An open label pilot study of [18F]AlF-RESCA-IL2 (Interleukin-2 PET tracer) for positron emission tomography imaging in patients treated with immune checkpoint inhibitors

Published: 30-08-2022
Last updated: 07-04-2024

Primary objectives:• To evaluate safety of repeat doses of [18F]AlF-RESCA-IL2.• To evaluate tumour uptake of [18F]AlF-RESCA-IL2 in patients with cancer.• To evaluate whole body distribution of [18F]AlF-RESCA-IL2 in cancer patients.Secondary…

Ethical review	Approved WMO
Status	Pending
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Observational invasive

Summary

ID

NL-OMON53936

Source
ToetsingOnline

Brief title
IL-2 PET imaging in advanced solid tumours

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
cutaneous squamous cell carcinoma, head and neck squamous cell carcinoma, non-small-cell lung cancer, renal cell carcinoma, urothelial cell carcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: [18F]AlF-RESCA-IL2, immune checkpoint inhibitors, PET imaging

Outcome measures

Primary outcome

• Safety evaluation through summaries of adverse events per NCI CTCAE v5.0 criteria, changes in laboratory test results and changes in vital signs after exposure to [18F]AlF-RESCA-IL2

• Evaluation of tumour [18F]AlF-RESCA-IL2 uptake by measuring standardised uptake values in tumour lesions.

• Evaluation of [18F]AlF-RESCA-IL2 biodistribution in cancer patients on the PET images by measuring standardised uptake values in healthy tissues and organs.

Secondary outcome

• Correlation of [18F]AlF-RESCA-IL2 uptake in tumours, with T cell infiltration in tumour biopsy samples, as determined by IHC.

• Correlation of [18F]AlF-RESCA-IL2 PET measurements with radiologic response to treatment, according to (i)RECIST v1.1 criteria.

• Assessment of changes in tumour and normal organ tracer uptake after 2 weeks of treatment, expressed as standardised uptake values.

Study description

Background summary

The rapidly evolving fields of tumour immunology and cancer immunotherapy have resulted in several Food and Drug Administration (FDA) and European Medicines Agency (EMA) approved immune checkpoint inhibitors (ICI) for different tumour types. However, not all patients respond to these drugs. Moreover, immunotherapeutic drugs require careful management of potential side effects. Therefore, it would be of major interest to be able to know whether a specific treatment induces an immune response.
The dynamic tumour microenvironment and tumour heterogeneity have raised significant interest in objectifying the status of the microenvironment. Still, the ability to monitor changes in the immune status of metastatic cancers is limited. Current methods to monitor lymphocytes from whole blood or biopsies from heterogeneous tumours do not necessarily reflect the dynamic and spatial information required to monitor immune responses to therapeutic intervention. Moreover, these responses may elicit whole body changes in immune cell numbers and localization. Molecular imaging can noninvasively monitor whole-body systemic and intratumoral alterations. Assessing abundance and localization of immune cells before and during therapy would increase the understanding of the dynamics of immunotherapeutic mechanisms, with the potential to provide translatable methods for predicting and/or assessing responses.
IL-2 is a 15 kDa cytokine that plays an important role in the cellular immune response. Its primary function involves stimulation of growth, proliferation, activation, and differentiation of T cells. IL-2 induces its effects by binding to transmembrane IL-2 receptors (IL-2Rs). The high-affinity IL-2R, consisting of all three subunits (CD25, CD122, and CD132), is primarily present on activated effector T cells and regulatory T cells (Treg). Whereas the low-affinity IL-2R, consisting of two subunits (CD122 and CD132), is generally found on naïve T cells and natural killer cells.
The migration of activated T cells was visualized using [18F]FB-IL2-PET in mouse xenograft models. Furthermore, a clinical PET study using the tracer [18F]FB-IL2 was performed in patients with metastatic melanoma before and during immune checkpoint inhibitor therapy. Also, single-photon emission computed tomography (SPECT) imaging of the IL-2R has previously been performed in three patients with metastatic melanoma. However, PET-imaging provides better spatial resolution and allows for more accurate quantification of tracer uptake in tumour lesions and other tissues.
[18F]AlF-RESCA-IL2 is an improved version of the PET tracer [18F]FB-IL2, with better imaging characteristics. The aim of this pilot study is to evaluate the safety and imaging performance of [18F]AlF-RESCA-IL2.

Study objective

Primary objectives:

• To evaluate safety of repeat doses of [18F]AlF-RESCA-IL2.
• To evaluate tumour uptake of [18F]AlF-RESCA-IL2 in patients with cancer.
• To evaluate whole body distribution of [18F]AlF-RESCA-IL2 in cancer patients.

Secondary objectives:
• To assess changes in tumour and normal organ uptake after 2 weeks of ICI therapy.
• To determine whether changes in visual and semi-quantitative [18F]AlF-RESCA-IL2 PET measurements correlate with RECIST v1.1. radiology responses.
• To correlate tumour tracer uptake with tumour immune cell infiltration as assessed by immunohistochemistry (IHC).

Study design

An investigator-initiated, open-label clinical trial designed to evaluate the safety and in vivo biodistribution of the PET tracer [18F]AlF-RESCA-IL2.

Intervention

Patients will be enrolled to undergo [18F]AlF-RESCA-IL2 PET imaging twice; the first [18F]AlF-RESCA-IL2 PET scan will be performed at baseline, before starting therapy. The second [18F]AlF-RESCA-IL2 PET scan will be performed after 2 weeks of treatment, to minimize morphological changes in tumours responding to the therapy.

Study burden and risks

For this study, patients have to make a maximum of 4 extra visits to the clinic for screening, to have 2 PET-scan visits, and one biopsy taken before starting treatment. In practice, most procedures will be combined with visits to the hospital in the context of clinical care to minimse the burden.
[18F]AlF-RESCA-IL2 is a radioactive compound and therefore, will cause radiation burden to the patient. The effective dose equivalent of [18F] tracers was estimated to be roughly 0.02 mSv/MBq (8). For a diagnostic dose of [18F]AlF-RESCA-IL2 equal to 200 MBq, the absorbed radiation dose will be around 4 mSv. Each PET scan will be made with a low dose attenuation correction CT scan, which has an effective dose of 1.5 mSv. The radiation exposure will be approximately (2x4) + (2x1.5) = 11 mSv.
Besides PET imaging, patients will be asked to provide a total of 5 blood samples (38 mL).
A tumour lesion will be biopsied. Based on a literature review, the risk of tumour biopsies is considered low, with a small risk of significant or major complications or death. To keep this risk as low as possible only patients that have safely accessible tumour lesions will be included in the study.
The risk associated with [18F]AlF-RESCA-IL2 is considered very low based on

preclinical testing. The tracer will be intravenously injected as a single dose that will not exceed 50 microgram of protein, which is substantially lower than the dose of interleukin-2 (Proleukin) that is clinically applied. Although patients do not directly benefit from this study, results from this study will be valuable for our understanding of the tumour immune response and will guide further prospective research and hopefully treatment decisions.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Age >= 18 years at the time of signing informed consent.
2. Patients with histologically confirmed diagnosis of locally advanced or metastatic solid cancer, eligible for ICI therapy as part of routine care.
3. At least 1 lesion that is accessible per investigator*s assessment and

eligible for biopsy according to standard clinical care procedures.
4. Measurable disease, as defined by standard RECIST v1.1. Previously irradiated lesions should not be counted as target lesions except for lesions that have progressed after radiotherapy.
5. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
6. Life expectancy >= 12 weeks.
7. Signed informed consent.
8. Willingness and ability to comply with all protocol required procedures.
9. 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. Treatment with any other investigational agent or participation in another clinical trial with therapeutic intent within 28 days prior to [18F]AlF-RESCA-IL2 injection.
2. Evidence of an active infection that requires systemic antibiotics within 2 weeks prior to [18F]AlF-RESCA-IL2 injection.
3. Active HIV, Hepatitis-B or Hepatitis-C infection.
4. Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of [18F]AlF-RESCA-IL2, or that may affect the interpretation of the results or render the patient at high risk from complications.
5. Altered mental status, or any psychiatric condition that would prohibit the understanding or rendering of informed consent.
6. Sponsor employee/member of the clinical site study team and/or his or her immediate family
7. Pregnant or lactating females.
8. Concurrent use of systemic corticosteroids > 10 mg daily prednisone equivalent.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2023
Enrollment:	14
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]AlF-RESCA-IL2
Generic name:	[18F]AlF-RESCA-IL2

Ethics review

Approved WMO Date:	30-08-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-03-2023
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-05-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-07-2023
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	EUCTR2022-000040-30-NL
ClinicalTrials.gov	NCT05471271
CCMO	NL81955.042.22