Expression of prostate specific membrane antigen (PSMA) in soft tissue sarcomas and urothelial cell carcinomas: implications for tumour-specific molecular imaging and treatment?

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This pilot study aims to investigate the PSMA expression in the biopsy material of advanced soft tissue sarcomas and advanced urothelial cell carcinomas, and in case of high PSMA expression, to investigate whether this correlates with high tracer...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Musculoskeletal and connective tissue neoplasms
Study type	Observational invasive

Summary

ID

NL-OMON54064

Source
ToetsingOnline

Brief title
PSMA expression & PSMA PET in soft tissue sarcoma/urothelial cell carcinoma

Condition

- Musculoskeletal and connective tissue neoplasms
- Bladder and bladder neck disorders (excl calculi)

Synonym
bladder cancer, cohort 1: soft tissue cancer, cohort 2: transitional cell carcinoma, soft tissue tumour

Research involving

Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: het onderzoek wordt deels gefinancierd door geld van het Topconsortium voor Kennis en Innovatie (TKI) Life Sciences and Health,de TKI subsidie is aangevuld door geld van het bedrijf Philips (via een public-private partnership;oftewel PPP-allowance). Het LUMC heeft niet specifiek voor dit onderzoek geld ontvangen. Dit onderzoek is onderdeel van een bredere samenwerking tussen LUMC;Philips en TKI. Het LUMC heeft 41000 euro beschikbaar voor dit onderzoek.,Philips Research,Topconsortium voor Kennis en Innovatie (TKI) Life Sciences and Health

Intervention

Keyword: PSMA expression, PSMA PET, soft tissue sarcoma, urothelial cell carcinoma

Outcome measures

Primary outcome

The correlation between the level of PSMA expression in biopsy material and the level of PSMA tracer uptake on [18F]-JK-PSMA-7 PET/CT in advanced soft tissue sarcomas (cohort 1) and advanced urothelial cell carcinomas (cohort 2).

Secondary outcome

The correlation between the level of PSMA expression in biopsy material and tumour grade, tumour stage and tumour type.

Quantification of the accumulation of [18F]-JK-PSMA-7 on PET/CT imaging by using SUV.

In case of metastasized disease, the differences in the level and heterogeneity of PSMA expression (if biopsy material is available) and PSMA tracer uptake on [18F]-JK-PSMA-7 PET/CT between primary tumours and metastases.

The agreement between [18F]-JK-PSMA-7 PET/CT and standard imaging (CT or [18F]-FDG PET/CT).

Study description

Background summary

Patients with advanced soft tissue sarcoma and advanced urothelial cell carcinoma have a poor prognosis, with a 3-year survival rate of 20-25% and a 5-year survival rate of 5-40%, respectively. This is due to limited treatment options and low response rates to systemic chemotherapy of approximately 25% in soft tissue sarcomas and 40-50% in urothelial cell carcinomas. In these patient groups there is a high need for new effective treatment options that can decrease burden of disease and increase survival benefit.

Prostate specific membrane antigen (PSMA) is a transmembrane metallopeptidase that is overexpressed in prostate cancer cells. For diagnostic purposes, PET/CT scans that target PSMA have found their way into the clinical routine of prostate cancer patients. However, currently we know that despite the name, PSMA is not prostate cancer specific. It is also found in the tumour-associated blood vessels of a wide variety of other tumours, including soft tissue sarcomas and urothelial cell carcinomas. In many different sarcoma types, PSMA expression is seen in the neovasculature with the highest detection rate of 46-60% in high grade and undifferentiated sarcomas (e.g. pleomorphic sarcoma types). The PSMA expression rate in the neovasculature of urothelial cell carcinomas still varies in literature, however, the most recently published article showed that PSMA expression was found in 93% of urothelial cell carcinoma tissues. Additionally, PSMA expression was seen in the tumour cells itself in 79% of the tissues. Because of the unique expression pattern which seems to be limited to tumour cells and tumour-associated endothelial cells, PSMA may represent an interesting target for molecular imaging using PSMA-targeting PET scans, and eventually for radionuclide targeted therapy, when coupled to an alpha- or beta-emitter. [225Act]-PSMA and [177Lu]-PSMA therapy have shown promising results in the treatment of advanced prostate cancer patients and might offer perspective and increase quality of life in patients with advanced soft tissue sarcoma and urothelial cell carcinoma, as well.

Study objective

This pilot study aims to investigate the PSMA expression in the biopsy material of advanced soft tissue sarcomas and advanced urothelial cell carcinomas, and in case of high PSMA expression, to investigate whether this correlates with high tracer uptake on PSMA-targeted PET. This way, (a subset of) patients can be selected that could benefit from radionuclide targeted therapy in the future.

Study design

This pilot study is a single centre, open-label, non-randomized, non-blinded phase II study with two patient cohorts.

Study burden and risks

When patients meet the in- and exclusion criteria, immunohistochemical PSMA staining is performed on already acquired biopsy material, which does not bring any burden or risks to the study participants. Written informed consent is required to use the immunohistochemistry results in this study. When high PSMA expression is found, a [18F]-JK-PSMA-7 PET/CT scan will be made, for which the patient will need to provide written informed consent as well. For the [18F]-JK-PSMA-7 PET/CT scan the patient will need to visit the hospital once for approximately 2 hours. When undergoing PET/CT imaging the patient will be exposed to radiation with an effective dose of approximately 8.8 mSv. The risk of adverse effects is low, as the tracer [18F]-JK-PSMA-7 is used on a daily basis for standard clinical care to perform PET/CT scans in prostate cancer patients and no adverse effects have been reported. No extra safety measurements will be taken. Patients do not directly benefit from participation in this study. In case of high PSMA uptake in the tumours of some patients, PSMA might provide a target for therapy in future 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

Age > 18 years at the time of informed consent.
Diagnosis of advanced (locally irresectable or metastasized) soft tissue sarcoma (cohort 1) or advanced (muscle invasive or metastasized) urothelial cell carcinoma (cohort 2).
Voluntary agreement to provide written informed consent and the willingness and ability to comply with all aspects of the protocol.
Recent (< 8 weeks) standard imaging (with CT or [18F]-FDG PET/CT) with measurable disease (lesion diameter > 1 cm).
Biopsy available of primary tumour and/or metastasis
WHO performance status of 0-2
Either :
- No previous systemic therapy for advanced soft tissue sarcoma or advanced urothelial cell carcinoma, or;
- Previous systemic therapy for advanced soft tissue sarcoma or advanced urothelial cell carcinoma with progression of disease during systemic therapy or progression of disease after discontinuation of systemic therapy, or;
- Previous systemic therapy for advanced soft tissue sarcoma or advanced urothelial cell carcinoma with partial response or stable disease, where the last dose of systemic therapy was given > 8 weeks before.

Exclusion criteria

Women who are pregnant and/or lactating.
Medical or psychiatric conditions that compromise the patient*s ability to give informed consent.
Known hypersensitivity to drugs comparative to [18F]-JK-PSMA-7, any of their excipients or to any component of [18F]-JK-PSMA-7.
Inability to undergo PET/CT scanning, e.g. claustrophobia, weight limits or inability to tolerate lying down for the duration of a PET/CT scan (~30 minutes).

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-08-2022
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Date:	11-04-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	21-11-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	19-06-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL78279.058.21