Integrated analyses of melanoma-T cell interactions; relevance for immunotherapy

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immune disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON29970

Source
ToetsingOnline

Brief title
Integrated analyses of melanoma-T cell interactions

Condition

- Immune disorders NEC
- Skin neoplasms malignant and unspecified
- Pigmentation disorders

Synonym
skin cancer

Research involving
Human

Sponsors and support

Primary sponsor: NKI-AVL

Source(s) of monetary or material Support: KWF kankerbestrijding

Intervention

Keyword: interaction, melanocyte, melanoma, T cell

Outcome measures

Primary outcome

The presence of melanoma-reactive T lymphocytes will be determined in the tumor tissue and in the blood of each patient. These T lymphocytes will subsequently be tested for the ability to lyse melanoma cells in the metastasis and/or melanocytes in the skin, using the skin/tumor explant system. The analyses in this system also incorporate the influence of the tissue microenvironment on the T cell functionality.

Secondary outcome

Our ex vivo in situ tumor and skin explant system is the first to integrate the multidimensionality of human tumor-host interactions, and can therefore predict the efficacy of these interactions in vivo more accurately than in vitro assays based on rather artificial interactions between cells in suspension.

This study provides insight in the defects in individual patients that cause failure of tumor regression by immunotherapy and may lead to novel strategies to overcome these defects and improved immunotherapy of melanoma in the future.

Study description

Background summary

Melanoma is an immunogenic tumor that arises from the melanocytes and occasionally triggers an immune response. Immune responses against melanoma can also be actively induced in melanoma patients by immunotherapy. However, the presence of an immune response against melanoma does not necesarily lead to regression of the tumor.

Study objective

Our purpose is to establish whether the frequently observed absence of tumor regression in the presence of infiltrating T lymphocytes is due to a lack of T cell effector function or due to an inhibitory influence of the tumor microenvironment on T cell-mediated lysis.

Study design

We have developed a skin/tumor explant system, in which the function of T lymphocytes in the skin and in the tumor can be studied within the tissue architecture. In this study we will compare the efficacy of T lymphocytes to kill melanoma cells in the tumor or their efficacy to kill normal melanocytes in the skin and cause depigmentation. T lymphoytes derived form both tumor tissue and peripheral will be analyzed.

The experiments will address the following questions:

1. Are patient-derived T lymphocytes that are reactive with antigens on both melanoma cells and melanocytes capable of killing melanoma cells in the tumor tissue as well as melanocytes in the skin?

2. What is the influence of the tissue microenvironment on the functionality of the
T lymphocytes?

3. What is the mechanism of cell death that is mediated by the T lymphocytes in the tumor or skin tissue?

Study burden and risks

hardly or no burden for the patient and no additional risks

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

Metastatic melanoma; (sub)cutaneous metastases

Exclusion criteria

Hemophilia en other blood coagulation disorders

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-08-2006
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	27-07-2006
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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
CCMO	NL12654.031.06