Prophylactic infusion of CD4 positive donor lymphocytes early after T-cell depleted stem cell transplantation

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In this phase II study, the toxicity and treatment effects of early donor derived CD4+ lymphocyte infusion, three months after SCT, will be evaluated

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

Summary

ID

NL-OMON30913

Source
ToetsingOnline

Brief title
CD4 positive lymphocyte infusion after alloSCT

Condition

- Leukaemias
- Lymphomas non-Hodgkin's unspecified histology

Synonym
leukemia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Donor lymphocyte infusion, Immune reconstitution, Stem cell transplantation

Outcome measures

Primary outcome

Primary Objective: To evaluate whether CD4+ lymphocytes infusion given three months after T-cell depleted allo-SCT improves immunological recovery, i.e. recovery of circulating CD4+ T cells with an incidence of GvHD requiring systemic treatment not exceeding 30%

Secondary outcome

Secondary Objective(s): To evaluate whether CD4+ lymphocytes infusion given three months after T-cell depleted allo-SCT influences chimerism, disease status as measured by minimal residual disease, appearance of virus specific T lymphocytes, and incidence of viral infections

Study description

Background summary

Allogeneic hematopoietic stem-cell transplantation (allo-SCT) regimens using the CD52 antibody alemtuzumab for T cell depletion demonstrate efficient engraftment and reduced graft-versus-host disease (GVHD). However, alemtuzumab-containing regimens result in decreased post-transplant anti-infection immunity. Due to poor T cell immune reconstitution, particularly of the CD4+ T-cell subset, T cell dependent anti-tumor effects are also impaired, requiring the administration of donor lymphocyte infusions (DLI) early after transplantation. Although unmanipulated DLI can induce considerable anti-tumor responses and immune reconstitution, morbidity and mortality due to GVHD occur frequently.
Several studies have shown the capacity of CD8 depleted DLI to improve immune reconstitution. In a small randomized trial, infusion of CD8 depleted DLI six months after T-cell depleted SCT was associated with considerable less severe GVHD than infusion of unmanipulated DLI with no difference in relapse rates.

However, CD8 depletion appears not to be able to completely eliminate GVHD, possibly due to residual low numbers of CD8+ cells. DLI based on selection of CD4+ positive donor cells may be more effective in preventing GVHD and may improve immune reconstitution.

Study objective

In this phase II study, the toxicity and treatment effects of early donor derived CD4+ lymphocyte infusion, three months after SCT, will be evaluated

Study design

Randomized open label single centre intervention study.

Intervention

The intervention is the infusion of a subset of donor lymphocytes (the CD4+ cells), three months after stem cell transplantation.

Study burden and risks

Participating patients will visit the outpatient clinic once every two weeks for physical examination and blood sampling, which is at this moment the standard care for patients during the first six months after allogeneic stem cell transplantation at our institution. The total amount of blood which will be taken for study purposes will be maximally 250 cc in a three months period. One extra bone marrow examination will be performed (six weeks after CD4+ infusion). Theoretically, the risk of CD4+ donor lymphocyte infusion is acute GVHD, as is seen in patients receiving total donor lymphocyte infusion after allogeneic stem cell transplantation.

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 AML, myelodysplasia (MDS), ALL, CML in accelerated phase or blastic transformation, CLL, MM or aggressive lymphoma, who are scheduled to receive an allogeneic stem cell transplantation.

Exclusion criteria

Systemic immunosuppressive treatment
Progressive GVHD
GVHD of the skin > grade 1
Progressive malignant disease needing cytoreductive treatment

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2007
Enrollment:	60
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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
Other	ISRTCN CCT-NAPN-16885
CCMO	NL18707.058.07