Natural killer cellen tegen acute myeloïde leukemie

No registrations found.

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

Summary

ID

NL-OMON25848

Source
NTR

Brief title
NK4AML

Health condition

Acute myeloid leukemia and Myelodysplastic syndrome with excess of blasts 2

Sponsors and support

Primary sponsor: Radboudumc
Source(s) of monetary or material Support: KWF

Intervention

Outcome measures

Primary outcome

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.

Secondary outcome

For both phases of the study secondary objectives include 1) evaluation of the in vivo lifespan and expansion potential of the donor NK cells following adoptive transfer, 2) exploration of the functional activity of the donor NK cells in peripheral blood (PB) and bone marrow (BM) and 3) evaluation of IL-2 serum levels and plasma cytokine concentrations pre- and post-administration of SC IL-2. An extra secondary objective for the phase IIa of the study is the number of patients bridged to transplant with this treatment protocol.

Study description

Background summary

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 x 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 adminstered 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.

Study objective

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.

Study design

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.

Intervention

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

Contacts

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Eligibility criteria

Inclusion criteria

- 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 ≥ 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

Exclusion criteria

- 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

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-11-2020
Enrollment:	23
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Plan description
N/A.

Ethics review

Positive opinion

Date:	15-10-2020
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 55708
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

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

Study results

Summary results
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-myeloide-leukemie/