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# 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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| **Submission date**<br>28/10/2009 | **Recruitment status**<br>No longer recruiting | [X] Prospectively registered<br>[ ] Protocol<br>[ ] Statistical analysis plan<br>[ ] Results<br>[ ] Individual participant data<br>[ ] Record updated in last year |
| **Registration date**<br>11/11/2009 | **Overall study status**<br>Completed | |
| **Last Edited**<br>11/11/2009 | **Condition category**<br>Cancer | |

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

## Contact information

**Type(s)**
Scientific

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## Additional identifiers

**EudraCT/CTIS number**

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
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 Fakultaet Heidelberg, University of Heidelberg, submission planned for November 2009

### Study design
Prospective multicentre multinational randomised parallel group open phase III clinical trial

### Primary study design
Interventional

### Secondary study design
Randomised controlled trial

### Study setting(s)
Hospital

### Study type(s)
Treatment

## Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

## 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^2 intravenous [iv] on days 1, 4, 8 and 11, doxorubicin 9 mg/m^2 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^2 iv on days 1, 4, 8 and 11, cyclophosphamide 900 mg/m^2 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^2 on day 1, doxorubicin 15 mg /m^2 iv on days 1  4, Dex po 40 mg/d on days 1 - 4) and G-CSF. At least 5 x 10^6 CD34+ cells/kg body weight have to be harvested.
5. High dose therapy (HDT, melphalan 200 mg/m^2) 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 measure
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

## Secondary outcome measures
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)

### Overall study start date
01/01/2010

### 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

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants
504

### 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)

**Sponsor details**
Im Neuenheimer Feld 672
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**Sponsor type**
University/education

**Website**
http://www.uni-heidelberg.de/index_e.html

**ROR**
https://ror.org/038t36y30

# Funder(s)

**Funder type**
Industry

**Funder Name**
Celgene (Eurpope) (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

**Publication and dissemination plan**
Not provided at time of registration

**Intention to publish date**

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**
Not provided at time of registration