



Record 1 of 1



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Recruiting ⓘ

Study Comparing AAA817+ARPI Versus Standard of Care in Adult Participants With PSMA-positive mCRPC (AcTFirst)

ClinicalTrials.gov ID ⓘ NCT06855277

Sponsor ⓘ Novartis Pharmaceuticals

Information provided by ⓘ Novartis (Novartis Pharmaceuticals) (Responsible Party)

Last Update Posted ⓘ 2025-11-12

Study Details Tab

Study Overview

Brief Summary

The purpose of this study is to determine whether [225Ac]Ac-PSMA-617 (AAA817), given for up to 6 cycles at a dose of 10 Megabecquerel (MBq) +/- 10%, plus androgen receptor pathway inhibitor (ARPI), improves the radiographic progression free survival (rPFS) compared to investigator's choice of standard of care (SOC) (ARPI change or taxane-based chemotherapy) in adult participants with PSMA-positive metastatic castration resistant prostate cancer (mCRPC) treated with another ARPI as last treatment and who have not been exposed to a taxane-containing chemotherapy in the mCRPC setting nor have received any prior PSMA-targeting radioligand therapy.

Detailed Description

This is a phase III, open label, multicenter randomized study. The study aims at evaluating the superiority of 225Ac-PSMA-617 combined with androgen receptor pathway inhibitor (ARPI) over a change of ARPI or chemotherapy in prolonging progression free survival (rPFS).

Screening period: At screening, the participants will be assessed for eligibility and will undergo a positron emission tomography (PET)/computed tomography (CT) scan to evaluate PSMA positivity. Only participants with PSMA positive cancer and confirmed eligibility criteria will be randomized.

Participants randomized to the investigational arms will receive up to 6 doses of AAA817 10 Mbq +/- 10% given intravenously with or without an ARPI (oral enzalutamide or oral abiraterone) per investigator's choice. Treatment with ARPI should continue as per protocol end of treatment criteria.

Study Start (Actual) ⓘ

2025-07-01

Primary Completion (Estimated) ⓘ

2028-02-29

Study Completion (Estimated) ⓘ

2032-11-04

Enrollment (Estimated) ⓘ

605

Study Type ⓘ

Interventional

Phase ⓘ

Phase 3

Patent Owner Exhibit 2084
IPR2025-01582



Participants randomized to SoC will be treated with an ARPI change (oral enzalutamide or oral abiraterone) or taxane-based chemotherapy (docetaxel or cabazitaxel) per investigator's choice. Treatment with ARPI should continue as per protocol end of treatment criteria. Treatment duration with taxane-based chemotherapy will depend on the chosen regimen per the investigator's discretion following local guidelines as per standard of care and product labels and adhere to the protocol end of treatment criteria.

Supportive care will be allowed in both arms at the discretion of the investigator and includes available care for the eligible participant according to best institutional practice for mCRPC treatment, including androgen deprivation therapy (ADT).

Safety will be assessed routinely during the study. Crossover is not allowed among study arms.

The study will be conducted in the USA among other countries globally.

Official Title
A Phase III, Open-label, Multi-center, Randomized Study Comparing AAA817+ARPI Versus Standard of Care in Adult Participants With PSMA-positive Metastatic Castration Resistant Prostate Cancer

Conditions
Prostate Cancer

Intervention / Treatment

- Drug: AAA817
- Drug: ARPI
- Drug: Standard of Care

Other Study ID Numbers

- CAAA817B12301
- 2024-512340-32-00 (Registry Identifier) (REGISTRY: EU CTIS)

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

[MedlinePlus Genetics](https://medlineplus.gov/genetics/) (https://medlineplus.gov/genetics/), related topics: [Spinal and bulbar muscular atrophy](https://medlineplus.gov/genetics/condition/spinal-and-bulbar-muscular-atrophy) (https://medlineplus.gov/genetics/condition/spinal-and-bulbar-muscular-atrophy).

[MedlinePlus](https://medlineplus.gov/) (https://medlineplus.gov/), related topics: [Prostate Cancer](https://medlineplus.gov/prostatecancer.html) (https://medlineplus.gov/prostatecancer.html).

[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
Name: Novartis Pharmaceuticals
Phone Number: 1-888-669-6682
Email: novartis.email@novartis.com

Study Contact Backup
Name: Novartis Pharmaceuticals
Phone Number: +41613241111

This study has 29 locations

United States

Kansas Locations

 **Kansas City, Kansas, United States, 66160**
Recruiting
University of Kansas Hospital
Contact : Gloria Rodriguez
grodriguez3@kumc.edu
Principal Investigator : Xinglei Shen

South Carolina Locations

 **Myrtle Beach, South Carolina, United States, 29572**
Recruiting
Carolina Urologic Research Center
Contact : Kate Valipour
843-839-1679 kate.valipour@startresearch.com
Principal Investigator : Neal D Shore

Australia

New South Wales Locations

 **Darlinghurst, New South Wales, Australia, 2010**
Recruiting
Novartis Investigative Site

South Australia Locations

 **Adelaide, South Australia, Australia, 5000**
Recruiting
Novartis Investigative Site

China

 **Beijing, China, 100036**
Recruiting
Novartis Investigative Site

 **Guangzhou, China, 510060**
Recruiting
Novartis Investigative Site

 **Shanghai, China, 200025**
Recruiting
Novartis Investigative Site

 **Shanghai, China, 200032**
Recruiting
Novartis Investigative Site

 **Shanghai, China, 200127**
Recruiting
Novartis Investigative Site

Guangdong Locations

 **Guangzhou, Guangdong, China, 510632**
Recruiting
Novartis Investigative Site

Hubei Locations

 **Wuhan, Hubei, China, 430022**
Recruiting
Novartis Investigative Site

 **Wuhan, Hubei, China, 430030**
Recruiting
Novartis Investigative Site

Jiangsu Locations

 **Nanjing, Jiangsu, China, 210006**
Recruiting
Novartis Investigative Site

 **Nanjing, Jiangsu, China, 210029**
Recruiting
Novartis Investigative Site

Liaoning Locations

-  Shenyang, Liaoning, China, 110011
Recruiting
Novartis Investigative Site

Sichuan Locations

-  Chengdu, Sichuan, China, 610041
Recruiting
Novartis Investigative Site

Hong Kong

-  Pokfulam, Hong Kong, 999077
Recruiting
Novartis Investigative Site

Japan

-  Chiba, Japan, 260-8717
Recruiting
Novartis Investigative Site
-  Fukuoka, Japan, 811-0213
Recruiting
Novartis Investigative Site
-  Kyoto, Japan, 606 8507
Recruiting
Novartis Investigative Site

Hokkaido Locations

-  Sapporo, Hokkaido, Japan, 060 8648
Recruiting
Novartis Investigative Site

Hyōgo Locations

-  Kobe, Hyōgo, Japan, 650-0047
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Novartis Investigative Site

Kanagawa Locations

-  Yokohama, Kanagawa, Japan, 236-0004
Recruiting
Novartis Investigative Site

Singapore

-  Singapore, Singapore, 119074
Recruiting
Novartis Investigative Site
-  Singapore, Singapore, 168583
Recruiting
Novartis Investigative Site
-  Singapore, Singapore, 169608
Recruiting
Novartis Investigative Site

Taiwan

-  Kaohsiung City, Taiwan, 83301
Recruiting
Novartis Investigative Site
-  Taoyuan District, Taiwan, 33305
Recruiting
Novartis Investigative Site

United Kingdom

Surrey Locations

-  Sutton, Surrey, United Kingdom, SM2 5PT
Recruiting
Novartis Investigative Site

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

Key Inclusion Criteria:

- Signed informed consent must be obtained prior to participation in the study.
- Participants must be adults ≥ 18 years of age.
- Participants must have an ECOG performance status of 0 to 2.
- Participants must have histological, and/or cytological confirmation of adenocarcinoma of the prostate. Participants with mixed histology (neuroendocrine) are not eligible.
- Participants who have received taxane-based chemotherapy in mHSPC setting are eligible if they are deemed appropriate for chemotherapy or ARPI change as the next line of therapy in the opinion of the Investigator. Note: Participants who have received taxane-based chemotherapy for mCRPC are excluded.
- Participants must not have received taxane-based chemotherapy in mCRPC setting (allowed in mHSPC setting).
- Participants must have PSMA-PET positive disease using a PSMA imaging agent that is approved as per protocol.
- Participant must have been diagnosed with mCRPC with documented progressive disease while on treatment with ARPI in mHSPC or earlier setting as their last treatment (and did not progress on more than one ARPI).

Key Exclusion Criteria:

- Previous treatment with any approved or investigational RLT, approved or investigational radioisotopes
- Previous treatment with any conventional external beam radiotherapy including hemi-body radiation within 6 weeks of randomization (within 2 weeks for radiotherapy of localized metastases).
- Participants with known or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer.
- Any approved or investigational agents/systemic anti-cancer therapy (e.g. other chemotherapy, investigational therapy, immunotherapy or biological therapy including monoclonal antibodies) within 28 days (or 5 times the half-life of that therapy whichever is longer) of the anticipated day C1D1.
- Diagnosed with other active malignancies that are expected to alter life expectancy or may interfere with disease assessment.

Other protocol-defined inclusion/exclusion criteria may apply.

Ages Eligible for Study

18 Years to 100 Years (Adult, Older Adult)

Sexes Eligible for Study

Male

Accepts Healthy Volunteers

No

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 ⓘ : Diagnostic

Allocation ⓘ : Randomized

Interventional Model ⓘ : Parallel Assignment

Masking ⓘ : None (Open Label)

Arms and Interventions

Participant Group/Arm 	Intervention/Treatment 
Experimental: Investigational Arm: AAA817+ARPI (enzalutamide or abiraterone) Participants will receive AAA817 infusion directly into a vein with ARPIs.	Drug: AAA817 - AAA817 is being studied for treating PSMA positive mCRPC. Inside the body, it attaches itself to PSMA on the cell surface of the prostate cancer cells and emits radiation to kill them. This treatment is also called a radioligand therapy. - Other Names: [225Ac]Ac-PSMA-617 Drug: ARPI - Androgen receptor pathway inhibitor (ARPI): An ARPI is approved for the treatment of prostate cancer. It works by blocking signals from male hormones, such as testosterone, that helps cancer cells grow. By blocking these signals, an ARPI slows down or stops the growth of prostate cancer cells. In this trial, participants will be given either enzalutamide or abiraterone. - Other Names: - Enzalutamide or Abiraterone
Experimental: Investigational Arm: AAA817 Participants will receive AAA817 infusion directly into a vein.	Drug: AAA817 - AAA817 is being studied for treating PSMA positive mCRPC. Inside the body, it attaches itself to PSMA on the cell surface of the prostate cancer cells and emits radiation to kill them. This treatment is also called a radioligand therapy. - Other Names: [225Ac]Ac-PSMA-617
Active Comparator: Control arm: Investigator's choice of SoC (ARPI or taxane-based chemotherapy) Participants will receive standard treatment as decided by the trial doctor either as a chemotherapy infusion directly into a vein or ARPI either as capsules or tablets.	Drug: ARPI - Androgen receptor pathway inhibitor (ARPI): An ARPI is approved for the treatment of prostate cancer. It works by blocking signals from male hormones, such as testosterone, that helps cancer cells grow. By blocking these signals, an ARPI slows down or stops the growth of prostate cancer cells. In this trial, participants will be given either enzalutamide or abiraterone. - Other Names: - Enzalutamide or Abiraterone Drug: Standard of Care - Standard treatment includes approved treatment for mCRPC. In this trial, the trial doctor will decide which available treatment participants will receive. The trial doctor will select either an ARPI of enzalutamide or abiraterone, or a taxane based chemotherapy of docetaxel or cabazitaxel. - Other Names: - ARPI enzalutamide - ARPI abiraterone - Taxane based chemotherapy of docetaxel - Taxane based chemotherapy of cabazitaxel

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Radiographic Progression Free Survival (rPFS)	Time to radiographic disease progression or death due to any cause.	From the date of randomization to the date of the first documented radiographic disease progression using conventional imaging, or death due to any cause, whichever occurs first, assessed up to approximately 40.0 months.

Secondary Outcome Measures ⓘ

Outcome Measure	Measure Description	Time Frame
Overall Survival (OS) (Key Secondary Endpoint)	Time to death due to any cause.	From the date of randomization to the date of death due to any cause, assessed up to approximately 40 months.
Radiographic Progression Free Survival by PSMA PET/CT and (rPSF-PET)(Key Secondary)	Time to radiographic disease progression, using PSMA PET/CT and (rPSF-PET), or death due to any cause.	From date of randomization to the date of the first documented radiographic disease progression or death due to any cause, whichever occurs first, assessed up to approximately 40.0 months.
Progression Free Survival (PFS)	Time to first documented progression or death due to any cause.	From date of randomization to the first documented progression by investigator's assessment or death due to any cause, whichever occurs first, assessed up to approximately 40.0 months.
Progression Free Survival (PFS2)	Time to first documented progression on next line of antineoplastic therapy or death from any cause.	From date of randomization until

		date of second progression or date of death from any cause, whichever comes first, assessed up to approximately 40.0 months.
Overall Response Rate (ORR)	The proportion of participants with best overall response (BOR) of confirmed complete response (CR) or partial response (PR) in soft tissue.	From the date of randomization to the date of the first documented radiographic disease progression, or death due to any cause, whichever occurs first, assessed up to approximately 40.0 months.
Disease Control Rate (DCR)	The proportion of participants with BOR of confirmed CR, PR, stable disease (SD) or non-CR/non-progressive disease (PD) in soft tissue.	From the date of randomization to the date of the first documented radiographic disease progression or death due to any cause, whichever occurs first, assessed up to approximately 40.0 months.
Duration of Response (DoR)	Time between the date of first documented response and the date of first documented radiographic progression or death due to any cause.	From the date of first documented response (CR or PR) for confirmed responders and the date of first documented radiographic progression in soft tissue or death due to any cause, whichever occurs first, assessed up to approximately 40.0 months.
Time to first radiographic soft tissue progression (TTSTP)	Time to radiographic soft tissue progression.	From the date of randomization to the date of radiographic soft tissue progression or death due to any cause, whichever occurs

		first, assessed up to approximately 40.0 months.
Time to first symptomatic skeletal event (TTSSE)	Time to date of first new symptomatic skeletal event of death due to any cause.	From the date of randomization to the date of the first documented radiographic disease progression, or death due to any cause, whichever occurs first, assessed up to approximately 40.0 months.
Prostate specific antigen response (PSA50 and PSA90)	The percentage of participants who achieved $\geq 50\%$ and $\geq 90\%$ decrease from baseline, respectively.	From the date of randomization to the date of safety follow up, assessed up to approximately 40.0 months.
Time-concentration profiles and PK parameters of AAA817	Time-concentration profiles and PK parameters of AAA817 (e.g. AUC, Cmax).	From Cycle 1 Day 1 up to approximately cycle 5 days 11 (each cycle is 8 weeks).
Change from baseline on FACT-P Prostate Cancer Subscale (PCS)	Change from baseline on FACT-P Prostate Cancer Subscale (PCS). FACT-P assesses symptoms/problems related to prostate carcinoma and its treatment.	From randomization to the first occurrence of worsening on the score or death due to any cause, whichever occurs first, assessed up to approximately 40.0 months.
Time to worsening on the Worst Pain	Time to worsening on the Worst Pain is defined as the time from randomization to the first occurrence of worsening on the Worst Pain item (BPI-SF) or death due to any cause, whichever occurs first.	From randomization to the first occurrence of worsening from baseline, or death due to any cause, whichever occurs first, assessed up to approximately 40.0 months.
rPFS in participants treated with AAA817	rPFS time to the date of first documented radiographic disease progression or death due to any cause, whichever occurs first.	From the date of randomization to the date of the first documented

		radiographic disease progression, or death due to any cause, whichever occurs first, assessed up to approximately 40.0 months.
OS in participants treated with AAA817	OS is time to death due to any cause.	From the date of randomization to the date of death due to any cause assessed up to approximately 40.0 months.

Collaborators and Investigators

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

Sponsor ⓘ

Novartis Pharmaceuticals

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 ⓘ

2025-02-18

First Submitted that Met QC Criteria ⓘ

2025-02-26

First Posted ⓘ

2025-03-03

Study Record Updates

Last Update Submitted that met QC Criteria ⓘ

2025-11-07

Last Update Posted (Estimated) ⓘ

2025-11-12

Last Verified ⓘ

2025-11

More Information

[HHS Vulnerability Disclosure](#)

Terms related to this study

Keywords Provided by Novartis (Novartis Pharmaceuticals)

Positive Metastatic Castration Resistant Prostate Cancer

PSMA

PSMA-positive

Additional Relevant MeSH Terms

Genital Neoplasms, Male

Urogenital Neoplasms

Neoplasms by Site

AAA817	Neoplasms
[225AC] AC-PSMA-617	Genital Diseases, Male
Radioligand Therapy	Genital Diseases
RLT	Urogenital Diseases
Androgen receptor pathway inhibitor	Prostatic Diseases
ARPI	Male Urogenital Diseases
Taxane	Prostatic Neoplasms
Metastatic castration resistant prostate cancer	Quality Indicators, Health Care
mCRPC	Quality of Health Care
AcTFirst	Health Services Administration
	Health Care Quality, Access, and Evaluation
	(225)Ac-PSMA-617
	enzalutamide
	abiraterone
	Standard of Care

Plan for Individual Participant Data (IPD)

Plan to Share Individual Participant Data (IPD)?

Yes

IPD Plan Description

Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent review panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

This trial data availability is according to the criteria and process described on www.clinicalstudydatarequest.com

IPD Sharing Url

<https://www.clinicalstudydatarequest.com> (<https://www.clinicalstudydatarequest.com>).

Drug and device information, study documents, and helpful links

Studies a U.S. FDA-Regulated Drug Product

Yes

Studies a U.S. FDA-Regulated Device Product

No