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A phase 3 randomized double-blinded, placebo-controlled study of JNJ-78278343, T-Cell redirecting agent targeting Human Kallikrein 2 with best supportive care (BSC) versus placebo with BSC for metastatic castration-resistant prostate cancer_KLK2 comPAS_78278343PCR3001

Submission date 22/07/2025	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol
Registration date 03/10/2025	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 26/10/2026	**Condition category** Cancer	[_] 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.

Metastatic castration-resistant prostate cancer (mCRPC) is an advanced cancer of the prostate that is resistant to hormone therapy and has spread beyond the prostate.

Although treatment options are available, cancer eventually progresses on these treatment options and gets worse. Hence, there is a significant need for easy to tolerate and better treatment options.

Pasritamig (JNJ-78278343) is a bispecific antibody* that targets a protein, human kallikrein 2 (hK2) (encoded by the KLK2 gene hereafter referred to as KLK2), on tumor cells as well as cluster of differentiation 3 protein on T-cells. This activates T-cells, which damage tumor cells and stop them from growing.

*Type of protein that recognizes and attaches to 2 different targets.

In this study the researcher want to evaluate if pasritamig with BSC is better when compared to placebo with BSC in overall survival in participants with mCRPC.

Who can participate?

Participants aged 18 years or older with mCRPC.

What does the study involve?
The study consists of the following phases:
•Screening Phase: (Up to 28 days before first dose of study drug)
•Treatment Phase: (From first dose of study treatment until discontinuation): Participants will be randomly (by chance) assigned to below 2 arms in a 2:1 ratio:
- Arm 1: Pasritamig with BSC
- Arm 2: Placebo with BSC
All participants must be receiving background androgen deprivation therapy (ADT) or had prior orchiectomy (surgical removal of testicles).
•End of Treatment (EOT) Visit: (42 days after last treatment dose or before the next treatment)
•Post-Treatment Follow-Up Phase: (Every 12 weeks until death): To monitor participants overall health and other anticancer therapy.

Safety assessments include monitoring adverse events, vital signs, Eastern Cooperative Oncology Group (ECOG; how well participants can take care of themselves) performance status, and clinical laboratory tests. The overall duration of the study will be up to approximately 2 years and 8 months.

What are the possible benefits and risks of participating?
There is no established benefit to participants of this study. Based on scientific theory, taking pasritamig may help treat mCRPC. However, this cannot be guaranteed because pasritamig is still under investigation as a treatment, and it is not known whether pasritamig will work.

In addition, if participants are put into the placebo treatment group, they will not receive pasritamig and will only receive placebo and BSC during this study.

Participants may experience some benefit from participation in the study that is not due to receiving pasritamig, but due to regular visits and assessments monitoring overall health. Participation may help other people with mCRPC in the future.

Participants may have side effects from the drugs or procedures used in this study that may be mild to severe and even life-threatening, and they can vary from person to person.

The most common, known risks are infusion-related reactions (IRRs; reactions during or after an intravenous drug), cytokine release syndrome (CRS; immune system overreaction causing fever and inflammation), and fatigue. Other potential risks include neurotoxicity including immune effector cell-associated neurotoxicity syndrome (ICANS; brain-related side effects from immune cell therapy), prostatitis (inflammation of the prostate; for participants with residual prostate or local tumor tissue), nausea, vomiting, diarrhea, anemia, and headache.

The participant information sheet and informed consent form, which will be signed by every participant agreeing to participate in the study, includes a detailed section outlining the known risks to participating in the study.

Not all possible side effects and risks related to pasritamig are known at this moment. During the study, the sponsor may learn new information about pasritamig. The study doctor will tell participants as soon as possible about any new information that might make them change their mind about being in the study, such as new risks.

To minimise the risk associated with taking part in the study, participants are frequently reviewed for any side effects and other medical events. Participants are educated to report any such events to their study doctor who will provide appropriate medical care. Any serious side

effects that are reported to the sponsor are thoroughly reviewed by a specialist drug safety team.

There are no costs to participants to be in the study. The sponsor will pay for the study drug and tests that are part of the study. The participant will receive reasonable reimbursement for study-related costs (e.g., travel/parking costs).

Where is the study run from?
Janssen Research and Development (UK)

When is the study starting and how long is it expected to run for?
July 2025 to May 2029

Who is funding the study?
Janssen-Cilag International NV (Netherlands)

Who is the main contact?
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Public, Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
1012341

Central Portfolio Management System (CPMS)
68039

Protocol serial number
78278343PCR3001

Study information

Scientific Title
A phase 3 randomized double-blinded, placebo-controlled study of JNJ-78278343, T-Cell redirecting agent targeting Human Kallikrein 2 with best supportive care (BSC) versus placebo with BSC for metastatic castration-resistant prostate cancer_KLK2 comPAS_78278343PCR3001

Acronym
KLK2-comPAS

Study objectives
1.1. Main objectives
•To evaluate if pasritamig with best supportive care (BSC) is better when compared to placebo (treatment with no medical effect) with BSC in overall survival*.
*The length of time from the randomization until a participant dies.
1.2. Secondary objectives
•To compare the clinical benefits (positive effects of a treatment) of pasritamig with BSC when compared to placebo with BSC.
•To compare how safe is pasritamig with BSC when compared to placebo with BSC

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 18/07/2025, London - Central Research Ethics Committee (3rd Floor, 3 Piccadilly Place, London Road, Manchester, M1 3BN, United Kingdom; +44 207 104 8061; londoncentral.rec@hra.nhs.uk), ref: 25/LO/0606

Primary study design
Interventional

Study design
Interventional double blind randomized placebo controlled trial

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Metastatic Castration-resistant Prostate Cancer

Interventions
Arm 1: Pasritamig with Best Supportive Care (BSC)
Participants in this arm receive pasritamig (JNJ-78278343), a bispecific antibody, administered as a solution for infusion using a step-up dosing schedule: Step-Up Dose 1 (SU1) on Cycle 1 Day 1 (C1D1), Step-Up Dose 2 (SU2) on C1D8, and the target dose on C1D15. From Cycle 2 Day 1 (C2D1) onwards, participants receive the target dose every 6 weeks (Q6W). Treatment continues until confirmed progressive disease, death, intolerable toxicity, withdrawal of consent, or end of study.

Arm 2: Placebo with Best Supportive Care (BSC)
Participants in this arm receive a matching placebo (solution for infusion) with the same step-up dosing schedule as the experimental arm: SU1 on C1D1, SU2 on C1D8, and target dose on C1D15. From C2D1 onwards, placebo is administered every 6 weeks (Q6W) until confirmed progressive disease, death, intolerable toxicity, withdrawal of consent, or end of study.

Treatment Duration and Follow-Up
The treatment phase begins on the first dose and continues until discontinuation criteria are met. An End of Treatment (EOT) visit occurs 42 days after the last dose. Post-treatment follow-up is conducted every 12 weeks until death to monitor overall health and subsequent anticancer therapies. The total study duration is approximately 2 years and 8 months.

Randomisation Process
Participants are randomised in a 2:1 ratio to receive either pasritamig with BSC or placebo with BSC.

Previous interventions:
Arm 1: Pasritamig with Best Supportive Care (BSC)
Participants in this arm receive pasritamig (JNJ-78278343), a bispecific antibody, administered as a solution for infusion using a step-up dosing schedule: Step-Up Dose 1 (SU1) on Cycle 1 Day 1 (C1D1), Step-Up Dose 2 (SU2) on C1D8, and the target dose on C1D15. From Cycle 2 Day 1 (C2D1) onwards, participants receive the target dose every 6 weeks (Q6W). Treatment continues until confirmed progressive disease, death, intolerable toxicity, withdrawal of consent, or end of study.

Arm 2: Placebo with Best Supportive Care (BSC)
Participants in this arm receive a matching placebo (solution for infusion) with the same step-up dosing schedule as the experimental arm: SU1 on C1D1, SU2 on C1D8, and target dose on C1D15. From C2D1 onwards, placebo is administered every 6 weeks (Q6W) until confirmed progressive disease, death, intolerable toxicity, withdrawal of consent, or end of study.

Treatment Duration and Follow-Up
The treatment phase begins on the first dose and continues until discontinuation criteria are

met. An End of Treatment (EOT) visit occurs 42 days after the last dose. Post-treatment follow-up is conducted every 12 weeks until death to monitor overall health and subsequent anticancer therapies. The total study duration is approximately 4 years and 8 months.

Randomisation Process
Participants are randomised in a 2:1 ratio to receive either pasritamig with BSC or placebo with BSC.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Overall Survival, defined as the time from randomisation to date of death from any cause. Participants alive at the time of analysis will be censored on the last date the participant was known to be alive. After the primary endpoint achieves statistical significance, the α will be passed to the key secondary endpoints of rPFS, time to symptomatic progression, time to skeletal-related events, and PFS

Key secondary outcome(s)
1. Radiographic progression-free survival is measured using investigator-assessed RECIST v1.1 and PCWG3 criteria at baseline and every 8 weeks until radiographic progression or death
2. Time to symptomatic progression is measured using protocol-specified clinical criteria at baseline and every scheduled clinical assessment until first occurrence
3. Time to skeletal-related event is measured using protocol-specified criteria based on clinical and imaging assessments at baseline and every scheduled visit until first occurrence
4. Progression-free survival is measured using radiographic imaging, clinical assessment, and survival status at baseline and every 8 weeks until radiographic or clinical progression or death
5. Time to prostate-specific antigen progression is measured using serum PSA levels assessed per PCWG3 criteria at baseline and every 4 weeks until progression
6. Time to pain progression is measured using the Brief Pain Inventory-Short Form (BPI-SF) item 3 “worst pain in 24 hours” at baseline and every 4 weeks until first observation of pain progression
7. Time to deterioration in fatigue is measured using the EORTC QLQ-C30 fatigue scale at baseline and every 4 weeks until first observation of deterioration
8. Incidence and severity of adverse events are measured using investigator assessment and graded per CTCAE v5.0 at baseline and throughout the treatment period until 30 days after last dose
9. Clinical laboratory test results are measured using standard haematology, biochemistry, and urinalysis panels at baseline and every 4 weeks during treatment

Completion date
03/05/2029

Eligibility

Key inclusion criteria

Current key inclusion criteria as of 01/07/2026:
1. Be 18 years of age or more at the point of informed consent.
2. Histologically confirmed adenocarcinoma of the prostate.
3. Metastatic castration-resistant prostate cancer (mCRPC): Disease that is metastatic either to bone, any lymph node, or both without clear evidence of other metastatic sites at the time of screening by conventional imaging with CT or MRI (chest, abdomen, and pelvis) and 99mTc bone scan.
4. Prostate specific antigen (PSA) greater than or equal to 2 ng/mL at screening.
5. In the opinion of the investigator, the next best treatment option is a clinical trial.
6. Participants should have had all life-prolonging therapies for which they are clinically eligible in the opinion of the investigator and to which they have access. Prior therapies could have been given in any disease setting (not limited to mCRPC). Prior treatment specifications are specified in full within the study protocol.
7. Use of any other anticancer therapy or investigational agent must be discontinued for at least 2 weeks before the first dose of study treatment.
8. Prior orchiectomy or medical castration (receiving ongoing androgen deprivation therapy [ADT] with a gonadotropin-releasing hormone [GnRH] analog [agonist or antagonist]) prior to the first dose of study treatment and must continue this therapy throughout the treatment phase.
9. Must be sufficiently recovered from any recent surgery or trauma.
10. Have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2.
11. Have an eGFR greater than or equal to 30 mL/min, calculated with the CKD-epi formula, before randomisation. Participants with obstructive uropathy should have treatment prior to randomisation.
12. Participants must meet the protocol specified hepatic function measures.
13. Participants must meet the protocol specified haematological value measures.
14. Participant must agree, while on study treatment and for 3 months after the last dose of study treatment, to not donate gametes (i.e., sperm) or freeze for future use for the purposes of assisted reproduction and to wear an external condom, when transmission of sperm/ejaculate can occur. If able to produce sperm and their partner is of childbearing potential, the partner must practice a highly effective method of contraception.
15. Must sign an Informed Consent Form (ICF) indicating that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study.
16. Participant must be willing and able to adhere to the lifestyle restrictions specified in this protocol.

Previous key inclusion criteria:
1. Be 18 years of age or more at the point of informed consent.
2. Histologically confirmed adenocarcinoma of the prostate.
3. Metastatic castration-resistant prostate cancer (mCRPC): Disease that is metastatic either to bone, any lymph node, or both without clear evidence of metastasis to visceral organs at the time of screening. Local-regional invasion (rectum, bladder) can be included.
4. Prostate specific antigen (PSA) greater than or equal to 2 ng/mL at screening.
5. In the opinion of the investigator, the next best treatment option is a clinical trial.
6. Participants should have had all life-prolonging therapies for which they are clinically eligible in the opinion of the investigator and to which they have access. Prior therapies could have been given in any disease setting (not limited to mCRPC). Prior treatment specifications are specified in full within the study protocol.
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Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
99 Years

Sex
Male

Total final enrolment
0

Key exclusion criteria
Current key exclusion criteria as of 01/07/2026:
1. Solid organ or bone marrow transplantation.
2. Venous thromboembolic events within 1 month prior to the first dose of study treatment.
3. Active autoimmune disease within the 12 months prior to signing consent that requires systemic immunosuppressive medications.
4. Participants with Grade 1 or higher fever (>=38°C) or active infection requiring systemic treatment within 7 days prior to randomization are ineligible. Participants must be afebrile (<38°C) at the time of study treatment dosing unless approved by medical monitor.

5. Clinically significant pulmonary compromise, particularly a requirement for supplemental oxygen use (greater than 2 L/min by nasal cannula) to maintain adequate oxygenation.
6. Suspected or known allergies, hypersensitivity, or intolerance to excipients of pasritamig.
7. Participant has a prior or concurrent second malignancy (other than the disease under study) for which natural history or treatment could likely interfere with any study endpoints of safety or the efficacy of the study treatment(s).
8. Any of the protocol-specified cardiac dysfunctions within 6 months prior to first dose of study treatment.
9. Has known history of either brain or leptomeningeal prostate cancer metastases.
10. Participants who are HIV-positive and meet any of the criteria specified in the study protocol.
11. Active or chronic HBV or HCV infection, as specified in the study protocol.
12. Prior treatment with KLK2-targeted therapy.
13. Prior treatment with any CD3-directed therapy.
14. Received immunosuppressive doses of systemic medications within 3 days prior to the first dose of study treatment. A single course of glucocorticoids is permitted as prophylaxis for imaging contrast. If glucocorticoids were used to treat immune-related adverse events associated with prior therapy, 7 or more days must have elapsed since the last dose of corticosteroid.
15. Received or plans to receive any live, attenuated vaccine within 4 weeks before the first dose of study treatment. Live, attenuated influenza vaccines are permitted as late as 7 days before the study treatment.
16. 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 study 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.

Previous key exclusion criteria:
1. Solid organ or bone marrow transplantation.
2. Venous thromboembolic events within 1 month prior to the first dose of study treatment.
3. Active autoimmune disease within the 12 months prior to signing consent that requires systemic immunosuppressive medications.
4. Active infection or condition that requires treatment with systemic antibiotics within 7 days prior to the first dose of study treatment. Prophylactic anti-infective agents are allowed.
5. Clinically significant pulmonary compromise, particularly a requirement for supplemental oxygen use (greater than 2 L/min by nasal cannula) to maintain adequate oxygenation.
6. Suspected or known allergies, hypersensitivity, or intolerance to excipients of pasritamig.
7. Participant has a prior or concurrent second malignancy (other than the disease under study) for which natural history or treatment could likely interfere with any study endpoints of safety or the efficacy of the study treatment(s).
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12. Prior treatment with KLK2-targeted therapy.
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14. Received immunosuppressive doses of systemic medications within 3 days prior to the first dose of study treatment. A single course of glucocorticoids is permitted as prophylaxis for imaging contrast. If glucocorticoids were used to treat immune-related adverse events associated with prior therapy, 7 or more days must have elapsed since the last dose of corticosteroid.

15. Received or plans to receive any live, attenuated vaccine within 4 weeks before the first dose of study treatment. Live, attenuated influenza vaccines are permitted as late as 7 days before the study treatment.
16. 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 study 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
14/10/2025

Date of final enrolment
14/06/2027

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Australia

Belgium

Brazil

Canada

China

France

Germany

Italy

Japan

Netherlands

Poland

Spain

Sweden

Taiwan

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Sponsor information

Organisation
Janssen-Cilag International NV

Funder(s)

Funder type
Industry

Funder Name
Janssen-Cilag International NV

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