mRNA-transfected dendritic cell vaccination in high risk uveal melanoma patients

Published: 27-10-2008
Last updated: 11-05-2024

The primary goal is to show the capability of monocyte-derived DC after RNA electroporation for melanoma antigens to induce an immune response.The secondary objective is to show clinical response.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Ocular neoplasms
Study type	Interventional

Summary

ID

NL-OMON33733

Source
ToetsingOnline

Brief title
mRNA-DC vaccination in high risk uveal melanoma

Condition

- Ocular neoplasms
- Ocular neoplasms

Synonym
melanoma of the eye

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Rotterdamse Vereniging Blindenbelangen

en Stichting Nijmeegs Offensief Tegen Kanker

Intervention

Keyword: DC vaccination, immune therapy, uveal melanoma

Outcome measures

Primary outcome

In vivo immune response to the tumor associated antigens in at least 16 out of

31 patients will be considered as a positive result.

Secondary outcome

An improvement in disease-free survival > 95 months as compared with the

control group (arm B) will be considered a positive end result.

Study description

Background summary

Patients with uveal melanoma will be initially treated locally (for example with enucleation of the effected eye), after which there is frequently a complete remission. Especially in the patient group with chromosomal abnormalities (eg loss of chromosome 3) a large group will develop metastases. An effective treatment for metastasized melanoma is not available. Standard treatment with chemotherapy is effective in only a very limited number of patients and is not lasting. In large studies treatment with chemotherapy did not shown a survival benifit.
In previous studies we have treated stage III and IV melanoma patients with mature dendritic cells loaded with tumor-specific antigens. We have shown that this approach is feasible, and leads to very limited toxicity.
In this study we will treat 30 patients with DC electroporated with mRNA coding for gp100 and tyrosinase. The vaccinations will be given intravenously and intradermally. A group of 30 patients who fulfill all inclusion criteria except for HLA-A2 phenotype, and therefore receive no vaccinations, will serve as a control.

Study objective

The primary goal is to show the capability of monocyte-derived DC after RNA

electroporation for melanoma antigens to induce an immune response.
The secondary objective is to show clinical response.

Study design

This is a two-armed study including two times 31 patients. Arm A will be treated with 3 DC vaccinations at 2 week interval. In case of response the procedure can be repeated to boost the immune response. Arm B will receive the standard treatment (observation).

Intervention

Arm A will be vaccinated with DC vaccine, intravenous and intradermal 3 times with 2 week intervals.

Study burden and risks

The burden and risk associated with participation can be considered minimal. Previous studies (200+ patients treated in our centre) showed that toxicity was limited to local reactions at the site of injection, activation of the immune system (elevated temperature, flu-like symptoms), furthermore a limited group showed allergic skin reactions and depigmentation of the skin.
Apheresis is a safe procedure. Patients will have to visit our outpatient clinic (aferese, vaccination 1-3, skin test), extra blood will be drawn (vaccination 2 and 3 and skin test). Furthermore patients will undergo a skin test by which 6 mm biopsies will be taken.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- histologically documented evidence of uveal melanoma
- HLA-A02.01 phenotype is required for treatment group
- melanoma expressing gp100 (compulsory) and tyrosinase (non-compulsory)
- high risk genetic profile (loss of chromosome 3) as determined by FISH
- interval since local treatment of uveal melanoma is <12 months
- no signs of liver metastasis as determined by diagnostic CT-abdomen
- normal serum LDH
- no clinical signs of CNS metastases
- WHO performance status 0-1 (Karnofsky 100-70%)
- life expectancy >3 months
- age 18-75 years
- expected adequacy of follow-up
- no pregnant or lactating women
- written informed consent

Exclusion criteria

- history of second malignancy, adequately treated basal cell carcinoma or carcinoma in situ of the cervix is acceptable
- serious active infections, HbsAg or HIV positive (test only in case of high risk or clinical suspicion)
- autoimmune diseases or organ allografts
- concomitant use of immunosuppressive drugs
- known allergy to shell fish (since it contains KLH)

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-06-2009
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Approved WMO Date:	27-10-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-04-2009
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-05-2010

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
EudraCT	EUCTR2008-001974-33-NL
CCMO	NL22553.000.08

Study results

Date completed:	29-06-2016
Actual enrolment:	38