Janssen Research & Development *

Clinical Protocol

Protocol Title

A Phase 3 Randomized, Open-label Study of Pasritamig (JNJ-78278343), a T-cell-redirecting Agent Targeting Human Kallikrein 2, With Docetaxel Versus Docetaxel for Metastatic Castration-resistant Prostate Cancer

KLK2-PASenger

Short Title: Pasritamig With Docetaxel vs Docetaxel in Metastatic Castration-resistant Prostate Cancer (mCRPC)

Protocol 78278343PCR3003; Phase 3
Version: Original

JNJ-78278343 (pasritamig)

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Studies conducted at sites in the United States (US) will be conducted under US Food & Drug Administration Investigational New Drug (IND) regulations (21 CFR Part 312).

Studies conducted at sites in the European Economic Area (EEA) will be conducted under Regulation [EU] No 536/2014.

Regulatory Agency Identifier Numbers:
IND: 157066
EU TRIAL NUMBER: 2025-522713-29-00

Status:	Approved
Date:	15 September 2025
Prepared by:	Janssen Research & Development, LLC; Janssen Research & Development, a division of Janssen Pharmaceutica NV
EDMS number:	EDMS-RIM-1590150, 1.0

GCP Compliance: This study will be conducted in compliance with Good Clinical Practice, and applicable regulatory requirements.

4.3.1.2. Docetaxel

Docetaxel will be administered at 75 mg/m^2 once every 3 weeks by IV administration per the approved label with a maximum of 10 doses.

The treatment label for docetaxel utilizes concomitant daily prednisone in mCRPC. Prednisone will be administered per the label in the comparator arm, but not in the experimental arm (see Section 2.3). Pre-dose medication will be administered in both arms per the label (see Section 6.9.1) to manage potential toxicities for both docetaxel and pasritamig.

4.4. End of Study Definition

The end of study/study completion is the last scheduled study assessment for the last participant in the study. The final data from the study site will be sent to the Sponsor (or designee) after completion of the final participant assessment at that study site, in the time frame specified in the Clinical Trial Agreement.

Participant Study Completion Definition

A participant is considered to have completed the study if the participant:

- died while on study OR
- remained on study at the time of the end of study (ie, did not meet the criteria for withdrawal from study, see Section 7.2).

5. STUDY POPULATION

Screening for eligible participants will be performed within 28 days prior to randomization. Imaging can be performed within 42 days prior to randomization. Refer to Section 5.4, for conditions under which repetition of any screening procedures is allowed.

The inclusion and exclusion criteria for enrolling participants in this study are described below. The investigator must consult with the appropriate Sponsor representative with any issues/questions related to entry criteria. Issues/questions must be resolved prior to participant enrollment into the study. Waivers are not allowed. For a discussion of the statistical considerations of participant selection, refer to Section 9.2.

5.1. Inclusion Criteria

All potential participants must satisfy all the following inclusion criteria to be enrolled into the study. Participants must:

Age

1. Be ≥18 years of age at the time of informed consent or at least the legal age of majority in the jurisdiction in which the study is taking place.

Disease Characteristics

2. Have histologically confirmed adenocarcinoma of the prostate. Participants with primary (or documented evidence of conversion to) small cell carcinoma, carcinoid tumor, mixed NE carcinoma, large cell NE carcinoma, or sarcoma of the prostate are excluded.

3. Have disease that is metastatic at the time of the screening as determined by the investigator.

4. Have progressive disease defined as at least one of the following:
   - PSA level ≥2 ng/mL that has increased on at least 2 successive occasions at least 1 week apart.
   - Progressive disease or new lesion(s) in the lymph nodes, bones, or viscera as defined by RECIST v1.1 and/or in bone scan per PCWG3 while on medical or surgical castration.

Prior Therapy Restrictions or Requirements

5. Participants must receive ongoing ADT with a GnRH analog (agonist or antagonist) throughout the Treatment Phase or have had prior bilateral orchiectomy, and have serum testosterone ≤50 ng/dL (≤1.73 nmol/L) at screening.

6. Have progressed on at least 1 novel ARPI but received no more than 2 different ARPI (eg, abiraterone acetate, apalutamide, enzalutamide, darolutamide) for any stage of disease. Must have discontinued ARPI before randomization into the study.

Performance Status

7. Have an ECOG performance status of 0 to 1 (Oken 1982).

Renal Function

8. Have an eGFR, calculated with the CKD-epi formula (at https://www.kidney.org/professionals/gfr_calculator), of >30 mL/min during the screening period. Participants with obstructive uropathy should have treatment prior to randomization (eg, foley catheter, nephrostomy tubes, etc).

Hepatic Function

9. Have the following laboratory values during the screening period:

	Hepatic metastases	
	No known	***Yes***
AST	<1.5 x ULN	<3 x ULN
ALT	<1.5 x ULN	<3 x ULN
Total bilirubin	Normal, except in case of known congenital nonhemolytic indirect hyperbilirubinemias such as Gilbert's Syndrome: if total bilirubin is >1.5 × ULN, eligible if direct bilirubin is ≤1.5 × ULN	

Hematologic Values

10. Have the following laboratory values during the screening period:
    - Hemoglobin ≥9.0 g/dL
    - Neutrophils ≥1.5 x 10^9/L
    - Platelets ≥100 x 10^9/L
    - **Note**, transfusion or growth factor usage within 14 days of randomization is not allowed.

Sex and Contraceptive/Barrier Requirements

13. Agree, while on study treatment and for 6 months after the last dose of study treatment, to:
    - Not donate gametes (ie, sperm) or freeze for future use for the purposes of assisted reproduction.
    - 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.

    See Appendix 3: Contraceptive and Barrier Guidance for details.

Informed Consent

14. Participant (or their legally designated representative) must sign an ICF.

15. Be willing and able to adhere to the lifestyle restrictions specified in this protocol.

5.2. Exclusion Criteria

Any potential participant who meets any of the following exclusion criteria will be excluded from participating in the study.

Medical Conditions

1. Known history of either brain or leptomeningeal prostate cancer metastases.
2. Patients with known BRCA 1/2 mutations (germline or somatic) who have not received treatment with a PARP inhibitor, unless not available or contraindicated.
3. Suspected or known allergies, hypersensitivity, or intolerance to pasritamig excipients (refer to the pasritamig IB and Addenda) or docetaxel excipients (Taxotere PI).
4. Not recovered from recent surgery.
5. Solid organ or bone marrow transplantation.
6. Active autoimmune disease within the 12 months prior to signing consent that requires systemic immunosuppressive medications (eg, chronic corticosteroid, methotrexate, or tacrolimus).

Cardiovascular Dysfunction

7. Any of the following within 6 months prior to first dose of study treatment:
   - severe or unstable angina,
   - myocardial infarction,
   - major thromboembolic events (eg, pulmonary embolism, cerebrovascular accident),
   - clinically significant ventricular arrhythmias or heart failure New York Heart Association functional classification Class II to IV.

   Note: Uncomplicated deep vein thrombosis is not considered exclusionary.

Prior Malignancies

8. Prior or concurrent second malignancy (other than the disease under study) because the natural history or treatment could interfere with study endpoints (see Appendix 5 on Allowed Recent Second or Prior Malignancies for details).

Disease Characteristics

9. Received cytotoxic chemotherapy for prostate cancer in any setting (eg, docetaxel, cabazitaxel, mitoxantrone, etc).

10. Received prior treatment with KLK-2-directed therapies.

11. Received prior treatment for prostate cancer with:
   - CD3 redirector therapies or
   - Radiopharmaceutical agents or
   - Immunotherapy agents for prostate cancer (eg, sipuleucel-T, PD-1 inhibitors, T-cell redirectors, costimulatory agents, etc) or
   - PARP inhibitors (other than for BRCA1/2 mutation) or
   - Any other investigational agent for the treatment of mCRPC.

HIV Status

12. Participants who are HIV-positive and meet any of the following:
   a) Detectable viral load (ie, ≥50 copies/mL) at screening.
   b) CD4+ count ≤300 cells/mm^3 at screening.
   c) AIDS-defining opportunistic infection within 6 months of screening.
   d) Receive treatment other than continued HAART. A change in HAART due to resistance/progression must occur at least 3 months prior to screening. A change in HAART due to toxicity is allowed up to 4 weeks prior to screening.

   Note: HAART that could interfere with study treatment is excluded (consult the Sponsor for a review of medications prior to enrollment).

Viral Hepatitis Assessments

13. Active hepatitis of infectious origin.

    a) Seropositive for hepatitis B: defined by a positive test for HBsAg. Participants with resolved infection (ie, participants who are HBsAg negative with positive antibodies to total hepatitis B core antigen [anti-HBc]) must be screened using RT-PCR measurement of HBV DNA levels. Those who are RT-PCR positive will be excluded. Participants with serologic findings suggestive of HBV vaccination (anti-HBs positivity as the only serologic marker) AND a known history of prior HBV vaccination, do not need to be tested for HBV DNA by RT-PCR (see Appendix 6).

    b) Known hepatitis C infection or positive serologic testing for hepatitis C virus (anti-HCV) antibody.
    Participants with positive hepatitis C antibody due to prior resolved disease can be enrolled only if a confirmatory negative hepatitis C RNA test is obtained at screening or within 3 months prior to first dose of study treatment.

    c) Other clinically active liver disease of infectious origin.

Prior/Concomitant Therapy or Clinical Study Experience

14. Received or plans to receive any live, attenuated vaccine within 4 weeks before the first dose of study treatment. Non-live and non-replication-competent vaccines are allowed.

15. Received systemic glucocorticoids (doses >10 mg/day prednisone or equivalent) within 3 days prior to the first dose of study treatment. A single course of glucocorticoids is permitted as prophylaxis for imaging contrast (ie, for participants with allergies to contrast). If glucocorticoids were used to treat immune-related adverse events associated with prior therapy, ≥7 days must have elapsed since the last dose of corticosteroid.

16. Received external beam radiation therapy within 14 days prior to start of study treatment. However, if palliative focal radiation was used, the participant is eligible regardless of date of radiation.

Other Exclusions

17. Any condition which, in the opinion of the investigator, would not be in the best interest of the participant (eg, compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.

    Note: Investigators must ensure that all study enrollment criteria have been met at screening. If a participant's clinical status changes (including any available laboratory results or receipt of additional medical records) after randomization but before the first dose of study treatment is given such that the participant no longer meets all eligibility criteria, the participant may still be eligible for participation in the study