[18F]FB-IL2 imaging of T cell response as biomarker to guide treatment decisions in metastatic melanoma patients

Published: 31-10-2014
Last updated: 21-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON44731

Source
ToetsingOnline

Brief title
IL2 imaging metastatic melanoma

Condition

- Metastases

Synonym
advanced melanoma, Metastastic melanoma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Genentech (Roche),Genentech (Roche) en ZonMw

Intervention

Keyword: Immune checkpoint inhibitors, PET scan, T cell respons

Outcome measures

Primary outcome

*To determine tracer kinetics of [18F]FB-IL2 PET.

*To determine if [18F]FB-IL2 PET is able to detect a treatment-induced immune response in tumors.

*To analyze if the tumor uptake of [18F]FB-IL2 correlates with the number of IL2 receptor positive immune cells.

Secondary outcome

*To correlate the tumor uptake of [18F]FB-IL2 with response to therapy.

*To analyze heterogeneity in immune response to treatment between separate lesions, as determined by [18F]FB-IL2 PET.

*To demonstrate treatment induced immune cell activation in non-target tissues and if possible to correlate PET observations with side effects related to the tissue involved.

*To provide a safety profile of [18F]FB-IL2 PET.

Study description

Background summary

T cell infiltration of tumor lesions is a known prognostic factor in several tumor types and is used as treatment mechanism in some of these tumor types. In metastatic melanoma, treatment with immune checkpoint inhibitors like ipilimumab induces clinical benefit in about 30% of the patients. These immune-based therapies are however accompanied by serious immune-related adverse events and high costs. Besides ipilimumab, the immune checkpoint

inhibitors pembrolizumab, nivolumab and the combination of ipilimumab and nivolumab are approved as treatment for advanced melanoma.
Tumor infiltrating T cells express a high affinity interleukin-2 (IL2) receptor on their surface. These T cells could therefore been visualized by the radio-labelled ligand of this receptor, [18F]FB-IL2. If [18F]FB-IL2 PET is able to detect a response to treatment it could serve as a non-invasive early indicator of response. If no treatment-induced T cell infiltrating of tumor lesions is seen, patient could be spared further treatment. Besides, accumulation in non-target tissue could predict the development of an immune-related adverse event. This finding could be anticipated by timely discontinuation of immunotherapy.
The value of the [18F]FB-IL2 PET is already tested in ex vivo and animal models, but has not been proven yet in human beings. We hypothesized that a high correlation exist between [18F]FB-IL2 uptake and the extend of T cell infiltration of tumor lesions.

Study objective

Main objective of this study is to determine if the [18F]FB-IL2 PET is able to detect a treatment-induced immune response in tumor lesions of patients with metastatic melanoma and if the tumor uptake of the tracer correlates with the number of IL2 receptor positive cells in these lesions. Besides, kinetics of the tracer will be measured with an extended PET protocol in the first 5 patients.
Secondary objectives are to correlate tumor uptake of [18F]FB-IL2 with response to therapy. In addition, heterogeneity of tracer uptake in tumor lesions and tracer uptake of non-target tissues will be investigated. Since this is the first study with application of [18F]FB-IL2 PET in humans, a safety profile of the [18F]FB-IL2 PET will be determined.

Study design

This study is a feasibility (observational) study for the use of [18F]FB-IL2 as a PET tracer, which will be conducted in a single center. Patients will be treated with ipilimumab, nivolumab, pembrolizumab or the combination of ipilimumab and nivolumab conform standard of care. The study will consist of two substudies. In both substudies patients will receive a [18F]FB-IL2 PET scan at baseline and at week 2 of treatment with immunotherapy. In patients participating in phase 2 of the study, two biopsies and two blood samples will be taken, of which the results will be correlated to the scan results. Adverse events of immunotherapy will be registrated and will be correlated to the amount of infiltrating T cells on the [18F]FB-IL2 PET. If adverse events occur in colon or skin and patients have given their consent, a biopsie can be taken from this non-target tissue. Response to treatment will be determined on the CT scans, which will made in week 12 and 16 as part of regular care.

Intervention

Main intervention of this study is a [18F]FB-IL2 PET-CT scan. This scan will be performed twice: at baseline and at week 2 of treatment with immunotherapy.

Study burden and risks

The investigational product, [18F]FB-IL2, is chemically almost identical to the drug Proleukin. Since it will be used in a sub-therapeutic dose of 50 µg or less, no drug interactions or adverse events are to be expected. Nevertheless, vital signs will be monitored until one hour after tracer injection and blood parameters will be checked before and after each scan. A total of 14 blood samples in phase 1 and 2 blood samples in phase 2 of the study will be obtained for study purposes, which will give minor discomfort. Subjects will undergo two PET-CT scans, which are estimated to carry an added radiation burden of 11.8 mSv, and a diagnostic CT with an additional radiation burden of 18 mSv. Thus, the total radiation burden (29.8 mSv) is substantial, but according to the investigators is justified by the possibility of finding a noninvasive biomarker for predicting response to immune-modulating therapy in metastatic melanoma patients, as these therapies are only of clinical benefit in part of the patients, but still can be accompanied by severe adverse effects. In patients participating in phase 2 of the study, after each PET scan a biopsy will be taken from an easy accessible lesion. This biopsy could be painful and carries the risk of bleeding. To minimize the burden to the patient, intervention and patients* visits are preferably planned on the same day.

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

1. Has signed informed consent.
2. Age18 years or older.
3. Histologically confirmed cutaneous metastatic melanoma (Stage IV).
4. At least one measurable metastatic lesion based on RECIST version 1.1.
5. At least one easy accessible metastatic melanoma lesion, which could be biopsied.
6. Eligible for treatment with ipilimumab, nivolumab, pembrolizumab or combination of ipilimumab and nivolumab.
7. No contraindication for performing a CT scan.
8. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-1.
9. Women with child-bearing potential and men with reproductive potential must be willing to practice acceptable methods of birth control during the study.
10. Must have adequate organ function (liver, kidney, cardiac).

Exclusion criteria

1. Pre-existing auto-immune disease, which could be exacerbated by immunotherapy.
2. Presence of malignancy other than the disease under study within 5 years of study enrolment.
3. Brain metastases that are symptomatic or not stable for 8 weeks
4. The use of corticosteroids (at the start of treatment).
5. Evidence of active infection requiring antibiotic therapy at start of treatment.
6. Current use of a prohibited medication for treatment with immunotherapy.
7. Known immediate or delayed hypersensitivity reaction to ipilimumab, nivolumab or pembrolizumab, or excipients.
8. Unresolved toxicity of National Cancer Institute Common CTCAE grade 2 or higher from previous anti-cancer therapy, except alopecia.
9. A history or evidence of cardiovascular risk.

10. Any serious or unstable pre-existing medical conditions, psychological, familial, sociological, or geographical conditions that do not permit compliance with the protocol; or unwillingness or inability to follow the procedures required in the protocol.
11. Altered mental status, or any psychiatric condition that would prohibit the understanding or rendering of informed consent.
12. Pregnant or nursing females.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-10-2016
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	31-10-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-10-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-10-2016
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-04-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-12-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2014-003387-20-NL
ClinicalTrials.gov	NCT02922283
CCMO	NL49939.042.14