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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

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

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 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

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^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(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
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69120

Sponsor information

Organisation
Heidelberg University (Germany)

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

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration