Bortezomib therapy combined with donor lymphocyte infusion in patients with relapsed Multiple Myeloma following allogeneic stem cell transplantation

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25090

Source
NTR

Brief title
DLI-Velcade studie

Health condition

Multiple Myeloma/ Multiple Myeloom/ Morbus Kahler
Allogeneic stem cell transplantation/allogene stamceltransplantatie
Donor lymphocyte infusion/Donor lymfocyten infusie
Bortezomib

Sponsors and support

Primary sponsor: UMC Utrecht, afdeling hematologie
Source(s) of monetary or material Support: geen

Intervention

Outcome measures

Primary outcome

The primary outcome is response rate. The included patients will be analysed with analysis of the m-protein at entry, after bortezomib cycle 2, 4, 6, 8 and before administration of DLI or before cycle 4,6,8 if no more DLI is given. After each DLI before administration of bortezomib cycle 3, 5, 7 and in follow up every 2 months. Bone marrow examination
will be done on indication, for example confirmation of CR.

Secondary outcome

Secondary outcomes are evaluated at the same time points as the primary outcome. Blood samples for experimental mmunology are taken before first gift bortezomib in cycle 1, before first DLI, before first gift bortezomib cycle 3, before DLI nr 2, before first gift bortezomib cycle 5, before DLI nr 3, before first gift bortezomib cycle 7 and by stopping treatment and/or by occurring GvHD.

Study description

Background summary

Patients with multiple myeloma treated with an allogeneic SCT who are candidated for a DLI intervention because of relapse of their disease. These patients will first receive 2 cycli of bortezomib, then the DLI, and then again 2 cycli of bortezomib. The DLI and the bortezomin can be repeated, maximum is 3 DLI and 8 cycli of bortezomib

Study objective

The combination of DLI with bortezomib given before and after the DLI improves the Graft versus Myeloma effect without effect on the Graft versus host disease

Intervention

The intervention consists of a sequential approach over bortezomib cycli (2) with DLI. The bortezemib cycli are given before and 2 weeks after the DLI infusion. If the patient reaches a CR the treatment is
stopped. If a PR is reached the patient continues with bortezomib, maximum 8 cycli. In case of a minimal reaction the patient can receive a second and third DLI, combined with bortezemib. During the study blood and bone marrow sampling will determine the response rate. This is no
control group, comparison with historical data will be performed.

Contacts

Public
University Medical Center Utrecht
Department of Hematology/B02.226
P.O. Box 85500

M.C. Minnema
Utrecht 3508 GA
The Netherlands
+31 30 2507230
Scientific
University Medical Center Utrecht
Department of Hematology/B02.226
P.O. Box 85500

M.C. Minnema
Utrecht 3508 GA
The Netherlands
+31 30 2507230

Eligibility criteria

Inclusion criteria

1. Male or female and at least 18 years-of-age;
2. MM patients with any type of relapse or progressive disease following (non) myeloablative allo-SCT for which DLI is considered a treatment option (including patients previously participating in Hovon 54 or Hovon 65 studies);
3. Informed consent;
4. Haematological parameters; Hb > 4.0 mmol/L, leucocytes > 1.0¡Á109/L , thrombocytes > 25 ¡Á109/L, with or without transfusion

Exclusion criteria

1. Use of the immunosuppressive drugs cyclosporin, MMF, or corticosteroids;
2. Existing GvHD > grade A;
3. Any non-hematological toxicity CTC grade ¡Ý 3;
4. Neuropathy and/or neuropathic pain CTC grade ¡Ý 2;
5. Pregnancy;
6. History of allergic reaction to compounds containing boron or mannitol;

7. Uncontrolled or severe cardiovascular disease, including myocardial infarctiin within 6 months, NYHA class III of IV heart failure (appendix E), uncontrolled angina, clinically significant pericardial disease or cardiac amyloidosis;
8. Previous use of bortezomib is not an exclusion criterion, however patients refractory to bortezomib during previous treatments are excluded from this study.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2007
Enrollment:	20
Type:	Anticipated

Ethics review

Positive opinion

Date:	11-04-2007
Application type:	First submission

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
NTR-new	NL925
NTR-old	NTR949
Other	:
ISRCTN	ISRCTN53810679

Study results

Summary results

1. Lokhorst HM, Wu K, Verdonck LF et al. The occurrence of graft-versus-host disease is the major predictive factor for response to donor lymphocyte infusions in multiple myeloma. Blood 2004;103:4362-4364.
2. van de Donk NW, Kroger N, Hegenbart U et al. Remarkable activity of novel agents bortezomib and thalidomide in patients not responding to donor lymphocyte infusions following nonmyeloablative allogeneic stem cell transplantation in multiple myeloma. Blood 2006;107:3415-3416.
3. Kroger N, Shimoni A, Zagrivnaja M et al. Low-dose thalidomide and donor lymphocyte infusion as adoptive immunotherapy after allogeneic stem cell transplantation in patients with multiple myeloma. Blood 2004;104:3361-3363.
4.Sun K, Welniak LA, Panoskaltsis-Mortari A et al. Inhibition of acute graft-versus-host disease with retention of graft-versus-tumor effects by the proteasome inhibitor bortezomib. Proc.Natl.Acad.Sci.U.S.A 2004;101:8120-8125