A phase I/II post-cord blood HCT dendritic cell vaccination trial directed against WT1 for pediatric acute myeloid leukemia: the U-DANCE-anti-AML trial

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27248

Source
NTR

Brief title
U-DANCE-anti-AML Trial

Health condition

Pediatric AML patient elegible for allogeneic hematopoietic cell transplantation

Sponsors and support

Primary sponsor: University Medical Center Utrecht,
The Netherlands

UMC Utrecht

Source(s) of monetary or material Support: NWO (ZonMW) & KiKa

Intervention

Outcome measures

Primary outcome

Primary endpoints:

Part A, Safety: Occurrence of DLTs including aGvHD (according to Glucksberg criteria1) from the first vaccination (t=0) until 84 days after the third CBDC vaccination.

Part B, Activity: One-year WT1+ AML relapse-free survival rate from the time of the first vaccination as compared to historical controls.

Secondary outcome

Secondary endpoints (part A):

- One-year cumulative incidence of WT1-specific immunity after the first vaccination.

- One-year overall survival rate, from the time of first vaccination

- One-year WT1+AML relapse-free survival rate, from the time of first vaccination.

- One-year cumulative incidence of cGvHD (according to NIH criteria2) from the first vaccination.

Secondary endpoints (part B):

- One-year cumulative incidence of WT1-specific immunity after the first vaccination.

- One-year cumulative incidence of cGvHD (according to NIH criteria2) from the first vaccination.

- One-year overall survival rate from the time of first vaccination.

Exploratory endpoints (part B):

- Changes in general immune parameters between those samples taken before and those taken after the first vaccination until one year of follow-up.

- Expression of inhibitory (immune checkpoint) molecules on the AML in the case of relapse occurring after the first vaccination until one year of follow-up

Study description

Background summary

Study design:
This is a single-arm open-label phase I/II intervention study in pediatric AML patients using an ATMP: cord blood-derived dendritic cell (CBDC) vaccine. Data from our historic cohort of pediatric patients with a WT1+ AML and receiving CBT will be used as control group for the primary objective in part B.

Study population:

All pediatric patients with an WT1+ AML and eligible for a CBT as ‘standard of care’ can be included in the current study, taking into account the age limits of the part A of the study (≥12 and ≤17 year of age) . Younger patients will only be included when safe dose has been determined in part A (≥0 - ≤17 year).

Intervention:

CBDC-vaccination (day 0, day 14 and day 28):
Patients will receive three “Full length WT1 encoding” mRNA-electroporated and WT1 15-mer-peptide pool loaded CBDC-vaccinations starting at 8 weeks post-CBT every 2 weeks (hence week 8, 10 and 12). The CBDC vaccine will be split into two equal doses that will be administered intradermally and intravenously.

Study objective

Cord Derived Dendritic Cell Vaccination directed against WT1 will prevent patients from relapse

Study design

In this study, all planned visits (see table 5 for details) are aligned with the “standard of care” SOP-follow-up visits with regard to CBT. As such, no additional visits are needed unless medically required.

Most parameters will be obtained by physical examination or assessed as part of “standard of

care” SOP diagnostics. When extra blood is collected for study specific assessments (WT1-specific immunity and WT1 MRD levels) this blood will always be collected in combination with the “standard of care” blood collection. As such, no extra vein punctures will need to be performed.

Intervention

CBDC vaccine.

This advanced therapy medicinal product (ATMP) is a full-length WT1-mRNA electroporated and WT1 peptide pool-loaded CBDC vaccine produced from CD34+ cells isolated from the 20% fraction of the CB graft under GMP conditions and cryopreserved in the “Cell Therapy Facility” of the UMC Utrecht.

All pediatric AML patients eligible for allo-HCT according to the international NOPHO AML protocol and the national (DCOG) guidelines, and undergoing a CBT at the pediatric blood and marrow transplantation program of the UMC Utrecht, are eligible for part A and B this study.

Although DC vaccinations have been used in allo-HCT settings, no previous studies have been performed using a CBDC vaccine after CBT. This study will therefore be subdivided into 2 parts: Part A to determine a safe dose of the vaccination and Part B to study its activity measured as the one-year relapse-free survival rate, based on an expansion cohort.

Part A: Safety: Occurrence of DLTs including aGvHD (according to Glucksberg criteria 1) from the first vaccination (t=0) until 84 days after the third CBDC vaccination

Part B: Activity: One-year WT1+ AML relapse-free survival rate from the time of the first vaccination as compared to historic controls.

Patients will be vaccinated three times biweekly by combined intradermal and intravenous administration of the WT1 loaded-CBDC vaccine, starting at 8 weeks after CBT.

Contacts

Public
room KC.03.065.2

J.J. Boelens
Wilhelmina Kinderziekenhuis, Lundlaan 6

Utrecht 3584 EA
The Netherlands
0031-88-754003
Scientific
room KC.03.065.2

J.J. Boelens
Wilhelmina Kinderziekenhuis, Lundlaan 6

Utrecht 3584 EA
The Netherlands
0031-88-754003

Eligibility criteria

Inclusion criteria

•Pediatric AML patients eligible for allo-HCT according to standard-of-care guidelines, with overexpression of WT1 mRNA in an AML sample (>50 copies WT1/10^4 copies ABL for PB and >250 copies WT1/10^4 copies ABL for BM 52 taken at diagnosis and/or relapse after (re-)induction chemotherapy.

•Indication for CB-HCT according to the UMC Utrecht guidelines

•CB selection criteria: the 80% fraction of the unit should contain a minimum total nucleated cell number of 3x10^7 NC/Kg criteria for any match grade (before cryo-preservation). Preferable CD34+/Kg dose: > 1x10e5 in the 80% fraction

•The whole CB unit should contain more than 7.5x10^6 total CD34+ before freeze.

•Karnofsky/Lansky score ≥70

•Age limits for part A (safety run) only: ≥12 and ≤17 years of age, and <18 years for part B of the study.

•Signed informed consent

Exclusion criteria

•Patients undergoing allo-HCT with stem cells derived from PBMCs or BM

•Patients who are pregnant or breast-feeding or unwilling to use adequate contraceptive methods

•Known allergies to compounds used in the CBDC production process or the local anaestetic “lidocaine-tetracaine (Rapydan®) plasters

•Patients included in other intervention studies influencing the endpoints of this study

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:	Pending
Start date (anticipated):	01-12-2016
Enrollment:	54
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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	NL5882
NTR-old	NTR6055
Other	EUDRA CT invullen : 2015-000827-94

Study results

Summary results
de Haar C, Plantinga M, Blokland NJ, et al. Generation of a cord blood-derived Wilms Tumor 1 dendritic cell vaccine for AML patients treated with allogeneic cord blood transplantation. oncoimmunology. 2015;4(11):e1023973–12.