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.

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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.

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22000

Bron
NTR

Verkorte titel
HaploCord

Aandoening

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

Allogene stamceltransplantatie
Haplo identiek

Navelstreng bloed
Hoog risico hematologische ziekte

Ondersteuning

Primaire sponsor: UMC Utrecht
Overige ondersteuning: None

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Safety: Transplantation related (non-relapse) mortality (TRM).
Biology: Investigate the anti-tumor response mechanism from both grafts.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

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.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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%.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-11-2011
Aantal proefpersonen:	37
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	24-09-2011
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2932
NTR-old	NTR3079
Ander register	METC UMCU : 11-313
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A