Umbilical cord blood transplantation in high-risk hematological patients using stemregenin-1 expanded hematopoietic stem cells.
A feasibility study focusing on engraftment and hematopoietic recovery.

No registrations found.

Ethical review	Positive opinion
Status	Other
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26058

Source
Nationaal Trial Register

Brief title
CORDEX

Health condition

single cord blood transplantation
stemregenin-1 expanded hematopoietic stem cells
engraftment

Sponsors and support

Primary sponsor: Erasmus MC
Source(s) of monetary or material Support: initiator

Intervention

Outcome measures

Primary outcome

Feasibility as defined by, and to be achieved in ≥ 80% of (evaluable) patients:

1. SR-1 mediated expansion, resulting in > 20-fold expansion of CD34+ cells, and

2. effective hematopoietic (neutrophils > 0.5 x 109/L) engraftment within 30 days upon transplantation

Secondary outcome

 Cumulative incidence of engraftment

 Cumulative incidence of graft failure

 Time to neutrophil recovery (> 0.5 x 109/L)

 Time to lymphocyte (T-cells + subsets; B-cells; NK-cells) recovery

 Time to platelet recovery (> 20 x 109/L)

 Time to red blood cell transfusion independence

 Absolute number of CD3+CD4+, CD3+CD8+, CD19+ and CD3-CD16/56+ cells at 1,2, 3, 6, 12 and 24 months after UCBT

 Incidence and grade of acute GVHD

 Incidence of chronic GVHD

 Incidence of infections

 Incidence of CTC grade 3-4 adverse events
 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. Patients still alive or lost to follow up are censored at the date they were last known to be alive

Study description

Background summary

Rationale:

Insufficient hematopoietic recovery following UCBT is considered to be primarily due to the low number of hematopoietic stem cells in UCB grafts. In-vitro stem cell expansion can be achieved by SCF, Flt3L, TPO and Stemregenin-1 (SR-1). Transplantation of double UCBT including one SR-1 expanded unit was recently demonstrated feasible and safe. The present study aims to evaluate feasibility, engraftment and recovery following transplantation of one expanded unit.

Study objectives:

 To study the feasibility of single UCBT with one ex-vivo SR-1 expanded unit

 To assess side effects and TRM after single UCBT with one expanded unit

 To assess engraftment and engraftment kinetics; to evaluate immune reconstitution, acute and chronic GVHD, chimerism, toxicity, progression-free survival and overall survival after single UCBT with one expanded unit.

Intervention:

Patients are treated with a reduced-intensity conditioning regimen, irrespective of patient age, followed by single UCBT, using one SR-1 expanded unit. Post grafting immunosuppression is performed by mycophenolate mofetil (30 days) and cyclosporine A (90 days, taper thereafter)

Duration of treatment:

Patients will be treated with a conditioning regimen during 7 days, followed by transplantation. Subsequent immunosuppression may take up to 180 days.

Patients will be followed until 5 years after registration

Expected duration of accrual: 1 year

Main study endpoint:

Feasibility as defined by, and to be achieved in ≥ 80% of (evaluable) patients:

1. SR-1 mediated expansion, resulting in > 20-fold expansion of CD34+ cells, and

2. effective hematopoietic (neutrophils > 0.5 x 109/L) engraftment within 30 days upon transplantation

Benefit and nature and extent of the burden and risks associated with participation

Benefits for individual patients may include a faster and better hematopoietic recovery, less opportunistic infections after transplantation and less graft versus host disease as compared to double UCBT

Risks of participation include graft failure and autologous recovery

Planned interim analysis and DSMB

An interim analysis will take place after the first 5 patients have been included and are found to be eligible and will be discussed with the DSMB.

Study design

 At entry: within 30 days before start of treatment

 After 1, 2, 3, 6, 12 and 24 months after transplantation and yearly therafter

Intervention

Patients are treated with a reduced-intensity conditioning regimen, irrespective of patient age, followed by single UCBT, using one SR-1 expanded unit. Post grafting immunosuppression is performed by mycophenolate mofetil (30 days) and cyclosporine A (90 days, taper thereafter)1.

Contacts

Public
Erasmus Medical Center, Daniel den Hoed Cancer Center, Department of Hematology,
P.O. Box 5201
J.J. Cornelissen
Rotterdam 3008 AE
The Netherlands

+31 (0)10 4391598 or +31 (0)10 4391367
Scientific
Erasmus Medical Center, Daniel den Hoed Cancer Center, Department of Hematology,
P.O. Box 5201
J.J. Cornelissen
Rotterdam 3008 AE
The Netherlands
+31 (0)10 4391598 or +31 (0)10 4391367

Eligibility criteria

Inclusion criteria

- Age 18-70 years inclusive

- Diagnosis of poor-risk hematological malignancy 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 1 (≥5/6) matched UCB graft with a nuclear cell count > 2,7 x 107/kg (see paragraph 8.2).

- Availability of an back-up autograft, harvested and frozen earlier in the course of treatment, (harvest according to local aphersis policies)

- 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 by:

Reduced left ventricular function with an ejection fraction < 45% as measured by MUGA scan or echocardiogram (another method for measuring cardiac function is acceptable)

Unstable angina

Unstable cardiac arrhythmias

- Pulmonary function test with VC, FEV1 and/ or DCO < 50%

- Active, uncontrolled infection

- History of high dose (≥ 8 Gy) total body irradiation

- Pregnant or lactating females

- HIV positivity

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Other
Start date (anticipated):	01-03-2017
Enrollment:	10
Type:	Unknown

Ethics review

Positive opinion

Date:	26-01-2017
Application type:	First submission

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
NTR-new	NL6082
NTR-old	NTR6229
Other	METC Erasmus MC : MEC 2016-689

Study results