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Recruiting ⓘ

Actium-225-Prostate Specific Membrane Antigen Imaging & Therapy (225AcPSMAI&T)

ClinicalTrials.gov ID ⓘ NCT05902247

Sponsor ⓘ Erasmus Medical Center

Information provided by ⓘ Tessa Brabander, Erasmus Medical Center (Responsible Party)

Last Update Posted ⓘ 2023-06-13

Study Details Tab

Study Overview

Brief Summary

225Ac-PSMA I&T is a radiopharmaceutical for therapy of prostate cancer. PSMA is overexpressed on prostate cancer cells. Actium-225 is an alpha emitting radionuclide. When PSMA I&T is labelled with Actium-225, it can be applied as therapy for prostate cancer.

Detailed Description

Rationale:

225Ac-PSMA I&T is a radiopharmaceutical for therapy of prostate cancer. PSMA is overexpressed on prostate cancer cells. Actium-225 is an alpha emitting radionuclide. When PSMA I&T is labelled with Actium-225, it can be applied as therapy for prostate cancer.

Objective:

Patent Owner Exhibit 2089
IPR2025-01582



To evaluate the tolerability and safety of 225Ac-PSMA I&T in patients with metastatic prostate cancer and recommend a dose for further phase 2 studies.

Study design:

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

Study population:

Up to 30 patients with advanced metastatic castration-resistant prostate cancer (mCRPC).

Intervention:

Patients with advanced mCRPC will receive therapy with 225Ac-PSMA I&T. The first dose-level will not exceed 8 megabecquerel (MBq), as this is reported in the literature as a safe activity for treatment. A Positron Emission Tomography - Magnetic Resonance Imaging (PET-MRI) with Gallium-68-PSMA I&T (68Ga) will be performed to calculate the precise dose-level needed and as a verification the precise dose-level will be compared with the dose-level of 8 MBq. In the first week after therapy, the PET-MRI will be repeated to observe any effects of the alpha radiation on the metastases and observe the potential changes in 68Ga-PSMA I&T uptake. Eight weeks after the first cycle, patients will receive the second cycle of 225Ac-PSMA I&T. If no Dose Limiting Toxicity (DLT) occurs, the dose can be increased for the next DL. If a DLT occurs, the cohort will be expanded to 6 patients. After establishing the recommended dose, an expansion cohort will be opened with a total of 12 patients.

Main study endpoints:

To investigate the safety, tolerability and biochemical effects of 225Ac-PSMA I&T injected in patients with metastatic prostate cancer.

Primary objective:

- To assess the safety and tolerability of 225Ac-PSMA I&T administered intravenously

Secondary objectives:

- To predict and calculate the absorbed-dose in critical organs (e.g. salivary glands, kidneys, bone marrow) by 68Ga-PSMA I&T PET-MRI
- To evaluate the effects of the radionuclide therapy on metastases in the days after therapy using 68Ga-PSMA I&T PET-MRI
- To evaluate the biochemical effects of 225Ac-PSMA I&T therapy in patients with metastatic prostate cancer

Official Title

Phase I Dose Escalation Study to Evaluate Tolerability and Safety of 225Ac-PSMA I&T in Patients With Metastatic Prostate Cancer

Conditions ⓘ

Intervention / Treatment ⓘ

- Radiation: Radionuclide Therapy

Other Study ID Numbers ⓘ

- NL73234.078.20

Study Start (Actual) ⓘ

2021-12-29

Primary Completion (Estimated) ⓘ

2025-12-29

Study Completion (Estimated) ⓘ

2025-12-29

Enrollment (Estimated) ⓘ

30

Study Type ⓘ

Interventional

Phase ⓘ

Phase 1

Resource links provided by the National Library of Medicine

[MedlinePlus](https://medlineplus.gov/) (https://medlineplus.gov/) related topics: [Prostate Cancer](https://medlineplus.gov/prostatecancer.html) (https://medlineplus.gov/prostatecancer.html).

[FDA Drug and Device Resources](https://clinicaltrials.gov/fda-links) (https://clinicaltrials.gov/fda-links).

Contacts and Locations

This section provides contact details for people who can answer questions about joining this study, and information on where this study is taking place.

To learn more, please see the [Contacts and Locations section in How to Read a Study Record](#) (<https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations>).

Study Contact ⓘ

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This study has 1 location

Netherlands

South Holland Locations

 Rotterdam, South Holland, Netherlands,
3015GD

Recruiting

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Participation Criteria

Researchers look for people who fit a certain description, called [eligibility criteria](#). Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read [Learn About Studies](#) (<https://clinicaltrials.gov/study-basics/learn-about-studies>).

Eligibility Criteria

Description

Inclusion Criteria:

- Histopathological proven metastatic castration resistant prostate cancer.
Castration-resistant disease is defined as a serum testosterone level of 50 nanogram per deciliter or lower (≤ 1.7 nanomol per liter) after bilateral orchiectomy or during maintenance treatment consisting of androgen-ablation therapy with a luteinizing hormone-releasing hormone agonist.
- Evidence of progressive disease, defined as 1 or more Prostate Cancer Work Grouping 3 (PCWG3) criteria: - PSA level ≥ 1 ng/mL that has increased on at least 2 successive occasions at least 1 week apart
- Progression as defined by RECIST 1.1 with PCGW3 modifications
- Progression after at least one line of chemotherapy and/or one line of nonsteroidal antiandrogen (NSAA).
- No active anti-tumor therapy, except for androgen deprivation therapy in combination with at least one androgen receptor-targeted agent
- Willing and able to undergo 2 cycles of ^{225}Ac -PSMA I&T therapy and 3 PET-MRI scans in 16 weeks and comply with protocol
- Signed and dated written informed consent by the patient (or legal representative) prior to any study-specific procedures.
- Age ≥ 18 years.
- Eastern Cooperative Oncology Group (ECOG) performance-status score 0-2.
- Use of highly effective methods of contraception (female partners of male participants)
- During the trial and 6 months after completion of the study or willing to practice sexual abstinence.

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 $\leq 3.5 \cdot 10^9/\text{L}$, absolute neutrophil count $\leq 1.5 \cdot 10^9/\text{L}$, platelet count $\leq 100 \cdot 10^9/\text{L}$, serum creatinine concentration ≥ 150 $\mu\text{mol/L}$ (≥ 1.7 mg/dL), serum albumin < 30 g/L, bilirubin ≥ 1.5 x upper limit normal (ULN), aspartate transaminase (ASAT) ≥ 3 x ULN and alanine aminotransferase (ALAT) ≥ 3 x ULN (or bilirubin ≥ 3 x ULN, ASAT ≥ 5 x ULN and ALAT ≥ 5 x ULN in the case of pre-existing liver metastases at baseline)
- Concurrent bladder outflow obstruction or unmanageable urinary incontinence
- Known or expected hypersensitivity to Gallium-68, Actinium-225, PSMA I&T, or any excipient present in $^{225}\text{Ac}/^{68}\text{Ga}$ -PSMA I&T

- Prior administration of a radiopharmaceutical within a period corresponding to 8 halflives of the radionuclide used on such radiopharmaceutical
- Prior treatment with any radionuclide therapy
- History of somatic or psychiatric disease/condition that may interfere with the objectives and assessments of the study
- Central nervous system (CNS) metastases, leptomenigeal disease, or spinal cord compression
- Radiation therapy within 4 weeks of first dose (or local or focal radiotherapy within 2 weeks of first dose)
- Male subjects unwilling to abstain from donating sperm during treatment and for an additional 6 months after the last dose

Gender-based Eligibility ⓘ

Yes

Gender Eligibility for Study

Male

Ages Eligible for Study ⓘ

18 Years and older (Adult, Older Adult)

Sexes Eligible for Study ⓘ

Male

Accepts Healthy Volunteers ⓘ

No

Study Plan

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose ⓘ : Treatment

Allocation ⓘ : N/A

Interventional Model ⓘ : Single Group Assignment

Interventional Model Description: A clinical prospective, single-center, single-arm, phase I dose escalation therapy study.

Masking ⓘ : None (Open Label)

Arms and Interventions

Participant Group/Arm ⓘ	Intervention/Treatment ⓘ
Experimental: 225Ac-PSMA I&T 225Ac-PSMA I&T	Radiation: Radionuclide Therapy - To evaluate the tolerability and safety of 225Ac-PSMA I&T in patients with metastatic prostate cancer - Other Names: 225Ac-PSMA I&T

What is the study measuring?

Primary Outcome Measures ⓘ

Outcome Measure	Measure Description	Time Frame
Incidence and severity of Adverse Events and Serious Adverse Events as assessed by CTCAE v5.0	Safety and tolerability assessment	4 years

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	Safety and tolerability assessment	4 years
Absolute values and changes from baseline in vital signs & ECG parameters	Safety and tolerability assessment	4 years

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
To predict and calculate the absorbed-dose in critical organs (e.g. salivary glands, kidneys, bone	Dosimetry	4 years

marrow) by 68Ga-PSMA I&T PET-MRI		
Changes in SUVmax of the target lesions on PET-MRI and morphological changes evaluated on MRI	Direct effect of 225Ac-PSMA I&T	4 years
Objective response rate (ORR) as measured by Response Evaluation Criteria in Solid Tumors (RECIST) criteria v.1.1.	Preliminary efficacy	4 years
Percent changes from baseline in tumor size where tumor size is defined as the sum of all target lesions as measured by RECIST criteria v.1.1.	Preliminary efficacy	4 years

Prostate Specific Antigen(PSA) response rate assessed from treatment visit 1 defined as a decrease in PSA of $\geq 50\%$ from baseline.	Preliminary efficacy	4 years
Percent change from baseline in PSA as a continuous endpoint by visit and maximum reduction during the study	Preliminary efficacy	4 years
Percent change from baseline values of pain questionnaire at every treatment visit	Preliminary efficacy	4 years
Overall Survival (OS) defined as the time from the date of first dose of 225Ac-PSMA I&T treatment to the date of	Preliminary efficacy	4 years

death due to any cause.			
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Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor ⓘ

Erasmus Medical Center

Collaborators ⓘ

- Dutch Cancer Society

Publications

From PubMed

These publications come from PubMed, a public database of scientific and medical articles. This list is automatically created by ClinicalTrials.gov Identifier (NCT Number), and these articles may or may not be about the study.

- [Ling SW, van der Veldt AAM, Konijnenberg M, Segbers M, Hooijman E, Bruchertseifer F, Morgenstern A, de Blois E, Brabander T. Evaluation of the tolerability and safety of \[225Ac\]Ac-PSMA-I&T in patients with metastatic prostate cancer: a phase I dose escalation study. BMC Cancer. 2024 Jan 29;24\(1\):146. doi: 10.1186/s12885-024-11900-y. \(https://pubmed.ncbi.nlm.nih.gov/38287346\)](https://pubmed.ncbi.nlm.nih.gov/38287346)

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted ⓘ

2023-05-24

First Submitted that Met QC Criteria ⓘ

2023-06-05

First Posted ⓘ

2023-06-13

Study Record Updates**Last Update Submitted that met QC Criteria** ⓘ

2023-06-05

Last Update Posted ⓘ

2023-06-13

Last Verified ⓘ

2023-06

More Information

Terms related to this study**Keywords Provided by Tessa Brabander, Erasmus Medical Center**

225Ac-PSMA

Prostate cancer

Additional Relevant MeSH Terms

Genital Neoplasms, Male

Urogenital Neoplasms

Neoplasms by Site

Neoplasms

Genital Diseases, Male

Genital Diseases

Urogenital Diseases

Prostatic Diseases

Male Urogenital Diseases

Prostatic Neoplasms, Castration-Resistant

Prostatic Neoplasms

Plan for Individual Participant Data (IPD)

Plan to Share Individual Participant Data (IPD)? [HHS Vulnerability Disclosure](#)

No

Drug and device information, study documents, and helpful links

Studies a U.S. FDA-Regulated Drug Product

No

Studies a U.S. FDA-Regulated Device Product

No