Flow cytometric analysis of circulating melanoma cells after enrichment by leukapheresis

Published: 16-11-2018
Last updated: 19-08-2024

The primary objective of this study is to optimize a workflow for identification of circulating melanoma cells in LA using flow cytometry. Secondary objectives include the detection of known mutations in different CMC subsets.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON49343

Source
ToetsingOnline

Brief title
FAME

Condition

- Skin neoplasms malignant and unspecified
- Skin neoplasms malignant and unspecified

Synonym
Metastatic melanoma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Circulating melanoma cells, Flow cytometry, Leukapheresis, Metastatic melanoma

Outcome measures

Primary outcome

The primary endpoint of this study will be to determine the percentage of patients with cells positive for any melanoma specific marker identified by flow cytometric analysis of LA product.

Secondary outcome

Secondary endpoints are the comparison of putative CMC counts as identified by flow cytometry and CellSearch in blood and LA product and mutation status of a mutation, present on primary- or metastatic tumor tissue, in different CMC subsets as identified by flow cytometry.

Study description

Background summary

Recent developments on the treatment of metastatic melanoma have changed perspectives of patients with a previously poor prognosis. Promising results of immuno- and targeted therapy in the metastatic setting has shifted current focus to the application of those treatments in the adjuvant setting. However, treatment with these modalities yields significant toxicity leading to hospitalization and treatment withdrawal 15% of the patients. Furthermore, in studies conducted in the adjuvant setting, the number needed to treat was rather high, indicating a significant proportion of the patients do not benefit from adjuvant systemic treatment. This emphasizes the need for the identification of a prognostic biomarker enabling to discriminate patients who would benefit from adjuvant therapy. In other cancer types, circulating tumor cells (CTCs) are of significant prognostic value. However, regular methods to identify CTCs are not suitable for identification of melanoma cells since those methods are based on Epithelial Cell Adhesion Molecule (EpCAM) isolation techniques. Moreover, literature has reported melanoma cells to be phenotypically heterogenic, complicating capture methods based on one or two

antibodies. Therefore, we plan to identify circulating melanoma cells (CMCs) using multicolor flow cytometry targeting different melanoma specific antigens. Given the expected low numbers of CMCs in the adjuvant setting, we aim to identify CMCs in leukapheresis (LA) material, enabling detection of CMCs in larger volumes of blood. Furthermore, we aim to confirm true CMC identity of cells designated as CMCs by flow cytometry by downstream identification of a known mutation.

Study objective

The primary objective of this study is to optimize a workflow for identification of circulating melanoma cells in LA using flow cytometry. Secondary objectives include the detection of known mutations in different CMC subsets.

Study design

Prospective, observational study

Study burden and risks

All patients are asked to undergo a single LA procedure which will take a maximum of 2 hours. A maximum volume of calculated total body volume, which is approximately 5 L peripheral blood will be processed with the use of an Optia Spectra Cell Separator. Patients do not benefit from this study. The most common adverse events to be expected are pain or bruising at the venipuncture site (1-5%), apprehension or fainting associated with venipuncture (1-5%), fluid imbalance (0.01-0.1%) and citrate anticoagulant infusion-related symptoms resulting in tingling or buzzing around the mouth or fingers (20-50%). All patients will receive intravenous calcium to prevent this. The risk of adverse events associated with LA is considered negligible.

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

* Patients with metastatic melanoma
* Starting new line of systemic treatment for metastatic disease, irrespective of treatment modality (i.e. BRAF-targeted therapy or immunotherapy) or with progression under current treatment
* Age *18 years

Exclusion criteria

* Known hypersensitivity to the anticoagulant used for apheresis
* Inadequate cardiac function or severe cardiovascular comorbidity
a. Heart failure NYHA class III/IV
* Hemoglobin level < 6.0 mmol/L
NOTE: red blood cell transfusions are allowed to increase the hemoglobin level at the discretion of the investigator
* Coagulation disorders as defined by one of the following:
NOTE: the use of all types of anticoagulant therapy is permitted
a. Coagulation disorder in medical history
b. Platelet count < 40 x 109/L;
Patients not on anticoagulant therapy which affects PT or APTT if:
c. PT > 1.5 x ULN or PT-INR > 1.5 x ULN
d. APTT > 1.5 x ULN
Patients who take anticoagulant therapy which affects PT or APTT if:
e. PT or APTT > 1.5 x the upper limit of the desired therapeutic window

f. Total bilirubin > 2.5 x ULN

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-04-2019
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	16-11-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	15-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	21-01-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL67262.078.18