PSMAfore: A phase III, Open-label, Multi-Center, Randomized Study Comparing 177Lu-PSMA-617 vs. a Change of androgen receptor-directed therapy in the Treatment of Taxane Naïve Men with Progressive Metastatic Castrate Resistant Prostate Cancer

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This study has been transitioned to CTIS with ID 2023-507772-50-00 check the CTIS register for the current data. The purpose of this study is to determine whether 177Lu-PSMA-617, given for 6 cycles at a dose of 7.4 Gigabecquerel (GBq) (200...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON52179

Source
ToetsingOnline

Brief title
CAAA617B12302

Condition

- Other condition

Synonym
uitgezaaide prostaatkanker

Health condition

prostaat kanker

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma BV (sponsor van dit onderzoek)

Intervention

Keyword: Phase III, Prostate cancer PSMA protein, Radioligand therapy

Outcome measures

Primary outcome

To evaluate whether treatment with 177Lu-PSMA-617 improves the time to

radiographic progression by BICR according PCWG3-modified RECIST v1.1 or death

in participants with progressive PSMA-positive mCRPC compared to participants

treated with ARDT

Secondary outcome

key secondary:

To evaluate whether treatment with 177Lu-PSMA-617 improves the overall survival

(OS) in participants with progressive PSMA-positive mCRPC compared to

participants treated with ARDT treatment

other:

To estimate the time to radiographic progression by BICR or death in

participants treated with ARDT who subsequently crossover to 177Lu-PSMA-617

after radiographic progression (rPFS2)

for more see page 14 in the protocol

Study description

Background summary

The preliminary clinical evidence indicates that 177Lu-PSMA-617 may demonstrate clinical benefit for men with mCRPC, improving rPFS and OS compared with a change in ARDT. The ongoing VISION study is investigating the efficacy and safety of 177Lu-PSMA-617 in mCRPC participants previously treated with ARDT and taxane-based chemotherapy. Data from this study will complement the data from the VISION study for 177Lu-PSMA-617 as a treatment in mCRPC prior to the use of taxanes.
The basic principle of 177Lu-PSMA-617 radioligand therapy is to systemically deliver low dose rate radiation specifically to multiple PSMA positive prostate cancer lesions, while sparing normal tissues. To date, 12 dosimetry studies have been conducted in 158 participants. The results are consistent across the studies and demonstrate exposure that correlates well with the expected rapid clearance of a small molecule, and the limited distribution pattern of a PSMA-targeted radionuclide.
177Lu-PSMA-617 is well tolerated according to the clinical experience that has been documented in over 53 publications, summarizing the safety and or efficacy information from over 1280 participants

Study objective

This study has been transitioned to CTIS with ID 2023-507772-50-00 check the CTIS register for the current data.

The purpose of this study is to determine whether 177Lu-PSMA-617, given for 6 cycles at a dose of 7.4 Gigabecquerel (GBq) (200 Millicuries (mCi)) +/- 10%, improves the radiographic progression free survival (rPFS) or death compared to a change in androgen receptor-directed therapy (ARDT) in metastatic castrate resistant prostate cancer (mCRPC) participants that were previously treated with an alternate ARDT and not exposed to a taxane-containing regimen in the castrate resistant prostate cancer (CRPC) or metastatic hormone-sensitive prostate cancer (mHSPC) settings.

Study design

This is a phase III, open label, multicenter randomized study for PSMA-positive mCRPC participants previously treated with an ARDT where it is considered appropriate to delay taxane-based chemotherapy.
The study aims at evaluating the superiority of 177Lu-PSMA-617 over a change of ARDT treatment in prolonging rPFS. The primary endpoint of rPFS will be assessed via blinded centralized review of radiographic images provided by the treating physician and as outlined in PCWG3 Guidelines.
The study will also evaluate whether 177Lu-PSMA-617 improves the overall survival (OS) in participants with progressive PSMA-positive mCRPC compared to participants treated with a change in ARDT treatment. OS is defined as the time from randomization to death due to any cause

Intervention

Intervention with 177Lu-PSMA-11 or anti-hormonal therapy and patients on anti-hormonal therapy can cross over to 177Lu-PSMA-11 treatment

Study burden and risks

Risk: potential side effects of study treatment and GA-PSMA-11 scan
Burden:
The patient will come to the study doctor*s clinic 6 times during the first 1 cycle (1 cycle is 6 weeks), thereafter 3 times during each following 5 cycles, thereafter every 12 weeks. After the patient discontinues study treatment, he/she will be followed for safety.
See question E4 for all study assessments.

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

• Participants must have an ECOG performance status of 0 to 1
• Participants must have histological pathological, and/or cytological confirmation of adenocarcinoma of the prostate
• Participants must be 68Ga-PSMA-11 PET/CT scan positive, and eligible as determined by the sponsor*s central reader
• Participants must have a castrate level of serum/plasma testosterone (< 50 ng/dL or < 1.7 nmol/L)
• Participants must have progressed only once on prior second generation ARDT (abiraterone, enzalutamide, darolutamide, or apalutamide).
• first generation androgen receptor inhibitor therapy (e.g. bicalutamide) is allowed but not considered as prior ARDT therapy
• second generation ARDT must be themost recent therapy received
• Participants must have progressive mCRPC. Documented progressive mCRPC will be based on at least 1 of the following criteria:
• Serum/plasma PSA progression defined as 2 increases in PSA measured at least 1 week apart. The minimal start value is 2.0 ng/mL; 1.0 ng.mL is the minimal starting value if confirmed rise in PSA is the only indication of progression
• Soft-tissue progression defined [PCWG3-modified RECIST v1.1 (Eisenhauer et al 2009, Scher et al 2016)]
• Progression of bone disease: two new lesions; only positivity on thebone scan defines
metastatic disease to bone (PCWG3 criteria (Scher et al 2016))
• Participants must have >= 1 metastatic lesion that is present on screening/baseline CT, MRI, or bone scan imaging obtained <= 28 days prior to beginning study therapy
• Participants must have recovered to <= Grade 2 from all clinically significant toxicities related to prior therapies (i.e. prior chemotherapy, radiation, etc.) except alopecia

• Participants must have adequate organ function

Exclusion criteria

- Previous treatment with any of the following within 6 months of randomization: Strontium-89, Samarium-153, Rhenium-186, Rhenium-188, Radium-223, hemi-body irradiation
- Previous PSMA-targeted radioligand therapy
- Prior treatment with cytotoxic chemotherapy for castration resistant or castrate sensitive prostate cancer (e.g., taxanes, platinum, estramustine, vincristine, methotrexate, etc.), immunotherapy or biological therapy [including monoclonal antibodies]) [Note: Taxane exposure (maximum 6 cycles) in the adjuvant or neoadjuvant setting is allowed if 12 months have elapsed since completion of this adjuvant or neoadjuvant therapy]. Prior treatment with sipuleucel-T is allowed
- Any investigational agents within 28 days prior to day of randomization
- Known hypersensitivity to any of the study treatments or its excipients or to drugs of similar classes
- Other concurrent cytotoxic chemotherapy, immunotherapy, radioligand therapy, PARP inhibitor, biologicals or investigational therapy
- Transfusion or use of bone marrow stimulating agents for the sole purpose of making a participant eligible for study inclusion
- Patients with a history of CNS metastases that are neurologically unstable, symptomatic, or receiving corticosteroids for the purpose of maintaining neurologic integrity. Participants with CNS metastases are eligible if received therapy (surgery, radiotherapy, gamma knife),

asymptomatic and neurologically stable without corticosteroids. Participants with epidural disease, canal disease and prior cord involvement are eligible if those areas have been treated, are stable, and not neurologically impaired.
- Symptomatic cord compression, or clinical or radiologic findings indicative of impending cord compression
- History or current diagnosis of the following ECG abnormalities indicating significant risk of safety for study participants:
- Concomitant clinically significant cardiac arrhythmias, e.g. sustained ventricular tachycardia, complete left bundle branch block, high-grade AV block (e.g., bifascicular block, Mobitz type II and third degree AV block)
- History of familial long QT syndrome or known family history of Torsades de Pointe
- Cardiac or cardiac repolarization abnormality, including any of the following: History of myocardial infarction (MI), angina pectoris, or

CABG within 6 months prior to starting study treatment

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-09-2021
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	gallium (68Ga) gozetotide
Generic name:	gallium (68Ga) gozetotide
Product type:	Medicine
Brand name:	lutetium(177Lu) vipivotide tetraxetan
Generic name:	177Lu-PSMA-617
Product type:	Medicine
Brand name:	XTANDI
Generic name:	ENZALUTAMIDE
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Zytiga

Generic name:	abiraterone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-02-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-06-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-12-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-02-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-04-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-04-2022
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-05-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-06-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-06-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-08-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-10-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-11-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-05-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-05-2023
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-07-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-07-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-09-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	CTIS2023-507772-50-00
EudraCT	EUCTR2020-003969-19-NL
ClinicalTrials.gov	NCT04689828
CCMO	NL75959.091.21