A Phase III Trial on the Effect of Elotuzumab in VRD Induction /Consolidation and Lenalidomide Maintenance in Patients With Newly Diagnosed Myeloma (GMMG-HD6)

This study is currently recruiting participants. (see Contacts and Locations)

Verified July 2015 by University of Heidelberg Medical Center

Sponsor:
University of Heidelberg Medical Center

Information provided by (Responsible Party):
Prof. Dr. Hartmut Goldschmidt, University of Heidelberg Medical Center

ClinicalTrials.gov Identifier:
NCT02495922

First received: June 24, 2015
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History of Changes

Purpose

Trial in patients with newly diagnosed myeloma to evaluate the effect of elotuzumab in induction and consolidation therapy with bortezomib/lenalidomide/dexamethasone and in lenalidomide maintenance treatment

Condition	Intervention	Phase
Multiple Myeloma	Drug: elotuzumab Drug: Lenalidomide Drug: Bortezomib Drug: Dexamethasone	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: A Randomized Phase III Trial on the Effect of Elotuzumab in VRD Induction /Consolidation and Lenalidomide Maintenance in Patients With Newly Diagnosed Myeloma

Resource links provided by NLM:

MedlinePlus related topics: Multiple Myeloma

Drug Information available for: Dexamethasone Dexamethasone sodium phosphate Dexamethasone acetate Bortezomib Lenalidomide

Genetic and Rare Diseases Information Center resources: Multiple Myeloma

U.S. FDA Resources

Further study details as provided by University of Heidelberg Medical Center:

Primary Outcome Measures:

- the best of four treatment strategies regarding Progression Free Survival (PFS) [Time Frame: time from randomization to progression or death from any cause whichever comes first, censored after two years of maintenance therapy (i.e. approx. after 36 months after randomisation)] [Designated as safety issue: No]

  response evaluation

Secondary Outcome Measures:

- overall survival [Time Frame: time from randomisation to time of death from any cause. Patients still being alive at the time of the analysis w ill be censored at the date last know n to be alive. (assessed up to 80 months)] [Designated as safety issue: No]

  survival status

- complete response rates after induction [Time Frame: approx. after 3 months (after induction therapy)] [Designated as safety issue: No]

  response evaluation

- complete response rates after consolidation [Time Frame: approx. after 9 months (after consolidation therapy)] [Designated as safety issue: No]

  response evaluation

- Progression Free Survival after end of trial [Time Frame: time from randomisation to progression or death from any cause w hichever comes first, censored at the end date of the trial (i.e. assessed up to 80 months)] [Designated as safety issue: No]

  response evaluation

- best response to treatment during the study [Time Frame: response assessment after ca. 3 months, 4 months, 7 months, 9 months,11 months, 14 months, and subsequently every 3 months during maintenance treatment, up to 35 months after start of study treatment.] [Designated as safety issue: No]

  response evaluation

- time to progression, censored at end of the trial [Time Frame: From date of randomization until the date of first documented progression, assessed up to 80 months] [Designated as safety issue: No]

  Response evaluation

- duration of response, censored at end of the trial [Time Frame: assessed up to 80 months] [Designated as safety issue: No]

  response evaluation

- toxicity during induction treatment, consolidation and maintenance treatment w ith respect to adverse Events of CTCAE grade 3 or higher [Time Frame: from first administration of study drug until 40 days after last administration of study drug or any drug of the study treatment or upon start of a new subsequent chemotherapy, w hichever occurs first] [Designated as safety issue: Yes]

  toxicity according CTCAE Version 4.0

- Quality of Life assessment [Time Frame: assessed at baseline, after ca. 3 months, 7 months, 9 months, subsequently every 6 months, up to 36 months] [Designated as safety issue: No]

  Questionnaires EORTC-QLQC30 and EORTC-QLQMY20

Estimated Enrollment:	516
Study Start Date:	June 2015
Estimated Study Completion Date:	March 2022
Estimated Primary Completion Date:	June 2021 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Active Comparator: A1 Induction therapy w ith 4 cycles VRD (Velcade, Revlimid, Dexamethasone), 21 days per cycle, intensification (mobilization and autologous stem cell transplantation), consolidation therapy w ith 2 cycles VRD (Velcade, Revlimid, Dexamethasone), 21 days per cycle. Maintenance therapy: 26 cycles (28 days) w ith lenalidomide (Dexamethasone on day 1 and 15 in cycles 1-6 and on day 1 in cycles 7 to 26).	Drug: Lenalidomide 25 mg per os on day 1-14 in induction cycle 1-4, 25 mg p.o. on day 1-14 in consolidation cycle 1 and 2, 10 mg p.o. on day 1-28 in maintenance cycle 1-3, 15 mg p.o. on day 1-28 in maintenance cycle 4-26 (all arms) Other Name: Revlimid Drug: Bortezomib all arms: 1,3 mg/m^2 subcutaneous on day 1, 4, 8 and 11 in 4 induction cycles, 1,3 mg/m^2 subcutaneous on day 1, 8 and 15 in 2 cycles of consolidation Other Name: Velcade

	Drug: Dexamethasone 20 mg per os on day 1,2 and 4,5 and 8,9 and 11,12 and 15 in induction cycles 1 and 2. 20 mg per os on day 1,2 and 4,5 and 8,9 and 11,12 in induction cycles 3 and 4 (Arms A1 and A2). 8 mg per os and 12 mg i.v. on day 1, 8 and 15 and 20 mg per os on days 2,4,5, 9, 11 and 12 in induction cycles 1 and 2. 8 mg per os and 12 mg i.v. on day 1, and 11, 20 mg per os on days 2,4,5,8, 9, and 12 in induction cycles 3 and 4 (Arms B1 and B2). 20 mg per os on days 1,2, 8,9, 15 and 16 in both cycles of consolidation (Arms A1 and B1). 8 mg per os and 12 mg i.v. on days 1, 8 and 15 and 20 mg per os on days 2, 9 and 16 in both consolidation cycles (Arms A2 and B2). 12 mg per os on day 1 and 15 in maintenance cycles 1-6, 12 mg per os on day 1 of maintenance cycles 7 and follow ing (Arms A1 and B1). 4 mg per os and 8 mg i.v. on day 1 and 15 in maintenance cycles 1-6, 4 mg per os and 8 mg i.v. on day 1 of maintenance cycles 7 and follow ing (Arms A2 and B2).
Experimental: A2 Induction therapy w ith 4 cycles VRD (Velcade, Revlimid, Dexamethasone) 21 days per cycle, intensification (mobilization and autologous stem cell transplantation), consolidation therapy w ith 2 cycles VRD (Velcade, Revlimid, Dexamethasone) + elotuzumab, 21 days per cycle. Maintenance therapy: 26 cycles (28 days) w ith lenalidomide + elotuzumab (Dexamethasone on day 1 and 15 in cycles 1-6 and on day 1 in cycles 7 to 26).	Drug: elotuzumab 10 mg/kg in the vein(i.v) on day 1,8 and 15 in induction cycle 1 and 2, on day 1 and 11 in induction cycle 3 and 4 (Arm B1 and B2). 10 mg/kg i.v. on day 1,8 and 15 in consolidation cycle 1 and 2 (Arm A2 and B2), 10 mg/kg i.v. on day 1 and15 in maintenance cycle 1-6, 10 mg/kg i.v. on day 1 in maintenance cycle 7-26 (Arm A2 and B2) Drug: Lenalidomide 25 mg per os on day 1-14 in induction cycle 1-4, 25 mg p.o. on day 1-14 in consolidation cycle 1 and 2, 10 mg p.o. on day 1-28 in maintenance cycle 1-3, 15 mg p.o. on day 1-28 in maintenance cycle 4-26 (all arms) Other Name: Revlimid Drug: Bortezomib all arms: 1,3 mg/m^2 subcutaneous on day 1, 4, 8 and 11 in 4 induction cycles, 1,3 mg/m^2 subcutaneous on day 1, 8 and 15 in 2 cycles of consolidation Other Name: Velcade Drug: Dexamethasone 20 mg per os on day 1,2 and 4,5 and 8,9 and 11,12 and 15 in induction cycles 1 and 2. 20 mg per os on day 1,2 and 4,5 and 8,9 and 11,12 in induction cycles 3 and 4 (Arms A1 and A2). 8 mg per os and 12 mg i.v. on day 1, 8 and 15 and 20 mg per os on days 2,4,5, 9, 11 and 12 in induction cycles 1 and 2. 8 mg per os and 12 mg i.v. on day 1, and 11, 20 mg per os on days 2,4,5,8, 9, and 12 in induction cycles 3 and 4 (Arms B1 and B2). 20 mg per os on days 1,2, 8,9, 15 and 16 in both cycles of consolidation (Arms A1 and B1). 8 mg per os and 12 mg i.v. on days 1, 8 and 15 and 20 mg per os on days 2, 9 and 16 in both consolidation cycles (Arms A2 and B2). 12 mg per os on day 1 and 15 in maintenance cycles 1-6, 12 mg per os on day 1 of maintenance cycles 7 and follow ing (Arms A1 and B1). 4 mg per os and 8 mg i.v. on day 1 and 15 in maintenance cycles 1-6, 4 mg per os and 8 mg i.v. on day 1 of maintenance cycles 7 and follow ing (Arms A2 and B2).

Experimental: B1 Induction therapy w ith 4 cycles VRD (Velcade, Revlimid, Dexamethasone) + elotuzumab , 21 days per cycle, intensification (mobilization and autologous stem cell transplantation), consolidation therapy w ith 2 cycles VRD (Velcade, Revlimid, Dexamethasone) 21 days per cycle. Maintenance therapy: 26 cycles (28 days) w ith lenalidomide (Dexamethasone on day 1 and 15 in cycles 1-6 and on day 1 in cycles 7 to 26).	Drug: elotuzumab 10 mg/kg in the vein(i.v) on day 1,8 and 15 in induction cycle 1 and 2, on day 1 and 11 in induction cycle 3 and 4 (Arm B1 and B2). 10 mg/kg i.v. on day 1,8 and 15 in consolidation cycle 1 and 2 (Arm A2 and B2), 10 mg/kg i.v. on day 1 and15 in maintenance cycle 1-6, 10 mg/kg i.v. on day 1 in maintenance cycle 7-26 (Arm A2 and B2) Drug: Lenalidomide 25 mg per os on day 1-14 in induction cycle 1-4, 25 mg p.o. on day 1-14 in consolidation cycle 1 and 2, 10 mg p.o. on day 1-28 in maintenance cycle 1-3, 15 mg p.o. on day 1-28 in maintenance cycle 4-26 (all arms) Other Name: Revlimid Drug: Bortezomib all arms: 1,3 mg/m^2 subcutaneous on day 1, 4, 8 and 11 in 4 induction cycles, 1,3 mg/m^2 subcutaneous on day 1, 8 and 15 in 2 cycles of consolidation Other Name: Velcade Drug: Dexamethasone 20 mg per os on day 1,2 and 4,5 and 8,9 and 11,12 and 15 in induction cycles 1 and 2. 20 mg per os on day 1,2 and 4,5 and 8,9 and 11,12 in induction cycles 3 and 4 (Arms A1 and A2). 8 mg per os and 12 mg i.v. on day 1, 8 and 15 and 20 mg per os on days 2,4,5, 9, 11 and 12 in induction cycles 1 and 2. 8 mg per os and 12 mg i.v. on day 1, and 11, 20 mg per os on days 2,4,5,8, 9, and 12 in induction cycles 3 and 4 (Arms B1 and B2). 20 mg per os on days 1,2, 8,9, 15 and 16 in both cycles of consolidation (Arms A1 and B1). 8 mg per os and 12 mg i.v. on days 1, 8 and 15 and 20 mg per os on days 2, 9 and 16 in both consolidation cycles (Arms A2 and B2). 12 mg per os on day 1 and 15 in maintenance cycles 1-6, 12 mg per os on day 1 of maintenance cycles 7 and follow ing (Arms A1 and B1). 4 mg per os and 8 mg i.v. on day 1 and 15 in maintenance cycles 1-6, 4 mg per os and 8 mg i.v. on day 1 of maintenance cycles 7 and follow ing (Arms A2 and B2).
Experimental: B2 Induction therapy w ith 4 cycles VRD (Velcade, Revlimid, Dexamethasone) + elotuzumab, 21 days per cycle, intensification (mobilization and autologous stem cell transplantation), consolidation therapy w ith 2 cycles VRD (Velcade, Revlimid, Dexamethasone) + elotuzumab, 21 days per cycle. Maintenance therapy: 26 cycles (28 days) w ith lenalidomide + elotuzumab (Dexamethasone on day 1 and 15 in cycles 1-6 and on day 1 in cycles 7 to 26).	Drug: elotuzumab 10 mg/kg in the vein(i.v) on day 1,8 and 15 in induction cycle 1 and 2, on day 1 and 11 in induction cycle 3 and 4 (Arm B1 and B2). 10 mg/kg i.v. on day 1,8 and 15 in consolidation cycle 1 and 2 (Arm A2 and B2), 10 mg/kg i.v. on day 1 and15 in maintenance cycle 1-6, 10 mg/kg i.v. on day 1 in maintenance cycle 7-26 (Arm A2 and B2) Drug: Lenalidomide 25 mg per os on day 1-14 in induction cycle 1-4, 25 mg p.o. on day 1-14 in consolidation cycle 1 and 2, 10 mg p.o. on day 1-28 in maintenance cycle 1-3, 15 mg p.o. on day 1-28 in maintenance cycle 4-26 (all arms) Other Name: Revlimid Drug: Bortezomib all arms: 1,3 mg/m^2 subcutaneous on day 1, 4, 8 and 11 in 4 induction cycles, 1,3 mg/m^2 subcutaneous on day 1, 8 and 15 in 2 cycles of consolidation Other Name: Velcade Drug: Dexamethasone 20 mg per os on day 1,2 and 4,5 and 8,9 and 11,12 and 15 in induction cycles 1 and 2. 20 mg per os on day 1,2 and 4,5 and 8,9 and 11,12 in induction cycles 3 and 4 (Arms A1

	and A2). 8 mg per os and 12 mg i.v. on day 1, 8 and 15 and 20 mg per os on days 2,4,5, 9, 11 and 12 in induction cycles 1 and 2. 8 mg per os and 12 mg i.v. on day 1, and 11, 20 mg per os on days 2,4,5,8, 9, and 12 in induction cycles 3 and 4 (Arms B1 and B2). 20 mg per os on days 1,2, 8,9, 15 and 16 in both cycles of consolidation (Arms A1 and B1). 8 mg per os and 12 mg i.v. on days 1, 8 and 15 and 20 mg per os on days 2, 9 and 16 in both consolidation cycles (Arms A2 and B2). 12 mg per os on day 1 and 15 in maintenance cycles 1-6, 12 mg per os on day 1 of maintenance cycles 7 and following (Arms A1 and B1). 4 mg per os and 8 mg i.v. on day 1 and 15 in maintenance cycles 1-6, 4 mg per os and 8 mg i.v. on day 1 of maintenance cycles 7 and following (Arms A2 and B2).

Detailed Description:

Prospective, multicentre, randomised, parallel group, open, phase III clinical trial, for patients with confirmed diagnosis of untreated multiple myeloma requiring systemic therapy .

Investigational Medicinal Products:Elotuzumab, lenalidomide

Patients are randomized in one of 4 study arms (A1, A2, B1, B2). Patients randomized in arm A1 or A2 will receive 4 cycles VRD (Bortezomib (Velcade®), Lenalidomide (Revlimid®), Dexamethasone). Patients in arm B1 or B2 will additionally receive the monoclonal antibody Elotuzumab in the 4 cycles VRD. After induction therapy patients undergo intensifying therapy according to GMMG standard (usually mobilization therapy followed by stem cell collection and autologous stem cell transplantation). After intensification a consolidation therapy will be performed with two cycles VRD (A1 und B1) or VRD+ Elotuzumab (A2 und B2), followed by Lenalidomide maintenance therapy with (arm A2 and B2) or without (arm A1 and B1) additional Elotuzumab. Maintenance therapy will be performed for 2 years.

Primary objective is the determination of the best of four treatment strategies regarding progression-free survival (PFS), defined as time from randomisation to progression or death from any cause whichever occurs first.

The duration of the trial for each patients is expected to be 36-39 months (induction and intensification treatment: 7-10 months, 3 months rest between intensification and start of consolidation, consolidation 2 months, maintenance phase 24 months).

Eligibility

Ages Eligible for Study:	18 Years to 70 Years
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Patients meeting all of the following criteria will be considered for admission to the trial:
- Confirmed diagnosis of untreated multiple myeloma requiring systemic therapy (diagnostic criteria (IMWG updated criteria (2014))
- Measurable disease, defined as any quantifiable monoclonal protein value, defined by at least one of the following three measurements:
  - Serum M-protein ≥ 10g/l (for IgA ≥ 5g/l)
  - Urine light-chain (M-protein) of ≥ 200 mg/24 hours
  - Serum FLC assay: involved FLC level ≥ 10 mg/dl provided sFLC ratio is abnormal
- Age 18 - 70 years inclusive
- WHO performance status 0-3 (WHO=3 is allowed only if caused by MM and not by co-morbid conditions)
- Negative pregnancy test at inclusion (women of childbearing potential)
- For all men and women of childbearing potential: patients must be willing and capable to use adequate contraception during the complete therapy. Patients must agree on the requirements regarding the lenalidomide pregnancy prevention programme described in chapter 6.
- All patients must
  - agree to abstain from donating blood while taking lenalidomide and for 28 days following discontinuation of lenalidomide therapy
  - agree not to share study drug lenalidomide with another person and to return all unused study drug to the investigator or pharmacist
- Ability of patient to understand character and individual consequences of the clinical trial
- Written informed consent (must be available before enrollment in the trial)

Exclusion Criteria:

- Patients presenting with any of the following criteria will not be included in the trial:
- Patient has known hypersensitivity to any drugs given in the protocol, notably bortezomib, lenalidomide, dexamethasone and elotuzumab or to any of the constituent compounds (incl. boron and mannitol).
- Systemic AL amyloidosis (except for AL amyloidosis of the skin or the bone marrow)
- Previous chemotherapy or radiotherapy during the past 5 years except local radiotherapy in case of local myeloma progression.
- Severe cardiac dysfunction (NYHA classification III-IV)
- Significant hepatic dysfunction (serum bilirubin ≥ 1,8mg/dl and/or ASAT and/or ALAT ≥ 2.5 times normal level), unless related to myeloma.
- Patients with renal insufficiency requiring hemodialysis
- HIV positivity
- Patients with active or history of hepatitis B or C
- Patients with active, uncontrolled infections
- Patients with peripheral neuropathy or neuropathic pain, CTC grade 2 or higher (as defined by the NCI Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 4.0)
- Patients with a history of active malignancy during the past 5 years with the exception of basal cell carcinoma of the skin or stage 0 cervical carcinoma treated with curative intent
- Patients with acute diffuse infiltrative pulmonary and/or pericardial disease
- Autoimmune hemolytic anemia with positive Coombs test or immune thrombocytopenia
- Platelet count < 75 x 109/l, or, dependent on bone marrow infiltration by plasma cells, platelet count < 30 x 109/l (patients with platelet count < 75 x 109/l, but > 30 x 109/l may be eligible if percentage of plasma cells in bone marrow is ≥ 50%), (transfusion support within 14 days before the test is not allowed)
- Haemoglobin ≤ 8.0 g/dl, unless related to myeloma
- Absolute neutrophil count (ANC) < 1.0 x 10^9/l (the use of colony stimulating factors within 14 days before the test is not allowed), unless related to myeloma
- Pregnancy and lactation
- Participation in other clinical trials. This does not include long-term follow-up periods without active drug treatment of previous studies during the last 6 months.

No patients will be allowed to enrol in this trial more than once.

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02495922

Contacts

Contact: GMMG Study Office	0049-6221-568198 ext n.a.	studiensekretariat.gmmg@med.uni-heidelberg.de
Contact: Uta Bertsch, Dr.	0049-6221-568015	uta.bertsch@med.uni-heidelberg.de

Locations

Germany

Asklepios Klinik Hamburg Altona, II. Med. Klinik — **Not yet recruiting**
Hamburg, Germany, D-22763
Contact: Hans Salwender, Dr.

University Hospital Heidelberg, Med. Klinik V — **Recruiting**
Heidelberg, Germany, D-69120
Contact: GMMG Study Office studiensekretariat.gmmg@med.uni-heidelberg.de
Principal Investigator: Hartmut Goldschmidt, Prof. Dr.

University Hospital Tübingen, Med. Klinik und Poliklinik, Abt. II — **Not yet recruiting**
Tübingen, Germany, D-72076
Contact: Katja Weisel, PD Dr.

Sponsors and Collaborators

University of Heidelberg Medical Center

Investigators

Principal Investigator: Hartmut Goldschmidt, Prof. Dr. Med. Klinik V, University Hospital Heidelberg

More Information

No publications provided

Responsible Party:	Prof. Dr. Hartmut Goldschmidt, Prof. Dr., University of Heidelberg Medical Center
ClinicalTrials.gov Identifier:	NCT02495922 History of Changes
Other Study ID Numbers:	**GMMG HD6**
Study First Received:	June 24, 2015
Last Updated:	July 10, 2015
Health Authority:	Germany: Paul-Ehrlich-Institut

Additional relevant MeSH terms:

Multiple Myeloma	Dexamethasone
Blood Protein Disorders	Dexamethasone 21-phosphate
Cardiovascular Diseases	Dexamethasone acetate
Hematologic Diseases	Lenalidomide
Hemorrhagic Disorders	Angiogenesis Inhibitors
Hemostatic Disorders	Angiogenesis Modulating Agents
Immune System Diseases	Anti-Inflammatory Agents
Immunoproliferative Disorders	Antiemetics
Lymphoproliferative Disorders	Antineoplastic Agents
Neoplasms	Antineoplastic Agents, Hormonal
Neoplasms by Histologic Type	Autonomic Agents
Neoplasms, Plasma Cell	Central Nervous System Agents
Paraproteinemias	Enzyme Inhibitors
Vascular Diseases	Gastrointestinal Agents
BB 1101	Glucocorticoids

ClinicalTrials.gov processed this record on December 06, 2015