An International Prospective Open-label, Randomized, Phase III Study comparing 177Lu-PSMA-617 in combination with Standard of Care, versus Standard of Care alone, in adult male patients with Metastatic Hormone Sensitive Prostate Cancer (mHSPC)

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This study has been transitioned to CTIS with ID 2023-507970-42-00 check the CTIS register for the current data. The purpose of this study is to evaluate the efficacy and safety of 177Lu-PSMA-617 in combination with Standard of Care, versus Standard…

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

Summary

ID

NL-OMON54006

Source
ToetsingOnline

Brief title
CAAA617C12301

Condition

- Other condition

Synonym
metastatic prostate cancer

Health condition

prostaatkanker

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

The primary objective of this study is to evaluate radiographic progression free survival (rPFS) as assessed by Blinded Independent Review Committee (BIRC) in patients with mHSPC receiving Standard of Care and 177Lu-PSMA-617 versus patients receiving Standard of Care without 177Lu-PSMA-617.The primary clinical question of interest: what is the treatment effect based on rPFS for 177Lu-PSMA-617 in combination with Standard of Care versus Standard of Care alone in the treatment of adult male patients with mHSPC as defined through inclusion/exclusion criteria, regardless of study treatment discontinuation (STD) or start of new antineoplastic therapy prior to rPFS event.

Secondary outcome

Key Secondary objective:

• To evaluate the contribution of 177Lu-PSMA-617 to Standard of Care in terms of overall survival (OS) in patients with mHSPC.

Other Secondary Objectives:

• To evaluate PSA90 response at 3, 6 and 12 months

• To evaluate the time to development of metastatic castration resistant prostate cancer (TTDm) as determined by investigators.

• To evaluate Progression Free Survival (PFS) by investigator

• To evaluate the second progression Free Survival (PFS2) by investigator

• To evaluate the change in the nadir levels of PSA < 0.2 ng/mL at months 3, 6 and 12 months

• To evaluate the overall response rate (ORR), disease control rate (DCR), time to response (TTR), duration of response (DOR) and Time to soft tissue progression (TTSTP) based on PCWG3-modified Response evaluation criteria in solid tumor (RECIST) 1.1 by Blinded Independent Review Committee (BIRC) assessment

• To evaluate safety and tolerability of 177Lu-PSMA-617

• To assess the effect of 177Lu-PSMA-617 on the health-related quality of life (HRQoL)

• To evaluate the time to first symptomatic skeletal event (SSE).

Study description

Background summary

An estimated 1.3 million new cases of prostate cancer (PC) and 359,000 cancer deaths were attributed to PC in 2018 worldwide (International Agency for Research on Cancer 2018) and a majority of patients who die of prostate cancer will pass through the metastatic hormone sensitive prostate cancer (mHSPC) phase of the disease. Historically mHSPC has been treated, since the discovery of its hormone dependence in the 1940s, with surgical or medical castration

resulting in frequent and rapid palliative benefits and a presumptive improvement in cancer-specific and overall survival. Attempts to improve survival and quality of life have included, but have not been limited to, earlier use of androgen deprivation therapy (ADT) for asymptomatic advanced disease, use of traditional anti-androgens to achieve combined androgen blockade (Prostate Cancer Trialists' Collaborative 2000), intermittent androgen therapy (Hussain et al 2013), early bisphosphonate use (Dearnaley et al 2009, James et al 2016b, James et al 2016a, Smith et al 2014), gonadotropin releasing hormone antagonists, targeted biologic agents (Yu et al 2015) and radiopharmaceuticals (Bilen et al 2014, James et al 2016a) with either absent, limited or controversial success.

Study objective

This study has been transitioned to CTIS with ID 2023-507970-42-00 check the CTIS register for the current data.

The purpose of this study is to evaluate the efficacy and safety of 177Lu-PSMA-617 in combination with Standard of Care, versus Standard of Care alone, in adult male patientswith mHSPC.
In this study, the SoC is defined as a combination of Androgen Receptor Directed Therapy + Androgen Deprivation Therapy.

Study design

In this international, open-label, prospective, phase III study, where approximately 1126 patients with treatment naïve or minimally treated PSMA-positive mHSPC will be randomized in a 1:1 ratio to receive Standard of Care (SoC) with or without the radioligand 177Lu-PSMA-617. In this study, the combination for Androgen Receptor Directed Therapy + Androgen Deprivation Therapy are allowed as SoC.
After patients randomized to the SoC alone (i.e., control) arm experience radiographic progression (the rPFS event) as confirmed by BIRC, they will be allowed to cross-over to receive 177Lu-PSMA-617 +/- SoC per the discretion of the treating physician. If cross-over to 177Lu-PSMA-617 is selected, then 177Lu-PSMA-617 will be administered with the same dose/schedule as participants who were initially randomized to receive 177Lu-PSMA-617.

Intervention

Intervention with 177Lu-PSMA-11 + standard of care versus standard of care alone. Crossover form standard of care alone to combination 177Lu-PSMA-11 + standard of care is possible

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 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

Public
Novartis

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Amsterdam 1101 BX
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients must have an ECOG performance status of 0 to 2
Patients must have a life expectancy >9 months as determined by the study

investigator
Patients must have metastatic prostate cancer with histologically or cytologically confirmed adenocarcinoma (current or prior biopsy of the prostate and/or metastatic site)
Patients must have evidence of PSMA-positive disease as seen on a 68Ga-PSMA-11 PET/CT scan, and eligible as determined by the sponsor's central reader
Patients must have at least one metastatic bone and/or soft tissue/visceral lesion documented in the following manners within 28 days prior randomization:
a. Metastatic disease to the bone (in any distribution) visible on 99Tc-MDP bone scintigraphy on either pre-ADT scans or baseline scans. OR
b. Lymph node metastases of any size or distribution. If lymph nodes are the only site of metastasis, then at least one must be at least 1.5 cm in short axis AND outside of the pelvis. OR
c. Visceral metastases of any size or distribution. If a participant has a history of visceral metastases at any time prior to randomization, he should be coded as having visceral metastases at baseline
Patients must have adequate organ function
Human immunodeficiency virus (HIV)-infected patients who are healthy and have a low risk of acquired immune deficiency syndrome (AIDS)-related outcomes can participate in this trial
other protocol-defined inclusion criteria may apply

Exclusion criteria

Patients with rapidly progressing tumor that requires urgent exposure to taxane-based chemotherapy
Any prior systemic anti-prostate cancer therapy, including chemotherapy, PARP inhibitors, immunotherapy or biological therapy (including monoclonal antibodies).
Concurrent cytotoxicity chemotherapy, immunotherapy, radioligand therapy, PARP inhibitors, biologicals or investigational therapy
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 is not allowed
Ongoing participation in any other clinical trial
Use of other investigational drugs within 30 days prior to day of randomization
Known hypersensitivity to any of the study treatments or its excipients or to drugs of similar chemical classes
Transfusion for the sole purpose of making a participant eligible for study inclusion
Patients with CNS metastases that are neurologically unstable, symptomatic, or receiving corticosteroids for the purpose of maintaining neurologic integrity.
Patients with epidural disease, canal disease and prior cord involvement are allowed if those areas have been treated, are

stable, and not neurologically impaired.
Diagnosed with other malignancies that are expected to alter life expectancy or may interfere with disease assessment. However, patients with a prior history of malignancy that has been adequately treated and who have been disease free for more than 3 years before randomization are eligible, as are patients with adequately treated non-melanoma skin cancer, superficial bladder cancer.

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):	25-11-2021
Enrollment:	39
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

Ethics review

Approved WMO Date:	29-03-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-04-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-04-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-06-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-06-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-12-2021
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:	30-04-2022
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:	23-05-2022
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:	10-06-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-07-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-10-2022
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:	16-02-2023

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-03-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-06-2023
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)
Approved WMO Date:	30-10-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-05-2024
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	CTIS2023-507970-42-00
EudraCT	EUCTR2020-003968-56-NL
ClinicalTrials.gov	NCT04720157
CCMO	NL75960.091.21