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KLK2-comPAS: A Phase 3, Randomized, Double-blind, Placebo-controlled Study of Pasritamig plus Best Supportive Care in Metastatic Castration-resistant Prostate Cancer

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KEY TAKE AWAYS

- Pasritamig (PAS) is a first-in class, KLK2xCD3 T cell engager targeting human kallikrein 2 (KLK2), a novel, prostate-specific target.[1]
- PAS demonstrated a favorable safety profile differentiated from prior T-cell engagers.[2,3]
- The comPAS study is evaluating PAS + BSC (best supportive care) vs placebo + BSC (NCT07164443).
- This phase 3 trial will open at 163 clinical sites across 16 countries worldwide.
- The trial is active and currently enrolling participants.

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Introduction

- Metastatic castration-resistant prostate cancer (mCRPC), also termed androgen pathway modulation-resistant (APMR) in PCWG4[4], remains an incurable disease with high morbidity and a median overall survival of approximately two years.[5]
- Human kallikrein 2 (KLK2) is highly specific to normal and malignant prostate tissue, including in late-stage mCRPC.[1]
- Pasritamig (PAS) s a novel T cell engager (TCE). PAS is a humanized, IgG1-based bispecific antibody that targets KLK2-expressing cells via CD3 engagement, inducing T cell-mediated targeted cytotoxicity.[1]
- In a first-in-human study in participants with mCRPC refractory to standard therapies, pasritamig demonstrated a favorable safety profile (<5% grade 3 or higher treatment-related adverse events and <10% cytokine release syndrome, all grade 1 – fever only) permitting fully outpatient administration.[2,3]
- PAS achieved durable disease control and rPFS (median 7.9 months) that compare favorably to historical data in heavily pretreated participants with mCRPC.[2,3]
- KLK2-comPAS is a double-blind, randomized, global phase 3 study to evaluate the safety and efficacy of pasritamig with BSC in participants with late-line mCRPC.

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

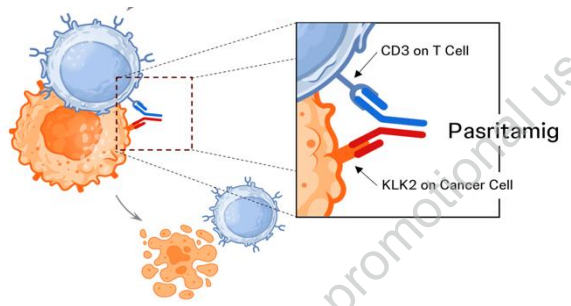
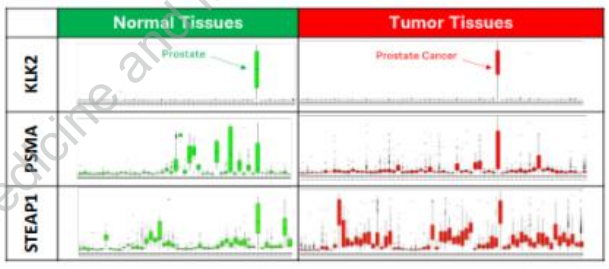


Figure 2: KLK2 is a novel target highly expressed on prostate cells (normal and malignant) with limited expression in other tissues.[1]



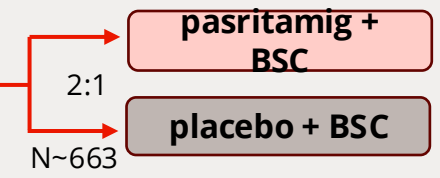
Methods

Key Eligibility

- Received all available life-prolonging therapies (ARPI, taxanes, RLT, PARPI for BRCAm) including at least one taxane and one ARPI
- ECOG 0-2
- PSA ≥2 ng/mL
- Adequate organ function
- Ongoing ADT or prior orchiectomy
- No visceral metastases
- No prior KLK2 or CD3 directed therapies
- No active autoimmune disease requiring immunosuppression

Study design

Figure 3: A global, randomized, double-blinded, placebo-controlled, phase 3 study evaluates the efficacy and safety of PAS plus best supportive care (BSC) or placebo plus BSC (NCT07164443)



Stratification factors:
- prior PSMA-targeted RLT
- number of prior taxanes
- ECOG PS

Primary endpoint: OS

Key secondary endpoints:
- rPFS (investigator-assessed per RECIST v1.1 and PCWG3)
- Time to symptomatic progression
- Time to skeletal-related event
- PFS (including clinical and/or unconfirmed bone progression)

Pasritamig (PAS) or placebo schedule

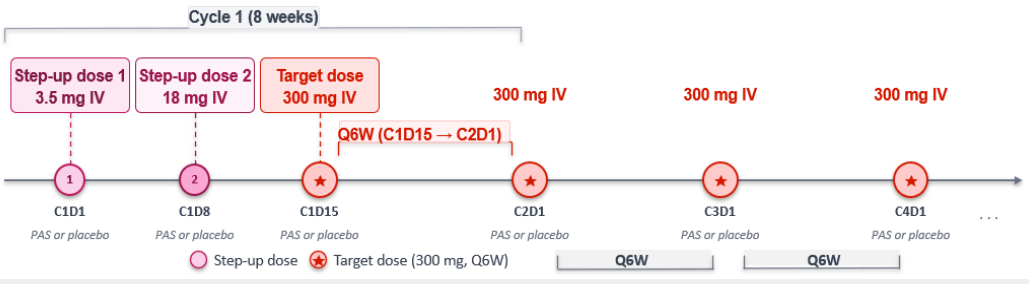
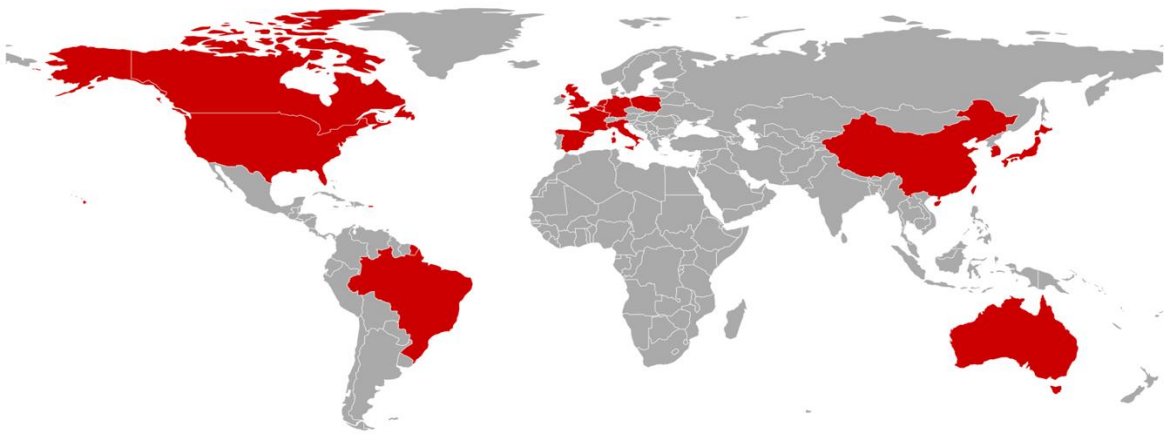


Figure 4: PAS is administered in the outpatient setting. Treatment begins with two step-up doses (3.5 mg IV on Day 1 and 18 mg IV on Day 8) followed by the target dose of 300 mg IV every 6 weeks until progression.

ADT = androgen deprivation therapy; APMR = androgen pathway modulation-resistant; ARPI = androgen receptor pathway inhibitors; BSC = best supportive care; CD3 = cluster of differentiation 3; KLK2 = human kallikrein 2; mCRPC = metastatic castration-resistant prostate cancer; PAS = pasritamig; PCWG = Prostate Cancer Clinical Trials Working Group; PARPi = poly ADP-ribose polymerase inhibitor; PSA = prostate-specific antigen; PSMA = prostate-specific membrane antigen; RLT = radioligand therapy; rPFS = radiographic progression free survival, RECIST 1.1 = Response Evaluation Criteria in Solid Tumors 1.1

Figure 5: Countries planned for participation in comPAS trial



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Prostate Cancer

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