Early Detection of Immunotherapy-mediated Toxicity

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON23691

Source
Nationaal Trial Register

Brief title
EDIT

Health condition

melanoma, renal cell carcinoma, autoinflammatory diseases

Sponsors and support

Primary sponsor: Erasmus MC
Source(s) of monetary or material Support: none

Intervention

Outcome measures

Primary outcome

The primary study endpoint is the detection of organspecific methylation patterns in cell-free DNA during an irAE.

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

Rationale: 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 (irAE) 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 disease burden from immunotherapy, in addition to reducing 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.
Objective: We hypothesize that during an irAE (immune-related adverse event), 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-inflammatory 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 population: Adult patients planned to receive or receiving immune checkpoint inhibitors
as anti-cancer treatment and adult patients with auto-inflammatory diseases directed to a specific organ
Main study parameters/endpoints: The primary study endpoint is the detection of organspecific
methylation patterns in cell-free DNA during an irAE. 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 objective

We hypothesize that during an irAE, 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 immunotherapyinduced
toxicity is directed, can be detected using epigenetic profiling of cell-free DNA. If this hypothesis is confirmed, epigenomic profiling of cell-free DNA should further be explored to test
Figure 2. Overview of MeD-seq technology. Active genes display gene body methylation (1), whereas inactive
genes show promoter and enhancer methylation. LpnPI digests methylated templates in 32 bp fragments (3)
surrounding the LpnPI containing reads and alignment to genome (7). Shown are gene tracks of MeD-seq readcounts
displaying differential DNA methylation of the HOXB locus in liver and ovary

whether it can serve as an early detection marker for ieAEs, i.e. before the patient experiences
symptoms or when the patient only experiences mild symptoms.

Study design

start immunotherapy, during immunotherapy, during irAE, after irAE

Contacts

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Eligibility criteria

Inclusion criteria

1. Population with immunotherapy-related organ specific toxicity
 Planned treatment with (intravenous) checkpoint inhibitors for any type of cancer according to standard of care.
 Age ≥18 years
 Able to understand the written information and able to give informed consent
2. Population with immune-mediated organ specific disease
 Patients with immune-mediated organ specific disease including, but not limited to, immune-mediated colitis such as ulcerative colitis, Crohn's disease or auto-immune hepatitis
 Age ≥18 years
 Able to understand the written information and able to give informed consent

Exclusion criteria

4.2 Exclusion criteria
 Unable to draw blood for study purposes

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2021
Enrollment:	50
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Not applicable
Application type: Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 57250
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9486
CCMO	NL77494.078.21
OMON	NL-OMON57250

Study results