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Recruiting ⓘ

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

ClinicalTrials.gov ID ⓘ NCT04597411

Sponsor ⓘ Endocyte

Information provided by ⓘ Endocyte (Responsible Party)

Last Update Posted ⓘ 2025-03-21

Study Details Tab

Study Overview

Brief Summary

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).

Detailed Description

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less than 6 cycles if they have disease progression, intolerable toxicity, started other anticancer therapy, or have withdrawn from treatment per participant or physician decision.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.

Official Title

Study Start (Actual) ⓘ

2021-04-01

Primary Completion (Estimated) ⓘ

2027-01-01

Study Completion (Estimated) ⓘ

2027-01-01

Enrollment (Estimated) ⓘ

99

Study Type ⓘ

Interventional

Phase ⓘ

Phase 1



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

Conditions ⓘ

Prostatic Neoplasms, Castration-Resistant

Intervention / Treatment ⓘ

- Radiation: 225Ac-PSMA-617
- Radiation: 68Ga-PSMA-11

Other Study ID Numbers ⓘ

- PSMA-617-100
- CAAA817A12101 (Other Identifier) (OTHER: Novartis)

Resource links provided by the National Library of Medicine  **NLM**

[MedlinePlus Genetics](https://medlineplus.gov/genetics/) (https://medlineplus.gov/genetics/) related topics: [Prostate cancer](https://medlineplus.gov/genetics/condition/prostate-cancer) (https://medlineplus.gov/genetics/condition/prostate-cancer)

[MedlinePlus](https://medlineplus.gov/) (https://medlineplus.gov/) related topics: [Prostate Cancer](https://medlineplus.gov/prostatecancer.html) (https://medlineplus.gov/prostatecancer.html) [Prostate Diseases](https://medlineplus.gov/prostatediseases.html) (https://medlineplus.gov/prostatediseases.html) [Cancer](https://medlineplus.gov/cancer.html) (https://medlineplus.gov/cancer.html) [Cancer Immunotherapy](https://medlineplus.gov/cancerimmunotherapy.html) (https://medlineplus.gov/cancerimmunotherapy.html) [Cancer in Children](https://medlineplus.gov/cancerinchildren.html) (https://medlineplus.gov/cancerinchildren.html) [Tumors and Pregnancy](https://medlineplus.gov/tumorsandpregnancy.html) (https://medlineplus.gov/tumorsandpregnancy.html)

[Drug Information](https://dailymed.nlm.nih.gov/dailymed/) (https://dailymed.nlm.nih.gov/dailymed/) available for: [Gallium Ga-68 gozetotide](https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Gallium+Ga-68+gozetotide) (https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Gallium+Ga-68+gozetotide)

[FDA Drug and Device Resources](https://www.clinicaltrials.gov/fda-links) (https://www.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://www.clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations) (<https://www.clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations>).

Study Contact ⓘ

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

Study Contact Backup

Name: Novartis Pharmaceuticals
Phone Number: +41613241111
Email: novartis.email@novartis.com

This study has 2 locations

Australia

 **Darlinghurst, Australia**
Recruiting
St. Vincent's Hospital Research Office-Translational Research Center
Principal Investigator : Louise Emmett, Prof

South Africa

 **Pretoria, South Africa**
Recruiting
Steve Biko Hospital-Department of Nuclear Medicine
Principal Investigator : Mike M Sathekge, Prof

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://www.clinicaltrials.gov/study-basics/learn-about-studies) (<https://www.clinicaltrials.gov/study-basics/learn-about-studies>).

Eligibility Criteria

Description

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 marrow 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

Ages Eligible for Study

18 Years and older (Adult, Older Adult)

Sexes Eligible for Study

Male

Accepts Healthy Volunteers

No

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).

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** ⓘ : Non-Randomized**Interventional Model** ⓘ : Parallel Assignment**Interventional Model Description:**

Study-eligible participants with PSMA-positive, metastatic, castration resistant (mCRPC) prostate cancer will be assigned to one of three groups, A, B, and C based on their prior prostate cancer treatment history:

1. Group A: Men that have received prior cytotoxic chemotherapy and an ARPI, who Have Not been previously treated with prior 177Lu-PSMA-617 radioligand therapy or 177Lu-PSMA I&T.
2. Group B: Men that Have Not received cytotoxic chemotherapies, ARPIs, and 177Lu-PSMA radioligand therapy or 177Lu-PSMA I&T. Due to geographical differences in disease presentation/aggressiveness and access to treatment of mCRPC, group B participants will be enrolled only in South Africa, after medical review determines the need for therapy as part of a clinical study.
3. Group C: Men who HAVE been previously treated with 177Lu-PSMA-617 radioligand therapy or 177Lu-PSMA I&T. Prior chemotherapy or ARPI is not required.

Masking ⓘ : None (Open Label)

Arms and Interventions

Participant Group/Arm 	Intervention/Treatment 
Experimental: Group A (mCRPC who have received prior ARPI and chemotherapy, but are PSMA RLT naïve) Men that have received prior cytotoxic chemotherapy and ARPI (e.g., abiraterone or enzalutamide), who HAVE NOT been previously treated with 177Lu-PSMA-617 radioligand therapy or 177Lu-PSMA I&T will receive a dose of 225Ac-PSMA-617 via intravenous injection every 8 weeks (+/- 1 week) for a maximum of 6 cycles.	Radiation: 225Ac-PSMA-617 - administered intravenously under the dose escalation schedule Radiation: 68Ga-PSMA-11 - administered intravenously at a dose of 111 - 185 MBq (3 - 5 mCi)
Experimental: Group B (mCRPC who have not had prior ARPI or chemotherapy, and are PSMA RLT naïve) Men previously treated with luteinizing hormone-releasing hormone (LHRH) agonists or orchiectomy and primary anti-androgen therapy that have not received prior cytotoxic chemotherapy or novel androgen axis drugs (e.g., abiraterone or enzalutamide) will receive a dose of 225Ac-PSMA-617 via intravenous injection every 8 weeks (+/- 1 week) for a maximum of 6 cycles.	Radiation: 225Ac-PSMA-617 - administered intravenously under the dose escalation schedule Radiation: 68Ga-PSMA-11 - administered intravenously at a dose of 111 - 185 MBq (3 - 5 mCi)
Experimental: Group C (mCRPC who have received prior PSMA RLT) Men with progressive metastatic castration resistant prostate cancer (mCRPC) who HAVE been previously treated with 177Lu-PSMA-617 radioligand therapy or 177Lu-PSMA I&T will receive a dose of 225Ac-PSMA-617 via intravenous injection every 8 weeks (+/- 1 week) for a maximum of 6 cycles. Prior chemotherapy and/or novel androgen axis drugs not required.	Radiation: 225Ac-PSMA-617 - administered intravenously under the dose escalation schedule Radiation: 68Ga-PSMA-11 - administered intravenously at a dose of 111 - 185 MBq (3 - 5 mCi)

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
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Recommended Phase 2 Dose (RP2D)	The RP2D for each group (Group A, B and C) is defined as the dose level that is well tolerated (i.e., at or below the MTD) and for which there may be additional findings (e.g., longer term tolerability) effecting the RP2D decision. In the case where an MTD is not identified, even at the highest dose level tested, the RP2D may be determined on the basis of data indicating adequate tolerability and therapeutic effectiveness.	6 weeks post Cycle 1 Day 1 (C1D1) of each dosing cohort through enrollment completion, an average of 1.5 years to determine RP2D
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Secondary Outcome Measures ⓘ

Outcome Measure	Measure Description	Time Frame
Percentage of Participants with treatment emergent adverse events	Safety measured by the percentage of participants with treatment emergent adverse events (events started after the first dose of study medication or events present prior to start of treatment but increased in severity based on preferred term).	Day 1/Infusion Day up to 60 days post infusion
Overall Response Rate (ORR)	Overall Response Rate (ORR) is defined as the proportion of participants with best overall response of Complete Response (CR) or Partial Response (PR) as measured by RECIST v1.1.	Every 8 weeks after first dose of 225Ac-PSMA-617 for the first 24 weeks, then every 12 weeks through the end of treatment visit, on average 2.5 years
Duration of Response (DOR)	Duration of Response (DOR) is the time from the date of the first documented response (CR or PR) to the date of the first radiologically documented disease progression or death due to disease according to RECIST v1.1.	Every 8 weeks after first dose of 225Ac-PSMA-617 for the first 24 weeks, then every 12 weeks through the end of treatment visit, on average 2.5 years
Disease Control Rate (DCR)	Disease Control Rate (DCR) is the percentage of participants with a best overall response of Complete Response (CR), Partial Response (PR) or Stable Disease (SD) according to RECIST v1.1.	Every 8 weeks after first dose of 225Ac-PSMA-617 for the first 24 weeks, then every 12 weeks through the end of treatment visit, on average 2.5 years

Progression Free Survival (PFS)	Progression Free Survival (PFS) is defined as the time from Cycle 1 Day 1 (C1D1) to the first of radiographic, clinical, or prostate-specific antigen [PSA] progression-free survival, or censorship with events defined as follows: 1. Radiographic disease progression as determined from bone scans and contrast CT/MRI as outlined in Prostate Cancer Working Group 3 (PCWG3) and RECIST 1.1 2. Unequivocal clinical progression 3. PSA progression, defined as the date that a $\geq 25\%$ increase in PSA and an absolute increase of 2 ng/mL or more from the nadir is documented and confirmed by a second consecutive value obtained 3 or more weeks later. Rises in PSA within the first 12 weeks will be ignored. Where no decline from baseline is documented, baseline PSA is the nadir. The date of progression is date of first occurrence, not date of confirmation (PCWG3 Guidance).	Every 8 weeks after first dose of 225Ac-PSMA-617 for the first 24 weeks, then every 12 weeks through the end of treatment visit, on average 2.5 years
Percentage of Participants with Biochemical Response as measured by Prostate Specific Antigen (PSA)	Prostate-specific antigen is a glycoprotein considered as a biomarker for the response to therapy in men with prostate cancer. A 50 percent (%) decline in PSA from Baseline to the PSA level at End of Study was considered as a PSA response.	Baseline, Days 1, 15, 29 and 43 of each Cycle (1 cycle = 8 weeks +/- 1 week), End of Treatment and every 3 months during the 12-month follow-up period
Notable Changes in Alkaline phosphatase (ALP) levels	Safety measured by the notable post-baseline changes in Alkaline phosphatase (ALP) levels compared to baseline.	Baseline, Cycle 1 and Cycle 2 (Weekly), Cycle 3 to Cycle 6 (Bi-weekly) (1 cycle = 8 weeks +/- 1 week)
Notable Changes in Lactate dehydrogenase (LDH) levels	Safety measured by the notable post-baseline changes in Lactate dehydrogenase (LDH) levels compared to baseline.	Baseline, Cycle 1 and Cycle 2 (Weekly), Cycle 3 to Cycle 6 (Bi-weekly) (1 cycle = 8 weeks +/- 1 week)
Change from Baseline in European Quality of Life (EuroQoL) - 5 Domain 5 Level scale (EQ-5D-5L)	EQ-5D-5L is a standardized participant completed questionnaire that measures health-related quality of life and translates that score into an index value or utility score. EQ-5D-5L consists of two components: a health state profile and an optional visual analogue scale (VAS). EQ-5D health state profile is comprised of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: 1= no problems, 2= slight problems, 3= moderate problems, 4= severe problems, and 5= extreme problems. Higher scores indicated greater levels of problems across each of the five dimensions.	Baseline, Day 1 of each Cycle (1 cycle = 8 weeks +/- week), End of Treatment, on average 2.5 years
Change from Baseline in Functional Assessment of Cancer Therapy - Prostate (FACT-P) Questionnaire	FACT-P assesses symptoms/problems related to prostate carcinoma and its treatment. It is a combination of the FACT- General + the Prostate Cancer Subscale (PCS). The FACT-General (FACT-G) is a 27 item Quality of Life (QoL) measure that provides a total score as well as subscale scores: Physical (0-28), Functional (0-28), Social (0-28), and Emotional Well-being (0-24). The total score range is between 1-108, higher scores indicates better for total score and subscale scores. PCS is a 12-item prostate cancer subscale that asks about symptoms and problems specific to prostate cancer (Range 0-48, higher scores better). The FACT-P total score is the sum of all 5 subscale scores of the FACT-P questionnaire and ranges from 0-156. Higher scores indicate higher degree of functioning and better quality of life.	Baseline, Day 1 of each Cycle (1 cycle = 8 weeks +/- week), End of Treatment, on average 2.5 years

Change from Baseline in Brief Pain Inventory - Short Form (BPI-SF) Questionnaire: Pain Severity Score	The BPI-SF is a publicly available instrument to assess the pain and includes severity and interference scores. BPI-SF is an 11-item self-report questionnaire that is designed to assess the severity and impact of pain on daily functions of a participant. Pain severity score is a mean value for BPI-SF questions 3, 4, 5 and 6 (questions inquiring about the extent of pain, where the extent is ranked from 0 [no pain] to 10 [pain as bad as you can imagine]). Pain severity progression is defined as an increase in score of 30% or greater from baseline without decrease in analgesic use.	Baseline, Day 1 of each Cycle (1 cycle = 8 weeks +/- week), End of Treatment, on average 2.5 years
Change from Baseline in Brief Pain Inventory - Short Form (BPI-SF) Questionnaire: Pain Interference Score	The BPI-SF is a publicly available instrument to assess the pain and includes severity and interference scores. BPI-SF is an 11-item self-report questionnaire that is designed to assess the severity and impact of pain on daily functions of a participant. Pain interference score is mean value for the 7 BPI-SF questions (questions inquiring about the extent of interference with activities by pain) where the extent is ranked from 0 (does not interfere) to 10 (completely interferes). Pain interference progression is defined as an increase in score of 50% or greater from baseline without decrease in analgesic use.	Baseline, Day 1 of each Cycle (1 cycle = 8 weeks +/- week), End of Treatment, on average 2.5 years
Change from Baseline in Xerostomia-Related Quality of Life Scale (XeQOLS)	The XeQOLS is a validated patient reported 15-item assessment scale with 4 domains: physical functioning, pain/discomfort, personal/psychologic functioning, and social functioning. The score is the average of all responses of all domains and can range from 0 to 4, with higher scores indicating increased xerostomia burden. A negative change from Baseline indicates an improvement of the xerostomia burden.	Baseline, Day 1 of each Cycle (1 cycle = 8 weeks +/- 1 week), End of Treatment and every 3 months during the 12-month follow-up period

Collaborators and Investigators

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

Sponsor ⓘ

Endocyte

Investigators ⓘ

- Study Director: Novartis Pharmaceuticals, Novartis Pharmaceuticals

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 ⓘ

2020-09-29

First Submitted that Met QC Criteria ⓘ

2020-10-16

First Posted ⓘ

2020-10-22

Study Record Updates

Last Update Submitted that met QC Criteria ⓘ

2025-03-20

Last Update Posted ⓘ

2025-03-21

Last Verified ⓘ

2025-03

More Information**Terms related to this study****Keywords Provided by Endocyte**

Androgen-Resistant Prostatic Neoplasms
 Castration-Resistant Prostatic Cancer
 Castration-Resistant Prostatic Neoplasms
 Prostatic Cancer, Castration-Resistant
 Prostatic Neoplasms
 Genital Neoplasms, Male
 Urogenital Neoplasms
 Neoplasms by Site
 Neoplasms
 Genital Diseases, Male
 Prostatic Diseases
 [225Ac]Ac-PSMA-617
 225Ac-PSMA-617
 [68Ga]Ga-PSMA-11
 68Ga-PSMA-11
 [177Lu]Lu-PSMA-617
 177Lu-PSMA-617
 [177Lu]Lu-PSMA I&T
 177Lu-PSMA I&T

Additional Relevant MeSH Terms

Genital Diseases
 Urogenital Diseases
 Male Urogenital Diseases
 Female Urogenital Diseases
 Female Urogenital Diseases and Pregnancy Complications
 Prostatic Neoplasms, Castration-Resistant
 Prostatic Neoplasms
 Genital Neoplasms, Male
 Urogenital Neoplasms
 Neoplasms by Site
 Neoplasms
 Genital Diseases, Male
 Prostatic Diseases
 (225)Ac-PSMA-617
 gallium 68 PSMA-11

Plan for Individual Participant Data (IPD)**Plan to Share Individual Participant Data (IPD)?**

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