

# The GMMG-HD5 trial: bortezomib-based induction prior to high dose therapy and autologous stem cell transplantation followed by lenalidomide-based consolidation and maintenance therapy in patients with multiple myeloma

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|----------------------------------------|---------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| <b>Submission date</b><br>28/10/2009   | <b>Recruitment status</b><br>No longer recruiting | <input checked="" type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol            |
| <b>Registration date</b><br>11/11/2009 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input type="checkbox"/> Results                       |
| <b>Last Edited</b><br>11/11/2009       | <b>Condition category</b><br>Cancer               | <input type="checkbox"/> Individual participant data<br><input type="checkbox"/> Record updated in last year |

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Protocol serial number**  
GMMG-HD5

# Study information

## Scientific Title

Phase III trial in patients with multiple myeloma to optimize bortezomib based induction (bortezomib, Adriamycin®, dexamethasone [PAd] vs. bortezomib, cyclophosphamide, dexamethasone [VCD]) prior to high dose therapy and autologous stem cell transplantation followed by lenalidomide based consolidation and maintenance therapy

## Acronym

GMMG-HD5

## Study objectives

The GMMG-HD5 trial is designed to address two independent primary objectives:

1. Demonstration of non-inferiority of VCD induction therapy compared to PAd induction therapy with respect to response rate (very good partial remission or better; response criteria of the International Myeloma Working Group [IMWG])
2. Determination of the best of four treatment strategies with respect to progression-free survival (PFS). The four treatment strategies are defined by PAd versus VCD induction treatment, High Dose melphalan Therapy (HDT) followed by autologous stem cell transplantation and maintenance treatment with lenalidomide for 2 years versus lenalidomide until complete remission (CR).

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Ethikkommission der Medizinischen Fakultät Heidelberg, University of Heidelberg, submission planned for November 2009

## Primary study design

Interventional

## Study design

Prospective multicentre multinational randomised parallel group open phase III clinical trial

## Study type(s)

Treatment

## Health condition(s) or problem(s) studied

Multiple myeloma

## Interventions

1. Patients are randomised into four treatment arms (A1, A2, B1, B2)
2. Patients included in arms A1/B1 are treated with 3 cycles PAd (bortezomib 1.3 mg/m<sup>2</sup> intravenous [iv] on days 1, 4, 8 and 11, doxorubicin 9 mg/m<sup>2</sup> iv on days 1, 4, dexamethasone [Dex] orally [po] 20 mg/d on days 1 - 4, 9 - 12 and 17 - 20)
3. Patients in arm A2/B2 are treated with 3 cycles VCD (bortezomib 1.3 mg/m<sup>2</sup> iv on days 1, 4, 8 and 11, cyclophosphamide 900 mg/m<sup>2</sup> iv on day 1, dexamethasone po 40 mg/d on days 1 - 2, 4 - 5, 8 - 9, 11 - 12)
4. Stem cells are mobilised by CAD (cyclophosphamide iv 1 g/m<sup>2</sup> on day 1, doxorubicin 15 mg

/m<sup>2</sup> iv on days 1 - 4, Dex po 40 mg/d on days 1 - 4) and G-CSF. At least 5 x 10<sup>6</sup> CD34+ cells/kg body weight have to be harvested.

5. High dose therapy (HDT, melphalan 200 mg/m<sup>2</sup>) is started 4 - 6 weeks after CAD

6. For patients not reaching a CR after HDT1, a second HDT is performed within 2 - 3 months after HDT1. Thereafter, two cycles of lenalidomide 25 mg/d on days 1 - 21 are given, followed by a lenalidomide maintenance treatment (lenalidomide po 10 mg/d in the first three months, thereafter 15 mg/d).

7. In arms A1 and A2 lenalidomide maintenance will be given for a period of 2 years, in arms B1 and B2 until a CR is reached

## **Intervention Type**

Drug

## **Phase**

Phase III

## **Drug/device/biological/vaccine name(s)**

PAd (bortezomib/PS341 [Velcade®], doxorubicin [Adriamycin®], dexamethasone), VCD (bortezomib, cyclophosphamide, dexamethasone), melphalan, lenalidomide

## **Primary outcome(s)**

1. Response to treatment (very good partial remission or better) after induction therapy
2. Progression free survival (i.e., time from randomisation to progression or death from any cause, whichever occurs first)

Patients will be investigated for progression after every treatment phase (induction, HDT, consolidation) and then every 3 months in maintenance treatment and follow up

## **Key secondary outcome(s)**

1. Overall survival defined as time from randomisation to death from any cause. Patients still alive or lost to follow up are censored at the date they were last known to be alive.
2. Response to be measured after induction, after transplantation, after consolidation and during maintenance
  - 2.1. Partial remission (PR)
  - 2.2. Very good partial remission (VGPR)
  - 2.3. Complete remission (CR)
  - 2.4. Molecular complete remission (mCR)
3. Toxicity ([serious] adverse events CTC grade 3 and grade 4, CTC-AE v4.0) related to induction, consolidation and maintenance treatment
4. Progression free survival from HDT (i.e., time from last HDT treatment to progression or death from any cause whichever occurs first)

## **Completion date**

01/01/2016

## **Eligibility**

### **Key inclusion criteria**

1. Confirmed diagnosis of multiple myeloma requiring systemic therapy
2. Measurable disease
3. Age 18 - 70 years inclusive, either sex

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

All

**Key exclusion criteria**

1. Previous chemotherapy or radiotherapy during the past 5 years except local radiotherapy in case of local myeloma progression
2. Severe cardiac dysfunction
3. Significant hepatic dysfunction
4. Patients known to be human immunodeficiency virus (HIV)-positive
5. Patients with active, uncontrolled infections
6. Patients with peripheral neuropathy or neuropathic pain, Common Toxicity Criteria (CTC) grade 2 or higher
7. Patients with a history of active malignancy during the past 5 years
8. Systemic AL amyloidosis

**Date of first enrolment**

01/01/2010

**Date of final enrolment**

01/01/2016

**Locations****Countries of recruitment**

France

Germany

**Study participating centre**

Universitätsklinikum Heidelberg

Heidelberg

Germany

69120

**Sponsor information**

**Organisation**

Heidelberg University (Germany)

**ROR**

<https://ror.org/038t36y30>

**Funder(s)****Funder type**

Industry

**Funder Name**

Celgene (Europe) (ref: RV-MM-GMMG-0423)

**Alternative Name(s)**

Celgene Corporation

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

For-profit companies (industry)

**Location**

United States of America

**Funder Name**

Janssen Cilag (Europe) (ref: 26866138MMY3026)

**Funder Name**

Chugai (UK)

**Funder Name**

The Binding Site (UK)

**Funder Name**

University Hospital Heidelberg (Germany)

# Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration