This is a multicentric study in which metastatic melanoma patients that have already been treated with at least 2 therapies, will be treated with their own white blood cells that are genetically transduced.

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Preclinical and clinical studies have shown that adoptive therapy with T cell receptor reactive lymphocytes leads to a clinical response in 13-45% of the patients.

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

Samenvatting

ID

NL-OMON28054

Bron
Nationaal Trial Register

Verkorte titel
TCR

Aandoening

metastasized melanoma
gemetastaseerde huidkanker

Ondersteuning

Primaire sponsor: NKI-AVL
Overige ondersteuning: Grant NKI-AVL

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1. Safety (CTCAE 4.0) of the TCR treatment;
2. Objective response rate according to RECIST 1.1.

Toelichting onderzoek

Achtergrond van het onderzoek

In this study up to 25 patients will be treated with T cell receptor gene therapy. The primary goal of this study is to provide a proof of principle by determining whether autologous T cells modified with a MART-1 specific TCR have sufficient biological activity in advanced stage melanoma patients in terms of classic tumor response. Patients must have had at least 2 lines of therapy before they can be treated in this study.

Doel van het onderzoek

Preclinical and clinical studies have shown that adoptive therapy with T cell receptor reactive lymphocytes leads to a clinical response in 13-45% of the patients.

Onderzoeksopzet

It is a two staged design. First 16 patients will be treated and reviewed. If more than 4 patients responded to the therapy another 9 patients will be treated.

Onderzoeksproduct en/of interventie

Patients will be hospitalized to first receive chemotherapy during one week, then they will receive their own transduced T cells intraveneously, which will be followed by a low-dose of interleukin-2.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Patients must be ≥ 18 years of age;

2. Patients must have inoperable stage IIIc or stage IV cutaneous melanoma (AJCC) progressing after at least two lines of therapy (DTIC, BRAF inhibitor, ipilimumab);

3. Patients must be HLA-A*0201 positive;

4. The primary tumor and/or metastasis have to be positive for MART-1 (>10% of tumor cells);

5. Patients with measurable disease (RECIST 1.1);

6. Patients must have a clinical performance status of ECOG 0 or 1;

7. Patients of both genders must be willing to practice a highly effective method of birth control during treatment and for four months after receiving the preparative regimen;

8. Patients must be able to understand and sign the Informed Consent document;

9. Absolute neutrophil count greater than 1.5 x 109/L without support of filgrastim;

10. Platelet count greater than 100 x 109/L;

11. Hemoglobin greater than 5 mmol/L or 8.0 in g/dl;

12. Chemistry;

13. Serum ALAT/ASAT less than 3 times the upper limit of normal, unless patients have liver metastases (< 5 times ULN);

14. Serum creatinine normal range or clearance at 50 ml/min or higher;

15. Total bilirubin less than or equal to 20 micromol/L, except in patients with Gilbert's Syndrome who must have a total bilirubin less than 50 micromol/L;

16. Seronegative for HIV antibody;

17. Seronegative for hepatitis B antigen, and hepatitis C antibody;

18. Seronegative for lues.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Life expectancy of less than three months;

2. Patients with metastatic ocular melanoma or mucosal melanoma;

3. Requirement for systemic steroid therapy;

4. Patients who have a history of more than two CNS metastases;

5. Patients who have any CNS lesion that is symptomatic, greater than 1 cm in diameter or show significant surrounding edema on MRI scan will not be eligible until they have been treated and demonstrated no clinical or radiologic CNS progression for at least 2 months;

6. Any immunosuppressive chemotherapy or systemic steroid therapy within the last 3 weeks;

7. Patients who have: history of coronary revascularization, documented LVEF of less than 45%, clinically significant atrial and/or ventricular arrhythmias including but not limited to atrial fibrillation, ventricular tachycardia, 2° or 3° heart block, documented FEV1 less than or equal to 60% predicted for patients with a history of cigarette smoking (greater than 20 pack/year within the past 2 years) and with symptoms of respiratory distress;

8. All patients' toxicities due to prior non-systemic treatment must have recovered to a grade

1 or less. Patients may have undergone minor surgical procedures or focal palliative radiotherapy (to non-target lesions) within the past 4 weeks, as long as all toxicities have recovered to grade 1 or less;

9. Women who are pregnant or breastfeeding, because of the potentially dangerous effects of the preparative chemotherapy on the fetus or infant. A negative pregnancy test before inclusion in the trial is required for all women of child bearing potential;

10. Any active systemic infections, coagulation disorders or other active major medical illnesses, such as active autoimmune disease requiring anti-TNF treatment.

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-04-2012
Aantal proefpersonen:	25
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	27-07-2012
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3396
NTR-old	NTR3539
Ander register	NKI-AVL / CCMO : M11TCR / NL37327.000.11;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A