Safety and Efficacy of Pasritamig (PAS) + Docetaxel (DOCE) in Participants With Metastatic Castration-Resistant Prostate Cancer (mCRPC): Initial Results of a Phase 1b Study

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Key Takeaway

PAS + DOCE demonstrated promising clinical activity, and PAS was well-tolerated, with an outpatient regimen in mCRPC[3]

Conclusions

PAS + DOCE demonstrated a safety profile consistent with the established profile of DOCE[5,6]. No CRS (of any grade) was reported

PAS + DOCE showed deep and durable PSA responses in participants previously treated with ARPI, Lu-177 PSMA RLT, and/or chemotherapy

A Phase 3 trial, **KLK2-PASenger**, evaluating PAS + DOCE is now enrolling (NCT07225946). Additional combinations with PAS are being explored in Phase 1 trials

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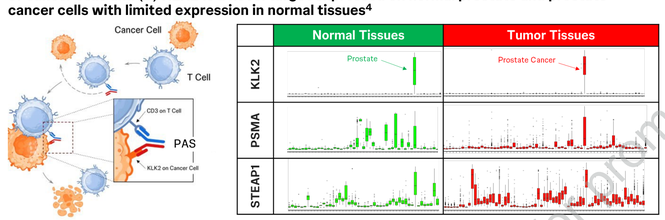
Introduction

- Docetaxel (DOCE) remains a standard of care for patients with metastatic castration-resistant prostate cancer (mCRPC) following disease progression on androgen receptor pathway inhibitors (ARPIs)[1]
- Median overall survival (OS) remains short (~2 years), and despite newer therapies, survival outcomes in mCRPC have not demonstrated meaningful improvement[2]
- Pasritamig (PAS) is a first-in-class human kallikrein 2 (KLK2) T-cell engager (TCE) (**Figure 1**) and was well-tolerated (<10% cytokine release syndrome [CRS], all grade 1; transient fever) with every 6 weeks (Q6W) outpatient dosing and promising single-agent activity in heavily pretreated mCRPC[3]
- We report the initial safety profile and early efficacy signals of PAS + DOCE in mCRPC previously treated with ≥1 ARPI, chemotherapy, and/or lutetium Lu 177 vipivotide tetraxetan prostate-specific membrane antigen radioligand therapy (Lu-177 PSMA RLT)

Objective

- To determine the recommended Phase 2 regimen of PAS + DOCE in an open-label, Phase 1b study in mCRPC (**NCT05818683**)

Figure 1: (A) PAS simultaneously binds KLK2 (encoded by the *KLK2* gene) on prostate cancer cells and CD3 receptor complexes on T cells, leading to T-cell activation and subsequent lysis of cancer cells and (B) KLK2 is a novel target expressed on normal prostate and prostate cancer cells with limited expression in normal tissues[4]



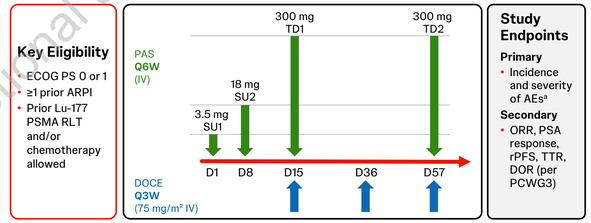
A. First-in-class KLK2xCD3 TCE

B. KLK2 is highly and uniquely expressed in prostate

CD, cluster of differentiation; KLK2, human kallikrein 2; PAS, Pasritamig; PSMA, prostate-specific membrane antigen; STEAP1, six-transmembrane epithelial antigen of the prostate 1; TCE, T-cell engager.

Methods

Figure 2: Study Design and Dosing Schema



[a]Based on NCI-CTCAE v5.0. AEs, adverse events; ARPI, androgen receptor pathway inhibitor; D, day; DOCE, docetaxel; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; Lu-177 PSMA RLT, lutetium Lu 177 vipivotide tetraxetan prostate-specific membrane antigen radioligand therapy; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; ORR, overall response rate; PAS, pasritamig; PCWG3, Prostate Cancer Clinical Trials Working Group 3; PSA, prostate-specific antigen; Q3W, every 3 weeks; Q6W, every 6 weeks; rPFS, radiographic progression-free survival; SU, step-up dose; TD, target dose; TTR, time to response.

Results

Baseline Characteristics

- Participants received a median of 3 prior lines of therapy (range, 1–9) (**Table 1**)

Table 1: Baseline Characteristics

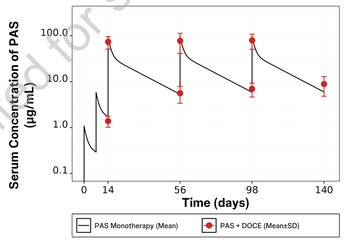
	Total (N=51)
Age, years, median (range)	70.0 (55–84)
ECOG PS, n (%)	
0	19 (37.3)
1	32 (62.7)
Baseline PSA, ng/mL (range)	23 (1.6–744.2)
Disease location, n (%)	
Bone only	26 (51.0)
Lymph node +/- bone without visceral	8 (15.7)
Any visceral	17 (33.3)
Liver	4 (7.8)
Non liver	13 (25.5)
Lines of prior systemic therapy, median (range)	3 (1–9)
Prior therapy, n (%)	
ARPI	51 (100.0)
Taxane chemotherapy	23 (45.1)
Docetaxel	22 (43.1)
Cabazitaxel	11 (21.6)
Lu-177 PSMA RLT	10 (19.6)

Data cut-off December 9, 2025. ARPI, androgen receptor pathway inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; Lu-177 PSMA RLT, lutetium Lu 177 vipivotide tetraxetan prostate-specific membrane antigen radioligand therapy; PSA, prostate-specific antigen.

Pharmacokinetics

- PAS serum concentrations measured at pre-dose and end-of-infusion (approximating C_{trough} and C_{max}, N=50) after 300 mg Q6W dose in combination with DOCE were similar to PAS monotherapy (**Figure 3**)

Figure 3: Pharmacokinetics of PAS + DOCE is Consistent With PAS Monotherapy



Data cut-off July 22, 2025. Profile of mean observed (plot with standard deviation error bars; semilogarithmic plots) serum concentrations of pasritamig administered in combination with docetaxel and mean predicted (solid line) serum concentrations of pasritamig established from monotherapy study (compartment model analysis). DOCE, docetaxel; PAS, pasritamig; SD, standard deviation.

Safety

- Median number of treatment doses for PAS Q6W is 8 (range, 3–12) and for DOCE every 3 weeks (Q3W) is 6 (range, 1–17) (**Table 2**)
- Participants who discontinued DOCE were allowed to continue PAS
- No participants discontinued PAS due to treatment-related adverse events (TRAEs), while 13 (25.5%) participants discontinued DOCE due to TRAEs
- No dose-limiting toxicities were observed
- The most common TRAEs are summarized (**Table 3**)
- No CRS (any grade) or fatal TRAEs were reported
- Most common TRAEs related to PAS included fatigue (33.3%), diarrhea (11.8%), and rash maculopapular (9.8%); no dose reductions were required

Table 2: Exposure and Duration of Treatment[a]

	All Treated (N=51)					
	PAS (Q6W)			DOCE (Q3W)		
	Overall	Taxane-Naive	Taxane-Exposed	Overall	Taxane-Naive	Taxane-Exposed
Duration of treatment, months, median (range)	7.39 (0.5–13.0)	7.51 (0.5–11.5)	6.01 (0.5–13.0)	3.48 (0.0–11.1)	3.81 (0.7–10.3)	3.48 (0.0–11.1)
Cumulative duration of treatment, months, n (%)						
<3 months	51 (100)	28 (100)	23 (100)	51 (100)	28 (100)	23 (100)
≥3 months	39 (76.5)	23 (82.1)	16 (69.6)	32 (62.7)	19 (67.9)	13 (56.5)
≥6 months	33 (64.7)	21 (75.0)	12 (52.5)	12 (23.5)	7 (25.0)	5 (21.7)
Number of treatment doses received, median (range)	8 (3–12)	8 (3–11)	7 (3–12)	6 (1–17)	6 (2–16)	6 (1–17)

[a]Duration of treatment to date. The trial is still ongoing and many participants are continuing treatment. Data cut-off December 9, 2025. DOCE, docetaxel; PAS, pasritamig; Q3W, once every 3 weeks; Q6W, once every 6 weeks.

Table 3: Most Common (≥10%, All Grade) PAS-Related and DOCE-Related TRAEs

	All Grade (N=51)			Grade ≥3 (N=51)		
Preferred Term, n (%)	Overall	PAS-Related	DOCE-Related	Overall	PAS-Related	DOCE-Related
≥1 TRAE	50 (98.0)	31 (60.8)	49 (96.1)	15 (29.4)	1 (2.0)	15 (29.4)
Fatigue	31 (60.8)	17 (33.3)	28 (54.9)	0	0	0
Alopecia	21 (41.2)	0	21 (41.2)	0	0	0
Diarrhea	16 (31.4)	6 (11.8)	15 (29.4)	1 (2.0)	0	1 (2.0)
Nausea	16 (31.4)	3 (5.9)	15 (29.4)	0	0	0
Peripheral edema	14 (27.5)	2 (3.9)	14 (27.5)	0	0	0
Peripheral sensory neuropathy	13 (25.5)	0	13 (25.5)	0	0	0
Dysgeusia	12 (23.5)	4 (7.8)	12 (23.5)	0	0	0
Anemia	9 (17.6)	2 (3.9)	9 (17.6)	4 (7.8)	1 (2.0)[a]	4 (7.8)
Decreased appetite	8 (15.7)	1 (2.0)	8 (15.7)	1 (2.0)	0	1 (2.0)
Nail discoloration	8 (15.7)	0	8 (15.7)	0	0	0
Stomatitis	8 (15.7)	1 (2.0)	8 (15.7)	0	0	0
Infusion-related reaction	6 (11.8)	0	6 (11.8)	0	0	0
Myalgia	6 (11.8)	4 (7.8)	3 (5.9)	0	0	0
Rash maculopapular	6 (11.8)	5 (9.8)	4 (7.8)	0	0	0
Neutropenia	5 (9.8)	0	5 (9.8)	4 (7.8)	0	4 (7.8)

Data cut-off December 9, 2025. Participants are counted only once for any given event, regardless of the number of times they experienced the event. [a]In 1 patient, Grade 3 anemia TRAE was attributed to both PAS and DOCE. DOCE, docetaxel; PAS, pasritamig; TRAE, treatment-related adverse event.

Efficacy

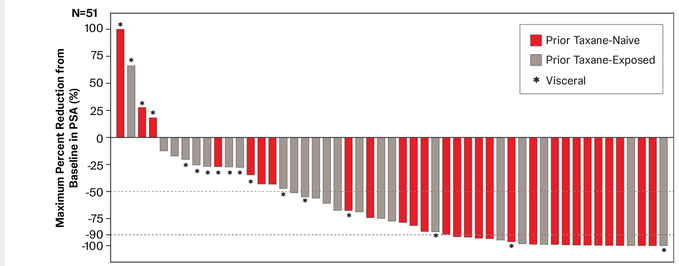
- Overall, the response rates for participants with confirmed reduction in prostate-specific antigen (PSA) levels by 50% (PSA50) and 90% (PSA90) were 64.7% (33/51) and 39.2% (20/51), respectively (**Table 4**)
  - When classified by disease extent, the taxane-naive, bone-only subgroup demonstrated the highest confirmed response rates, with PSA50 at 88.2% (15/17) and PSA90 at 76.5% (13/17)
- PSA50 and PSA90 responses, together with disease control, were observed despite prior taxane exposure (**Table 4, Figure 4, Figure 5**)
- Overall response rates (ORR) of 28.6% (2/7) and 6.7% (1/15) were observed in participants with Response Evaluation Criteria in Solid Tumors (RECIST) measurable disease in the non-visceral and any visceral subgroups, respectively

Table 4: Summary of Confirmed PSA Responses

	Taxane-Naive				Prior Taxane				Overall			
	Bone Only	Lymph Node ± Bone Without Visceral	Any Visceral	Total	Bone Only	Lymph Node ± Bone Without Visceral	Any Visceral	Total	Bone Only	Lymph Node ± Bone Without Visceral	Any Visceral	Total
Analysis set: All Treated, N	17	4	7	28	9	4	10	23	26	8	17	51
PSA50 (confirmed), n (%)	15 (88.2)	4 (100)	2 (28.6)	21 (75.0)	7 (77.8)	2 (50.0)	3 (30.0)	12 (52.2)	22 (84.6)	6 (75.0)	5 (29.4)	33 (64.7)
PSA90 (confirmed), n (%)	13 (76.5)	1 (25.0)	1 (14.3)	15 (53.6)	3 (33.3)	1 (25.0)	1 (10.0)	5 (21.7)	16 (61.5)	2 (25.0)	2 (11.8)	20 (39.2)

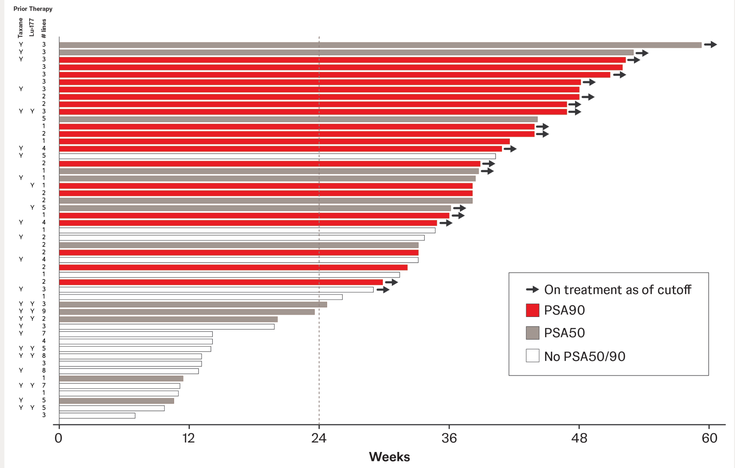
Data cut-off December 9, 2025. PSA, prostate-specific antigen; PSA50, 50% reduction in PSA levels; PSA90, 90% reduction in PSA levels.

Figure 4: Waterfall Plot of Maximum Reduction in PSA



Data cut-off December 9, 2025. The dashed reference lines represent 50% and 90% decrease. Increase greater than 100% is set to 100%. "N" is the number of participants with both baseline and at least one post-baseline assessment. PSA, prostate-specific antigen.

Figure 5: Swimmer Plot Showing Duration on Study and PSA Responses



Data cut-off December 9, 2025. The reference line represents 24 weeks on treatment. Lu-117, lutetium Lu 177 vipivotide tetraxetan; PSA, prostate-specific antigen; PSA50, 50% reduction in PSA levels; PSA90, 90% reduction in PSA levels; Y, yes.

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