

Natural killer cellen tegen acute myeloïde leukemie

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Natural killer cells are cells of the innate immunesystem and can kill tumor cells without prior sensitization. By infusing these cells hematologic cancer cells can be killed. IL-2 will activate the cells and prolong survival of the natural killer...

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

Samenvatting

ID

NL-OMON25848

Bron

NTR

Verkorte titel

NK4AML

Aandoening

Acute myeloid leukemia and Myelodysplastic syndrome with excess of blasts 2

Ondersteuning

Primaire sponsor: Radboudumc

Overige ondersteuning: KWF

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The study is divided in two phases.

The primary objective of phase I of the study is to evaluate the safety and toxicity of the

infusion of ex vivo-expanded UCB-NK cells, both with and without SC IL-2, following a non-myeloablative immunosuppressive conditioning regimen in patients with AML or MDS with excess blasts-2 (EB-2).

The primary objective of phase IIa of the study is to evaluate the effect of UCB-NK cell adoptive immunotherapy in combination with SC IL-2 following a non-myeloablative immunosuppressive conditioning regime on disease activity in patients with AML/MDS-EB-2.

Toelichting onderzoek

Achtergrond van het onderzoek

In this study we will combine infusion of ex-vivo generated allogeneic natural killer cells with subcutaneous IL-2 to treat residual disease in AML or MDS-EB-2 patients. NK cells are generated from CD34+ hematopoietic stem and progenitor cells from umbilical cord blood (UCB-NK cells). A previous trial (PLMA25) has shown that administration of these cells is safe. This study is divided in two phases. In phase I of the study we will evaluate the safety and toxicity of the NK-cell product in combination with IL-2, following a non-myeloablative immunosuppressive conditioning regimen. All patients will receive a fixed dose of $1.0-3.0 \times 10^9$ UCB-NK cells. The first 3 patients will receive no IL-2, the next 3 patients will receive IL-2 in a low dose and the next 6 patients IL-2 in a higher dose. IL-2 will be administered with a subcutaneous injection for 6 doses given every other day. After establishing the safety of UCB-NK cells combined with sc IL-2, we will continue with phase IIa of the study, evaluating the effect on disease activity of this treatment. We will use the highest tolerable IL-2 dose. Therefore another 11 patients will be included. The patients will be monitored for clinical toxicity, biological parameters in peripheral blood and bone marrow and disease activity.

Doel van het onderzoek

Natural killer cells are cells of the innate immunesystem and can kill tumor cells without prior sensitization. By infusing these cells hematologic cancer cells can be killed. IL-2 will activate the cells and prolong survival of the natural killer cells.

Onderzoeksopzet

For phase 1 of the study dose-limiting toxicities (DLTs) have been defined for both UCB-NK cell or IL-2 toxicity. These will be evaluated at Day 28 after NK cell administration. The next cohort can start if all patients of the previous cohort reached day 28 after NK cell infusion.

For phase 2 of the study the effect on disease activity will also be evaluated on day 28 after NK cell infusion, by performing bone marrow examination.

Onderzoeksproduct en/of interventie

Intravenous natural killer cell therapy with a preconditioning chemotherapy regimen with and without subcutaneous IL-2 administration.

Contactpersonen

Publiek

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Wetenschappelijk

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0243613223

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Newly diagnosed AML or MDS EB-2 defined according to WHO 2016 criteria; AML may be secondary to prior hematological disorders, including MDS, and/or therapy-related.
- Stable or at least non-rapidly progressive disease with or without disease controlling medication.
- Patients may belong to any of the following categories:
 - o Relapsed/refractory disease after treatment with intensive chemotherapy, hypomethylating agents, targeted agents, autologous or allo-SCT (at least 6 months ago) and DLI
 - o Newly diagnosed, untreated patients ineligible for allo-SCT
- Age $\geq$ 18 years
- WHO performance 0- 2 (Appendix 2)
- Life expectancy of $>$ 4 months
- Written informed consent
- Hydrea is allowed as pre-treatment to control blast count until day -3
- Hypomethylating agents decitabine or azacitidine are allowed until day -7

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Rapid-progressive disease in case of previous therapy (see Appendix 1).
- Patients on immunosuppressive drugs or active GvHD
- Patients with active infections (viral, bacterial or fungal); acute anti-infectious therapy must have been completed within 14 days prior to study treatment
- Severe cardiovascular disease (CTCAE III-IV)
- Severe pulmonary dysfunction (CTCAE III-IV)
- Severe renal dysfunction (CTCAE III-IV)
- Severe hepatic dysfunction (CTCAE III-IV)
- Severe neurological or psychiatric dysfunction (CTCAE III-IV)
- Presence of anti-HLA class I antibodies
- Patients on concurrent chemotherapy or interferon-alpha treatment
- Pregnancy or breastfeeding

Onderzoeksopzet

Opzet

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

Deelname

Nederland	
Status:	Werving gestart
(Verwachte) startdatum:	15-11-2020
Aantal proefpersonen:	23
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Toelichting

N/A.

Ethische beoordeling

Positief advies

Datum: 15-10-2020

Soort: Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 55708

Bron: ToetsingOnline

Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9001
CCMO	NL67150.000.19
OMON	NL-OMON55708

Resultaten

Samenvatting resultaten

<https://www.ntvh.nl/journal-article/nk4aml-toediening-van-ex-vivo-gegenereerde-allogene-natural-killer-cellen-in-combinatie-met-subcutaan-il-2-bij-patienten-met-acute-myeloïde-leukemie/>