MiHA-DC vaccinatie na allogene stamceltransplantatie.

Gepubliceerd: 19-08-2013 Laatst bijgewerkt: 19-03-2025

N/A

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

Samenvatting

ID

NL-OMON29214

Bron
NTR

Verkorte titel
PSCT16

Aandoening

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

Ondersteuning

Primaire sponsor: Radboud University Nijmegen Medical Centre
Overige ondersteuning: ZonMW, Dutch Cancer Society (KWF), NOTK

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

N/A

Onderzoeksopzet

- 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.

Onderzoeksproduct en/of interventie

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).

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- 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.

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	19-08-2013
Aantal proefpersonen:	0
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	19-08-2013
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 40014
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten
N/A