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

Submission date
18/07/2016

Recruitment status
No longer recruiting

Registration date
22/07/2016

Overall study status
Completed

Last Edited
25/09/2017

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English Summary

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 hypothesis
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)

Condition
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 100µg 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

Overall study end date
01/07/2017

Eligibility

Participant 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

Participant 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

Recruitment start date
01/06/2004

Recruitment end date
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
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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 stutus 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