Study of 225Ac-PSMA-617 in Men With PSMA-positive Prostate Cancer

Last Update: Mar 21, 2025
AcTION: A Phase I Study of [225Ac]Ac-PSMA-617 in Men With PSMA-positive Prostate Cancer With or Without Prior [177Lu]Lu-PSMA-617 Radioligand Therapy
ClinicalTrials.gov Identifier:
NCT04597411
Novartis Reference Number:PSMA-617-100
See if you Pre-qualify
All compounds are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation.

Study Description

This is a Phase 1, open-label, international, dose escalation study to evaluate the safety of \[225Ac\]Ac-PSMA-617 (225Ac-PSMA-617) in men with PSMA-positive prostate cancer who have and have not had prior exposure to \[177Lu\]Lu-PSMA-617 (177Lu-PSMA-617) or \[177Lu\]Lu-PSMA I\&T (177Lu-PSMA I\&T). Total duration of study participation of each participant is approximately 18-24 months (12 months from enrollment to end of each treatment (EOT) plus 12 months of long-term follow up (LTFU). The total duration of the study, from first patient in (FPI) to last LTFU will be approximately 48 months.

A minimum of 3 patients will be treated in each patient group at each dose level and evaluated for the occurrence of dose-limiting toxicity (DLT) during the first 6 weeks of treatment before consideration will be given to enrolling patients into the next dose level. Dose modifications for toxicity are allowed and defined per protocol.

No more than 6 cycles of 225Ac-PSMA-617 will be administered. Patients may receive less than 6 cycles if they have disease progression, intolerable toxicity, started other anticancer therapy, or have withdrawn from treatment per participant or physician decision.

Participants may also receive supportive care therapy, as determined by the study physician, however, participants cannot receive concurrent investigational agents, cytotoxic chemotherapy, biological agents, targeted therapy, immunotherapy, other systemic radioisotopes, and hemi-body radiotherapy until completion of treatment with 225Ac-PSMA-617.

Condition
Prostatic Neoplasms, Castration-Resistant
Phase
Phase1
Overall Status
Recruiting
Number of Participants
99

Start Date
Apr 01, 2021
Completion Date
Jan 01, 2027
Gender
Male
Age(s)
18 Years - (Adult, Older Adult)

Interventions

Radiation

225^Ac-PSMA-617

administered intravenously under the dose escalation schedule
Radiation

68^Ga-PSMA-11

administered intravenously at a dose of 111 - 185 MBq (3 - 5 mCi)

Eligibility Criteria

Inclusion Criteria:

* Patients must have the ability to understand and sign an approved ICF.
* Patients must have the ability to understand and comply with all protocol requirements.
* Patients must be \>=18 years of age.
* Patients must have an ECOG performance status of 0 to 2.
* Patients must have had histological, pathological, and/or cytological confirmation of prostate cancer.
* Patients must have a positive 68Ga-PSMA-11 PET/CT scan performed within 28 days of study entry. If a patient also has soft tissue or visceral disease, it must be PSMA-positive on 68Ga-PSMA-11 PET/CT scan.
* Patients may not participate in the study if their baseline scan shows PSMA-negative disease (defined as disease that expresses PSMA at a level equal to or less than liver by visual assessment) in any of the following regions:

A) One or more PSMA negative lymph nodes \>2.5 cm on short axis B) Bone metastasis with PSMA-negative soft tissues component \> 1 cm in short axis

* Note that PSMA-negative osseous metastases without a soft tissue component \>1 cm does not exclude the subject C) PSMA-negative solid organ metastases (i.e. lung, liver, adrenal glands, etc) that are PSMA-negative and ≥ 1cm in short axis
* Patients must have recovered or stabilized to =\< Grade 2 or baseline from all clinically significant toxicities related to prior prostate cancer therapy.
* Determination of disease progression on treatment prior to enrollment. Progressive disease for study entry is defined as any one or more of the following:

1. PSA progression: minimum of two rising PSA values from a baseline measurement with an interval of \>= 1 week between each measurement. 2.0 ng/mL is the minimal starting value if PSA rise is only indication of

progression.
2. Soft tissue or visceral disease progression as per RECIST 1.1 criteria: increase \>= 20% in the sum of the diameter (SOD) (short axis for nodal lesions and long axis for non-nodal lesions) of all target lesions based on the smallest SOD since treatment started or the appearance of one or more new lesions.
3. Bone progression: \>= 2 new lesions on bone scan.
* Patients must have adequate organ function (bone morrow reserve, hepatic function and renal function).
* Known HIV-positive patients who are healthy and have a low risk of AIDS-related outcomes are eligible. HIV testing is required.
* For patients who have partners of childbearing potential, patient must use a method of birth control with adequate barrier protection, deemed acceptable by the principal investigator during the study and for 6 months after last study drug administration.
* Group A Subjects: Patients must have prior orchiectomy and/or ongoing androgen-deprivation therapy, a castrate level of serum testosterone (\< 50 ng/dL or \< 1.7 nmol/L) and must have received prior cytotoxic chemotherapy and a novel androgen axis drug (e.g., abiraterone or enzalutamide). Patients must also be naïve to prior 177Lu-PSMA radioligand therapy (177Lu-PSMA-617 or 177Lu-PSMA I\&T)
* Group B Subjects (South-Africa only): Patients must have ongoing androgen deprivation therapy (ADT) and either prior orchiectomy or be medically castrate using LHRH agonists/antagonists in order to achieve adequate suppression of serum testosterone (\< 50 ng/dL) but must not have received prior cytotoxic chemotherapy or novel androgen axis drugs (e.g., abiraterone or enzalutamide). These patients are naïve to 177Lu-PSMA radioligand therapy (177Lu-PSMA-617 or 177Lu-PSMA I\&T).
* Group C Subjects: Patients must have ongoing androgen deprivation therapy (ADT) and either prior orchiectomy or be medically castrate using LHRH agonists/antagonists in order to achieve adequate suppression of serum testosterone (\< 50 ng/dL). Patients must have been treated with prior 177Lu-PSMA radioligand therapy (177Lu-PSMA-617 or 177Lu-PSMA I\&T) for at least one cycle administered greater than 6 weeks from study enrollment, and been evaluated for biochemical and radiological response to therapy. Prior exposure to ARPI and/or chemotherapy is not required.

Exclusion Criteria:

* Previous treatment with Strontium-89, Samarium-153, Rhenium-186, Rhenium-188, Radium-223 or hemi-body irradiation.
* Any investigational agents within 28 days of study enrollment.
* Known hypersensitivity to the components of the study therapy or its analogues.
* Other concurrent cytotoxic chemotherapy, targeted therapy, biologic agents, immunotherapy, radioligand therapy, or investigational therapy.
* Transfusion for the sole purpose of eligibility into the study.
* Patients with a history of CNS metastases must have received therapy (surgery, radiotherapy, gamma knife) and be neurologically stable, asymptomatic, and not receiving corticosteroids for the purposes of maintaining neurologic integrity. Patients 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.
* Concurrent serious (as determined by the Principal Investigator) medical conditions, including, but not limited to, uncontrolled infection, active hepatitis B or C, or other significant co-morbid conditions that in the opinion of the investigator would impair study participation or cooperation.
* Diagnosed with other malignancies that are expected to alter life expectancy or may interfere with disease assessment. Patients with a prior history of malignancy who have been disease free for more than 3 years are eligible.
* Participants with an active documented COVID-19 infection (any grade of disease severity) at the time of informed consent may be included only when completely recovered (in accordance with local guidance).

Australia

St. Vincent's Hospital Research Office-Translational Research Center

Recruiting

Darlinghurst,Australia

Louise Emmett, Prof

South Africa

Steve Biko Hospital-Department of Nuclear Medicine

Recruiting

Pretoria,South Africa

Mike M Sathekge, Prof

Worldwide Contacts

If the location of your choosing does not feature any contact detail, please reach out using the information below.

Novartis Pharmaceuticals

Phone: +41613241111
Email: novartis.email@novartis.com

Novartis Pharmaceuticals

Phone: 1-888-669-6682
Email: novartis.email@novartis.com

Source URL: *https://prod1.novartis.com/clinicaltrials/study/nct04597411*

List of links present in page

1. https://clinicaltrials.gov/ct2/show/NCT04597411
2. #trial-eligibility
3. tel:+41613241111
4. mailto:novartis.email@novartis.com
5. tel:1-888-669-6682
6. mailto:novartis.email@novartis.com