Lenalidomide maintenance combined with Bortezomib following tandem autologous stem cell and non myeloablative allogeneic transplantation for patients with multiple myeloma <= 66 years.

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To study the efficacy of low dose Lenalidomide maintenance combined with bortezomib treatment following non myeloablative Allo-SCT on Event Free Survival.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Plasma cell neoplasms
Study type	Interventional

Summary

ID

NL-OMON35414

Source
ToetsingOnline

Brief title
HOVON 76 MM

Condition

- Plasma cell neoplasms

Synonym
Kahlers disease, multiple myeloma

Research involving
Human

Sponsors and support

Primary sponsor: HOVON
Source(s) of monetary or material Support: stichting HOVON

Intervention

Keyword: kahlers disease, multiple myeloma, Phase II, plasma cell neoplasm

Outcome measures

Primary outcome

Progression Free Survival (PFS)

Secondary outcome

1 Overall survival

2 Safety of lenalidomide

3 Possible in vivo immune modulation of lenalidomide.

Study description

Background summary

Although NMA allogeneic SCT results in a high percentage of complete remissions in multiple myeloma these remissions are not long lasting. Most patients have a recurrence during follow up. One of the potential opportunities to prevent recurrences may be to give maintenance therapy after SCT.
Lenalidomide is currently one of the most promising effective anti-myeloma products. The working mechanism involves the stimulation of the immune system of the patient. The expectation is that maintenance therapy with lenalidomide with its direct anti-myeloma effects will also enhance the Graft versus myeloma reaction of the donor T cells.

Study objective

To study the efficacy of low dose Lenalidomide maintenance combined with bortezomib treatment following non myeloablative Allo-SCT on Event Free Survival.

Study design

The study is designed as a prospective phase 2 study for administration of lenalidomide and bortezomib following non myeloablative Allo-SCT.

Intervention

Non myeloablative allogeneic stem cell transplantation followed by the planned dose of lenalidomide for investigation (which is 10 mg/day), orally for 21 days with 7 days rest (28 day cycle) for in total 2 years or earlier in case of relapse. Bortezomib 1,3 mg/m2 iv, days 1,8,15 monthly for first 3 cycles

Study burden and risks

Due to the immune modulating effects of lenalidomide there remains the possibility of an enhanced Graft versus Host reaction, which may occur after an allogeneic SCT. At this moment it is not known if lenalidomide actually increases Graft versus Host disease and if so to which extent. The investigators expect the probability of increased Graft versus Host reaction to be minor. In case a serious Graft versus Host reaction occurs lenalidomide will be stopped and standard anti-Graft versus Host treatment will be given.
First intrim analysis data:
After 2 cycles of lenalidomide, 41% of patients were withdrawn from the study and 54 %of patients were withdrawn after 4 cycles of lenalidomide. The major cause was rapid development of GvHD after start of lenalidomide. As in the protocol strict stopping rules were defined (development of GvHD >= 2) this was responsible for the high percentage of drop out.
Addition in amendment 4:
After the amendment is in place bortezomib will be added for 3 months to temper the immune side effects of lenalidomide. Bortezomib will be given once weekly, day 1,8,15 of a monthly cycle, in stead of twice weekly. This once weekly administration of Bortezomib has been shown to reduce the incidence of polyneuropathy while its anti myeloma efficacy is probably not reduced (Jesus San Miguel: Personal communication; First results of MP combined with weekly bortezomib).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Age 18-66 years;
-Patients with, before start of induction therapy, a confirmed diagnosis of multiple myeloma stage II or III according to the Salmon & Durie criteria (see appendix A), included in or treated according to the HOVON 65/GMMG-HD4, HOVON 95 or treated according to the guidelines of Hovon Myeloma Study Group for patients <= 66 years group;
-Patient has received 3 cycles induction therapy, followed by stem cell mobilization and 1 cycle of high dose Melphalan with autologous stem cell reinfusion;
-Allogeneic transplantation planned between 2 and 6 months after autologous SCT;
-WHO performance status 0-2 (see appendix D);
-HLA-identical family donor;
-Disease free of prior malignancies for >= 5 years with exception of currently treated basal cell, squamous cell carcinoma of the skin, or carcinoma *in situ* of the cervix or breast.
-Written informed consent for allo SCT treatment as well as lenalidomide maintenance, preferably signed in the presence of both patient and investigator and signed on the same date.;Eligibility for Lenalidomide maintenance combined with bortezomib:
- Laboratory test results within these ranges:
*Absolute neutrophil count >= 1.0 x 109/L
*Platelet count >= 75 x 109/L
*Serum creatinine cleareance >= 50 ml/min
*Total bilirubin <= 30 µmol/l
*AST (SGOT) and ALT (SGPT) <= 3 x Upper Limit of Normal (ULN);
-Negative pregnancy test before inclusion if female of child baring potential;
-Sexually active women of child bearing potential must agree to use 1 adequate contraceptive method while on study drug (and 4 weeks before and after study drug) (for

detailed information see section 9.2.2);
-Men must agree not to father a child and to use a condom if his partner is of childbearing potential.

Exclusion criteria

-Creatinin clearance < 50 ml/min;
-Severe cardiac dysfunction (NYHA classification II-IV, see appendix E);
-Significant hepatic dysfunction (serum bilirubin >= 30 micromol/l or transaminases >= 2.5 times normal level), unless related to myeloma;
-Known positive for HIV;
-Patients with active, uncontrolled infections;
-Patients with brain disease with the exception of those patients whose brain disease has been treated with either radiotherapy or surgery and remains asymptomatic, with no active brain disease, as shown by CT scan or MRI, for at least 6 months;
-Progressive disease / relapse from CR / progression from MR or PR after HDM with autologous stem cell reinfusion;;Exclusion criteria for lenalidomide maintenance combined with bortezomib:
-Progressive myeloma (see appendix B)(within 3 weeks before start therapy, response must be checked and patients who developed progressive myeloma must be excluded);
-Acute Graft versus host Disease >= grade 2 (at time of registration);
-Pregnant or lactating females;
-Concurrent use since NMA Allo SCT of other anti-cancer agents or treatments or use of any other experimental drug or therapy within 28 days of planned start lenalidomide;
-Known hypersensitivity to thalidomide;
-The development of erythema nodosum if characterized by a desquamating rash while taking thalidomide or similar drugs;
-Any prior use of lenalidomide;
-Severe cardiac dysfunction (NYHA classification II-IV, see appendix E);
-Polyneuropathy >= grade 2

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-01-2008
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	revlimid
Generic name:	lenalidomide
Product type:	Medicine
Brand name:	Velcade
Generic name:	Bortezomib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	09-03-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	28-08-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	04-03-2008
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	13-03-2008
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO	

Date:	20-01-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	18-02-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	03-03-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	22-09-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-12-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-02-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2005-003891-39-NL
CCMO	NL15579.041.07