

Immunological effects of local low-dose immunotherapy in early stage melanoma patients

Submission date 18/07/2016	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 22/07/2016	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 25/09/2017	Condition category Cancer	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Melanoma is a type of skin cancer that is able to spread to other organs in the body. The most common sign of the disease is a new mole appearing or a change in appearance of an existing mole. At the moment, there isn't a widely used treatment option for early stage melanoma patients after they have had their initial therapy that will help prevent the cancer reoccurring. Indeed, the disease coming back remains the biggest challenge in the management of early stage melanoma. This study is investigating the use of stimulators of the immune system, namely unmethylated CpG type-B oligodeoxynucleotide (CpG type B) and Granulocyte /Macrophage-Colony Stimulating Factor (GM-CSF). The researchers want to know whether these substances can improve the immune response in order to fight the melanoma.

Who can participate?

Adults diagnosed with melanoma

What does the study involve?

Participants are randomly allocated to one of five groups. Those in group 1 are given an injection of CpG type B seven days at the tumour excision site (that is the site where the tumour is about to be removed) before undergoing a sentinel node biopsy (an operation that determines whether a cancer has spread beyond the original tumour into the lymphatic system). Those in group 2 are given an injection of CpG type B at the tumour excision site seven days and two days before the sentinel node biopsy. Those in group 3 are given an injection of CpG type B and GM-CSF at the tumour excision site seven days and two days before the sentinel node biopsy. Those in group 4 are given an injection of saline at the tumour excision site seven days before the sentinel node biopsy. Those in group 5 are given an injection of saline at the tumour excision site seven days and two days before the sentinel node biopsy. All participants are followed up two days after the biopsy and again after seven days to assess their immune response.

What are the possible benefits and risks of participating?

A possible benefit of participating in this trial might be that the immune system can effectively fight the melanoma cells that remain in the body after surgery. The side effects of these treatments are mild (symptoms of fever may occur) and are often easy to control.

Where is the study run from?

VU University Medical Center (Netherlands)

When is the study starting and how long is it expected to run for?

August 2003 to July 2017

Who is funding the study?

Fritz Ahlqvist Foundation

Who is the main contact?

Professor Tanja de Gruijl

Contact information

Type(s)

Scientific

Contact name

Prof Tanja de Gruijl

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1081 HV

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

03.199

Study information

Scientific Title

Immune response in the sentinel node in melanoma patients after the pre-operative administration of immune modulators GM-CSF and / or CpG 7909

Study objectives

It is expected that local administration of CpG 7909 around the primary tumor site in melanoma patients will result in an increased size of the sentinel lymph node (SLN) and we expect to see higher frequencies and activations states of DC and T cells due to the production of Th-1 type cytokines (IL-12, IL-2, IFN- γ , IFN- α).

The researchers also expect to see an increase in specific cytotoxic T-cells under the influence of both CpG 7909 and GM-CSF in the tumor positive SLN since CpG and GM-CSF can probably enhance the response against specific tumor antigens more effectively when tumor cells are present in the lymph nodes.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Institutional Review Board of the VU University Medical Centre, 16/03/2004, ref: IRB00002991

Study design

Single-center single-blinded randomized and placebo (saline) controlled phase-II clinical trial

Primary study design

Interventional

Secondary study design

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details to request a patient information sheet (in Dutch)

Health condition(s) or problem(s) studied

Clinical stage I-II melanoma

Interventions

There are three treatment arms and two saline (placebo) controlled arms.

Treatment arm 1: Intradermal injection at the tumor excision site with 8 mg CpG-B (PF-3512676, formerly named CPG 7909, Coley Pharmaceutical Group, Wellesley, MA) 7 days prior to the sentinel node biopsy.

Treatment arm 2: Intradermal injection at the tumor excision site with 1 mg CpG-B, 7 and 2 days prior to the sentinel node biopsy.

Treatment arm 3: Intradermal injection at the tumor excision site with 1 mg CpG-B and 100 μ g GM-CSF (Leukine®, Berlex Laboratories Inc. Montville, NJ) 7 and 2 days prior to the sentinel

node biopsy.

Placebo arm 1: Intradermal injection at the tumor excision site with saline (0.9% NaCl) 7 days prior to the sentinel node biopsy.

Placebo arm 2: Intradermal injection at the tumor excision site with saline (0.9% NaCl) 7 and 2 days prior to the sentinel node biopsy.

All patients are followed up at day 7 and day 14 (after the sentinel node biopsy).

Intervention Type

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

1. Unmethylated CpG type-B oligodeoxynucleotide; PF-3512676 (cpg7909) 2. Granulocyte /Macrophage-Colony Stimulating Factor; Leukine

Primary outcome measure

Immune status in the sentinel lymph node (SLN), specifically DC activation state and melanoma antigen specific T cells, measured using flow cytometry, interferon (IFN) gamma Elispot and tetramer analysis on immune cells that are harvested from the SLN at the day of the biopsy. .

Secondary outcome measures

Systemic anti melanoma activity measured using flow cytometry, IFN gamma Elispot and tetramer analysis on peripheral mononuclear blood cells from day -7, 0 and 14 (day 0 is the day of the SLN biopsy).

Overall study start date

01/08/2003

Completion date

01/07/2017

Eligibility

Key inclusion criteria

Patients with histologically proven primary melanoma, who are eligible for a SLN biopsy.

Participant type(s)

Patient

Age group

Adult

Sex

Both

Target number of participants

52

Key exclusion criteria

1. Treated with chemotherapy or immunotherapy in the last ten years
2. Autoimmune diseases
3. Congenital or acquired immunodeficiency
4. Use of immunosuppressive medications

Date of first enrolment

01/06/2004

Date of final enrolment

30/06/2007

Locations**Countries of recruitment**

Netherlands

Study participating centre

VU University Medical Center

De Boelelaan 1117

Amsterdam

Netherlands

1081 HV

Sponsor information**Organisation**

VU University Medical Center

Sponsor details

De Boelelaan 1117

Amsterdam

Netherlands

1081 HV

Sponsor type

Hospital/treatment centre

Website

<https://www.vumc.com/>

ROR

<https://ror.org/00q6h8f30>

Funder(s)

Funder type

Charity

Funder Name

Fritz Ahlqvist Foundation

Results and Publications

Publication and dissemination plan

Primary outcome; i.e. immune status SLN has been published in four papers.

Clinical follow-up will be published in separate paper in conjunction with an earlier clinical study (preceding 2004) in which, in a similar set-up, the effects of single administration of GM-CSF were studied (Vuysteke et al Cancer Res 2004).

Intention to publish date

30/10/2016

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	15/05/2007		Yes	No
Results article	results	15/07/2008		Yes	No
Results article	results	01/05/2015		Yes	No
Results article	results	01/04/2016		Yes	No