68Ga-PSMA-PET/CT and genomic alterations for future selection of patients with metastatic castration resistant prostate cancer (mCRPC) for Radium-223 treatment.

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Primary Objective: • To determine the clinical Progression Free Survival (cPFS) in our study cohort of patients with mCRPC and 68Ga-PSMA-PET/CT selected bone-only disease (PET-bone only group). The cPFS will be compared to the cPFS of patients with…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON57275

Source
ToetsingOnline

Brief title
The Radium-select study

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
Prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Bayer

Intervention

Keyword: 68Ga-PSMA-PET/CT, metastatic castration resistant prostate cancer, Radium-223

Outcome measures

Primary outcome

Clinical progression free survival (cPFS). cPFS will be defined as the time from first Radium-223 treatment to the date of confirmed progression: clinical progression (WHO PS * 3, new prostate cancer symptoms, skeletal related events, a persisting rise in both PSA and ALP) or radiographic progression based on ceCT or bone scan; start of subsequent treatment (including External Beam Radiotherapy: EBRT and radionuclide therapy to treat generalized pain); death or censored at last follow-up. Whichever comes first. Routine interim imaging in patients that do not show clinical signs of disease progression will not be permitted.

Secondary outcome

• Patient reported outcome measures (PROMs). Each participant will be asked to complete questionnaires on health related quality of life (HRQoL), including the FACT-P, pain (BPI-SF) and analgesics use after every treatment cycle.

• Overall Survival (OS). OS will be defined as time from first Radium-223 treatment to the date of death, or censored at last follow-up.

• 68Ga-PSMA-PET/CT parameters will be assessed at end of treatment. 68Ga-PSMA-PET/CT will be used to evaluate whether clinical progression was

driven by bone lesions or (new) extraskeletal lesions.

• Genomic biomarkers in ctDNA. We will determine whether homologous recombination deficiency (HRD) assessment in ctDNA correlates with a favorable therapy response. We will perform deep whole genome sequencing (WGS) of ctDNA before and after treatment to determine the clonal evolution of prostate cancer during Radium-223 therapy.

Study description

Background summary

Radium-223 is an established radionuclide therapy for patients with metastatic castration resistant prostate cancer (mCRPC) and symptomatic bone metastasis. Patients are eligible for this treatment when they have mCRPC and bone metastases; limited extraskeletal lesions (local prostate, lymph nodes <3 cm) on conventional contrast enhanced CT (ceCT) were allowed in the registration trial(1). Previous research revealed that extraskeletal disease on ceCT and bone scans correlates with a poor response. Meanwhile, 68Ga-PSMA-PET/CT emerged as more sensitive imaging strategy that increases the detection of extraskeletal prostate cancer metastases. It is unclear whether these extraskeletal lesions harbour any predictive value in the treatment of mCRPC patients with Radium-223.

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Study objective

Primary Objective:
• To determine the clinical Progression Free Survival (cPFS) in our study cohort of patients with mCRPC and 68Ga-PSMA-PET/CT selected bone-only disease (PET-bone only group). The cPFS will be compared to the cPFS of patients with on PSMA PET/CT-detected extra-skeletal disease (control group). In addition, cPFS will be compared to an historical cohort of patients that received standard of care Radium-223 therapy in the ROTOR registry (retrospective control group).

Secondary Objectives:
• To determine the impact of Radium-223 treatment on patient reported outcome measures (PROMs) in the selected bone-only group, as compared to the control

group, and in addition, to the retrospective control cohort (ROTOR).
• To determine the overall survival (OS) in our selected bone-only cohort of patients in comparison to the control group and to the retrospective control cohort (ROTOR).
• To determine the correlation between genomic biomarkers (HRD) in ctDNA and Radium-223 treatment response in the selected bone-only cohort.
• To evaluate whether clinical progression was driven by bone lesions or (new) extraskeletal lesions. 68Ga-PSMA-PET/CT will be used to assess these lesions.

Study design

We will conduct a prospective clinical study to determine the clinical response to Radium-223 therapy among patients with mCRPC with bone only disease according to 68Ga-PSMA-PET/CT scan. We will include patients (n=60) with mCRPC that are commencing standard-of-care Radium-223 therapy based on results of ceCT and bone scans. Each patient will undergo an additional 68Ga-PSMA-PET/CT scan to determine the presence of potential extra-skeletal disease according to this imaging modality and plasma sampling for ctDNA analysis. The treating physician*s will be blinded to the 68Ga-PSMA-PET/CT scan result during treatment. All imaging should be performed in the 8 weeks prior to start of Radium-223 therapy. Subsequently, all patients will receive a maximum number of 6 cycles of Radium-223 therapy according to current clinical guidelines (Figure 1). From each participant, data will be collected about clinical (skeletal related events, SREs), biochemical (alkaline phosphatase: ALP, PSA) and conventional imaging (ceCT, bone scans) response. We will also measure quality of life (QoL) parameters by serial assessment of PROMs. Upon clinical progression, the result of the baseline 68Ga-PSMA-PET/CT will be unblinded to allow monitoring of inclusions in the *PET-bone-only* cohort. All patients will undergo a second 68Ga-PSMA-PET/CT in addition to routine ceCT- bone scans to determine the location of the disease progression. The clinical results obtained with the 68Ga-PSMA-PET/CT selection strategy, will be compared to the treatment outcomes collected in our previously reported ROTOR registry(3).

Study burden and risks

All patients will receive standard of care Radium-223 treatment. Study participation will require completion of two 68Ga-PSMA-PET/CT scans (1), a maximum number of 4 plasma samplings (2x 10 mL Streck tubes) for genomics analysis (2) and monthly PROM assessments from inclusion until disease progression (3). Each PROM assessment will consist of either a digital completion of two questionnaires about quality of life (FACT-P) and pain (BPI-S) and registration of pain medications. Patients will be exposed to a total 12 mSv of radiation due to the two additional 68Ga-PSMA-PET/CT scans, which is a low dose of radiotion relative to Radium-223 radionuclide treatment to which to patient consented. We therefore consider the risks of these study procedures negligible. Radium-223 treatment is currently only registered for

the treatment of patients with mCRPC, based on ALSYMPCA inclusion criteria (i.e. no extra-skeletal disease on ceCT and bone scan). This study can therefore only be performed among these patients. Patients that will have extra-skeletal metastases on 68Ga-PSMA PET/CT (control group), will be treated with Radium-223 according to current clinical guidelines as well, as the predictive value of having extra-skeletal metastases on PET has not been shown. We hypothesize that clinical response among these patients will last shorter, because extra-skeletal metastases will by definition not be treated by Radium-223.

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

1) Histologically confirmed adenocarcinoma of the prostate.

2) Progressive disease after previous treatment defined as a rise in serum PSA (PCWG3 criteria(22), see appendix 1) and/or progression on conventional imaging (PCWG3).
3) A positive bone scan (osteoblastic bone metastases), with at least two metastases.
4) Hemoglobin concentration >10 g/dl (6.2 mmol/l) and thrombocytes >100 109/l at baseline.
5) Each patient will need to (continue to) receive adequate bone protective agents (e.g. bisphosphonates) and androgen deprivation therapy (ADT) according to current clinical guidelines.

Exclusion criteria

1) ECOG performance score >2
2) Life expectancy < 6 months.
3) Detected extra-skeletal metastases or lymph node metastases (>3 cm short axis) as identified by conventional imaging (ceCT thorax/abdomen)

Study design

Design

Study phase:	4
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-03-2025
Enrollment:	60
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	30-01-2025
Application type:	First submission
Review commission:	METC NedMec

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	NL86928.041.24