MiHA-DC vaccinatie na allogene stamceltransplantatie.

No registrations found.

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

Summary

ID

NL-OMON29214

Source
NTR

Brief title
PSCT16

Health condition

Patients with AML, MDS, ALL, CML (accelerated or blast phase), CLL, MM or malignant NHL, who underwent HLA-matched allo-SCT.

Sponsors and support

Primary sponsor: Radboud University Nijmegen Medical Centre
Source(s) of monetary or material Support: ZonMW, Dutch Cancer Society (KWF), NOTK

Intervention

Outcome measures

Primary outcome

The primary study parameters are to evaluate the safety, toxicity, development of GVHD and the immunological response by appearance of MiHA-specific CD8+ T cells following vaccination with monocyte-derived donor DC electroporated with mRNA encoding hematopoietic-restricted MiHA in patients who had undergone allo-SCT with stem cells from a

HLA-matched, MiHA-mismatched donor.

Secondary outcome

The secondary study parameters are to evaluate the clinical effect of MiHA-DC vaccination in case of detectable minimal residual disease and mixed chimerism.

Study description

Background summary

Allogeneic stem cell transplantation (allo-SCT) is a potent treatment and sometimes the only curative treatment for aggressive hematological malignancies. The therapeutic efficacy is attributed to the graft-versus-tumor (GVT) response, during which donor-derived CD8+ T cells become activated by recipient minor histocompatibility antigens (MiHA) presented on dendritic cells (DC). Consequently, these alloreactive donor T cells clonally expand, acquire effector functions and kill MiHA-positive malignant cells. However, in a substantial number of patients persistence and recurrence of malignant disease is observed, indicating that insufficient GVT immunity is induced. This is reflected by our observation that not all patients develop a productive CD8+ T cell response towards MiHA mismatched between the recipient and donor. A promising strategy to induce or boost GVT immune responses is pre-emptive or therapeutic vaccination with ex vivo-generated donor DC loaded with MiHA that are exclusively expressed by recipient hematopoietic cells and their malignant counterparts. In contrast to pre-emptive donor lymphocyte infusion (DLI) with polyclonal donor T cells, this MiHA-DC vaccination approach has less risk of inducing GVHD and the potency to induce more efficient GVT-associated T cell immunity.

This study will be performed in the Netherlands.

Study objective

N/A

Study design

- Safety, toxicity and development of GVHD will be monitored with standard physical examination at weekly or two-weekly visits to the outpatient clinic. General toxicity of the DC vaccinations will be measured using the NCI CTCAE criteria (http://ctep.cancer.gov/reporting/ctc/html).

- Immunological responses will be monitored in peripheral blood samples obtained at day 0 (prior to first DC vaccination) and day 7, 14, 21, 28, 42, 63 and 84 after DC vaccination.

Peripheral blood will be used for monitoring of T cell responses: changes in T/B/NK subsets by flow cytometry immunophenotyping, detection of MiHA-specific CD8+ T cells (% MiHA-tetramer-positive cells with flow cytometry), specific T cell proliferative and cytokine responses against KLH (in vitro restimulation assay). In addition, serum samples will be collected at each time point and stored at -20°C until use for monitoring of humoral immune responses: presence of antibodies against KLH will be examined by ELISA.

- Chimerism in peripheral blood (day 0, 14, 28, 63 and 84) will be measured by SNP Q-PCR analysis according to standard practice in the molecular diagnostic unit of the Department of Laboratory Medicine.

- In case of presence of detectable residual or persistent disease before DC vaccination, clinical effects will be investigated by monitoring residual disease in peripheral blood (day 0, 14, 28, 63 and 84) or bone-marrow aspirates (day 0, 42 and 84) using quantitative real-time bcr-abl PCR (CML, Ph+ ALL), WT1-specific PCR (AML, MDS), M-protein (MM), immunophenotyping (CLL, AML, ALL, MDS) or radiological examination (NHL) after vaccination.

Intervention

Eligible patients will receive once cycle of DC vaccination consisting of maximal 3 immunizations, given at 2 week intervals. MiHA mRNA-electroporated donor DC will be infused intravenously (2.5x105/kg body weight).

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Eligibility criteria

Inclusion criteria

- Patients positive for HLA-A2 and/or HLA-B7.

- Patients positive for HA-1, LRH-1 and/or ARHGDIB transplanted with the corresponding MiHA-negative donor.

- Patients >18 and <65 years of age.

- WHO performance status 0-2.

Exclusion criteria

- Life expectancy < 3 months.

- Severe neurological or psychiatric disease.

- Progressive disease needing cytoreductive therapy.

- HIV positivity.

- Patients with acute GVHD grade 3 or 4.

- Patients with extensive chronic GVHD.

- Patients with active infections (viral, bacterial or fungal) that requires specific therapy. Acute anti-infectious therapy must have been completed within 14 days prior to study treatment.

- Severe cardiovascular disease (arrhythmias requiring chronic treatment, congestive heart failure or symptomatic ischemic heart disease).

- Severe pulmonary dysfunction (CTCAE III-IV).

- Severe renal dysfunction (serum creatinine > 3 times normal level).

- Severe hepatic dysfunction (serum bilirubin or transaminases > 3 times normal level).

- Patients with known allergy to shell fish.

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):	19-08-2013
Enrollment:	0
Type:	Anticipated

Ethics review

Positive opinion

Date:	19-08-2013
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 40014
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL3969
NTR-old	NTR4128
CCMO	NL41183.000.12
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON40014

Study results

Summary results
N/A