Natural Killer cell alloreactive bone marrow transplantation for Multiple Myeloma

Published: 03-03-2015
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The aim of the study is demonstrating that progression free survival will improve after KIR-mismatched haploidentical bone marrow transplantation.

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

Summary

ID

NL-OMON41842

Source
ToetsingOnline

Brief title
Haplo-identical bone marrow transplantation in multiple myeloma

Condition

- Plasma cell neoplasms

Synonym
Plasmaceldyscrasia ; Multiple Myeloma

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Haploidentical bone marrow transplantation, KIR-mismatch, Multiple Myeloma, Natural Killer Cells

Outcome measures

Primary outcome

Progression free survival 18 weeks after transplantation.

Secondary outcome

1. Response rate

2. Incidence of graft failure, engraftment and time to neutrophil and platelet

recovery

3. Incidence and Severity of Acute and Chronic GVHD

4. Non-Relapse Mortality

5. Evaluation of infections after haploBMT and T cell reconstitution

6. NK cell repertoire reconstitution and maturation rates including

alloreactivity

7. NK cell repertoire in the Bone Marrow before and after (6 weeks)

transplantation

8. Cost calculation

9. Quality of Life

Study description

Background summary

Eventually almost all multiple myeloma patients will succumb to the disease. Mainly for patients with an early recurrence after standard therapy further treatment options are limited. Therefore, new treatment options are necessary.

An option is a bone marrow transplantation with donors selected on NK cell alloreactivity. In the laboratory and in mouse models, our group and others have shown that this alloreactivity results in antitumor responses. For NK cell alloreactivity an haploidentical stemcel transplantation is used in this study. This form of transplantation is being utilized for leukemia in many centers all over the world (also in Maastricht). For multiple myeloma there is not yet a study published demonstrating the effect of haploidentical transplantation focusing on NK cell alloreactivity.

Study objective

The aim of the study is demonstrating that progression free survival will improve after KIR-mismatched haploidentical bone marrow transplantation.

Study design

Fase II study in which a maximum of 24 patients will be treated by haploindetical bone marrow transplantation with NK cell alloreactivity. Primary objective is progression free survival after 18 months.

Intervention

Donor KIR-ligand mismatched haploidentical bone marow transplantation.

Study burden and risks

We expect that a substantial number of subjects will develop severe complications (infections, graft versus host disease or organ failure) due to treatment, even though the treatment protocol is focused on prevention of these complications. Treatment related mortality is expected to occur.
The subject will be admitted for a few weeks after which intensive follow-up in the out-patient department will follow. Readmissions are likely to occur.

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

- Patients with MM <66 years.
- Poor prognosis MM patients, permissive for KIR-ligand mismatch and with a KIR-ligand mismatched haploidentical donor. Poor prognosis is based on:
o Patients with early disease recurrence (within 12 months after first ASCT) or
o Patients after a minimum of three lines of chemotherapy (including high dose therapy followed by ASCT rescue therapy) or
o Poor risk based on the cytogenetic profile.
- Written informed consent
- If there is no HLA identical related or 10/10 matched unrelated donor
- Permissive for KIR-ligand mismatch
- At least partial response after reinduction therapy
- Measurable disease

Exclusion criteria

- Active uncontrolled infections
- Patients that are known to be HIV positive.
- Patients with Donor specific HLA-antibodies
- Uncontrolled CNS involvement by the malignant disease
- Severe cardiovascular disease (arrhythmias requiring chronic treatment, congestive heart failure or symptomatic ischemic heart disease)
- Severe pulmonary dysfunction (CTCAE grade III-IV)
- Severe neurological or psychiatric disease

- Significant hepatic dysfunction (serum bilirubin or transaminases >= 3 times upper limit of normal)
- Significant renal dysfunction (creatinine clearance < 30 ml/min after rehydration)
- History of active malignancy during the past 5 years with the exception of basal cell carcinoma of the skin or stage 0 cervical carcinoma
- Any psychological, familial, lingual, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule
- Breast-feeding female patients.
- Concurrent severe and/or uncontrolled medical condition (DM, hypertension, cancer).
- Pregnant female patient. During the study pregnancy must be prevented by the use of contraceptives.

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):	08-04-2016
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	03-03-2015
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO

Date:	02-02-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
CCMO	NL49476.000.14

Study results

Date completed:	23-09-2019
Actual enrolment:	12