Natural killer cell infusion after stem cell transplantation for leukemia

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Adoptive transfer of ex vivo IL15-activated donor NK cells enhance immune reconstitution and reduce residual tumor burden in the early post transplant setting.

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

Samenvatting

ID

NL-OMON26066

Bron
Nationaal Trial Register

Verkorte titel
IL-15 activated NK cells

Aandoening

Acute lymphoblastic leukemia (ALL)
Acute myeloid leukemia (AML)
Allogeneic stem cell transplantation

Ondersteuning

Primaire sponsor: Leiden University Medical Center
Overige ondersteuning: Dutch Cancer Society
Miltenyi Biotec GmbH

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

In addition to the standard evaluation following HSCT of children treated for leukemia, the following investigations will be performed in the context of the investigational NK cell infusion:
- To determine the number of patients for whom an investigational medicinal product (IMP), meeting all release criteria, can be generated. The protocol is considered feasible if:
> 50 % of transplanted patients can be included
> 66 % of included patients can be infused with the IMP.
- Registration of post infusion status of the patient, fever, nausea, chills, rash, erythema, and all serious adverse events, potentially linked to infusion. The IMP is considered safe and well-tolerated if no more than 2 out of 12 patients develop severe adverse reactions that are likely due to the NK cell infusion.

Toelichting onderzoek

Achtergrond van het onderzoek

Children with leukemia are treated with standardized chemotherapy and in most cases this treatment is curative. However, and in accordance with international guidelines, patients are eligible for allogeneic hematopoietic stem cell transplantation (HSCT) in case of leukemia characterized by well defined high-risk parameters and in case of relapsed disease following initial successful remission induction therapy. Historically, HLA-matched sibling donors were the first donors to be used, but due to ongoing improvements in HLA typing technology, graft manipulation and supportive care, a matched unrelated (MUD) or mismatched family donor (MMFD) is nowadays a feasible and widely accepted alternative. However, leukemia relapse after HSCT remains the main reason for treatment failure. Following HSCT with MUD and MMFD, T cell reconstitution is delayed up to 6-12 months post transplant, and thus a potential T cell mediated graft versus leukemia (GvL) effect may be impaired. In contrast, there is rapid recovery of natural killer (NK) cells, which have been reported to exert an anti-leukemic effect. Still, the functional capacity of the early regenerating NK cells seems limited. In vitro, the functional and cytolytic properties of NK cells can be augmented by stimulation with cytokines, e.g. interleukin 15 (IL-15). We aim to exploit this NK-cell mediated potential by adoptive transfer of ex vivo IL15-activated donor NK cells with the final aim to enhance immune reconstitution and reduce residual tumor burden in the early post transplant setting when tumor levels are low.

Doel van het onderzoek

Adoptive transfer of ex vivo IL15-activated donor NK cells enhance immune reconstitution and reduce residual tumor burden in the early post transplant setting.

Onderzoeksopzet

During the first year after transplantation and NK cell infusion, patients will be monitord frequently, according to our current standards for follow-up of pediatric HSCT recipients, to

address primary and secondary objectives. Timepoints are pre-SCT, weekly after SCT in the first 10 weeks, 12, 16, 20, 24, and 52 weeks post-SCT. Thereafter, patients will be followed until adulthood and subsequently transferred to the late feects clinic according to our standard procedures for allogeneic stem cell tranplantation recipients.

Onderzoeksproduct en/of interventie

Patients will receive one infusion of 5-10x10e6 ex vivo IL-15-activated donor NK cells per kg body weight (maximum dose: 200x10e6) at 4-12 weeks after transplantation.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Aged between 1-18 years at the time of hematopietic stem cell tranplantation (HSCT)

- Undergoing HSCT for acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) according to existing indications
- Receiving a stem cell graft from a mismatched family or volunteer unrelated donor
- Life expectancy>3 months
- Availability of a stem cell donor willing to donate white blood cells by means of a non-mobilized leukapheresis procedure

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Progressive uncontrollable malignant disease after HSCT but before or at the day of NK cell infusion, defined as overt leukemia relapse, i.e., ¡Ý 25% blasts in the marrow and/or 5% circulating blasts in the peripheral blood or progressive extra-medullary disease
- Lack of evidence for donor myeloid engraftment at the day of infusion (< 0.5 x 10e6 neutrophils/L);
- Active acute GvHD ¡Ý grade II (overall grade)
- Administration of steroids >1 mg/kg/day for any indication at the day of infusion
- Any medical condition, which in the opinion of the treating physician, would interfere with the adequate evaluation of the patient (e.g. end-stage irreversible multi-system organ failure)
- Cord blood stem cell donor

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 gestart
(Verwachte) startdatum:	17-07-2013
Aantal proefpersonen:	12
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	17-01-2014
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	NL4267
NTR-old	NTR4403
Ander register	Leiden University Medical Center, CCMO, EUdract : P12.022, NL38836.000.11, 2011-001514-34

Resultaten