Early detection of immunotherapy-mediated toxicity

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We hypothesize that during an episode of immune-mediated organ specific toxicity, as a result of inflammation and damage to the specific organ, organ-derived DNA will be detectable in blood of patients. The aim of this project is to investigate...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON57250

Source
ToetsingOnline

Brief title
EDIT

Condition

- Autoimmune disorders
- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
immunotherapy, toxicity

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: cell-free DNA, immunotherapy, toxicity

Outcome measures

Primary outcome

The primary study endpoint is the detection of organ-specific methylation patterns in cell-free DNA during an episode of immunotherapy-mediated toxicity.

Secondary outcome

Secondary endpoints are the levels of other biomarkers of inflammation during immunotherapy-mediated toxicity and the comparison organ-specific methylation profiles in blood with other biomarkers of inflammation.

Study description

Background summary

The number of tumor types and settings in which immune checkpoint inhibitors (immunotherapy) is standard treatment is rapidly expanding. However, toxicity is a frequent adverse event often necessitating high-dose of immunosuppressant treatments such as corticosteroids and sometimes even requiring permanent discontinuation of checkpoint inhibitors. Early detection of immunotherapy-mediated toxicity and early initiation of immunosuppressant treatment might reduce the total dose of glucocorticoids and other immunosuppressants needed for clinical management. More importantly, it might result in a lower discontinuation rate of treatment due to severe toxicity.

Study objective

We hypothesize that during an episode of immune-mediated organ specific toxicity, as a result of inflammation and damage to the specific organ, organ-derived DNA will be detectable in blood of patients. The aim of this project is to investigate whether the presence of cell-free DNA originating from the organ towards which immunotherapy-induced toxicity is directed, can be detected using epigenetic profiling of cell-free DNA.

Study design

Organ specific methylation patterns in cell-free DNA will be derived from 1) paired blood samples collected from patients during an episode of immunotherapy-mediated toxicity and in absence of immunotherapy-mediated toxicity and 2) samples from patients without checkpoint inhibitor treatment but with organ confined auto-immune diseases. Optionally, feces will be collected at the same time points to investigate inflammation biomarkers during an episode of immunotherapy-mediated colitis. In addition, blood will be drawn for investigation of other biomarkers of inflammation.

Study burden and risks

The risk of blood withdrawals is negligible.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Planned treatment with (intravenous) checkpoint inhibitors for any type of cancer according to standard of care.
- Patients with immune-mediated organ specific disease including, but not limited to, immune-mediated colitis such as colitis ulcerosa or auto-immune hepatitis
- Age >=18 years
- Able to understand the written information and able to give informed consent

Exclusion criteria

- Unable to draw blood for study purposes

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-09-2021
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	06-09-2021
Application type:	First submission

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

ID: 23691
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL77494.078.21
OMON	NL-OMON23691