Nivolumab dose optimization during nivolumab therapy in melanoma patients after achieving a complete, partial or stable response (NIVOPTIMIZE-trial)

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This study has been transitioned to CTIS with ID 2024-516718-39-00 check the CTIS register for the current data. The primary objective is to demonstrate that the nivolumab steady-state level after 3 cycles with a reduced nivolumab dosage (240 mg...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Skin neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON54156

Source
ToetsingOnline

Brief title
NIVOPTIMIZE-trial

Condition

- Skin neoplasms malignant and unspecified

Synonym
melanoma, skin cancer

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: dose reduction, nivolumab, Oncology, pharmacokinetics

Outcome measures

Primary outcome

Difference between the nivolumab mean trough level after 3 reduced doses (240 mg every 4 weeks) and after the first dose of 480 mg or 6mg/kg.

Secondary outcome

- PD-1 receptor occupancy in PBMCs, measured 4 weeks after 3 reduced nivolumab doses

- Grade >=3 adverse events during reduced doses

- Number of patients with new PD during 3 reduced doses

- Pharmacokinetic profile of nivolumab

- Cost effectiveness

Study description

Background summary

Patients with advanced melanoma or renal cell carcinoma are, amongst others, currently treated with nivolumab monotherapy or with nivolumab and ipilimumab followed by nivolumab. Even though registration studies administered nivolumab in a 3 mg/kg 2 weekly scheme, currently, nivolumab monotherapy is either administered in a 240 mg 2-weekly scheme or in a 480 mg of 6mg/kg 4-weekly scheme. With the current dosing regimen, steady-state is achieved after approximately 5 to 6 months, whereas a tumor response is usually observed earlier in patients with metastatic melanoma and renal cell carcinoma. Moreover, PD-1 receptor occupancy is almost saturated above doses of 0.3 mg/kg, or at nivolumab serum levels of 10 mg/L, which is a concentration that is achieved after one treatment cycle. In melanoma patients, the additional probability on response in patients treated with 3 mg/kg compared to 1 mg/kg

seems limited. PFS and OS for 3 mg/kg were not superior to 1 mg/kg. Therefore, in this study, our aim is to investigate nivolumab trough levels and pharmacokinetic parameters after 3 reduced nivolumab doses.

Study objective

This study has been transitioned to CTIS with ID 2024-516718-39-00 check the CTIS register for the current data.

The primary objective is to demonstrate that the nivolumab steady-state level after 3 cycles with a reduced nivolumab dosage (240 mg every 4 weeks) is not lower than the nivolumab concentration 4 weeks after the first 480 mg or 6mg/kg dose. Secondary objectives are to explore the cost-effectiveness of the alternative dosing regimen, the pharmacokinetic profile of nivolumab, the safety and efficacy of the alternative dosing regimen, and the PD-1 receptor occupancy in PBMCs.

Study design

Single-centre, single-arm, pharmacokinetic intervention trial.

Intervention

Three reduced doses of nivolumab 240 mg every 4 weeks in patients having a confirmed CR, PR or SD at least 6 months after treatment start.

Study burden and risks

Patients with a confirmed response or stable disease (CR, PR or SD) and are at least 6 months on treatment, will be asked to participate in this trial and receive three doses of 240 mg nivolumab instead of 480 mg or 6mg/kg. Therefore, theoretically, participation in this trial may affect clinical outcome in these patients. However, an increasing number of physicians discontinues treatment early at achieving CR, PR or SD, based on durable responses after treatment discontinuation. Therefore, the additional risk of participation in this trial is considered limited compared to daily clinical practice.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Age >= 18 years
2. Advanced or metastatic melanoma or renal cell carcinoma
3. Current treatment with nivolumab in a 480 mg or 6mg/kg, 4 weekly scheme
4. Documented confirmed and ongoing CR, PR or SD according to RECIST v1.1
5. On treatment for at least 6 months

Exclusion criteria

- Unable to draw blood for study purposes
- Patients willing to participate or already included in the SAFE-STOP trial

Study design

Design

Study type: Interventional

Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-01-2022
Enrollment:	34
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	opdivo
Generic name:	nivolumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	22-04-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-07-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-04-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	30-06-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-01-2024
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
EU-CTR	CTIS2024-516718-39-00
EudraCT	EUCTR2021-001707-32-NL
CCMO	NL77343.078.21