Prospective, single-centre, feasibility study to evaluate the use of 18F-PSMA PET/CT in patients with biochemically active medullary thyroid cancer.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Thyroid gland disorders
Study type	Observational invasive

Summary

ID

NL-OMON51749

Source
ToetsingOnline

Brief title
MIMETIC

Condition

- Thyroid gland disorders

Synonym
Medullary thyroid cancer, thyroid cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: 18F-PSMA PET/CT, Disease staging, Medullary thyroid cancer, Nucleair imaging

Outcome measures

Primary outcome

1. To evaluate whether the 18F-PSMA tracer is capable of detecting of medullary thyroid carcinoma lesions in patients with biochemically active and cytological/histological proven medullary thyroid cancer.

Composite reference standard:

A composite reference standard will be determined. This is required to answer the primary and secondary study parameters. A composite reference is a way to combine information from multiple tests/procedures to determine the presence or absence of the target disease. All available information from imaging procedures and cytological, histologic and follow-up data will be used to determine the composite reference standard. PSMA uptake is considered positive when there is visual uptake in that lesion higher than surrounding background, and the uptake is not attributable to the normal physiological uptake pattern of PSMA. The lesion with increased uptake is considered an MTC lesion if confirmed histologically. It is ethically not feasible to obtain histological or cytological proof of disease for all lesions. Therefore, the clinical context of the lesion (e.g. in relation to other imaging modalities, laboratory parameters, follow-up) will classify the lesion in an MTC or non-MTC lesion.

Secondary outcome

1. Comparison of the performance of the 18F-PSMA PET/CT and the 18F-FDG PET/CT

in terms of:

- Patient-based sensitivity

- Lesion-based sensitivity

- Region-based sensitivity

2. Quantification of:

- 18F-FDG uptake in tumor lesions (expressed as Standardized Uptake Values)

- 18F-PSMA uptake in tumor lesions (expressed as Standardized Uptake Values)

- Comparison of the 18F-FDG uptake and 18F-PSMA uptake in tumor lesions

(comparison of Standardized Uptake Values)

3. Association between 18F-PSMA uptake in tumor lesions (expressed as

Standardized Uptake Values) and clinical parameters (see below).

4. Describe clinical and demographic parameters of included patients

Study description

Background summary

More than 10% of patients with medullary thyroid carcinoma have distant metastases at initial presentation1. Diagnostic procedures are necessary to determine the extent of disease and the extent of the initial surgical approach. 18F-FDG is the most widely used tracer to evaluate the presence of distant metastases. It accumulates in cancer cells due to their high glucose metabolism. In MTC, it has an overall sensitivity of 62-76%, with higher uptake in patients with aggressive tumors (calcitonin-doubling times <9 months) 2,3. However, this method is less appropriate in patients with indolently growing tumors. The other molecular imaging modality that is used in MTC, is the 18F-DOPA PET. This tracer binds to an amino acid transporter after which it is metabolized in the catecholamine pathway that is commonly active in neuroendocrine tumors 4. In contrast to the 18F-FDG PET, it shows a better performance for indolently growing MTC with low calcitonin doubling-times.4,5 However, 18F-DOPA is not as widely available as 18F-FDG, e.g. due to lack of

commercial availability, and/or higher costs compared to 18F-FDG. Therefore, there is a need to explore additional tracers for (re)staging patients with MTC.

A tracer that is worth exploring is 18F-PSMA, targeting the prostate specific membrane antigen (PSMA). PSMA is a transmembrane protein found on the apical membrane of virtually all prostate cancer cells. Multiple PSMA-directed radio-labelled tracers have been developed for PET scanning. 18F-PSMA and 68Ga-PSMA are both used in clinical practice to detect (recurrent) prostate cancer. They have been compared but neither is clearly superior6. In the UMCG, the 18F-PSMA-1007 tracer has been used since mid-2019. This tracer has demonstrated high tumor uptake, creates high contrast to background images and does not have physiological uptake in the thyroid gland, as demonstrated in previous studies for prostate cancer patients. Moreover, its relatively long half-life allows transportation, improving its accessibility in medical centers without a cyclotron on-site7.

PSMA was thought to be very specific for prostate cancer. However, the past decades multiple studies have reported the expression of PSMA in the neovasculature of several other solid tumors, including MTC8. A recent pathology study showed PSMA expression in 92% of >100 included specimens of MTC patients 9. Moreover, there are case reports that incidentally found thyroid tumors after focal uptake in the thyroid on a 68Ga-PSMA PET or 18F-PSMA PET for prostate cancer staging8,10,11. Currently a clinical trial is studying 68Ga-PSMA uptake in thyroid cancer in general (clinicaltrials.gov; NCT03463889) highlighting the relevance to study a PSMA directed tracer in thyroid cancer patients. It is unclear whether the study also includes medullary thyroid tumors. Thus far, no clinical trials have been registered studying 18F-labelled PSMA in MTC patients.

Study objective

Therefore, this feasibility study will evaluate whether the 18F-PSMA PET/CT is capable of MTC lesion detection. Moreover, we will compare its ability to detect MTC lesions with a routinely used PET scan, the 18F-FDG PET. By exploring new tracers in PET scanning for MTC, we aim to ultimately 1) improve disease staging in the primary diagnostic process to adjust treatment accordingly (e.g. establish extent of surgery) and; 2) improve the detection of disease progression in the follow-up (e.g. allowing treatment of an oligometastasis or support decisions to start systemic therapy).

Study design

This study will be a single-center feasibility study to evaluate the clinical value of the 18F-PSMA PET/CT in patients with medullary thyroid carcinoma. After ethical approval of the study, inclusion will start and 10-15 patients

will been included until the end of 2024, until 15 patients have been included. The entire study will take place in the UMCG.

Patients are eligible when diagnosed with MTC and when an indication for an 18F-FDG PET/CT is present 1) during the work-up for disease extent in the primary diagnostic process, prior to (surgical) treatment or 2) during follow-up, to evaluate for the presence of disease progression or recurrence. Patients will subsequently be informed and asked for inclusion in the study by their treating physician, during their outpatient appointment. If patients have not sent their informed consent form within two weeks after this appointment, patients will be approached by the coordinating investigator and asked for written informed consent.

The 18F-FDG PET/CT and 18F-PSMA PET/CT will be planned on different days, requiring patients to come to the hospital one extra time. The order of the two scans is not relevant and therefore dependent on availability in the clinic. Both scans will be performed on the same camera in the Medical Imaging Centre of the UMCG to allow adequate comparison. The 18F-FDG-PET/CT is part of routine clinical patient care. Patients will need to make one additional visit to the UMCG for the 18F-PSMA PET/CT.

The 18F-PSMA PET/CT will be analyzed in two steps. Firstly, the nuclear medicine specialist (Dr. A.H. Brouwers) will be blinded from patient/clinical information when analyzing the 18F-PSMA PET/CT. Afterwards, all information will become available to the nuclear medicine specialist, including the results of the 18F-FDG PET/CT, and the 18F-PSMA PET/CT will be re-analyzed. Lesions will be considered abnormally avid when there is uptake above normal background activity which cannot be attributed to the known physiological uptake pattern of 18F-PSMA uptake.

The results of the 18F-PSMA PET/CT will be compared with the 18F-FDG PET/CT. Other potentially available radiological imaging studies performed as part of clinical practice will also be studied to establish a composite reference standard (see also section statistical analysis). The 18F-FDG PET/CT will be analyzed by the nuclear medicine specialist working on duty as part of the standard clinical routine.

Study burden and risks

Benefits
At this point, it is unknown whether the 18F-PSMA PET/CT detects MTC tumor lesions. It is possible that the 18F-PSMA PET/CT detects (an) MTC lesion(s) not detected by routine clinical imaging with CT, MRI and/or other PET scans. However, as this is a feasibility study, the possible detection of new lesions will not lead to diagnostic or treatment consequences. Participation in this study will therefore not directly benefit the included patients.

Radiation burden and risks
Since patients undergo an extra PET scan (the 18F-PSMA PET/CT) when participating in this study, there is an additional radiation burden to the patient. The 18F-PSMA PET/CT implements a radiation burden of 3.9 mSv. There are no known adverse events from intravenous injection of 18F-PSMA. As patients require an intravenous line for administration of the tracer, there is a small risk of adverse events related to this (i.e. hematoma, accidental subcutaneous injection).

Time investment:
Patients are required to invest time in this study in the form of an extra hospital visit. The whole procedure is expected to take maximum 3 hours total (excluding travel time).

Incidental uptake in the prostate gland: if incidental uptake of PSMA is seen in the prostate gland in male participants, the patient will be referred to the urologist for an assessment.

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)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following inclusion criteria:
- At least 18 years of age
- Histological or cytological proven MTC
- Biochemical evidence of disease activity (elevated/increasing calcitonin and/or CEA)
- Clinical indication for an 18F-FDG PET/CT
- Able to follow instructions to participate in the study
- Able to give informed consent

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study: - Patients with prostate cancer or renal cell carcinoma - Pregnant patients - Recent neck surgery (<3 months ago)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-09-2022
Enrollment:	15

Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	18F-PSMA-1007
Generic name:	18F-PSMA-1007

Ethics review

Approved WMO Date:	20-07-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-08-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-06-2024
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	EUCTR2022-000123-20-NL
ClinicalTrials.gov	NCT05534594
CCMO	NL80399.042.22