89Zr-pembrolizumab-PET imaging in patients with locally advanced or metastatic melanoma or non-small cell lung cancer

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Primary objective: To evaluate whole body distribution of 89Zr-pembrolizumab in patients with locally advanced or metastatic melanoma or NSCLC. Secondary objectives: i) To evaluate pharmacokinetics of 89Zr-pembrolizumab; ii) To assess the…

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

Summary

ID

NL-OMON43013

Source
ToetsingOnline

Brief title
Pembrolizumab-PET imaging

Condition

- Skin neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym
Melanoma and non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: projectfinanciering

Intervention

Keyword: 89Zr-pembrolizumab, melanoma, non-small cell lung cancer, PET imaging

Outcome measures

Primary outcome

To evaluate whole body distribution of 89Zr-pembrolizumab in patients with

locally advanced or metastatic melanoma or NSCLC.

Secondary outcome

i) To evaluate pharmacokinetics of 89Zr-pembrolizumab;

ii) To assess the heterogeneity of 89Zr-pembrolizumab tumor uptake;

iii) To describe safety of 89Zr-pembrolizumab

iv) To correlate the response of pembrolizumab, as measured by objective

response rate (ORR) according to standard RECIST v1.1 with specific tumor

tracer uptake.

Study description

Background summary

Immunotherapy targeting specific immune-regulatory checkpoints, mainly cytotoxic T-lymphocyte antigen-4 (CTLA-4) and Programmed Death (PD1) or PD ligand 1 (PD-L1) have shown spectacular effects in a broad range of solid malignancies, including melanoma and NSCLC. MK-3475, also known as pembrolizumab, is a monoclonal antibody that blocks the interaction between PD-1 on T-cells with its ligands PD-L1 and PD-L2. Anti-tumor activity with an acceptable side effect profile could been shown in melanoma and NSCLC. Radio-labeling of pembrolizumab with the positron emission tomography (PET) radionuclide 89Zirkonium (89Zr) enables serial non-invasive imaging and

quantification of distribution of PD-1 in melanoma or NSCLC patients. By performing a 89Zr-pembrolizumab-PET scan prior to treatment with pembrolizumab, the uptake of the tracer in the tumor lesions and normal organ distribution can be evaluated, this could lead to new insights about heterogeneity of PD-1 expression, as well as the use of a 89Zr-pembrolizumab-PET as a complementary tool for patient selection in the future.

Study objective

Primary objective: To evaluate whole body distribution of 89Zr-pembrolizumab in patients with locally advanced or metastatic melanoma or NSCLC. Secondary objectives: i) To evaluate pharmacokinetics of 89Zr-pembrolizumab; ii) To assess the heterogeneity of 89Zr-pembrolizumab tumor uptake; iii) To describe safety of 89Zr-pembrolizumab; iv) to correlate the response of pembrolizumab, as measured by objective response rate (ORR) according to standard RECIST v1.1 with specific tumor tracer uptake.

Study design

This is a two center, single arm, investigator sponsored trail (IST) with the PET tracer 89Zr-pembrolizumab to evaluate in vivo whole body distribution of 89Zr-embrolizumab in a registered indication: locally advanced metastatic melanoma or NSCLC before Pembrolizumab treatment.

Intervention

In part A of the imaging trial, a dose finding imaging study will be performed to assess the optimal tracer protein dose of 89Zr-pembrolizumab and the optimal interval between tracer injection and scanning. Approximately 3 cohorts of about 2-3 patients each will undergo 89Zr-pembrolizumab-PET imaging before start of treatment with pembrolizumab. In part B, 12 eligible patients will undergo 89Zr-pembrolizumab-PET imaging at baseline, with the optimal tracer protein dose and scanning schedule as determined in part A. The purpose of part B of the study is to analyze the whole body distribution and pharmacokinetics (PK) of 89Zr-Pembrolizumab in patients with locally advanced or metastatic melanoma. Tumor and normal organ radioactive tracer uptake will be quantified as standardized uptake values (SUV). Tumor biopsies will be collected at baseline and studied for various characteristics including PDL-1, PD-1 expression and tumor infiltrating lymphocytes. Pembrolizumab treatment will be administered as standard of care.

Study burden and risks

For this imaging study patients have to make maximal 6 extra visits to the clinic for screening, to receive tracer injection and for maximal 3 PET/CT scans and the biopsy before start of standard treatment with pembrolizumab. The

study ends after the last imaging or biopsy (whichever comes first) and will approximately take 5-7 days. 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.
89Zr-pembrolizumab*PET/CT implements a radiation burden of about 20 mSv, and 1.5 mSv per low-dose CT scan. Besides PET imaging, patients will be asked to give in total 12 blood samples (85 mL), which will give minor discomfort. A metastases biopsy will be performed, preferably from an easily accessible lesion to minimize the burden and risk for the patient. Based on a literature review, the risk of tumor biopsies is considered low with a small risk on significant/major complications or death. The risk associated with the 89Zr-pembrolizumab seems minor and although patients do not directly benefit from this study, results of this study will be valuable for our understanding of the tumor immune response and will guide further prospective research.

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

* Age *18 years.
* Histologically or cytologically documented locally advanced or metastatic melanoma or non-small cell lung cancer.
* Patients must be eligible for treatment with pembrolizumab. For patients with NSCLC this includes PD-L1 expression (>1% based on IHC assay) on tumor material.
* Metastatic lesion(s)(*1,0 cm) of which a histological biopsy can safely be obtained according to standard clinical care procedures.
* ECOG performance status 0 or 1.
* Life expectancy * 12 weeks .
* Signed Informed Consent Form.
* Ability to comply with protocol.
* Measurable disease, as defined by standard RECIST v1.1. Previously irradiated lesions should not be counted as target lesions.
* Adequate hematologic and end organ function, defined by the following laboratory results obtained within * 14 days prior to 89Zr-pembrolizumab injection:
* ANC * 1500 cells/*L (without granulocyte colony-stimulating factor support within 2 weeks prior to 89Zr-pembrolizumab injection)
* WBC * 2500/*L
* Lymphocyte count * 500/*L
* Platelet count * 100,000/*L (without transfusion within 2 weeks prior to 89Zr-Pembrolizumab injection)
* Hemoglobin *9.0 g/dL. Patients may be transfused or receive erythropoietic treatment to meet this criteria.
* AST, ALT, and alkaline phosphatase *2.5 x the upper limit of normal (ULN), with the following exceptions:
o Patients with documented liver metastases: AST and/or ALT * 5 x ULN
o Patients with documented liver or bone metastases: alkaline phosphatase * 5 x ULN
* Serum bilirubin * 1.5 x ULN. Patients with known Gilbert disease who have serum bilirubin level *3 x ULN may be enrolled.
* INR and aPTT *1.5 x ULN. This applies only to patients who are not receiving therapeutic anticoagulation; patients receiving therapeutic anticoagulation should be on a stable dose.
* Creatinine clearance *30 mL/min
* For female patients of childbearing potential and male patients with partners of childbearing potential, agreement (by patient and/or partner) to use a highly effective form(s) of contraception (i.e., one that results in a low failure rate [< 1% per year] when used consistently and correctly).

Exclusion criteria

1. Any approved anti-cancer therapy, including chemotherapy of hormonal therapy within *14 days prior to 89Zr-pembrolizumab injection; the following exceptions are allowed:

* Hormone-replacement therapy or oral contraceptives.
2. Treatment with any other investigational agent or participation in another clinical trial with therapeutic intent within 28 days prior to the 89Zr-pembrolizumab injection.
3. Malignancies other than melanoma or NSCLC within 5 years prior to 89Zr-pembrolizumab injection, with the exception of those with a negligible risk of metastasis or death treated with expected curative outcome (such as adequately treated carcinoma in situ of the cervix, basal or squamous cell skin cancer, localized prostate cancer treated with curative intent or ductal carcinoma in situ treated surgically with curative intent).
4. Pregnant and lactating women.
5. Symptomatic brain metastasis.
6. History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins.
7. Known hypersensitivity or allergy to any component of the pembrolizumab formulation.
8. History of autoimmune disease, including but not limited to myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, vascular thrombosis associated with antiphospholipid syndrome, Wegener*s granulomatosis, Sjögren*s syndrome, Guillain-Barré syndrome, multiple sclerosis, vasculitis, or glomerulonephritis.
* Patients with a history of autoimmune-related hypothyroidism on a stable dose of thyroid replacement hormone may be eligible for this study.
* Patients with controlled type I diabetes mellitus on a stable dose of insulin regimen may be eligible for this study.
9. Positive test for HIV.
10. Patients with active hepatitis B (chronic or acute; defined as having a positive hepatitis B surface antigen [HBsAg] test at screening) or hepatitis C.
* Patients with past hepatitis B virus (HBV) infection or resolved HBV infection (defined as the presence of hepatitis B core antibody [HBcAb] and absence of HBsAg) are eligible. HBV DNA test must be performed in these patients prior to 89Zr-pembrolizumab injection.
* Patients positive for hepatitis C virus (HCV) antibody are eligible only if polymerase chain reaction is negative for HCV RNA.
11. Signs or symptoms of infection within 2 weeks prior to 89Zr-pembrolizumab injection.
12. Major surgical procedure other than for diagnosis within 28 days prior to 89Zr-pembrolizumab injection or anticipation of need for a major surgical procedure during the course of the study.
13. Prior allogeneic bone marrow transplantation or solid organ transplant.
14. Treatment with systemic immunosuppressive medications (including but not limited to prednisone, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor agents) within 2 weeks prior to 89Zr-pembrolizumab injection.
* Patients who have received acute, low-dose, systemic immunosuppressant medications (e.g. a one-time dose of dexamethasone for nausea) may be enrolled in the study after discussion with and approval by the sponsor.
* The use of inhaled corticosteroids for chronic obstructive pulmonary disease, mineralocorticoids (e.g. fludrocortisone) for patients with orthostatic hypotension, and low-dose supplemental corticosteroids for adrenocortical insufficiency are allowed.
15. Inability to comply with other requirements of the protocol.

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):	24-10-2016
Enrollment:	21
Type:	Actual

Ethics review

Approved WMO Date:	02-05-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-08-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-08-2016
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	EUCTR2016-000941-30-NL
ClinicalTrials.gov	NCT02760225
CCMO	NL57160.042.16