PD-L1 PET/CT to predict avelumab treatment response in NSCLC

Published: 19-06-2018
Last updated: 13-04-2024

The aim of the study is to develop PD-L1 PET/CT imaging in patients with NSCLC to noninvasively image PD-L1 expression in tumors and to determine the correlation with response to avelumab. For this purpose, two studies will be carried out to1:...

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

Summary

ID

NL-OMON48833

Source
ToetsingOnline

Brief title
PD-L1 imaging in NSCLC

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lungcancer, non-small cell lungcancer

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: industrie,Merck

Intervention

Keyword: anti-PD-L1, immunotherapy, molecular imaging, NSCLC

Outcome measures

Primary outcome

Primary end points

Study 1: Tumor uptake of 89Zr-avelumab

Study 2: Validation of PD-L1 imaging

Secondary outcome

Secondary end points

Study 1:

1. Heterogeneity of 89Zr-avelumab uptake within and between tumor lesions

2. Correlation between 89Zr-avelumab tumor uptake and PD-L1 expression

Study 2:

1. Correlation between tumor uptake of 89Zr-avelumab in the individual tumor lesions and pathologic response after neo-adjuvant avelumab treatment

2. Correlation between tumor uptake of 89Zr-avelumab in the individual tumor lesions and overall survival after neo-adjuvant avelumab treatment and surgery

3. Correlation between PD-L1 expression on tumor cells before and after neo-adjuvant avelumab treatment

4. Pathological response to neo-adjuvant avelumab treatment in patients with resectable stage Ia (*T1b tumor) -IIIa NSCLC

5. Local increase in CD8+ T-cells and tumor infiltration of CD8+ T-cells together with a cytokine influx after neo-adjuvant treatment

6. Safety of neo-adjuvant avelumab in NSCLC

7. The number of treatment-related delays in surgical resections

8. The number of VATS conversions after neo-adjuvant avelumab

9. Post-operative complications incl. length of hospital stay and 30 and 90 day

mortality.

Study description

Background summary

Novel immune therapies with anti-PD-1 and PD-L1 immune checkpoint inhibitors (ICI) have shown impressive and durable antitumor responses. However, only 15-20% of patients respond to these drugs. This means that non-responders are exposed to expensive, ineffective treatment, and
its associated side effects, while alternative treatment is delayed.
Avelumab is an ICI shown to be effective in patients with stage IIIb/IV non-small cell lung cancer (NSCLC).To predict its effect, there is an urgent need for a predictive biomarker to select patients which could benefit from ICI therapy. The aim of the study is to develop PD-L1 PET/CT imaging in patients with NSCLC to noninvasively image PD-L1 expression in tumors and to determine the correlation with response to avelumab

Study objective

The aim of the study is to develop PD-L1 PET/CT imaging in patients with NSCLC to noninvasively image PD-L1 expression in tumors and to determine the correlation with response to avelumab. For this purpose, two studies will be carried out to
1: Determine the correct 89Zr-avelumab dose to image NSCLC lesions
2: Assess the potential of PD-L1 PET/CT to image PD-L1 expression in tumor lesions

Study design

non-randomized, non-blinded, prospective study among 37 patients with NSCLC

Intervention

1: Dose optimization for PD-L1 PET/CT
In three groups of five patients with NSCLC, the first 5 receive an antibody

dose of 2 mg, the following two groups will receive 10 and 50 mg 89Zr-avelumab. Whole body PET/CT scans will be acquired two and four days after injection of 37 MBq 89Zr-avelumab. After the PET/CT scan, patients will start treatment with avelumab, which is administered IV every 2 weeks (q2w, 10 mg/kg). The antibody dose resulting in the highest tumor uptake and highest tumor-to-background ratios will be selected for the phase II study. (archival) biopsy material will be used to determine PD-L1 expression immunohistochemically. Patients with stage IIIb-IV NSCLC will continu treatment untill disaese progression or unacceptable toxicity. Patients with resectable disease a maximum of 2 cycles avelumab. Treatment evaluation will be assessed by pathologic response in the latter, and assessed by CT/MRI according to RECIST 1.1 in stage IIIb-IV disease.

2: Predictive value of PD-L1 PET/CT
Twenty-two patients will undergo PD-L1 PET/CT with the correct dose as assessed in part I. Treatment with avelumab will be administered IV every 2 weeks (q2w, 10 mg/kg). Surgery is scheduled after a maximum of 2 cycles of avelumab treatment. Treatment evaluation will be assessed by pathologic respons. Tumor uptake assessed with PD-L1 PET/CT will be correlated to response to treatment with avelumab.

Study burden and risks

Part 1: At baseline laboratory analysis will be performed and a PET/CT scan will be planned. Prior to the PET/CT scan, patients will receive an intravenous injection of 37 MBq 89Zr-avelumab (2, 10, or 50 mg). Two and four days later, patients will undergo whole body PET/CT imaging. Immediately after injection and at day of scanning, 3 ml blood will be collected and serum radioactivity will be measured. In addition a blood sample must be performed at baseline, prior to each avelumab dose, at end of treatment visit and at 30 days post-treatment safety follow-up. A second PET/CT scan will be acquired 4 days after injection. After the last PET/CT scan, patients will start treatment with avelumab within 7 days. Avelumab is administered IV every 2 weeks (q2w) at a dose of 10 mg/kg.
Part 2: Patients will undergo only one pre-treatment PET/CT before 2 cycles of avelumab treatment, followed by surgical resection of the tumor.
Treatment response will be assessed by pathologic respons in patients with resectable disease. Infusion-related reactions including drug hypersensitivity reactions and immune-mediated adverse reactions might occur and require treatment according to local protocol. To date, 89Zr-labeled antibodies have been evaluated in patients without any sign of toxicity. The risks of exposure to ionizing radiation are considered minimal due to a relative low cumulative radiation.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 8
Nijmegen 6500 HB
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 8
Nijmegen 6500 HB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Male or female subjects aged * 18 years and >50 years in patients with resectable stage Ia (*T1b tumor) - IIIa NSCLC
2. Histological or cytologic proven stage IIIb/IV NSCLC or resectable stage Ia (*T1b tumor) - IIIa NSCLC
3. ECOG performance score (0-1)Karnofsky performance score * 70
4. At least one lesion with a tumor size * 1 cm
5. Hematologic function: absolute neutrophil count (ANC) * 1.5 × 109/L, platelet count * 100 × 109/L, and hemoglobin * 9 g/dL (may have been transfused)
6. Hepatic function: total bilirubin level * 1.5 × the upper limit of normal (ULN) range and AST and ALT levels * 2.5 × ULN for all subjects or AST and ALT levels * 5 x ULN (for subjects with documented metastatic disease to the liver).
7. Estimated creatinine clearance * 30 mL/min according to the Cockcroft-Gault

formula (or local institutional standard method)
8. Highly effective contraception for both male and female subjects throughout the study and for at least 60 days after avelumab treatment administration if the risk of conception exists. (Note: The effects of the trial drug on the developing human foetus are unknown; thus, women of childbearing potential and men able to father a child must agree to use 2 highly effective contraception, defined as methods with a failure rate of less than 1 % per year. Highly effective contraception is required at least 28 days prior, throughout and for at least 60 days after avelumab treatment.)
9. Fit for surgery (for patients with resectable stage Ia-IIIa disease), as assessed by treating thoracic surgeon / anesthesiologists based on sufficient cardiopulmonary status and absence of major contra-indications for surgery according to local guidelines

Exclusion criteria

1. All subjects with brain metastases, except those meeting the following criteria:
* Brain metastases that have been treated locally and are clinically stable for at least 2 weeks prior to enrollment
* No ongoing neurological symptoms that are related to the brain localization of the disease (sequelae that are a consequence of the treatment of the brain metastases are acceptable)
* Subjects must be either off steroids or on a stable or decreasing dose of < 10mg daily prednisone (or equivalent)
2. Prior organ transplantation, including allogeneic stem cell transplantation
3. Significant acute or chronic infections including, among others:
* Active infection requiring systemic therapy
* Known history of testing positive test for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS)
* Positive test for HBV surface antigen and / or confirmatory HCV RNA (if anti-HCV antibody tested positive)
4. Active autoimmune disease that might deteriorate when receiving an immunostimulatory agent:
-. Subjects with diabetes type I, vitiligo, psoriasis, hypo- or hyperthyroid disease not requiring immunosuppressive treatment are eligible
5. Hypersensitivity to study drug: *Known prior severe hypersensitivity reactions to investigational product or any component in its formulations, including known severe hypersensitivity reactions to antibodies (Grade * 3 NCI CTCAE v 4.03)
6. Persisting toxicity related to prior therapy of Grade >1 NCI-CTCAE v 4.03; however, alopecia and sensory neuropathy Grade * 2 is acceptable
7. Pregnancy or lactation
8. Known alcohol or drug abuse
9. Other severe acute or chronic medical conditions including colitis,

inflammatory bowel disease, pneumonitis, pulmonary fibrosis or psychiatric conditions including recent (within the past year) or active suicidal ideation or behavior; or laboratory abnormalities that may increase the risk associated with study participation or study treatment administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the patient inappropriate for entry into this study.
10. Any psychiatric condition that would prohibit the understanding or rendering of informed consent
11. Vaccination within 4 weeks of the first dose of avelumab and while on trial is prohibited except for administration of inactivated vaccines
12. Immunosuppressants: *Current use of immunosuppressive medication, EXCEPT for the following: a. intranasal, inhaled, topical steroids, or local steroid injection (eg, intra-articular injection); b. Systemic corticosteroids at physiologic doses * 10 mg/day of prednisone or equivalent; c. Steroids as premedication for hypersensitivity reactions (eg, CT scan premedication).*
13. Cardiovascular disease: *Clinically significant (i.e., active) cardiovascular disease: cerebral vascular accident/stroke (< 6 months prior to enrollment), myocardial infarction (< 6 months prior to enrollment), unstable angina, congestive heart failure (* New York Heart Association Classification Class II), or serious cardiac arrhythmia requiring medication.*
14. Prior anti-PD-1 or anti-PD-L1 therapy

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):	26-10-2018
Enrollment:	37
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Avelumab
Generic name:	Avelumab

Ethics review

Approved WMO Date:	19-06-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-07-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-02-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-04-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-08-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-03-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2017-002103-10-NL
CCMO	NL62026.091.17