89Zirconium-labeled pembrolizumab as predictive imaging biomarker of response and toxicity in pembrolizumab treated patients with non-small-cell lung cancer - a feasibility study

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To assess the safety and biodistribution of 89Zr-pembrolizumab and its uptake in tumor and target irAE tissues

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

Summary

ID

NL-OMON46216

Source
ToetsingOnline

Brief title
89Zr-labeled pembrolizumab in patients with non-small-cell lung cancer

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Lung cancer, lung malignancy

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Merck Sharp & Dohme

Intervention

Keyword: 89Zirconium-labeled, NSCLC, Pembrolizumab

Outcome measures

Primary outcome

To assess the safety of 89Zr-pembrolizumab. To assess uptake (visual and quantitatively, expressed as SUVmax, SUVmean and SUVpeak) of 89Zr-pembrolizumab in tumor lesions. Characterize tumor uptake heterogeneity between patients and within and between tumor lesions of the same patient

Secondary outcome

Correlate 89Zr-pembrolizumab tumor uptake with tumor and TIL PD-1 and PD-L1 expression as well as other blood and tissue parameters as outlined in section 7.1.2.7.

Correlate 89Zr-pembrolizumab organ uptake with irAEs. The focus will be on the gut, lung, liver, thyroid and pituitary.

Assess uptake (visual and quantitatively expressed as SUVmax, SUVmean and SUVpeak) of 89Zr-pembrolizumab in normal tissues to evaluate the biodistribution and dosimetry.

Study description

Background summary

Tumor PD-L1+ immunohistochemistry (IHC) seems to be related to pembrolizumab

response, but the signal is not straightforward. Temporal and spatial variation of tumor PD-L1 expression (within and between tumor lesions) might be responsible for its suboptimal predictive value as biomarker of response. Therefore there is a need to further validate tumor PD-L1 IHC as predictive biomarker, as well as looking at alternatives. Biological imaging of the PD-1 pathway allows to monitor the PD-1/PD-L1 interaction non-invasively. To visualize the PD-1 pathway positron emission tomography (PET) can be combined with radiolabeled monoclonal antibodies, a technique called immuno-PET. Imaging with radiolabelled pembrolizumab (89Zr-pembrolizumab) allows for non-invasive quantification of its direct target, the PD-1 receptor on tumor infiltrating lymphocytes. Because the technique is non-invasive and whole body, it allows for serial measurements of tumor uptake as well as looking at heterogeneity within and between tumor lesions.
89Zr-pembrolizumab might also predict for immune related adverse events (irAE). Whole body imaging with 89Zr-pembrolizumab allows to quantify pembrolizumab binding in target irAE tissues and the level of tracer uptake might predict for irAEs.

Study objective

To assess the safety and biodistribution of 89Zr-pembrolizumab and its uptake in tumor and target irAE tissues

Study design

Single arm open label exploratory pilot (imaging) biomarker study.

Intervention

Not applicable

Study burden and risks

Use of positron emitting radionuclides means exposure to ionizing radiation. On the longterm, there is a slighty increased risk of development of cancer elsewhere due to the ionizing radition in this trial.

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

Have a histologically or cytologically confirmed diagnosis of stage IV, EGFR wt and EML4/ALK fusion negative NCSLC and have received at least one line of platinum based doublet chemotherapy and disease progression by RECIST 1.1 on the last systemic treatment.
Be willing and able to provide written informed consent/assent for the trial.
Be 18 years of age or older on day of signing informed consent.
Have measurable disease based on RECIST 1.1.
Must provide newly obtained tissue from a core or excisional biopsy of a tumor lesion and are willing to undergo a second biopsy when the 89Zr-pembrolizumab PET scan shows heterogeneous uptake.
Have a performance status of 0-2 on the ECOG Performance Scale.
Demonstrate adequate organ function.
Female subject of childbearing potential should have a negative urine or serum pregnancy within 72 hours prior to receiving the first dose of study medication. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required.
Female subjects of childbearing potential should be willing to use 2 methods of birth control or be surgically sterile, or abstain from heterosexual activity for the course of the study through 120 days after the last dose of study medication. Subjects of childbearing potential are those who have not been surgically sterilized or have not been free from menses for > 1 year.
Male subjects should agree to use an adequate method of contraception starting with the

first dose of study therapy through 120 days after the last dose of study therapy.

Exclusion criteria

Is currently participating in or has participated in a study of an investigational agent or using an investigational device within 4 weeks of the first dose of treatment.
Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy in a dose higher than the equivalent of 10 mg prednisolone once daily or any other form of immunosuppressive therapy within 7 days prior to the first dose of trial treatment.
Has had a prior monoclonal antibody within 4 weeks prior to study Day 1 or who has not recovered (i.e., <= Grade 1 or at baseline) from adverse events due to agents administered more than 4 weeks earlier.
Has had prior chemotherapy, targeted small molecule therapy, or radiation therapy within 2 weeks prior to study Day 1 or who has not recovered (i.e., <= Grade 1 or at baseline) from adverse events due to a previously administered agent.
Has a known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or in situ cervical cancer that has undergone potentially curative therapy.
Has symptomatic central nervous system (CNS) metastases and/or carcinomatous meningitis. Subjects with asymptomatic CNS metastases are allowed to enter the study. Subjects with previously treated brain metastases may participate provided they are stable and are not using steroids for at least 7 days prior to trial treatment.
Has an active autoimmune disease requiring systemic treatment within the past 3 months or a documented history of clinically severe autoimmune disease, or a syndrome that requires systemic steroids or immunosuppressive agents. Subjects with vitiligo or resolved childhood asthma/atopy would be an exception to this rule. Subjects that require intermittent use of bronchodilators or local steroid injections would not be excluded from the study. Subjects with hypothyroidism stable on hormone replacement or Sjorgen*s syndrome will not be excluded from the study.
Has evidence of interstitial lung disease or active, non-infectious pneumonitis.
Has an active infection requiring systemic therapy.
Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the trial, interfere with the subject*s participation for the full duration of the trial, or is not in the best interest of the subject to participate, in the opinion of the treating investigator.
Has known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial.
Is pregnant or breastfeeding, or expecting to conceive or father children within the projected duration of the trial, starting with the pre-screening or screening visit through 120 days after the last dose of trial treatment.
Has received prior therapy with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody (including ipilimumab or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways).
Has a known history of Human Immunodeficiency Virus (HIV) (HIV 1/2 antibodies).
Has known active Hepatitis B (e.g., HBsAg reactive) or Hepatitis C (e.g., HCV RNA

[qualitative] is detected).
Has received > 30 Gy of thoracic radiotherapy within 6 months of starting Pembrolizumab.
Has received a live vaccine within 30 days prior to the first dose of trial treatment.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-06-2017
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	KEYTRUDA
Generic name:	Pembrolizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Zirconium-89-Pembrolizumab
Generic name:	Zirconium-89-Pembrolizumab

Ethics review

Approved WMO

Date:	01-12-2016
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-01-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-08-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2015-004260-10-NL
CCMO	NL55135.029.15