18F]FB-IL2 PET combined with multi-parametric MRI to analyze treatment-induced changes in tumor microenvironment in advanced cervical cancer

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To assess the potential of [18F]FB-IL2 PET to detect the infiltration of IL2 receptor (IL2R) positive immune cells in cervical cancer tissue during radiochemotherapy treatment using IL2 receptor positive cells in tumor biopsies as (golden standard...

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

Summary

ID

NL-OMON45627

Source
ToetsingOnline

Brief title
IL2 PET imaging and MRI in T cell respons

Condition

- Reproductive neoplasms female malignant and unspecified

Synonym
cervical cancer

Research involving
Human

Sponsors and support

Primary sponsor: Afdeling Gynaecologische Oncologie
Source(s) of monetary or material Support: deels vanuit ZonMW

Intervention

Keyword: 18F]FB-IL2 PET imaging, Multi-parametric MRI, T cell respons

Outcome measures

Primary outcome

The [18F]FB-IL2 uptake in tumor lesions and its relationship with the number of

CD25+ T lymphocytes in biopsy specimens.

Secondary outcome

To assess changes in perfusion, diffusion restriction on MRI in response to

chemoradiotherapy

To correlate the findings between [18F]FB-IL2 PET and pathology with possible

changes in perfusion and diffusion, as observed by multi-parameter MRI.

Study description

Background summary

Currently, treatment options for cervical cancer, more specificly for metastatic, recurrent and persistent disease, are essentially non-existent. There is clearly a need for innovative therapies for this disease. In recent years immunotherapy is gaining its place as single or combined treatment modality in the field of cancer , however for the use in cervical cancer, immunotherapy is still in early developmental stages. Immunotherapy is often accompanied by serious immune-related adverse events and high costs. Selecting the right patients for this kind of treatment and tailoring their therapy is therefore crucial. This not only applies to immunotherapy, but also to other treatment strategies. For this purpose, adequate predictors or early read-outs are essential, but are currently lacking.
The [18F]FB-IL2 PET scan is developed to detect T cell influx and changes in T cell status within the tumor which might reflect response to treatment . The

combination with an MRI scan, which is used in the standard diagnostic work-up of cervix cancer, should provide exact the anatomical location. In addition, MRI can give information on tumor perfusion and diffusion restriction in the tumor. Aberrant microvasculature can not only hamper the influx of immune cells, but also affect the delivery of therapeutic drugs to the tumor. For this reason, immunotherapies may need to be combined with drugs targeting tumor angiogenesis. MRI could help in determining whether these drugs are able to normalize the tumor vasculature and thus increase the potential efficacy of immunotherapy. This study could aid the clinical validation of [18F]FB-IL2 by enabling assessment of the impact of perfusion and diffusion on the uptake of [18F]FB-IL2 in tumor lesions. Since immunotherapies are currently not standard treatment for cervical cancer, the feasibility of the [18F]FB-IL2 PET scan to detect tumor infiltrating T cells will be assessed in patients that are being treated with radiochemotherapy according to the standard of care. Like immunotherapy, radiochemotherapy is also accompanied by enhanced tumor infiltration of activated T cells.

Study objective

To assess the potential of [18F]FB-IL2 PET to detect the infiltration of IL2 receptor (IL2R) positive immune cells in cervical cancer tissue during radiochemotherapy treatment using IL2 receptor positive cells in tumor biopsies as (golden standard).

Study design

This study is a single-center feasibility (observational) study for the use of [18F]FB-IL2 PET and multiparametric MRI to monitor changes in CD25+ T cell influx and changes in microvasculature in tumors of patients with locally advanced cervical cancer during radiochemotherapy. These changes will be compared to tumor biopsies (golden standard).

Study burden and risks

The toxicity profile of IL2 (Proleukin®) in humans and animals is well known. In fact, the first patients that underwent an [18F]FB-IL2 PET scan did not show any signs of toxicity. The radiation burden will add up to a total dose of 12.3 mSv. This complies with category III (moderate risk ICRP 62). In comparison to the radiotherapy dose (80Gy) given to the primary tumor site during radio chemotherapy this is negligible. In addition to the [18F]FB-IL2 PET IL2 PET a multiparametric MRI will be performed. This will take 45 minutes. MRI poses no additional radiation burden. Side effects to MRI contrast agents are extremely rare. The risk of an acute reaction for a gadolinium based contrast agent is lower than the risk with a iodine-based contrast agent. Besides imaging, patients will be asked to give 3 blood samples and 3 biopsies which will be taken at baseline, during and at the end of treatment, if

feasible. Biopsies at baseline and at the end of treatment will be taken during the examination under general anesthesia which is part of the standard care at that time point. The biopsy during treatment will be performed without anesthesia in the outpatient clinic and is optional. We aim to combine all study procedures with a regular visit to the hospital in order to reduce the burden of the study. This study will not have a direct benefit for the participants, but is the first step towards the clinical validation of a new diagnostic tool that could aid the stratification of patients, thus avoiding ineffective and expensive treatments that can be accompanied by potentially life-threatening side effects.

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

has signed informed consent
histologically confirmed advanced cervical cancer and eligible for chemoradiotherapy

Exclusion criteria

Pre-existing auto-immune disease
The use of corticosteroids (at the start of treatment).
Contraindication for MRI (e.g. metallic foreign body, heart pacemaker, severe claustrophobia)
eGFR<60 ml/min

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-02-2018
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO

Date:	24-08-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	09-05-2019
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
CCMO	NL61032.042.17