This study is currently recruiting participants.

**Verified September 2012** by Wuerzburg University Hospital

**Sponsor:**
Wuerzburg University Hospital

**Collaborators:**
ClinAssess GmbH
Celgene Corporation

**Information provided by (Responsible Party):**
Wuerzburg University Hospital

**ClinicalTrials.gov Identifier:**
NCT01685814

**First received:** June 27, 2012
**Last updated:** September 11, 2012
**Last verified:** September 2012

**History of Changes**

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**Purpose**

The investigators propose this study utilizing Lenalidomide, Adriamycin, Dexamethasone (RAD) as comparator arm for Lenalidomide, Bortezomib, Dexamethasone (VRD) with the latter being considered a novel "standard" as an induction protocol, since response in general occurs early after starting treatment we decided to choose three cycles of either induction regimen.

Together with the "novel compounds", tandem high-dose melphalan is still the standard of care; it seems desirable to re-address the question of the number of transplant (single vs. double high-dose melphalan) procedures required in the context of triplet-induction protocols utilizing at least one of the novel compounds.

Thus, the question to be asked in the current protocol is whether immediate lenalidomide maintenance (i.e. following one cycle of high-dose therapy) as an investigational agent will result in identical progression free survival (PFS) when compared to tandem high-dose melphalan with deferred maintenance therapy.

Despite induction with novel compounds, approximately 25 - 40% of patients will be in less than very good partial response. Very recently, achievement of less than VGPR was confirmed to negatively impact on both PFS as well as overall survival (OS). Therefore, allogeneic stem cell transplantation is considered the standard of care in patients with suboptimal response to a first autograft.

In the current protocol, the standard for favourable responders (tandem-autologous transplant) is combined with 3 years of lenalidomide maintenance. This approach will be investigated for patients with less than VGPR following a first autotransplant and compared to the current standard of intensification in poor responders (allogeneic transplantation).

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**Condition**

Previously Untreated Symptomatic Multiple Myeloma

**Intervention**

Drug: Lenalidomide, Bortezomib

Biological: autologous stem cell transplant

Biological: allogeneic stem cell transplant

**Phase**

Phase 3

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**Study Type:** Interventional

**Study Design:**
Allocation: Randomized

Endpoint Classification: Efficacy Study

Intervention Model: Parallel Assignment

Masking: Open Label

Primary Purpose: Treatment

**Official Title:** Lenalidomide, Adriamycin, Dexamethasone (RAD) Versus Lenalidomide, Bortezomib, Dexamethasone (VRD) for Induction in Newly Diagnosed Multiple Myeloma Followed by Response-adapted Consolidation and Lenalidomide Maintenance - A Randomized Multicenter Phase III Trial by Deutsche Studiengruppe Multiples Myelom (DSMM XIV

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**Resource links provided by NLM:**

MedlinePlus related topics: Multiple Myeloma

Drug Information available for: Dexamethasone, Dexamethasone acetate, Dexamethasone sodium phosphate, Doxorubicin, Doxorubicin hydrochloride, Bortezomib, Lenalidomide

Genetic and Rare Diseases Information Center resources: Multiple Myeloma
Further study details as provided by Wuerzburg University Hospital:

Primary Outcome Measures:
- The primary efficacy endpoint for the induction phase is the rate of patients with CR at first restaging [Time Frame: within 8 days after end of last induction cycle (Day 92(RAD); Day 71(VRD))] [Designated as safety issue: No]
- In the consolidation phase the primary efficacy endpoint for comparison II (response <VGPR after first ASCT) is the PFS rate [Time Frame: 3 years after the first ASCT, calculated from day 1 of ASCT.] [Designated as safety issue: No]

Secondary Outcome Measures:
- ORR following 3 cycles of induction treatment (VRD vs RAD) [Time Frame: within 8 days after end of last induction cycle] [Designated as safety issue: No]
- CR and ORR at the end of the whole treatment programme [Time Frame: at the end of the whole treatment programme (approx. 8 years)] [Designated as safety issue: No]
- Overall survival (OS) [Time Frame: 8 years from study entry] [Designated as safety issue: No]
- Incidence, severity and relationship of SAEs [Time Frame: 30 days post last dosing of study drug] [Designated as safety issue: Yes]
- Numbers of hospital stays and hospitalization days [Time Frame: within two years from second restaging] [Designated as safety issue: No]

Estimated Enrollment: 406
Study Start Date: May 2012
Estimated Study Completion Date: May 2020
Estimated Primary Completion Date: May 2015 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
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<tbody>
<tr>
<td>Active Comparator: single stem cell transplant, 3-year lenalidomide maintenance Arm A</td>
<td>Drug: Lenalidomide, Bortezomib Induction: two versus one novel drug maintenance: lenalidomide as a maintenance therapy Biological: autologous stem cell transplant</td>
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<td>Experimental: tandem autologous transplant, lenalidomide maintenance Arm B</td>
<td>Drug: Lenalidomide, Bortezomib Induction: two versus one novel drug maintenance: lenalidomide as a maintenance therapy Biological: autologous stem cell transplant</td>
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**Eligibility**

Ages Eligible for Study: 18 Years to 65 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

**Criteria**

Inclusion Criteria:
- Understand and voluntarily sign an informed consent form
- Patients willing and able to undergo autologous and allogeneic transplantation
- no previous systemic therapy for the treatment of multiple myeloma (dexamethasone at a cumulative dose of 320 mg; plasmapheresis/dialysis without concomitant chemotherapy, local irradiation of bone lesions; and surgical intervention is accepted as pretreatment)
- Newly diagnosed multiple myeloma according to common diagnostic criteria including presence of CRAB and measurable disease parameters
- Cardiac ejection fraction (LVEF) of at least 50%
- Corrected DLCO of at least 50% ; alternatively pO2 [art.] of at least 70mmHg
- Karnofsky performance status of greater or equal to 50%
- adequate bone marrow function
- adequate serum chemistry values
- Use of adequate contraception for female subjects with childbearing potential and male subjects

For more information, visit: http://clinicaltrials.gov/ct2/show/NCT01685814?term=myeloma&cntr...
Bone marrow sample available for analysis of molecular cytogenetics

Able to administer low molecular-weight heparin as a prophylactic anticoagulation therapy for the first three months (applicable for subjects randomized to RAD) and able to administer ASS 100 mg/d (applicable for subjects randomized to VRD)

Exclusion Criteria:
- Any serious medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from signing the informed consent form
- Pregnant or lactating females
- Any condition, including the presence of laboratory abnormalities, which places the subject at unacceptable risk
- History of myocardial infarction; NYHA Class III or IV heart failure, uncontrolled angina, severe uncontrolled ventricular arrhythmias; concomitant pericarditis or peri-/myocarditis
- Use of any other experimental drug or therapy within 28 days of baseline
- Greater or equal to Grade 2 peripheral neuropathy on clinical examination within 14 days before enrollment
- Known intolerance of boron
- Hypersensitivity to acyclovir or similar anti-viral drug
- Prior malignancy except adequately treated basal cell or squamous cell skin cancer, in situ cervical, breast or prostate cancer
- HIV positive, active hepatitis B, C or D viral infection, known CMV reactivation/active infection, EBV reactivation/active infection or treponema pallidum infection
- Uncontrolled diabetes mellitus
- Non-secretory MM
- Clinically relevant active infection or serious co-morbid medical conditions

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01685814

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<thead>
<tr>
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</thead>
<tbody>
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Lenalidomide, Adriamycin, Dexamethasone (RAD) Versus Lenalidomide... http://clinicaltrials.gov/ct2/show/NCT01685814?term=myeloma&cntr... 27.02.2014 09:58
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More Information
No publications provided

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Study First Received: June 27, 2012
Last Updated: September 11, 2012
Health Authority: Germany: Federal Institute for Drugs and Medical Devices

Keywords provided by Wuerzburg University Hospital:
multiple myeloma
autologous stem cell transplant
allogeneic stem cell transplant
lenalidomide
bortezomib

Additional relevant MeSH terms:
Multiple Myeloma
Neoplasms, Plasma Cell
Neoplasms by Histologic Type
Neoplasms
Hemostatic Disorders
Vascular Diseases
Cardiovascular Diseases
Paraproteinemias
Blood Protein Disorders
Hematologic Diseases
Hemorrhagic Disorders
Lymphoproliferative Disorders
Immunoproliferative Disorders
Immune System Diseases
Dexamethasone acetate

Dexamethasone
Dexamethasone 21-phosphate
Bortezomib
Lenalidomide
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Antiemetics
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Central Nervous System Agents

ClinicalTrials.gov processed this record on February 25, 2014

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