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A study of JNJ-78278343 in combination with JNJ-95298177 for treatment of prostate cancer

Submission date
21/05/2025

Recruitment status
Recruiting

Registration date
15/08/2025

Overall study status
Ongoing

Last Edited
26/10/2026

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Prostate cancer is a cancer that forms in the prostate, a male reproductive gland found below the bladder. Cancer is considered “advanced” if it spreads extensively to other parts of the body. Although treatments are available, they do not cure cancer. Over time, disease gets worse and progresses to metastatic castration-resistant prostate cancer (mCRPC)*, showing the need for better treatment.
*prostate cancer that grows despite low levels of male hormones JNJ-78278343 is a bispecific antibody** that targets a protein, human kallikrein 2, on tumor cells and cluster of differentiation 3 protein on T-cells (key cell in the immune system). This activates T-cells, which damage tumor cells and stop them from growing.
**type of protein that recognizes and attaches to 2 different targets
JNJ-95298177 is an antibody drug conjugate*** that targets proteins present on the surface of cancer cells. Once it attaches, it enters the cell and delivers a cancer-fighting drug, which stops thecancer from growing.
***treatment combining antibody with drug to attack cancer cells

In this study, researchers want to identify the most suitable dose of JNJ-78278343 and JNJ-95298177 and to find out how safe it is at the recommended dose.

Who can participate?
Men with prostate cancer

What does the study involve?
Study will be conducted in 2 parts:
1. Dose Confirmation (Part 1): Participants will receive JNJ-78278343 and JNJ-95298177 to confirm the combination dose (s).
2. Dose Expansion (Part 2): Participants will receive JNJ-78278343 and JNJ-95298177 at the doses determined in Part 1 to assess safety and anti-tumor activity.
Safety assessments include physical examinations, vital signs, Eastern Cooperative Oncology Group

(ECOG; how well participants can take care of themselves) performance status, clinical laboratory tests and electrocardiogram (ECG; test to record heart activity). All side effects will be recorded until study ends (around 2 years 2 months).

What are the possible benefits and risks of participating?
Participants will not receive any benefit from taking part in this study, but the information that is learned from the study may help people with advanced prostate cancer in the future. This is a first-in-human study, which means that JNJ-78278343 with JNJ-95298177 in combination have not been given to people before, although each of these drugs has been given by itself to participants with prostate cancer.
The expected risks for JNJ-78278343 based on how the drug works and results from clinical studies are as follows: cytokine release syndrome (inflammation condition that may occur after treatment with some types of immunotherapy), neurological side effects that may include headaches, changes in mental status, or seizures, and systemic administration-related reaction or infusion related reactions, which can include chills, low blood pressure, or feeling short of breath after the drug infusion. For participants with residual prostate or local tumour issue, prostatitis (inflammation in prostate) is possible. The expected risks for JNJ-95298177 based on how the drug works and results from clinical studies are as follows: excess protein in urine, nerve damage that causes pain, numbness, tingling, swelling, or muscle weakness in different parts of the body, harm to the eyes, kidneys, or liver, a low number of platelets (which can lead to bleeding), and inflammation of the lungs. The participant information sheet and informed consent form, which will be signed by every participant agreeing to take part in the study, includes a detailed section outlining the risks to participating in the study. Participants may have none, some, or all of the possible side effects listed, and they may be mild, moderate, or severe. To minimise the risk associated with taking part, participants are frequently reviewed for any side effects and other medical events. If they have any side effects or are worried about them, or have any new or unusual symptoms, participants will be encouraged to talk with their study doctor. The study doctor will also be looking out for side effects and will provide appropriate medical care. There may also be side effects that the researchers do not expect or do not know about and that may be serious. Many side effects go away shortly after the intervention ends. However, sometimes side effects can be serious, long-lasting, or permanent. If a severe side effect or reaction occurs, the study doctor may need to withdraw the participant from the study treatment. The study doctor will discuss the best way of managing any side effects with participants. There is always a chance that an unexpected or serious side effect may happen. This can happen to people who take this or any other drug.

Where is the study run from?
Janssen Research & Development, LLC (USA)

When is the study starting and how long is it expected to run for?
July 2025 to September 2027

Who is funding the study?
Janssen Research & Development, LLC (USA)

Who is the main contact?
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Contact information

Type(s)

Public

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Additional identifiers

Integrated Research Application System (IRAS)
1011800

Central Portfolio Management System (CPMS)
67465

Protocol serial number

78278343PBPCR1004

Study information

Scientific Title
A phase 1b study of JNJ-78278343, a T-cell redirecting agent targeting human kallikrein 2 (KLK2), in combination with JNJ-95298177, an antibody drug conjugate targeting prostate specific membrane antigen, for prostate cancer

Study objectives
Primary objectives:
Part 1 (Dose Finding): To find out the most suitable dose for the combination regimen (recommended phase 2 combination dose[s] [RP2CDs]) of JNJ-78278343 with the combination agent (JNJ-95298177).
Part 2 (Dose expansion): To find out how safe is the combination of JNJ-78278343 and the combination agent is at the recommended dose(s).

Secondary objectives:
1. To assess the preliminary antitumor (cancer-fighting) activity of JNJ-78278343 and combination agent.
2. To evaluate the pharmacokinetics* of JNJ-78278343 and combination agent.
*Process by which drug gets absorbed, distributed in the body, and excreted.
3. To evaluate immunogenicity (immune response against the drug) of JNJ-78278343 and the combination agent.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 07/07/2025, North West - Haydock Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 2071048117; haydock.rec@hra.nhs.uk), ref: 25/NW/0170

Primary study design
Interventional

Study design
Interventional non randomized

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Prostate cancer

Interventions
The study will be conducted in 2 Parts:

Part 1: Dose Confirmation Participants will receive JNJ-78278343 (Pasritamig) in combination with JNJ-95298177 (ARX517) in a dose de-escalation schedule in accordance with the Bayesian

Optimal Interval
Design (BOIN) design to determine the recommended phase 2 combination dose (RP2CD) regimen.

Part 2: Dose Expansion Participants will receive JNJ-78278343 in combination
with JNJ-95298177 at the RP2CD as determined in Part 1 of the study to confirm the safety and anti-tumor
activity.

Both drugs will be administered intravenously.

Follow up for around 2 years 2 months.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
JNJ-78278343, JNJ-95298177

Primary outcome(s)
1. Number of Participants With Adverse Events (AEs) by Severity
An AE is any untoward medical occurrence in a participant participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Severity will be graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0. Severity scale ranges from Grade 1 (Mild) to Grade 5 (Death). Grade 1= Mild, Grade 2= Moderate, Grade 3= Severe, Grade 4= Life-threatening and Grade 5= Death related to adverse event. Cytokine release syndrome (CRS) and immune effector cell associated neurotoxicity syndrome (ICANS) will be graded according to the American Society for Transplantation and Cellular Therapy (ASTCT) guidelines and ocular events will be graded using the alternative scale provided in the protocol. Up to 2 years 2 months.
2. Part 1: Number of Participants With Dose-Limiting Toxicity (DLT)
High grade hematologic or non-hematologic toxicities with exceptions and/or toxicities leading to treatment discontinuation will be regarded as DLT. Up to Day 22.

Key secondary outcome(s)
1. Objective Response Rate (ORR) ORR is defined as the percentage of participants who have a partial response (PR) or better according to the response evaluation criteria in solid tumors (RECIST) version 1.1 response criteria without evidence of bone progression
according to prostate cancer working group 3 (PCWG3). [Time Frame: Up to 2 years 2 months]
2. Prostate-Specific Antigen (PSA) Response Rate PSA response rate is defined as the percentage of participants with a decline of PSA of 50% or more from baseline. [Time Frame: Up to 2 years 2 months]
3. Radiographic Progression-Free Survival (rPFS) rPFS is defined as the time from the date of first dose of JNJ-78278343 or JNJ-95298177 until the date of radiographic disease progression or death, whichever comes first. [Time Frame: Up to 2 years 2 months]
4. Time to Response (TTR) TTR is defined for the responders as the time from the date of first dose of any study treatment to the date of first
documented response. [Time Frame: Up to 2 years 2 months]

5. Duration of Response (DOR) DOR will be calculated among responders (PR or better) from the date of initial documentation of a response (PR or better) to the date of first documented evidence of progressive disease, as defined in the PCWG3 or RECIST version 1.1 response criteria, or death due to any cause, whichever occurs first. [Time Frame: Up to 2 years 2 months]
6. Serum Concentration of JNJ-78278343 Serum samples will be analyzed to determine concentrations of JNJ-78278343.
[Time Frame: Up to 2 years 2 months]
7. Serum Concentration of JNJ-95298177 Serum samples will be analyzed to determine concentrations of JNJ-95298177 (including ADC, total antibody and payload pAF-AS269). [Time Frame: Up to 2 years 2 months]
8. Number of Participants With Anti-JNJ-78278343 Antibodies Serum samples will be analyzed for the detection of anti-JNJ-78278343 antibodies using a validated assay method. [Time Frame: Up to 2 years 2 months]
9. Number of Participants With Anti-JNJ-95298177 Antibodies Serum samples will be analyzed for the detection of anti-JNJ-95298177 antibodies using a validated assay method. [Time Frame: Up to 2 years 2 months]

Completion date
15/09/2027

Eligibility

Key inclusion criteria
1. Histologically confirmed adenocarcinoma of the prostate. Primary small cell carcinoma, carcinoid tumor, neuroendocrine (NE) carcinoma,
or large cell NE carcinoma arising in the prostate are not allowed; however, adenocarcinomas with NE features (for example [e.g.],
immunohistochemistry [IHC] with both androgen receptor [AR]- and NEmarker positivity) are allowed
2. Must have metastatic castration-resistant prostate cancer (mCRPC)
3. PSA must measure at least 2 nanograms per milliliters (ng/mL) at screening
4. Measurable or evaluable disease
5. Prior orchiectomy or medical castration; or, for participants who have not undergone orchiectomy, must be receiving ongoing androgen deprivation therapy with a gonadotropin-releasing hormone (GnRH) analog (agonist or antagonist) prior to the first dose of study drug and must continue this therapy throughout the treatment phase
6. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Male

Total final enrolment

0

Key exclusion criteria

Current key exclusion criteria as of 16/04/2026:

1. Toxicity related to prior anticancer therapy that has not returned to grade less than or equal to (≤) 1 or baseline levels (except for alopecia and vitiligo)
2. Known allergies, hypersensitivity, or intolerance to any of the components (e.g., excipients) of JNJ-78278343 or JNJ-95298177
3. Participants with leptomeningeal disease or brain metastases, with the exception of participants with definitively, locally treated brain metastases that are clinically stable and asymptomatic greater than (>) 2 weeks, and who are off corticosteroid treatment for at least 2 weeks prior to first dose of study treatment
4. Treatment with any anti-cancer or investigational agents within 14 days prior to the first dose of study treatment; specific requirements for certain anti-cancer therapies are as follows:
4.1. Any T-cell redirecting treatment (e.g., CD3-directed bispecific or Chimeric Antigen Receptor T-cell [CAR-T] therapy) within 90 days prior to the first dose of study treatment
4.2. Immune checkpoint inhibitors within 6 weeks prior to the first dose of study treatment
4.3. Radium (Ra) 223 dichloride within 28 days prior to the first dose of study treatment
4.4. Any prior treatment with kallikrein-related peptidase 2 (KLK2)-targeted therapy
4.5. Any prior prostate-specific membrane antigen (PSMA)-targeting therapy (i.e., participants who received PSMA-targeting radioconjugates are excluded) [Parts 2A and 2B only]. Prior PSMA RLT is allowed in Part 1 and required for Part 2C and Part 2D but last dose must be >3 months prior to the first dose of study treatment
4.6. Any prior antibody drug conjugates (ADCs) with microtubule inhibitor payloads (e.g., auristatins, maytansinoids, tubulysins)
5. Any serious underlying medical conditions or other issue that would impair the ability of the participant to receive or tolerate the planned treatment at the investigational site, to understand the informed consent, or any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant or that could prevent, limit, or confound the protocol-specified assessments.

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Previous key exclusion criteria:

1. Toxicity related to prior anticancer therapy that has not returned to grade less than or equal to (≤) 1 or baseline levels (except for alopecia and vitiligo)
2. Known allergies, hypersensitivity, or intolerance to any of the components (e.g., excipients) of JNJ-78278343 or JNJ-95298177
3. Participants with leptomeningeal disease or brain metastases, with the exception of participants with definitively, locally treated brain metastases that are clinically stable and asymptomatic greater than (>) 2 weeks, and who are off corticosteroid treatment for at least 2 weeks prior to first dose of study treatment
4. Treatment with any anti-cancer or investigational agents within 14 days prior to the first dose of study treatment; specific requirements for certain anti-cancer therapies are as follows:
4.1. Any T-cell redirecting treatment (e.g., CD3-directed bispecific or Chimeric Antigen Receptor T-cell [CAR-T] therapy) within 90 days prior to the first dose of study treatment
4.2. Immune checkpoint inhibitors within 6 weeks prior to the first dose of study treatment
4.3. Radium (Ra) 223 dichloride within 28 days prior to the first dose of study treatment
4.4. Any prior treatment with kallikrein-related peptidase 2 (KLK2)-targeted therapy
4.5. Any prior prostate-specific membrane antigen (PSMA)-targeting therapy (i.e., participants

who received PSMA-targeting radioconjugates are excluded) [Parts 2A and 2B only. Prior 177-Lu-PSMA radionuclide therapy is allowed in Part 1 and required for Part 2C], but last dose must be >6 weeks prior to the first dose of study treatment
4.6. Any prior antibody drug conjugates (ADCs) with microtubule inhibitor payloads (e.g., auristatins, maytansinoids, tubulysins)
5. Any serious underlying medical conditions or other issue that would impair the ability of the participant to receive or tolerate the planned treatment at the investigational site, to understand the informed consent, or any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant or that could prevent, limit, or confound the protocol-specified assessments.

Date of first enrolment
17/07/2025

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
United Kingdom

England

United States of America

Study participating centre
The Christie NHS Foundation Trust
550 Wilmslow Road
Withington
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Study participating centre
The Royal Marsden Hospital (surrey)
Downs Road
Sutton
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Study participating centre
University Hospitals Cleveland Medical Center
11100 Euclid Ave
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United States of America
44106

Study participating centre
Florida Cancer Specialists
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Sarasota
United States of America
34232

Study participating centre
Fred Hutchinson Cancer Center
1100 Fairview Avenue N
Seattle
United States of America
98109

Study participating centre
Columbia University Medical Center
177 Fort Washington Avenue
New York
United States of America
10032

Sponsor information

Organisation
Janssen-Cilag International NV

Funder(s)

Funder type
Industry

Funder Name
Janssen Research and Development

Alternative Name(s)

Janssen R&D, Janssen Research & Development, Janssen Research & Development, LLC, Janssen Research & Development LLC, Janssen Pharmaceutical Companies of Johnson & Johnson, Research & Development at Janssen, JRD, J&J PRD

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing policy of the Janssen Pharmaceutical Companies of Johnson and Johnson is available at www.janssen.com/clinical- trials/transparency. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at yoda.yale.edu

IPD sharing plan summary
Available on request