A clinical imaging study using [18F]F-AraG PET to visualize Tumor infiltrating T-cell Activation in Non-small cell lung cancer

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• To perform full kinetic modeling of [18F]F-AraG for the uptake in tumor lesions and healthy organs (e.g. spleen) by exploring different kinetic models and outcome measures as well as its test-retest (TRT) variability to guide the selection of an…

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

Summary

ID

NL-OMON50793

Source
ToetsingOnline

Brief title
ATTAIN

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified
- Congenital respiratory tract disorders

Synonym
lung cancer, lung carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Boehringer Ingelheim

Intervention

Keyword: [18F]F-AraG, neoadjuvant, NSCLC, PET imaging

Outcome measures

Primary outcome

Dynamic tumor tracer uptake parameters will be summarized to perform tracer kinetic modeling using standard nonlinear regression techniques to fit the dynamic [18F]F-AraG tumor time activity curves (TACs) to different (i.e., 1-tissue, irreversible 2-tissue, and reversible 2-tissue) compartment models using the measured metabolite corrected plasma time-activity curve as input function. The optimal model will be selected based on the goodness of fit. The most appropriate parameter will be chosen depending on the optimal model and its test-retest variability. Dynamic uptake parameters of interest will be correlated with simplified static uptake parameters derived from the whole-body scans. Correlations will be made between hotspots and cold-spots as seen on the [18F]F-AraG PET and the corresponding spots on the resection specimen for automated quantification of CD8+ cells using VECTRA and tumor inflammation signature using gene expression analyses.

Secondary outcome

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Study description

Background summary

The efficacy of immunotherapy and patient selection for combinatorial immunotherapy strategies would greatly improve if the tumor microenvironment (TME) could be characterized more accurately. Positron emission tomography (PET) using tracers that target immune cell subsets may provide a non-invasive means to immune profile the TME. Imaging T-cells can help in identifying *hot* tumors, or parts of the tumor mass that have high concentrations of tumor infiltrating T-cells and also provide information on its activation.
A promising tracer to image activated T-cells is [18F]F-AraG. We hypothesized that [18F]F-AraG will accumulate in activated T-cells. Therefore, we expect that [18F]F-AraG and PET will enable to (reproducibly) identify tumors and tumor areas with high concentrations of tumor infiltrating activated T-cells on pathological assessment.

Study objective

• To perform full kinetic modeling of [18F]F-AraG for the uptake in tumor lesions and healthy organs (e.g. spleen) by exploring different kinetic models and outcome measures as well as its test-retest (TRT) variability to guide the selection of an optimal PET pharmacokinetic model
• To correlate the relationship between the tumor uptake of [18F]F-AraG and the number of CD8 T-cells amongst others as measured by Immunohistochemistry (IHC) and gene expression

Study design

Open-label, non-controlled, non-randomized single center, single arm, imaging trial

Intervention

All patients will undergo [18F]F-AraG PET scanning according to the institutional pharmacokinetic tracer modeling protocols

Study burden and risks

Prior to the injection of the tracer, venous blood will be drawn for immunological assessment of T-cell subsets. All patients will undergo 2 extra scanning procedures (test and re-test on consecutive days). Per scanning procedure, patients will be lying for approximately 90 minutes on the scanner and will receive a total radiation burden of approximately 12 mSv for both procedures. In the first 5 patients (part-1), a cannula will be inserted in an

arm vein and in the radial artery (only test, not re-test) to draw blood (7cc), manually at 7 time points. In part-1, no more than 147+30cc (for test+retest, respectively) blood will be drawn per patient. In the other 5 patients (part-2), all procedures will be the same except for the arterial cannula, which will not be inserted, so, no arterial blood will be drawn, meaning that no more than 98+30cc of blood will be drawn per patient in part-2. Patients will derive no direct benefit from participating in this trial. The insights obtained in the translational part of this study can be of high interest and benefit assessment of T cell activation state and its treatment related changes in future cohorts of NSCLC patients.

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. Histologically confirmed NSCLC, a histological biopsy is mandatory.
2. Patients that are resectable upfront as per multidisciplinary tumor board evaluation.
3. Be willing and able to provide written informed consent for the trial.
4. Be above 18 years of age on day of signing informed consent.
5. Have a performance status of 0-1 on the ECOG Performance Scale at screening.

Exclusion criteria

1. Subjects with a condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalent) or other immunosuppressive medications within 14 days of screening. Inhaled or topical steroids, and adrenal replacement steroid >10 mg daily prednisone equivalent, are permitted in the absence of active autoimmune disease.
2. Psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial.
3. Patient is pregnant or breastfeeding or expecting to conceive within the projected duration of the trial, starting with the screening visit through 12 weeks after the last [18F]F-AraG PET scan.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-01-2022
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]F-AraG
Generic name:	[18F]F-AraG

Ethics review

Approved WMO Date:	18-08-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-10-2021
Application type:	First submission
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	EUCTR2021-001489-40-NL
CCMO	NL77310.029.21