Phase I dose escalation study to evaluate tolerability and safety of 225Ac-PSMA in patients with metastatic prostate cancer

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This study has been transitioned to CTIS with ID 2024-513729-22-01 check the CTIS register for the current data. 1.1 Primary study objectives To investigate the safety, tolerability and biochemical effects of 225Ac-PSMA injected in patients with...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52446

Source
ToetsingOnline

Brief title
Phase I study of 225Ac-PSMA in prostate cancer

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,KWF

Intervention

Keyword: 225Ac-PSMA, Prostate cancer

Outcome measures

Primary outcome

Primary study endpoints

· Safety and tolerability of 225Ac-PSMA in patients with mCRPC as assessed by:

o Incidence and severity of adverse events and serious adverse events

o Absolute values and changes from baseline in laboratory parameters

(hematology, blood chemistry and urinalysis), including assessment of shifts

from baseline to abnormal values on treatment

o Absolute values and changes from baseline in vital signs & ECG parameters

Secondary outcome

Secondary study endpoints

· The following 68Ga-PSMA distribution and radiation dosimetry endpoints will

be calculated:

o Volume calculations of critical organs and tumor by PET-MRI.

o Expected radiotracer uptake calculated as a percentage of the injected dose

per gram of tissue (%ID/g)

o Expected absorbed doses and effective whole body dose of 225Ac-PSMA

· Direct effect of 225Ac-PSMA will be monitored by:

o Changes in SUVmax of the target lesions on PET-MRI

o Changes in perfusion measured on MRI

· The preliminary action of the therapeutic doses of 225Ac-PSMA will be

assessed according to the last PET-MRI. These imaging techniques will be used

to derive the following endpoints where relevant:

o Objective response rate (ORR) as measured by RECIST criteria v.1.1. This is defined as the number of patients with either a complete response (CR) or partial response (PR) at any time point which is confirmed a minimum of 4 weeks later, divided by the total number of patients with visceral disease at baseline.

o Percent changes from baseline in tumor size where tumor size is defined as the sum of all target lesions as measured by RECIST 1.1. Only patients with measurable disease at baseline (i.e. target lesions identified and measured) will contribute to these analyses.

o PSA response rate assessed from treatment visit 1 defined as a decrease in PSA of >= 50% from baseline.

o Percent change from baseline in PSA as a continuous endpoint by visit and maximum reduction during the study

o Percent change from baseline values of pain questionnaire at every treatment visit

o Overall Survival defined as the time from the date of first dose of 225Ac-PSMA treatment to the date of death due to any cause. Any subject not known to have died at the time of the analysis will be censored based on the last recorded date on which the subject was known to be alive.

Study description

Background summary

PSMA is a type II transmembrane glycoprotein with a domain both intracellular and extracellular. PSMA is expressed on benign prostate epithelium and on prostate cancer cells. There is also expression of PSMA in other tissues such as the kidneys, small intestine and the salivary glands. However, the expression on prostate cancer cells is a thousand-fold higher than expression on normal tissues and therefore a target for both imaging and therapy of prostate cancer. PSMA has a large extracellular domain and specific inhibitors can internalize after binding to the receptor. Imaging with Gallium-68 or Fluor-18 labeled PSMA-ligands is now widely used for primary staging of prostate cancer, but also for detection of recurrent disease in patient with a biochemical recurrence. In the recent years different PSMA-ligands were developed for imaging and therapy. In the Netherlands, the most frequently used tracer for imaging is 68Ga-PSMA-11. For therapy, both PSMA-617 and PSMA I&T are used. With the use of PSMA I&T, the same ligand can be used for imaging and therapy when labeled to different radionuclides.

Study objective

This study has been transitioned to CTIS with ID 2024-513729-22-01 check the CTIS register for the current data.

1.1 Primary study objectives
To investigate the safety, tolerability and biochemical effects of 225Ac-PSMA injected in patients with metastatic prostate cancer.

Primary objective:
- To assess the safety and tolerability of 225Ac-PSMA administered intravenously

Secondary study objectives
Secondary objectives:
- To predict and calculate the absorbed-dose in critical organs (e.g. salivary glands, kidneys, bone marrow) by 68Ga-PSMA PET/MRI
- To evaluate the effects of the radionuclide therapy on metastases in the days after therapy using 68Ga-PSMA PET/MRI
- To evaluate the biochemical effects of 225Ac-PSMA therapy

Study design

A clinical prospective, single-center, single-arm, phase I dose escalation therapy study.

Intervention

Ac-PSMA

Study burden and risks

Participation in this study requires additional blood draws, imaging, infusion of the IMP, hospitalization and follow-up visits.

Total needed blood volume varies between 30-80 ml per blood draw. Blood draws will take place before each cycle and during follow-up visits. Additionally, blood will be drawn direct after infusion of the IMP and then over time (in total 13 times) to measure the radioactivity of the tracer and its daughters in blood, which is necessary for good dosimetry. The risk of blood being drawn is minimal.

Patients will undergo additionally three times imaging with PET-MRI, two times with SPECT/CT and five times with a gamma-camera during the study. From protocol version 3 patients will undergo additionally three times imaging with PET-MRI, one time with SPECT/CT and three times with a gamma-camera during the study. Scans for dosimetry will add an extra radiation dose of 2,5 mSV from the low-dose CT to the patients. Considering the age of the patients, the prognosis and the potential benefit of this study for future treatment of prostate cancer patients, the radiation burden of the protocol is considered justified.

Due to the Dutch safety regulations regarding dose limitations for hospital discharge, all patients should be hospitalized during one night after each treatment. From literature, it is not expected that patients will have acute side-effects from the IMP infusion. Expected side-effect will be subacute, therefore follow-up visits are necessary to monitor each patient close.

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

- Histopathological proven metastatic castration resistant prostate cancer
- Progression after at least one line of chemotherapy and one line of nonsteroidal antiandrogen

Exclusion criteria

- Concurrent severe illness or clinically relevant trauma within 2 weeks before the administration of the investigational product that might preclude study completion or interfere with study results
- Serum hemoglobin <= 6.2 mmol/L, total white blood cell (WBC) count <= 2·109/L, platelet count <= 100·109/L, serum creatinine concentration >= 150 umol/L (>= 1.7 mg/dL), serum albumin <30 g/L
- Concurrent bladder outflow obstruction or unmanageable urinary incontinence
- Known or expected hypersensitivity to Gallium-68, Actinium-225, PSMA, or any excipient present in 225Ac/68Ga-PSMA

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-03-2022
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	225Ac-PSMA

Ethics review

Approved WMO Date:	09-02-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-12-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-06-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-07-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-01-2023

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-02-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-02-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-05-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-07-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
EU-CTR	CTIS2024-513729-22-01
EudraCT	EUCTR2020-001089-13-NL
CCMO	NL73234.078.20