Safe Stop Trial: observational study of the STOP & GO strategy of PD-1 blockade in advanced melanoma patients upon achieving a complete or partial response

Published: 07-06-2018
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This study has been transitioned to CTIS with ID 2024-516937-10-01 check the CTIS register for the current data. The primary objective of this study is to evaluate ongoing responses in patients with advanced and metastatic melanoma who discontinue...

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

Summary

ID

NL-OMON55748

Source
ToetsingOnline

Brief title
Safe Stop Trial Melanoma

Condition

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

Synonym
malignant melanoma, Melanoma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Zilveren Kruis,CZ groep Zorgverzekeringen,KWF ,Menzis,Stichting Volksgezondheidszorg Zuid Nederland (VGZ),Zorgverzekeraars Zilveren Kruis;CZ;VGZ en Menzis;KWF

Intervention

Keyword: Melanoma, Nivolumab, Pembrolizumab, Response

Outcome measures

Primary outcome

The primary endpoint is the rate of ongoing responses (CR and PR) according to

RECIST v1.1 at 24 months after first start of nivolumab or pembrolizumab.

Secondary outcome

The secondary endpoints include:

1a. Total duration of response after first documented CR or PR followed by

treatment interruption

1b. Duration of response (CR and PR) after discontinuation of nivolumab or

pembrolizumab

2. Progression-free survival (PFS) from start of nivolumab/pembrolizumab until

first PD (PFS1)

3a. Rate of reintroduction of nivolumab/pembrolizumab upon first PD

3b. Rate of introduction of other systemic therapy (i.e. other than

nivolumab/pembrolizumab) upon first PD

4a. Best response on rechallenge with nivolumab/pembrolizumab

4b. Best tumor response after introduction of other systemic therapy (i.e.

other than monotherapy PD-1 blockade)

5a. PFS after reintroduction of nivolumab/pembrolizumab (PFS2a)

5b. PFS after introduction other systemic therapy (i.e. other than monotherapy PD-1 blockade) (PFS2b)

6. Total PFS (PFSTotal) defined as the period from initial start of PD-1 blockade until final PD (including period after discontinuation and (re)introduction of nivolumab/pembrolizumab or other salvage therapy)

6b. Overall survival (OS)

7. Rate of grade 3-4 adverse events (AEs) after discontinuation or reintroduction of nivolumab/pembrolizumab

8. Change in tumor burden since the start and after early discontinuation of PD-1 blockade

9. Change in QoL after discontinuation of PD-1 blockade

10. Change in fear of disease recurrence/progression

11. Change in productivity (paid and unpaid work) after discontinuation of PD-1 blockade

12. Change in healthcare resource (within and outside the hospital) after discontinuation of PD-1 blockade

13. Change in hours of informal care after discontinuation of PD-1 blockade

14. QoL at disease progression and restart of systemic therapy (when applicable)

15. Change in QoL after discontinuation of radiological follow-up

Study description

Background summary

Based on the pivotal clinical trials, PD-1 blockade with nivolumab or pembrolizumab is usually discontinued in case of disease progression, severe toxicity, or after a treatment duration of maximum 2 years. However, durable tumor responses have been observed after early discontinuation of PD-1 blockade in patients with advanced and metastatic melanoma who achieve a tumor response. In clinical practice, an increasing number of physicians discontinues treatment on an individual basis, for example at achieving complete (CR) or partial response (PR), or on patients* request. From a toxicity, economic, and patient perspective, a shorter treatment duration is obviously to be preferred, however, early discontinuation of PD-1 blockade has not been prospectively evaluated in clinical practice.

Study objective

This study has been transitioned to CTIS with ID 2024-516937-10-01 check the CTIS register for the current data.

The primary objective of this study is to evaluate ongoing responses in patients with advanced and metastatic melanoma who discontinue first-line monotherapy with nivolumab or pembrolizumab upon achieving CR or PR according to RECIST v1.1

Study design

This is a multicenter prospectively collected single arm study in the Netherlands. The initial protocol (v1.0, 20 October 2018) is extended with the QoL amendment.

Intervention

Discontinuation of PD-1 blockade (nivolumab or pembrolizumab) at achieving CR or PR.

Study burden and risks

Patients are treated and evaluated according to standard of care in the Netherlands. As PD-1 blockade will be discontinued earlier than 2 years, participation is this trial may affect treatment efficacy, which will be evaluated as primary objective of this study. As a result, participation in this trial may affect clinical outcome and even survival of these patients. On the other hand, early discontinuation may reduce the toxicity rate. However, as an increasing number of physicians discontinues treatment on an individual basis at achieving CR or PR, the additional risk of participation in this trial is considered limited as compared to daily clinical practice.

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

- advanced or metastatic melanoma
- current treatment with first-line nivolumab or pembrolizumab for advanced or metastatic melanoma; previous systemic treatment, including immunotherapy, in (neo)adjuvant setting for resectable melanoma is allowed
- documented diagnostic CT at start of PD-1 blockade with nivolumab or pembrolizumab
• For patients with CR on a diagnostic CT at response evaluation, a low dose-CT (which is usually part of 18FDG-PET/CT) is allowed at baseline
• For patients with PR on a diagnostic CT at response evaluation, a low dose-CT (which is usually part of 18FDG-PET/CT) is allowed if sufficient target lesions are measurable for response evaluation according to RECIST v1.1 criteria. In this specific case the sponsor should be consulted.

- documented tumor response evaluation every 12 (±1) weeks according to RECIST v1.1 (34) using a diagnostic CT as per standard practice
- presence of MRI brain for the screening of brain metastases (prior to discontinuation of PD-1 blockade)
- willingness to discontinue nivolumab or pembrolizumab within 6 (+1) weeks weeks after
confirmation of CR or PR before the full period of 2 years therapy

Exclusion criteria

Concomitant systemic therapies with other anti-cancer agents, e.g. BRAF-inhibitor, anti-CTLA4 (e.g. ipilimumab), or other PD-1 blockade than nivolumab or pembrolizumab

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-02-2019
Enrollment:	200
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Keytruda
Generic name:	pembrolizumab
Registration:	Yes - NL intended use
Product type:	Medicine

Brand name:	Opdivo
Generic name:	nivolumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-06-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-11-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	18-03-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-06-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-01-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-03-2024
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	CTIS2024-516937-10-01
EudraCT	EUCTR2018-001384-23-NL
CCMO	NL65512.078.18