TPS5139

KLK2-PASenger: A Phase 3 Randomized, Open-label Study of Pasritamig, a T-cell-engager, Targeting Human Kallikrein 2 with Docetaxel versus Docetaxel in Metastatic Castration-resistant Prostate Cancer

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KEY TAKE AWAYS

- PAS is a first-in class, specific T cell engager targeting human kallikrein 2 (KLK2), a novel, highly prostate-specific target[1,2,3]
- PAS + DOCE demonstrated a safety profile consistent with the established profile of DOCE.[4,5,6] No CRS (of any grade) was reported in the Phase 1 study at the RP2D.
- The PASenger study (NCT07225946) is evaluating PAS + DOCE vs DOCE in adult participants with mCRPC.
- This phase 3 trial will open at 97 clinical sites across 16 countries worldwide.
- The trial is active and currently enrolling participants.

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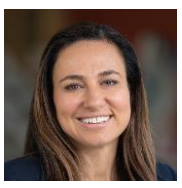

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Introduction

- Metastatic castration-resistant prostate cancer (mCRPC), also termed androgen pathway modulation-resistant (APMR) in PCWG4[7], remains an incurable disease with high morbidity and a median overall survival (OS) of approximately two years.[8]
- Docetaxel (DOCE) is a standard of care for patients with mCRPC after progression on androgen receptor pathway inhibitors (ARPIs).[9]
- Human kallikrein 2 (KLK2) is highly specific to normal and malignant prostate tissue, including in late stage mCRPC.[1] Pasritamig (PAS) is a first-in-class KLK2 T-cell engager (TCE) (Figure 1) and was well-tolerated with Q6W outpatient dosing (<10% CRS [cytokine release syndrome], all grade 1 [fever only]) and promising single-agent activity in heavily pretreated mCRPC in the early phase study.[2,3]
- In the Phase 1b study (NCT05818683), PAS was combined with DOCE to treat patients with pre-treated mCRPC, including 43% with prior docetaxel exposure.[6]
  - The safety of PAS+DOCE appears consistent with DOCE studies and no CRS, of any grade, was reported (0 of 51 patients).[4,5,6]
  - Promising anti-tumor activity was observed in patients with both taxane-naïve and heavily pretreated disease. Overall, response rates with confirmed PSA50 were 64.7% (33/51) and confirmed PSA90 were 39.2% (20/51).[6]
    - PSA90 in taxane-naïve (as in KLK2-PASenger) was 54%.

Figure 1: PAS simultaneously binds KLK2 on prostate cancer cells and CD3 receptor complexes on T cells, leading to T-cell activation and subsequent lysis of cancer cells

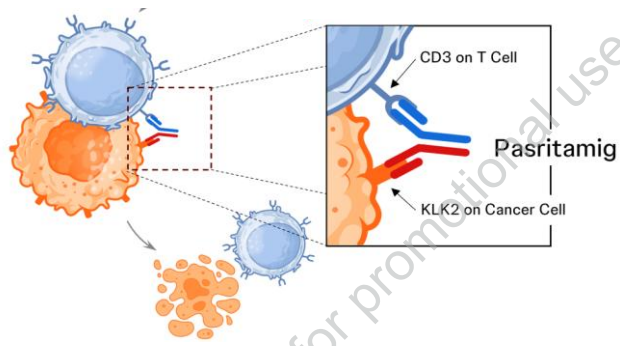
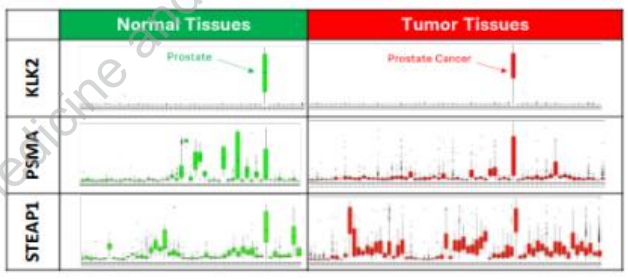


Figure 2: KLK2 is a novel target highly expressed on prostate cells (normal and malignant) with limited expression in other tissues.[1]



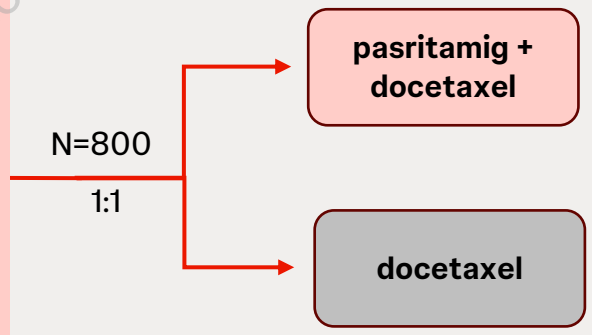
Methods

Key Eligibility

- Histologically confirmed adenocarcinoma of the prostate
- Evidence of metastatic disease on conventional imaging and PSA or radiographic progression at screening
- Progression on 1-2 novel ARPI for any stage of prostate cancer
- No prior treatment with T-cell redirecting therapies, chemotherapy, or radiopharmaceutical therapy
- No significant comorbidities that could interfere with study participation.

Study design

Figure 3: A global, randomized, open-label, phase 3 study evaluates the efficacy and safety of PAS + DOCE versus DOCE alone in adult chemo-naïve participants (≥18 years) with mCRPC (NCT07225946).



Primary endpoint: rPFS by BICR per PCWG3 and RECIST v1.1 criteria.

Key secondary endpoints:

- OS
- Time to symptomatic progression
- Time to subsequent therapy
- Time to skeletal-related event

Stratification factors:

- sites of metastases (on conventional imaging)
- LDH
- ECOG PS
- prior PARP inhibitor use

- PAS is administered in the outpatient setting at a target dose of 300 mg IV Q6W with two step-up doses of 3.5 mg IV on day 1 and 18 mg IV on day 8.
- DOCE is planned for 10 doses in both arms unless limited by toxicity despite optimal supportive care.
- Pre-medications including dexamethasone are administered in both treatment arms
- Participants in the DOCE alone arm will also receive continuous prednisone per label.

APMR = androgen pathway modulation-resistant; ARPI = androgen receptor pathway inhibitors; CD3 = cluster of differentiation 3; DOCE = docetaxel; KLK2 = human kallikrein 2; mCRPC = metastatic castration-resistant prostate cancer; PAS = pasritamig; PCWG= Prostate Cancer Clinical Trials Working Group; PARP = poly ADP-ribose polymerase; PSA = prostate-specific antigen; PSMA = prostate-specific membrane antigen; rPFS = radiographic progression free survival; RECIST 1.1 = Response Evaluation Criteria in Solid Tumors 1.1

Figure 3: Countries planned for participation in PASenger trial

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Prostate Cancer

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