Co-infusion of haematopoietic stem cells from a haplo-identical donor and single unit unrelated cord blood in patients with a high risk of relapse:
A Phase I/II study to assess safety and to investigate the biological mechanism of the anti-tumor response.

No registrations found.

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

Summary

ID

NL-OMON22000

Source
NTR

Brief title
HaploCord

Health condition

Allogeneic stem cell transplantation
Haplo identical
Cord blood
High risk Hematological disease

Allogene stamceltransplantatie
Haplo identiek
Navelstreng bloed
Hoog risico hematologische ziekte

Sponsors and support

Primary sponsor: UMC Utrecht
Source(s) of monetary or material Support: None

Intervention

Outcome measures

Primary outcome

Safety: Transplantation related (non-relapse) mortality (TRM).

Biology: Investigate the anti-tumor response mechanism from both grafts.

Secondary outcome

1. Acute- GVHD (Grade II-IV: Gluckberg Criteria);

2. Engraftment: Neutrophils > 500K/uL for 3 consecutive days and Platelet (day 180 > 50 K) engraftment;

3. Loss of CB chimerism (<25%) at 6 mths post HSCT;

4. Event Free Survival (>6 mths follow up). Event defined as: Death, graft-failure (<25% total donor chimerism) or relapse;

5. Non-Relapse Mortality;

6. Overall Survival;

7. Chronic GVHD: Limited and extensive (Shulman Criteria);

8. VOD (Seattle Criteria);

9. Mucositis ≥ CTC grade 3.

Study description

Background summary

Although haematopoietic stem cells transplantation (HSCT) has become much safer over the last decade the major limitation remain “transplantation related mortality (TRM; e.g. due to

viral reactivations/disease)" and relapse (in malignancies). Within the group of malignancies there is a subgroup of patients with a "very high risk (of relapse) profile" (e.g. relapse AML, refractory lymphoma, relapse after first allo-HSCT). Although this "very high risk group" may potentially benefit from allo-HSCT with the currently available "standard" transplant protocols the expected survival rates are very low <20%. Cord blood (CB) is emerging as stem cell source for HSCT because it has many advantages above the conventional bone marrow grafts. Disadvantages are however low stem cell count/kg for adults associated with prolonged neutropenia and a slower T cell recovery. T cell depleted haplo-grafts have the advantage of early neutrophil engraftment but are associated with higher rates of secondary graft-failure and poor T-cell reconstitution associated with viral infections. KIR-mismatching in Haplo-grafting is suggested to have anti-leukemic potential.

RATIONALE:

Combining cord blood and readily available haplo-identical family donor-HSCT combines beneficial effects of both allogeneic transplantations strategies, such as the in the long term excellent T-cell recovery after CB HSCT, and the NK-cell mediated anti-tumor activity of CB with the early haplo-mediated neutrophil recovery and the targeted anti-leukemia effect of NK (KIR mismatch) and T-cells after selected haplo-HSCT. We propose therefore that this multimodal treatment protocol may be a treatment option in the selected group of patients with a "very high risk (on relapse) profile". These patients with the very high risk profile may profit for from this double grafting because of:

Multi-modal cellular therapy: Strong early (first 2-4 weeks) NK + T-cells mediated anti-tumor activity from the haplo-graft and NK + T-cellular anti-tumor activity (> 4 weeks) from the CB-graft, without increasing the risk of aGVHD.

OBJECTIVE:

To study the safety of co-infusion of a T-/CD19 B-cell depleted haematopoietic stem cells from haplo-identical donor and a single unit cord blood unit and to investigate the anti-tumor responses from both grafts.

STUDY DESIGN:

Prospective study, Phase l/ll trial with an optimal 2-stage design.

Study objective

To study the safety of co-infusion of a T-/CD19 B-cell depleted haematopoietic stem cells from haplo-identical donor and a single unit cord blood unit and to investigate the anti-tumor

responses from both grafts.

Study design

T= 0 is inclusion till 12 months after allogeneic stem cell transplantation.

Intervention

For a group of patients with a very high risk malignancy: Instead of using a single donor, or no transplantation at all, a combination of a cord blood unit and selected cells from a haplo-identical family-donor are infused at the day of transplant. The selection procedure of the haplodonor allows mismatch NK-cells and T-cells in the graft for extra anti-tumor effect.

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Eligibility criteria

Inclusion criteria

1. Patients with either:

A. No standard HSCT protocol available and any of the following malignancies: NHL or HD (refractory, ≥2CR); relapse AML/refractory AML, MDS, SAA, ALL ≥CR2;

B. Relapse after first allo-HSCT with either SIB or MUD/UCB donor;

C. With a leukemia/lymphoma indication, qualifying for HSCT but without donor available according to ongoing, open study protocols no fully matched family donor or matched (9-10/10) unrelated donor available and / or no single or double unit cord blood available with sufficient cell numbers according to ongoing, open study protocols.

2. With having a single matching (≥ 4/6) umbilical CB unit available with total NC count > 1,5 E7/kg;

3. Lansky / Karnofsky > 40;

4. Age 18-65 * (*= age ≤ 65 and 364 days);

5. Signed Informed Consent.

Exclusion criteria

1. Creatinine clearance < 40 ml/min;

2. Cardiac dysfunction (SF < 30%) (Ejection fraction < 45%), unstable angina, or unstable cardiac arrhythmias;

3. Pulmonary function test VC, FEV1 and/ or DOC< 50%.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2011
Enrollment:	37

Type:	Anticipated

Ethics review

Positive opinion Date:	24-09-2011
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	NL2932
NTR-old	NTR3079
Other	METC UMCU : 11-313
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A