LUMC 2014-01 - Transfer of Streptamer selected multiantigen-specific T cells to prevent infections and relapse after allogeneic Stem Cell Transplantation - a phase I/II study

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• To evaluate the efficacy of the transfer of multiantigen specific T cells by measuring the appearance or expansion (if antigenic specific donor derived cells are already present in the circulation of the patient at time of infusion) of antigen...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON40919

Source
ToetsingOnline

Brief title
T control

Condition

- Leukaemias

Synonym
hematological malignancy, leukemia

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Europees

Intervention

Keyword: allogeneic stem cell transplantation, immunetherapy, t cells

Outcome measures

Primary outcome

- Cumulative incidence of acute GVHD overall grade 3 or higher needing prolonged systemic immune suppressive treatment in the three months after infusion of multi antigen-specific T cells.

Secondary outcome

- The appearance or doubling of antigenic specific donor derived T cells in the circulation during eight weeks after the infusion of multi antigen specific T cells

- Chimerism in bone marrow and peripheral lymphocytes

- Loads of circulating viruses (CMV, EBV, Adenovirus)

- Disease activity

Study description

Background summary

Patients with hematological malignancies can be successfully treated with allogeneic hematopoietic stem cell transplantation (allo-SCT). One of the major challenges in the field of allo-SCT is to find a balance between the harmful induction of graft-versus-host disease (GVHD) and the beneficial graft-versus-leukemia (GVL) response, both mediated by donor T cells recognizing antigens expressed on cells of the recipient. Complete removal of T cells from the graft results in abrogation of severe GVHD, but is associated

with impaired resistance to infections and abrogation of the anti-tumor efficacy (GVT effect). We hypothesize that the infusion of Streptamer selected multiantigen specific donor derived T cells early after T cell depleted allo-SCT is a feasible method to improve anti-viral and anti tumor immunity without an increased risk of severe GVHD.

Study objective

• To evaluate the efficacy of the transfer of multiantigen specific T cells by measuring the appearance or expansion (if antigenic specific donor derived cells are already present in the circulation of the patient at time of infusion) of antigen specific donor derived T cells during eight weeks after the infusion of donor derived multi antigen specific T cells.
• To assess the feasibility and safety (toxicity) of the administration of donor derived multi antigen specific T cells early after T cell depleted allo-SCT.
• To evaluate whether the appearance or expansion of antigen specific donor derived T cells coincides with the clearance or prevention of circulating viruses (EBV, CMV, Adenovirus) or with an improvement in bone marrow chimerism or with a control in disease burden (malignant cells in blood or bone marrow or tumor size in case of malignant lymphoma)

Study design

This is a non-randomized phase I/II safety and feasibility study.

Intervention

Patients will receive donor derived multi-antigen specific T cells 6 to 8 weeks after the transplantation.

Study burden and risks

All study related procedures will be performed during regular control visits which are scheduled during the first six months after the allogeneic SCT. Patients will receive one intravenous injection with multi-antigen specific donor derived T cells to enhance the immune reconstitution. In order to evaluate the effects of this infusion, one extra bone marrow examination (30 ml) will be performed. In addition, extra blood will be taken during regular blood examinations (in total 190 ml extra, divided over 5 time points)
A theoretical risk of the infusion of donor derived T cells is the development of acute Graft Versus Host Disease. Based on our experience maximal 10% of the patients develops de novo acute GVHD between week 6 and 26 after a T cell depleted allogeneic SCT. Although the donor derived T cells which are transferred to the patient in this study are specific for viruses, tumor associated antigens or haematopoiesis restricted minor antigens, they could

theoretically increase this existing risk on GVHD by intensifying an immune response towards non-hematopoietic patient tissue.
The potential benefit of the infusion of multi antigen specific T cells is an increase in donor derived immunity towards viruses and malignant cells in the patients.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Before allo-SCT:
- Age 18-75 years
- Planned T cell depleted allo-SCT for one of these diagnoses:
* Acute Lymphoblastic Leukemia in CR after prephase and first induction and consolidation therapy and WBC < 30 x 109/l in B-ALL or < 100 x 109/l in T-ALL at initial diagnosis. ALL with

t(9;22), t(4;11), complex karyotype or 11q23 abnormalities will be excluded.
* Acute Myeloid Leukemia in CR excluding AML with:
0 Monosomal Karyotype
- Abn3q26
- EVI1 overexpression
* Multiple myeloma at least in stable PR (no treatment foreseen in first 6 months after allo-SCT)
* Non high grade B-NHL (B-CLL, Mantle cell lymphoma, Follicular Lymphoma, MALT, LPL) at least in stable PR (no treatment foreseen in first 6 months after allo-SCT)
* Myeloprolypherative disorder at least in stable PR (no treatment foreseen in first 6 months after allo-SCT), excluding CML blastic phase
* Myelodysplastic/myeloprolypherative neoplasms at least in stable PR (no treatment foreseen in first 6 months after allo-SCT)
* Myelodysplastic syndrome at least in stable PR (no treatment foreseen in first 6 months after allo-SCT)
- HLA type A*0201.
- Written informed consent of the patient
- Availability of a stem cell donor who meets the following inclusion criteria:
* HLA type A*0201
* CMV and/ or EBV seropositivity
* Written informed consent
4-6 weeks after allo-SCT:
- Stable engraftment of the allogeneic graft (platelets >20 *10E9/L, granulocytes > 0.5 *10E9/L)

Exclusion criteria

Before allo-SCT:
- Disease specific treatment foreseen in the first 6 months after SCT
- Life expectation < 6 months.
- End stage irreversible multi-system organ failure (need for mechanical ventilation, hypotension for which admission to ICU, hepatic encephalopathy, coma)
- Pregnant or lactating women or women unwilling or not capable to use effective means of birth control
- Severe psychological disturbances.
4-6 weeks after allo-SCT:
- Histologically proven acute GVHD > grade I for which immune suppressive treatment is given
- Progressive disease for which therapy is needed
- Use of > 20 mg prednisone a day
- Life expectation < 12 weeks.
- End stage irreversible multi-system organ failure (need for mechanical ventilation, hypotension for which admission to ICU, hepatic encephalopathy, coma, start of dialysis after allo-SCT)
6-8 weken na allo-SCT:

- Acute GVHD (preferentially histologically proven) GVHD > grade I for which immune suppressive treatment is given
- Progressive disease for which therapy is needed
- Use of > 20 mg prednisone a day
- Life expectation < 12 weeks.
- End stage irreversible multi-system organ failure (need for mechanical ventilation, hypotension for which admission to ICU, hepatic encephalopathy, coma, start of dialysis after allo-SCT)
- Uncontrolled bacterial or fungal infection.
- Evidence of rejection

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-11-2014
Enrollment:	17
Type:	Actual

Ethics review

Approved WMO

Date:	19-09-2014
Application type:	First submission
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	NL48393.000.14