



Record 1 of 1



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Not yet recruiting ⓘ

Comparison of 177Lu-PSMA-617 and 225Ac-PSMA-617 (LUTACT)

ClinicalTrials.gov ID ⓘ NCT07054346

Sponsor ⓘ Thomas Hope

Information provided by ⓘ Thomas Hope, University of California, San Francisco (Responsible Party)

Last Update Posted ⓘ 2025-07-08

Study Details Tab

Study Overview

Brief Summary

There is evidence that Actinium-225 Prostate-Specific Membrane Antigen (225Ac-PSMA) has a potentially higher level of efficacy than 177 Lutetium Prostate-Specific Membrane Antigen (177Lu-PSMA) as a radioligand therapy. This single center, pilot study will compare differences in the mechanisms of actinium-225 and lutetium-177 radioligand therapies (RLT) in participants with high or very high risk localized or locoregional prostate cancer planning on undergoing a prostatectomy.

Detailed Description

PRIMARY OBJECTIVES:

- 1. Compare the tumor absorbed dose between 177Lu-PSMA-617 and 225Ac-PSMA-617.
- 2. Compare the immunologic priming of 177Lu-PSMA-617 and 225Ac-PSMA-617 with controls in prostatectomy specimens.

SECONDARY OBJECTIVES:

- 1. Determine the safety and tolerability of neoadjuvant 177Lu-PSMA-617 and 225Ac-PSMA-617 in participants with high or very high-risk prostate cancer planning to undergo radical prostatectomy.
- 2. Estimate PSA response for 177Lu-PSMA-617 and 225Ac-PSMA-617 treatment.
- 3. Estimate the rate of pathologic response in participants treated with 177Lu-PSMA-617 and 225Ac-PSMA-617.

EXPLORATORY OBJECTIVES:

Study Start (Estimated) ⓘ

2025-06-30

Primary Completion (Estimated) ⓘ

2027-04-30

Study Completion (Estimated) ⓘ

2028-04-30

Enrollment (Estimated) ⓘ

45

Study Type ⓘ

Interventional

Phase ⓘ

Phase 1

Patent Owner Exhibit 2082
IPR2025-01582



- 1. Determine the relationship between percent cell necrosis and tumor absorbed dose for both 177Lu-PSMA-617 and 225Ac-PSMA-617.
- 2. Compare the heterogeneity of cell necrosis for 177Lu-PSMA-617 and 225Ac-PSMA-617.
- 3. Compare messenger ribonucleic acid (mRNA) expression profiles of tumor treated with 177Lu-PSMA-617, 225Ac-PSMA-617, and controls.
- 4. Compare mRNA expression profiles of tumors in participants who achieve a PSA50 response and those that do not.
- 5. Compare mRNA expression profiles of tumors from archival tissue and at time of prostatectomy.
- 6. Compare the percent cell necrosis between participants receiving a single cycle of PSMA RLT versus participants receiving two cycles of PSMA RLT.
- 7. Compare the change in uptake on PSMA Positron Emission Tomography (PET) to PSA response and percent cell necrosis.
- 8. Descriptively evaluate cell necrosis at the tumor margins.

OUTLINE:

Participants will be assigned to 1 of 2 cohorts to receive 177Lu-PSMA-617 or 225Ac-PSMA-617. Additional participants undergoing prostatectomy without RLT will be enrolled as a control group. Participants enrolled in the RLT cohorts will receive 1 to 2 cycles of PSMA radioligand therapy up to 6 weeks apart before a scheduled, non-investigational, prostatectomy four weeks after PSMA radioligand therapy. Participants receiving RLT will be followed up for a safety assessment 6 weeks after surgery and for up to 60 months after prostatectomy for long term follow-up. Participants in the prostatectomy only cohort will have safety and long-term follow-up performed as part of clinical care up to 24 months after surgery.

Official Title

Comparison of 177Lu-PSMA-617 and 225Ac-PSMA-617 in a Prostatectomy Model (LUTACT Trial)

Conditions

- Prostate Cancer
- Prostate Cancer (Diagnosis)
- High-risk Prostate Cancer
- Localized Prostate Carcinoma
- Very High Risk Prostate Carcinoma

Intervention / Treatment

- Drug: 177 Lutetium Prostate-Specific Membrane Antigen 617
- Drug: Actinium-225 Prostate-Specific Membrane Antigen 617
- Procedure: Non-investigational, Prostatectomy
- Procedure: Prostate Tissue Collection
- Procedure: Single-photon emission computed tomography (SPECT)/Computerized tomography (CT)
- Procedure: Blood Sample Collection

Other Study ID Numbers

- 25922
- NCI-2025-04497 (Registry Identifier) (REGISTRY: NCI Clinical Trials Reporting Program (CTRP))

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 Surgery](https://medlineplus.gov/) (https://medlineplus.gov/)

[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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This study has 1 location

United States

California Locations

📍 **San Francisco, California, United States, 94143**

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Principal Investigator : Thomas A Hope, MD

Sub-Investigator : Carissa Chu, MD

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:**

1. Histologically confirmed prostate adenocarcinoma.
2. Willing to undergo prostatectomy with or without lymph node dissection, and candidate for prostatectomy as determined by urologic oncology.
3. High-risk disease as defined as meeting 1 or more of the 3 following criteria:
 1. Gleason score of 4+5 disease or higher.
 2. Pelvic nodal metastases on PSMA PET.
 3. Extracapsular extension or seminal vesicle invasion on MRI.
4. No evidence of distant metastatic disease as determined by PSMA PET. Nodal disease below the iliac bifurcation (clinical stage N1) is allowed.
5. Maximum Standardized Uptake Value (SUVmax) in the primary tumor greater than 10 on PSMA PET using Gallium-68 (68Ga)-PSMA-11 or piflufolastat F 18 (18F-DCFPyL).
6. Target tumor in the prostate measuring greater than 2 cm on MRI.
7. Age ≥ 18 years.
8. Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 (Karnofsky $\geq 60\%$).
9. Demonstrates adequate organ function as defined below:
 1. Platelets $\geq 100,000/\text{mL}$, independent of transfusions or growth factors within 3 months of treatment start.
 2. Hemoglobin $\geq 10 \text{ g/dL}$, independent of transfusions or growth factors within 3 months of treatment start.
 3. Absolute Neutrophil Count (ANC) $\geq 1,500/\text{microliter (mL)}$.
 4. Creatinine clearance Glomerular filtration rate (GFR) $\geq 60 \text{ mL/min/1.73 m}^2$, calculated using the Cockcroft-Gault equation.
 5. Albumin $\geq 2.5 \text{ g/dL}$.
 6. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) $\leq 3.0 \times \text{ULN}$.
 7. Total bilirubin (TBIL) $\leq 2 \times$ the institutional upper limit of normal (ULN). For participants with known Gilbert's Syndrome $\leq 3 \times \text{ULN}$ is permitted.
10. Ability to understand and the willingness to sign a written informed consent document.
11. Participants must provide consent to comply to recommended radioprotection precautions during study.
12. Participants must use adequate contraception and not donate sperm while on study drug and for at least 14 weeks after the last study treatment.

Exclusion Criteria:

1. Has received prior prostate cancer therapy.
 - a. Prior 5-alpha reductase inhibitors (e.g. finasteride, dutasteride) allowed if discontinued at least 3 weeks prior to treatment start.
2. Has participated in a study of an investigational therapeutic product and received study treatment or used an investigational device within four weeks of the first dose of treatment.
3. Dry mouth that impacts the eating of food (i. e. requiring mouthwash prior to eating).
4. Concurrent serious (as determined by the principal investigator) medical conditions including but not limited to New York Heart Association class III or IV congestive heart failure, history of congenital prolonged QT syndrome, uncontrolled infection, known active hepatitis B or C or other significant co-morbid conditions that in the opinion of the investigator would impair study participation or cooperation.
5. Diagnosed with other malignancies that are expected to alter life expectancy or may interfere with disease assessment. However, participants with a prior history of malignancy that has been adequately treated and who have been disease free, treatment free for more than 3 years prior to

Ages Eligible for Study

18 Years and older (Adult, Older Adult)

Sexes Eligible for Study

Male

Accepts Healthy Volunteers

No

randomization, or participants with adequately treated non-melanoma skin cancer, superficial bladder cancer are eligible.

6. Individuals with a prior or concurrent malignancy whose natural history or treatment has the potential to interfere with the safety or efficacy assessment of the investigational regimen.

Additional exclusion criteria applicable only to participants undergoing intraarterial administration of PSMA RLT:

1. Severe allergy to iodinated contrast.
2. Severe atherosclerosis from prior CT imaging study, or greater than 10 pack-year smoking history if no prior imaging available.

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

Masking : None (Open Label)

Arms and Interventions

Participant Group/Arm 	Intervention/Treatment 
Experimental: Cohort 1 (177Lu-PSMA-617) Five participants will receive a single dose of 177Lu-PSMA-617 radioligand therapy intravenously (IV), five participants will receive a single dose of 177Lu-PSMA-617 intra-arterially (IA), and five participants will receive two doses over 6 weeks intravenously. In participants receiving two doses, the dose will be divided so that the cumulative dose will be equivalent to participants receiving a single dose. All participants will undergo prostatectomy four weeks after completing radioligand therapy and will be followed up 6 weeks after surgery for safety assessments and at 3, 6, 12, and 60 months for long-term outcomes.	Drug: 177 Lutetium Prostate-Specific Membrane Antigen 617 - Given intravenously (IV) or intra-arterially (IA) - Other Names: 177Lu-PSMA-617 - Pluvicto - lutetium Lu 177 vipivotide tetraxetan Procedure: Non-investigational, Prostatectomy - Undergo non-investigational surgical procedure to remove prostate. - Other Names: - Prostatectomy Procedure: Prostate Tissue Collection - Whole prostate tissue will be collected for correlative research at time of prostatectomy. - Other Names: - Biospecimen Collection Procedure: Single-photon emission computed tomography (SPECT)/Computerized tomography (CT) - Imaging procedure - Other Names: - SPECT/CT Procedure: Blood Sample Collection - Blood samples will be obtained for research purposes - Other Names: - Blood Specimen
Experimental: Cohort 2 (225Ac-PSMA-617) Five participants will receive a single dose of 225Ac-PSMA-617 radioligand therapy IV, five participants will receive a single dose of 225Ac-PSMA-617 IA, and five participants will receive two doses over 6 weeks IV. In participants receiving two doses, the dose will be divided so that the cumulative dose will be equivalent to participants receiving a single dose. All participants will undergo prostatectomy four weeks after completing radioligand therapy and will be followed up 6 weeks after surgery for safety assessments and at 3, 6, 12, and 60 months for long-term outcomes.	Drug: Actinium-225 Prostate-Specific Membrane Antigen 617 - Given IV or IA - Other Names: 225Ac-PSMA-617 - Radioligand 225Ac-PSMA-617 Procedure: Non-investigational, Prostatectomy - Undergo non-investigational surgical procedure to remove prostate. - Other Names: - Prostatectomy Procedure: Prostate Tissue Collection - Whole prostate tissue will be collected for correlative research at time of prostatectomy. - Other Names: - Biospecimen Collection Procedure: Single-photon emission computed tomography (SPECT)/Computerized tomography (CT) - Imaging procedure

	- Other Names: - SPECT/CT Procedure: Blood Sample Collection - Blood samples will be obtained for research purposes - Other Names: - Blood Specimen
Other: Control Group (Prostatectomy only) Participants will obtain a non-investigational prostatectomy. Tumor tissue obtained at the time of surgery will be utilized for comparisons with the cohorts receiving study therapies. All participants will undergo prostatectomy four weeks after completing radioligand therapy and will be followed up 6 weeks after surgery for safety assessments and up to 24 months after surgery.	Procedure: Non-investigational, Prostatectomy - Undergo non-investigational surgical procedure to remove prostate. - Other Names: - Prostatectomy Procedure: Prostate Tissue Collection - Whole prostate tissue will be collected for correlative research at time of prostatectomy. - Other Names: - Biospecimen Collection Procedure: Blood Sample Collection - Blood samples will be obtained for research purposes - Other Names: - Blood Specimen

What is the study measuring?

Primary Outcome Measures ¹

Outcome Measure	Measure Description	Time Frame
Mean of tumor absorbed dose (Cohorts 1 and 2)	The mean tumor absorbed dose on post-treatment SPECT imaging within 7 days of the first radioligand treatment (RLT) will be obtained by using MIM Software to measure absorbed dose and researchers will manually segment activity in the dominant prostate tumor while carefully excluding any activity within the bladder using a threshold of 5 Gray. Using this segmented volume, the mean dose within the tumor in Gray for each participant and standard deviation will be calculated and reported descriptively for Cohorts 1 and 2. A two-sample t-test comparing the dose between Cohort 1 and Cohort 2 and Analysis of Variance (ANOVA) model to compare the dose between different treatment/fractionation modalities within each cohort will be performed.	1 week
Rate of Cluster of differentiation 3 positive (CD3+) T cell infiltration	Immunohistochemistry will be performed using standard methods, and stained slides will be scanned using an automated microscope scanner. Five randomly selected fields (0.25 mm ²) from each participant's primary tumor will be captured. Using color-specific algorithms, CD3+ cell counts will be determined, and the mean of each of the five quantified fields will be used. We will use a two-sample t-test or ANOVA model comparing the CD3+ cell counts between Cohort 1 and Cohort 2 with participants who have not undergone prostatectomy enrolled in the biospecimen protocol, respectively.	1 day, at time of prostatectomy

Secondary Outcome Measures ¹

Outcome Measure	Measure Description	Time Frame
Proportion of participants with reported treatment-emergent	The proportion of participants with treatment-emergent adverse events, as classified by the National Cancer Institute Common Terminology Criteria for Adverse Events version 5 (NCI CTCAE	Up to 6 weeks after last PSMA RLT

adverse events (Cohorts 1 and 2)	v5.0) will be reported for participants receiving RLT.	administration
Proportion of participants with perioperative complications	The Clavien-Dindo classification is a widely used system for grading and classifying surgical complications. The Proportion of participants with documented perioperative complications following prostatectomy per the Clavien-Dindo classification will be reported.	Up to 6 weeks after prostatectomy
Median scores on the xerostomia-quality-of-life-scale (XeQoLS)	The XeQoLS questionnaire measures the effects of salivary gland dysfunction and xerostomia on the four major domains of oral health-related quality of life: physical, pain, personal, and social. The questionnaire consists of 15 items, each rated on a 0-to-4 point Likert scale, with higher scores indicating more severe symptom burden. Median scores for each domain and global score and interquartile ranges will be reported.	Up to 12 months after prostatectomy
Proportion of participants with 50% decrease in level of prostate specific antigen (PSA50)	The proportion of participants who achieve a greater than 50% decline from baseline PSA drawn prior to Cycle 1 Day 1 (C1D1), up to the day of prostatectomy, will be descriptively reported along with 95% binomial confidence interval. It will be compared between the two treatment Cohorts using a Fischer's test.	Up to 8 weeks
Proportion of participants with complete pathologic response	Using the prostatectomy specimen, a board certified pathologies will determine pathologic complete response for each participant at time of prostatectomy. The pathologic response to the treatment in the prostate will be evaluated by percentage (0%, <10%, 10-25%, 50-75%, 75-100%) of viable tumor in the formalin-fixed paraffin embedded specimen. Complete pathologic response will be defined as no viable tumor (0%), and minimal residual disease will be defined as <10% of viable tumor. The number of participants in Cohorts 1 and 2 with complete pathologic response or minimal residual disease will be counted and the number of participants between the two cohorts will be compared using a Fisher's exact test. The proportion of complete pathologic response and minimal residual disease will be descriptively reported along with 95% binomial confidence interval.	1 day, at time of prostatectomy

Collaborators and Investigators

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

Sponsor ⓘ

Thomas Hope

Collaborators ⓘ

- Novartis

Investigators ⓘ

- Principal Investigator: Thomas A Hope, MD, University of California, San Francisco

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 ⓘ

2025-06-28

First Submitted that Met QC Criteria ⓘ

2025-06-28

First Posted ⓘ

Study Record Updates

Last Update Submitted that met QC Criteria ⓘ

2025-06-28

Last Update Posted ⓘ

2025-07-08

Last Verified ⓘ

2025-07-08

2025-06

More Information

Terms related to this study

[HHS Vulnerability Disclosure](#)

Keywords Provided by Thomas Hope, University of California, San Francisco

Radioligand Therapy

Additional Relevant MeSH Terms

Genital Neoplasms, Male
Urogenital Neoplasms
Neoplasms by Site
Neoplasms
Genital Diseases, Male
Genital Diseases
Urogenital Diseases
Prostatic Diseases
Male Urogenital Diseases
Pathologic Processes
Pathological Conditions, Signs and Symptoms
Prostatic Neoplasms
Disease
Urologic Surgical Procedures, Male
Urologic Surgical Procedures
Urogenital Surgical Procedures
Surgical Procedures, Operative
Specimen Handling
Clinical Laboratory Techniques
Diagnostic Techniques and Procedures
Diagnosis
Punctures
Investigative Techniques
Pluvicto
(225)Ac-PSMA-617
Prostatectomy
Blood Specimen Collection

Plan for Individual Participant Data (IPD)

Plan to Share Individual Participant Data (IPD)?

Yes

IPD Plan Description

De-identified data may be shared with study collaborators during the course of the study.

IPD Sharing Supporting Information Type

Study Protocol
Statistical Analysis Plan (SAP)
Informed Consent Form (ICF)

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