Double umbilical cord blood transplantation in high-risk haematological patients.
A phase II study focussing on the mechanism of graft predominance

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haematological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON39426

Source
ToetsingOnline

Brief title
HOVON 115 Double UCBT

Condition

- Haematological disorders NEC

Synonym
poor-risk hematological malignancy

Research involving
Human

Sponsors and support

Primary sponsor: HOVON
Source(s) of monetary or material Support: KWF

Intervention

Keyword: Double cord blood transplantation, Engraftment, Graft predominance

Outcome measures

Primary outcome

- The proportion of patients with activated class II-specific T-cells (aTCs),

defined as: the number of patients with aTCs, divided by the number of patients

with class II mismatches for which there are tests available (defined as

evaluable patients).

- Transplant related mortality (TRM; defined as non-relapse mortality)

Secondary outcome

- Cumulative incidence of engraftment

- Cumulative incidence of graft failure

- Time to neutrophil recovery

- Time to lymphocyte recovery

- Time to platelet recovery

- Time to red blood cell transfusion independence

- Count of total CD3+, CD4+ and CD8+ cells and CD3-CD16/56+ cells at 3, 6, 12

and 24 months after UCBT

- Incidence and grade of acute GVHD

- Incidence of chronic GVHD

- Incidence of infections

- Progression free survival (PFS, i.e. time from transplantation until

progression/relapse or death from any cause, whichever comes first)

- Overall survival (OS) calculated from transplantation.

Study description

Background summary

Many adults with high risk hematological disease can not proceed to allogeneic stem cell transplantation because they
lack a matched unrelated stem cell donor. Cord blood transplantation has shown to be an important alternative stem
cell source in children. The major problem after a single cord blood transplantation in adults appears to be primary graft
failure and a delayed hematopoietic recovery caused by the small number of hematopoietic stem cells in cord blood
grafts. Double cord blood transplantation has shown to be a safe and promising approach in adult to overcome this
problem and has become standard treatment in adult patients who qualify for alternative donor transplantation and lack a properly matched unrelated donor. Sustained hematopoiesis is usually derived from a single donor after double umbilical cord blood
transplantation.So far, the distinct contributing factors which lead to the predominance of the prevailing cord blood graft
are not known.

Study objective

Objective of the study is to evaluate whether parameters can be identified that predict which graft ultimately prevails following cord blood transplantation after a reduced intensity conditioning regimen in adult patients .
In addition engraftment, transplant related mortality and disease-free survival will be evaluated .

Study design

Prospective phase II study. Patients eligible for allogeneic stem cell transplantation lacking a matched unrelated donor
are transplanted with a double cord blood graft. Transplantation will be preceded by a reduced-intensity conditioning
regimen. After transplantation blood samples and bone marrow samples will be

collected at certain time points.

Intervention

Patients are treated with a reduced-intensity conditioning regimen, irrespective of patient age, followed by double UCBT. Post grafting immunosuppression is performed by mycophenolate mofetil (30 days) and cyclosporine A (90 days, taper thereafter)

Study burden and risks

Nature and extend of the burden and risks associated with participation. Burden and risk are comparable to burden and risk of a standard cord blood transplant procedure. Collection of blood
samples may be a small extra burden if extra venous puncture is necessary. Collection of bone marrow samples can
give a small inconvenience because a larger volume of bone marrow has to be collected compared to standard bone
marrow examination.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age 18-70years inclusive
- Diagnosis of poor-risk hematological malignancy or (V)SAA relapsing after or failing immunosuppressive therapy and meeting the criteria for a MUD allo SCT
- Lacking a sufficiently matched volunteer unrelated donor or lacking such a donor within the required time period of <= 2 months in case of urgently needed alloSCT
- Availability of 2 (>=4/6) matched UCB grafts with a total nuclear cell count > 4 x 107/kg (see paragraph 8.2).
- WHO performance status 0-2
- Written informed consent

Exclusion criteria

- Bilirubin and/or transaminases > 2.5 x normal value
- Creatinine clearance < 40 ml/min
- Cardiac dysfunction (as defined in protocol in 8.1.2)
- Pulmonary function test with VC, FEV1 and/ or DCO < 50%
- Active, uncontrolled infection
- History of high dose total body irradiation
- Pregnant or lactating female
- HIV positivity;

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):	22-08-2012
Enrollment:	70
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cels allogenic

Ethics review

Approved WMO Date:	15-05-2012
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-07-2012
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-03-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-10-2013
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-10-2013
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
EudraCT	EUCTR2012-001188-55-NL
CCMO	NL40329.000.12