Early response evaluation with 18F-FDG PET/CT and immunological profiling of circulating immune cells and tumor-draining lymph nodes in non-small cell lung cancer patients treated with immunotherapy.

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A) To quantify the difference in 18F-FDG uptake (expressed as SUVmax, SUVmean and SUVpeak) in tumor lesions within 7 days before and between 7 and 14 days after treatment initiation with immune checkpoint inhibitors with or without chemotherapy. B)...

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

Summary

ID

NL-OMON48669

Source
ToetsingOnline

Brief title
Early response evaluation in NSCLC patients treated with immunotherapy

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lung cancer, lung malignancy

Research involving

Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: farmaceutische industrie: Bristol-Myers Squibb (BMS)

Intervention

Keyword: EBUS, Immunotherapy, Non-small cell lung cander, PET

Outcome measures

Primary outcome

For each tumor, a volume of interest (VOI) will be drawn on the PET scan images and standard uptake values (SUVmax, SUVmean, SUVpeak), metabolically active tumor volume (MATV) and total lesion glycolysis (TLG) will be measured and the change in parameter values calculated and related to treatment outcome in terms of PFS and OS; response evaluation criteria in solid tumors). Change in the percentage, activation status and ratio of selected immune cells in PBMC's and if avaible in TDLNs will be calculated and related to the PET results and outcome in terms PFS and OS.

Secondary outcome

N.A.

Study description

Background summary

To identify patients that will benefit from treatment with mAbs like nivolumab or pembrolizumab, it is important to find a predictive biomarker. In this study we will explore potential biomarkers, 18F-FDG uptake assessed by FDG-PET and immunophenotyping of peripheral blood mononuclear cells (PBMC) and if avaible

tumor-draining lymph nodes (TDLNs).
In the research setting, PET is increasingly being used to study early changes of biologic effects during and after cancer therapy. Migration and activation of immune cells lead to an increase of FDG uptake. In the early phase of immune therapy, we expect an influx of inflammatory cells in the tumor to cause a higher metabolic activity in patients who respond to immune checkpoint inhibitors.
Change in subsets of immunce cells in peripheral blood cells after nivolumab treatment is known. We will explorate these changes further and correlate them with respons to nivolumab.
Recently we showed in a pilot study that fine needle aspiration (FNA) combined with multi parameter flow cytometry (FACS) immunophenotyping is a feasible, rapid and sensitive method to detect lymphoid marker expression that is unique to TDLNs and different from blood and non-tumor draining lymph nodes (NTDLNs) (manuscript in preparation). We hypothesize that an early read-out of TDLN immunophenotyping predicts the efficacy of immune checkpoint inhibitors.

Study objective

A) To quantify the difference in 18F-FDG uptake (expressed as SUVmax, SUVmean and SUVpeak) in tumor lesions within 7 days before and between 7 and 14 days after treatment initiation with immune checkpoint inhibitors with or without chemotherapy.
B) To analyse immune cell subsets in PBMC and TDLNs and compare changes before and one week after treatment initiation.

Study design

A pilot study with biomarker exploration

Study burden and risks

The burden and risks associated with participation are considered low. The study procedures are part of the routine diagnostic workup of NSCLC patients and thus common practice for pulmonologists on a weekly basis. Use of positron emitting radionuclides means exposure to ionizing radiation. The radiation exposure will be 9 mSv in total per patient (4.5 mSv per PET scan). One PET scan is part of routine care and the other is solely for the purpose of this study. The long term risk of developing a secondary malignancy due to radiation exposure is theoretical, because of the limited life expectancy of patients with stage IV NSCLC. Patients do not derive benefit from the PET scan results. Patients who will be approached for study participation already have an indication for a pretreatment PET-CT and EBUS procedure. The early on-treatment endoscopy (not mandatory) and PET scan are however not part of regular care and are performed for the purpose of this study. Since there is a lack of a well performing predictive biomarker of response, the results of this imaging

biomarker study can be of high interest for NSCLC patients that are eligible for treatment with checkpoint inhibitors in the future. Blood withdrawal is considered as a safe procedure.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
* willing and able to provide written informed consent for the study.
* * 18 years of age on day of signing informed consent.
* confirmed diagnosis of NSCLC.
* Histological tumor biopsy for PD-L1 IHC assessment (DAKO assay) available.
* Eligible for first line chemo-immunotherapy or 2nd line and beyond PD-(L)1

immunotherapy monotherapy.
* Measurable disease according to RECIST v1.1.
* WHO performance status of 0*2.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
* Has had prior chemotherapy, targeted small molecule therapy, or radiation therapy within 2 weeks prior to the baseline PET-scan.
* Has an active infection or had an active infection within 2 weeks prior to baseline PET-scan.
* Has a known history of hypersensitivity to contrast material.

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):	01-09-2017
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO

Date:	02-01-2018
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO Date:	07-12-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-03-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-07-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-01-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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
CCMO	NL62294.031.17