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.

No registrations found.

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

Summary

ID

NL-OMON28054

Source
Nationaal Trial Register

Brief title
TCR

Health condition

metastasized melanoma
gemetastaseerde huidkanker

Sponsors and support

Primary sponsor: NKI-AVL
Source(s) of monetary or material Support: Grant NKI-AVL

Intervention

Outcome measures

Primary outcome

1. Safety (CTCAE 4.0) of the TCR treatment;

2. Objective response rate according to RECIST 1.1.

Secondary outcome

1. 1-year progression free survival (PFS) and median overall survival;

2. Efficacy of induction of tumor specific T cell responses (as measured by the persistence of Melan-A/MART1 specific T cells in peripheral blood samples at several time points following adoptive transfer and in tumor biopsies when possible).

Study description

Background summary

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.

Study objective

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.

Study design

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.

Intervention

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.

Contacts

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Eligibility criteria

Inclusion criteria

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.

Exclusion criteria

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.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-04-2012
Enrollment:	25
Type:	Anticipated

Ethics review

Positive opinion

Date:	27-07-2012
Application type:	First submission

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	NL3396
NTR-old	NTR3539
Other	NKI-AVL / CCMO : M11TCR / NL37327.000.11;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A