PD-L1 PET imaging in patients with melanoma or NSCLC with brain metastasis and eligible for treatment with nivolumab

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Phase one: To assess the dynamics and kinetics of [18F]PD-L1 in human subjects to establish optimal tracer dose and scan schedule.Phase two: To validate the [18F]PD-L1 PET tracer by association of PD-L1 tumor expression as determined on PET and PD-...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON46055

Source
ToetsingOnline

Brief title
PD-L1 PET imaging in brainmets

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Melanoma / non small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Bristol-Myers Squibb,Industrie

Intervention

Keyword: Brain metastases, Melanoma, PD-L1, PET imaging

Outcome measures

Primary outcome

Phase one: To determine the optimal tracer dose and schedule for performing

[18F]PD-L1 PET scans.

Phase two: To assess the association of PD-L1 expression as measured by PD-L1

tracer uptake on PET with PD-L1 expression as measured by immunohistochemical

(IHC) staining for PD-L1 of corresponding tumor lesions.

Secondary outcome

To determine between-subject and within-subject variability in [18F]PD-L1

uptake in melanoma or non small cell lung cancer metastases and to assess the

association between the radiological response to anti-PD1 treatment and PD-L1

expression as measured by PET scanning and by immunohistochemistry.

Study description

Background summary

Clinical trials have shown efficacy of PD1/PD-L1 checkpoint inhibitors in multiple solid tumors, including melanoma and non small cell lung cancer. Whole body information with regard to target presence, drug kinetics and dynamics, as well as binding of PD-L1 targeting agents to the immune system cells is lacking. Molecular imaging of PD-L1 could lead to new insights on heterogeneity of PD-L1 expression in metastatic lesions and be of help in the prediction of

response to PD1/PD-L1 inhibitors in a non-invasive manner.

Study objective

Phase one: To assess the dynamics and kinetics of [18F]PD-L1 in human subjects to establish optimal tracer dose and scan schedule.
Phase two: To validate the [18F]PD-L1 PET tracer by association of PD-L1 tumor expression as determined on PET and PD-L1 expression as determined by immunohistochemistry

Study design

This is a feasibility study for the use of [18F]PD-L1 as a PET tracer that will be conducted in a single center. The study consists of two phases. The aim of phase one is to provide pharmacokinetic information on the tracer and to determine the optimal time point for imaging. In the second phase the main study objective will be assessed.

Study burden and risks

The expected applied injected activity of [18F]PD-L1 is 200 MBq, as is the case for most other 18F-labeled tracers. The radiation burden for a dose of 200 MBq is approximately 4.4 mSv. Patients will receive 2 serial PET scans each accompanied by a low dose CT scan which adds up to a total dose of 11.8 mSv. The radiation burden of these patients complies with category III (moderate risk) according to the International Commission on Radiological Protection (ICRP) guidelines (ICRP publication 62).
The biopsies needed in phase two of this study are obtained using an invasive procedure. Although biopsies are generally considered to be safe, they can be painful and carry certain risks, such as bleeding at the puncture site.
Biopsies will preferably been taken from easily accessible lesions to minimize the burden and risk for the patient.
Whenever possible, all procedures that are part of the study protocol will be planned during regular visits to the hospital as part of care as usual.

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. Subjects must sign informed consent prior to inclusion in this trial.
2. Subjects must be *18 years of age and competent to give informed consent.
3. Subjects must be diagnosed with histologically confirmed stage IV melanoma of non-small celllungcancer.
4. At least one radiologic new lesion in the brain by MRI, which should be measurable by RANO-BM criteria (longest diameter * 10 mm and perpendicular diameter * 5 mm). Lesions with prior local treatment (i.e., SRT or surgical resection) can be considered measurable if there has been demonstrated progression since the time of local treatment. Leptomeningeal involvement is allowed, but cannot be used as target lesion.
5. At least one easy accessible metastatic melanoma lesion of which a biopsy can be taken.
6. Subjects must be treatment-naive to nivolumab. (also as adjuvant treatment)
7. Subjects must score at least 1 or higher on the Eastern Cooperative Oncology Group (ECOG) Performance Status.(21)
8. Subjects must have adequate organ function as defined by the following laboratory values (determined within 28 days prior to randomization/registration):
1. White blood cells (WBC) * 2000 /µL
2. Absolute neutrophil count (ANC) * 1500 /µL
3. Platelets * 100 x103 /µL
4. Hemoglobin * 9 g/dL or * 5.6 mmol/L
5. Serum creatinine * 1.5 times upper limit of normal (ULN) or creatinine clearance > 40 ml/min (using the Cockcroft-Gault formula)
6. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) * 3 times ULN

7. Bilirubin * 1.5 times ULN (Except patients with the Gilbert Syndrome, for whom a maximum of * 3.0 mg/dL is acceptable)
9. Women of childbearing potential (WOCBP) should have a negative urine or serum pregnancy test within 7 days prior to receiving the first administration of nivolumab. Women with non-childbearing potential may be included if they are either surgically sterile or have been postmenopausal for * 1 year.
10. WOCBP and men who are sexually active with WOCBP must agree to use appropriate method(s) of contraception. (see section 5.2)

Exclusion criteria

1. Prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2 antibody, or any other antibody or drug specifically targeting T-cell costimulation or immune checkpoint pathways, except anti-CTLA4 antibody.
2. Subjects who have not recovered to Common Terminology Criteria for Adverse Events (CTCAE) v4.0 Grade 1 or better from the adverse events due to previous cancer therapy.
3. Evidence for an active, known or suspected autoimmune disease. Subjects diagnosed with vitiligo, type I diabetes mellitus, residual hypothyroidism due to autoimmune condition only requiring hormone replacement, psoriasis not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger are permitted to enroll.
4. Treatment with corticosteroids in an increasing dosage in the 7 days prior to the first administration of nivolumab. (A stable or decreasing dosage of * 4 mg dexamethasone or equivalent is allowed. In addition, inhaled or topical steroids and adrenal replacement doses are permitted in the absence of active autoimmune disease.)
5. Previous malignancies (except non-melanoma skin cancers, in situ bladder cancer, gastric or colon cancers, cervical cancers/dysplasia or breast carcinoma in situ) unless a complete remission was achieved at least 1 years prior to study entry and no additional therapy is required or anticipated to be required during the study period.
6. A severe hypersensitivity reaction to prior treatment with a monoclonal antibody, or known hypersensitivity to study drugs components.
7. A positive test for hepatitis B virus surface antigen (HBV sAg) or hepatitis C virus ribonucleic acid (HCV antibody) indicating acute or chronic infection.
8. Known history of testing positive for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS).
9. Any serious or uncontrolled medical disorder or active infection that, in the opinion of the investigator, may increase the risk associated with study participation, study drug administration, or would impair the ability of the patients to receive protocol therapy.
10. A known psychiatric or substance abuse disorder that could interfere with cancer therapy.
11. Women of childbearing potential with a positive serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG) within 24 hours prior to the start of nivolumab.
12. Breastfeeding women.
13. Inability to comply with other requirements of the protocol.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-05-2017
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO Date:	20-06-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-10-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-11-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-12-2017
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	EUCTR2016-002308-22-NL
CCMO	NL58038.042.16
Other	volgt