe neurological or psychiatric disease;
- Patients with neuropathy, CTC grade 3 or higher;
- Significant hepatic dysfunction (serum bilirubin or transaminases ≥ 3 times upper limit of normal);
- Significant renal dysfunction (creatinine clearance < 30 ml/min after rehydration);
- Concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled diabetes, infection, hypertension, cancer, etc.);
- History of active malignancy during the past 5 years with the exception of basal carcinoma of the skin or or carcinoma "in situ" of the cervix or breast;
- Patient known to be HIV-positive;
- Patients with brain disease with the exception of those patients whose brain disease has been treated with either radiotherapy or surgery and remains asymptomatic, with no active brain disease, as shown by CT scan or MRI, for at least 6 months;

Investigational Medicinal Product(s), dose and mode of administration:

Bortezomib 1,3 mg/m^2 iv days 1, 8 and 15 for 3 cycles

Duration of treatment:

9 months

Comparator(s), dose and mode of administration:

No comparator

Duration of treatment:

Not applicable, no comparator

Criteria for evaluation - Efficacy:

- To investigate the efficacy of this regimen in terms of complete remission rate, overall and progression free survival;

However due to the low numbers of patients included a reliable evaluation of efficacy is not possible

Criteria for evaluation - Safety:

We had the policy of Rapid Toxicity Reporting and immediate SAE evaluation. Criteria for safety were SAE's, SUSAR's, early death, acute GvHD grade 4 and chronic extensive GvHD. Definite evaluation of safety was done by the DSMB.

Statistical methods:

Not relevant as not enough patients were included for a valuable statistical analysis

Summary of efficacy results:

Not relevant as not enough patients were included for a valuable statistical analysis

Summary of safety results:

Based in the opinion of the DSMB and subsequently by HOVON it was decided to stop the trial due to unexpected toxicity not related to the IMP Bortezomib

Conclusions:

Allogeneic–SCT for relapsed myeloma with melphalan and fludarabine conditioning and T cell depletion with alemtuzumab was not feasible in a multi center setting. For safety reasons the study was stopped prematurely. Analysis of efficacy was not possible due to the low numbers of patients included.

Investigational sites & investigators

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