Early Detection of Immunotherapy-mediated Toxicity

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Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON23691

Bron
Nationaal Trial Register

Verkorte titel
EDIT

Aandoening

melanoma, renal cell carcinoma, autoinflammatory diseases

Ondersteuning

Primaire sponsor: Erasmus MC
Overige ondersteuning: none

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

start immunotherapy, during immunotherapy, during irAE, after irAE

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

4.2 Exclusion criteria
 Unable to draw blood for study purposes

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-07-2021
Aantal proefpersonen:	50
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Niet van toepassing
Soort: Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 57250
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten