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A randomised phase III study on the effect of bortezomib combined with adriamycin, dexamethasone (AD) for induction treatment, followed by high dose melphalan and bortezomib alone during maintenance in patients with multiple myeloma

Submission date 13/09/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 03/11/2005	**Overall study status** Completed	
Last Edited 03/09/2013	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Pieter Sonneveld

Contact details
Erasmus MC
Dept of Hematology
P.O. Box 2040
Rotterdam
Netherlands
3000 CA
p.sonneveld@erasmusmc.nl

Additional identifiers

Clinical Trials Information System (CTIS)
2004-000944-26

Protocol serial number
26866138MMY3003; HO65

Study information

Scientific Title

Acronym
HOVON65/GMMG-HD4

Study objectives
Bortezomib combined with intensive chemotherapy and in maintenance therapy is superior in comparison with intensive therapy with vincristine followed by thalidomide maintenance in patients with previously untreated multiple myeloma, as measured by response rate and progression-free and overall survival.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the local medical ethics committee

Study design
Prospective, multicentre, randomised, active controlled, parallel group trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Multiple myeloma

Interventions
Arm A: Standard Vincristine, Adriamycin and Dexamethasone (VAD) induction, followed by intensive chemotherapy with melphalan 200 mg/m^2 and autologous blood stem cell transplantation, followed by maintenance therapy with thalidomide.

Arm B: Induction chemotherapy with Bortezomib, Adriamycin and Dexamethasone (BAD) followed by intensive chemotherapy with melphalan 200 mg/m^2 and autologous blood stem cell transplantation, followed by maintenance with bortezomib.

Duration of treatment:
Expected duration of induction, stem cell collection and intensification (with or without Bortezomib) is six to seven months. Maintenance therapy with Bortezomib or Thalidomide will be given for two years.

Please note that the anticipated end date of this trial has been shortened to 22nd April 2007.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Bortezomib, vincristine, adriamycin, dexamethasone and melphalan

Primary outcome(s)
Progression Free Survival (PFS), i.e. time from registration to progression, relapse or death from any cause.

Key secondary outcome(s))
1. Response (Partial Remission [PR], very Good Partial Remission [vGPR] and Complete Remission [CR])
2. Overall Survival (OS)
3. PFS from High-Dose Therapy (HDT) i.e. time from last High-Dose Melphalan (HDM) treatment to progression, relapse or death from any cause whichever occurs first for patients who received at least PR on HDT
4. Toxicity
5. PFS analysed as primary endpoint, but patients with an allogeneic transplant not censored. This primarily to check whether censoring has a major impact.

Completion date
30/09/2011

Eligibility

Key inclusion criteria
1. Patients with a confirmed diagnosis of multiple myeloma stage II or III according to the Salmon and Durie criteria
2. Age 18 to 65 years inclusive
3. World Health Organisation (WHO) performance status zero to three (WHO = three is allowed only when caused by multiple myeloma and not by co-morbid conditions)
4. Negative pregnancy test at inclusion if applicable
5. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Known intolerance of thalidomide or boron
2. Systemic AL amyloidosis
3. Non-secretory multiple myeloma
4. Previous chemotherapy or radiotherapy except two cycles of melphalan/prednisone or local radiotherapy in case of local myeloma progression
5. Severe cardiac dysfunction (New York Heart Association [NYHA] classification II - IV)
6. Significant hepatic dysfunction (serum bilirubin more than or equal to 30 µmol/l or transaminases more than or equal to 2.5 times normal level), unless related to myeloma
7. Patients known to be Human Immunodeficiency Virus (HIV) positive
8. Patients with active, uncontrolled infections
9. Patients with neuropathy, CTC grade two or higher
10. Patients with a history of active malignancy during the past five years with the exception of basal carcinoma of the skin or stage zero cervical carcinoma
11. Patients who will not give permission for collection of Bone Marrow (BM) aspirate at entry
12. Patients who are not willing or capable to use adequate contraception during the therapy (all men, all pre-menopausal women)
13. Patients 65 years or less with a Human Leukocyte Antigen (HLA) identical sibling who will undergo non-myeloablative AlloSCT
14. Lactating women

Date of first enrolment
01/05/2005

Date of final enrolment
30/09/2011

Locations

Countries of recruitment
Germany

Netherlands

Study participating centre
Erasmus MC
Rotterdam
Netherlands
3000 CA

Sponsor information

Organisation
Dutch Haemato-oncology Association (Stichting Haemato-Oncologie voor Volwassenen Nederland [HOVON])

ROR
https://ror.org/056kpdx27

Funder(s)

Funder type
Industry

Funder Name
Johnson & Johnson

Alternative Name(s)
Johnson & Johnson, Johnson & Johnson Services, Inc., Johnson&Johnson, Johnson & Johnson Private Limited, , , J&J, JNJ

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Funder Name
Amgen

Alternative Name(s)
Amgen Inc., Applied Molecular Genetics Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Funder Name
Chugai

Funder Name
Novartis

Alternative Name(s)
Novartis AG, Novartis International AG

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Funder Name
Roche

Alternative Name(s)
F. Hoffmann-La Roche Ltd, F. Hoffmann-La Roche & Co, F. Hoffmann-La Roche AG, Roche Holding AG, Roche Holding Ltd, Roche Holding, Roche Holding A.G., Roche Holding, Limited, F. Hoffmann-La Roche & Co., Roche Holdings, Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Funder Name
German Federal Ministry of Education and Research

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/11/2011		Yes	No
Results article	results	26/01/2012		Yes	No
Results article	results	24/01/2013		Yes	No
Results article	results	01/01/2014		Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes