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	Recruitment stopped
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON31838

Source
ToetsingOnline

Brief title
CD4 positive lymphocyte infusion after alloSCT

Condition

- Leukaemias

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

Deelnemende patiënten zullen elke twee weken de polikliniek bezoeken voor lichamelijk onderzoek en bloedafname, wat op dit moment reeds de standaard controles zijn na een allogene stamceltransplantatie in het LUMC. De totale hoeveelheid bloed die gedurende 12 weken extra zal worden afgenomen is 250 ml. Er zal één extra beenmerg onderzoek verricht worden (zes weken na de CD4+ infusie).
Het theoretische risico van CD4+ infusie is het ontstaan van acute GVH ziekte. Na een stamceltransplantatie komt dit in ernstige mate voor in 10% van de patiënten en na ongeselecteerde donor lymfocyten infusie in 20% van de patiënten.
Gebasseerd op eerdere publicaties over het verwijderen van CD8+ cellen uit de donor lymfocyten verwachten we dat de prevalentie van ernstige GVH ziekte in deze studie lager zal zijn dan 30%.

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 2
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:	Recruitment stopped
Start date (anticipated):	04-07-2008
Enrollment:	70
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cels allogenic

Ethics review

Approved WMO Date:	19-03-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	27-05-2008
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
EudraCT	EUCTR2008-001447-19-NL
Other	ISRTCN CCT-NAPN-168
CCMO	NL22441.000.08

Study results

Date completed:	01-05-2020
Actual enrolment:	67