Phase 1 Study Results of Pasritamig (JNJ-78278343) in Metastatic Castration-Resistant Prostate Cancer

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Pasritamig | Key Takeaways

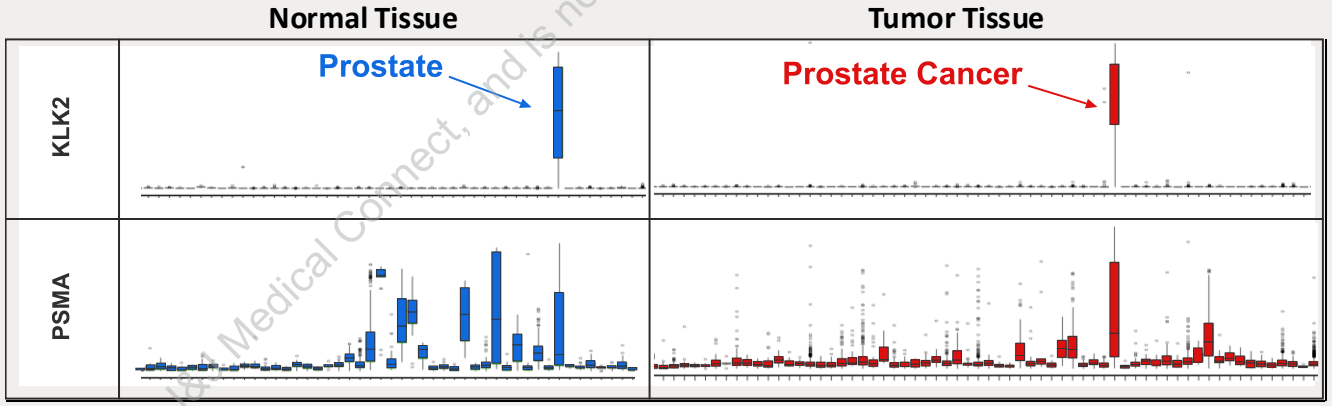
Pasritamig is a first-in-class, first-in-human, bispecific T-cell engager targeting human kallikrein 2, a novel, highly specific, prostate cancer antigen

- **Pasritamig** demonstrated a **remarkable safety** profile **differentiated** from **prior T-cell engagers**
  - **Low rates** of **TRAEs** and **infrequent CRS** (Grade 1 only) with no tocilizumab use at the RP2D
  - Safety of the **RP2D regimen** allowed for **outpatient dosing** on a **patient-friendly, every-6-week** schedule
- Pasritamig achieved **durable disease control** and **rPFS** that **compare favorably** to historical data in heavily pretreated participants with mCRPC[1,2]

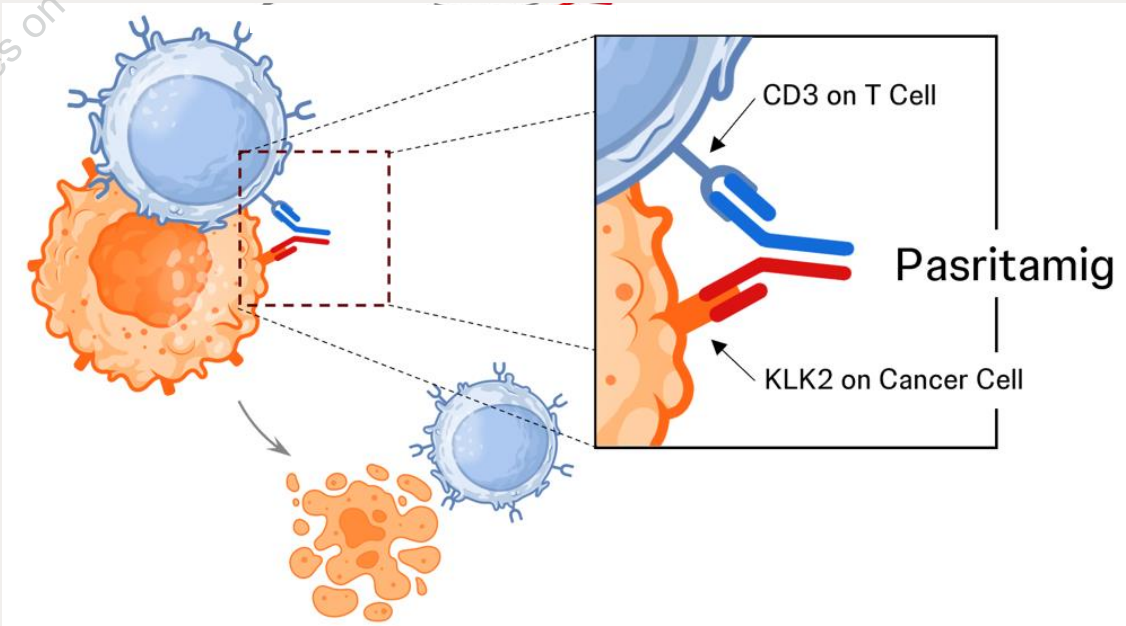
1. Sartor O, de Bono J, Chi KN, et al. Lutetium-177-PSMA-617 for metastatic castration-resistant prostate cancer. N Engl J Med 2021;385(12):1091-1103. 2. De Wit R, de Bono J, Sternberg CN, et al. Cabazitaxel versus abiraterone or enzalutamide in metastatic prostate cancer. N Engl J Med 2019;381(26):2506-2518. CRS, cytokine release syndrome; mCRPC, metastatic castration-resistant prostate cancer; rPFS, radiographic progression-free survival; RP2D, recommended phase 2 dose, TRAEs, treatment-related adverse events.

Pasritamig Is a First-in-Class, Bispecific T-Cell Engager Targeting Human Kallikrein 2, a Novel, Highly Specific, Prostate Cancer Antigen

- **Human kallikrein 2** (encoded by the *KLK2* gene and hereafter referred to as KLK2) is a **novel target** expressed on **prostate cancer** cells with **limited expression in normal tissues**



- **Pasritamig** 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

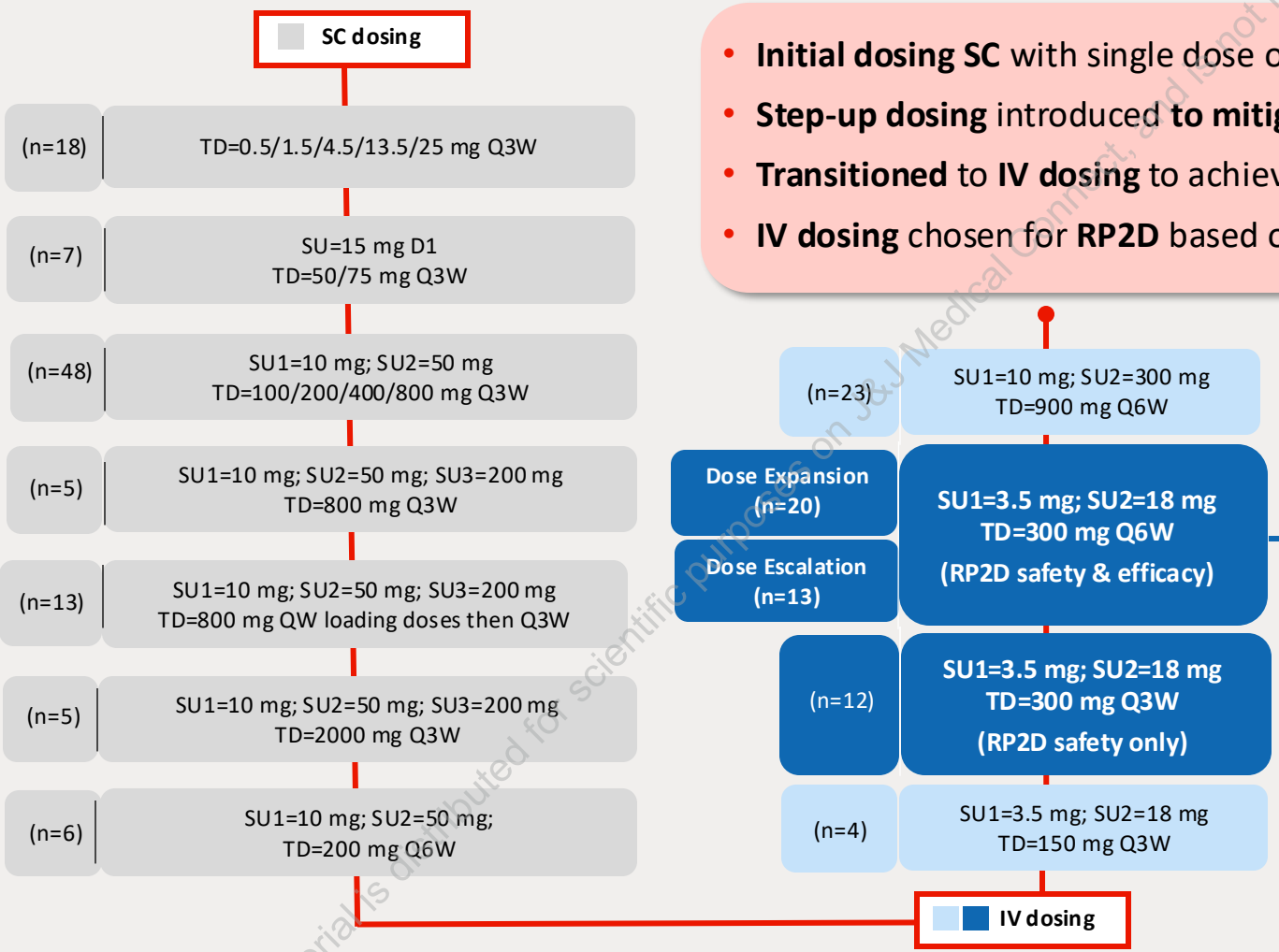


PSMA, prostate-specific membrane antigen.

Phase 1, First-in-Human Study (NCT04898634) of Pasritamig: Dose Escalation and Dose Expansion in mCRPC

Key eligibility

- ECOG PS 0 or 1
- Prior ARPI and/or chemotherapy
- Prior Lu-177 PSMA RLT allowed
- PSA >2 ng/mL and no visceral disease (dose expansion only)



- **Initial dosing SC** with single dose of steroid premedication
- **Step-up dosing** introduced **to mitigate CRS**
- **Transitioned** to **IV dosing** to achieve **higher doses** with **fewer injections**
- **IV dosing** chosen for **RP2D** based on **improved** safety and efficacy profile

Recommended Phase 2 Dose and Schedule

Intravenous

SU1: 3.5 mg Day 1
SU2: 18 mg Day 8
*TD: 300 mg Day 15, then **300 mg Q6W***

All Outpatient

ARPI, androgen receptor pathway inhibitor; CRS, cytokine release syndrome; ECOG; Eastern Cooperative Oncology Group; IV, intravenous; Lu-177 PSMA RLT, lutetium Lu 177 vipivotide tetraxetan prostate-specific membrane antigen radioligand therapy; mCRPC, metastatic castration-resistant prostate cancer; PS, performance status; PSA, prostate-specific antigen; QW, once weekly; Q3/6W, every 3/6 weeks; RP2D, recommended phase 2 dose; SC, subcutaneous; SU, step-up dose; TD, treatment dose.

Baseline Characteristics

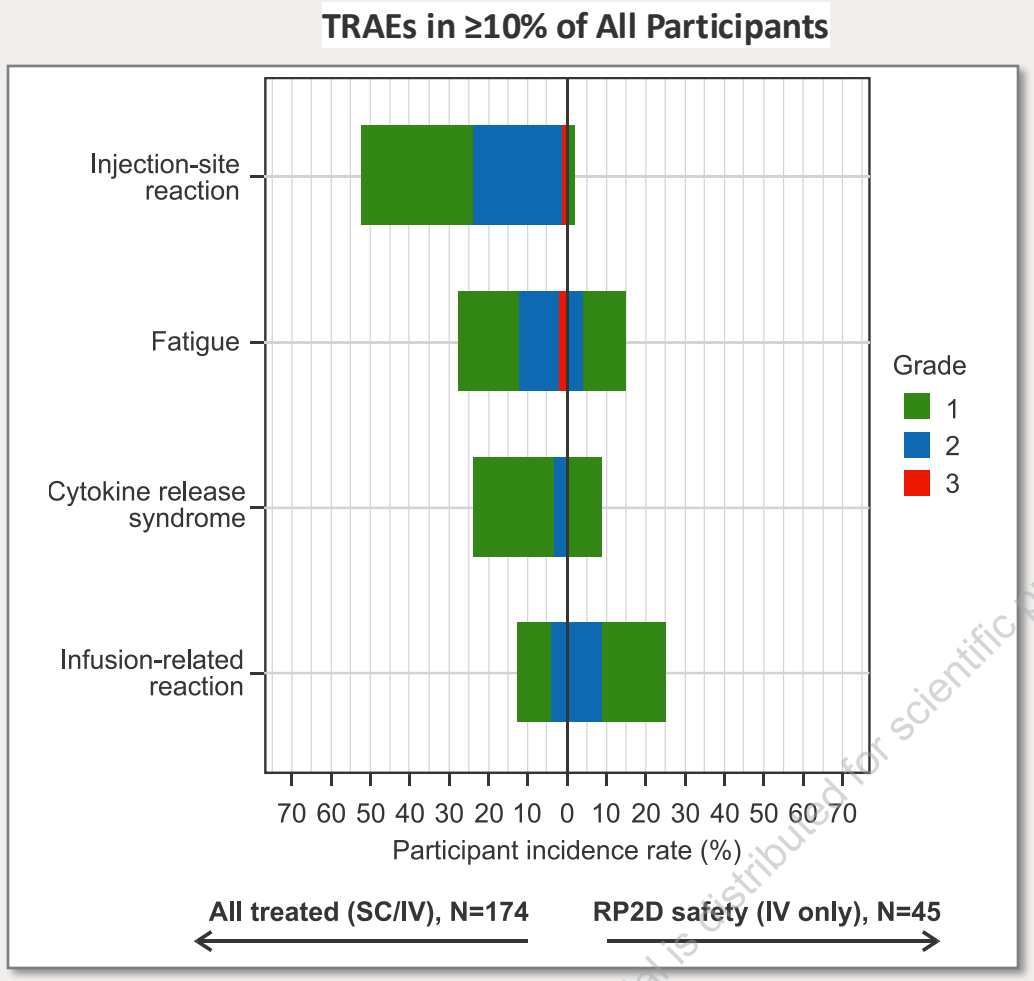
Participants Were Heavily Pre-Treated With a Median of 4 Prior Lines (Range 1–13)

	All-Treated Population (SC/IV)	RP2D Safety Population (IV Only)[a]
	Total N=174	Total N=45[a]
Age, years, median (range)	69.0 (36, 89)	70.0 (36, 89)
ECOG PS, n (%)		
0	88 (50.6)	25 (55.6)
1	86 (49.4)	20 (44.4)
Baseline PSA, ng/mL (range)	74.8 (0.0, 2612.0)	58.4 (0.1, 2117.6)
Disease location,[b] n (%)		
Bone	153 (88.4)	40 (90.9)
Lymph node	81 (46.8)	17 (38.6)
Visceral	42 (24.3)	5 (11.4)
Liver	18 (10.4)	1 (2.3)

	All-Treated Population (SC/IV)	RP2D Safety Population (IV Only)[a]
	Total N=174	Total N=45[a]
Lines of prior systemic therapy, median (range)	**4.0 (1.0, 13.0)**	**4.0 (1.0, 10.0)**
Prior therapy, n (%)		
ARPI	173 (99.4)	45 (100.0)
Taxane chemotherapy[c]	136 (78.2)	34 (75.6)
1 regimen	46 (26.4)	14 (31.1)
>1 regimen	90 (51.7)	20 (44.4)
Lu-177 PSMA RLT	31 (17.8)	17 (37.8)

Data cut-off March 7, 2025. [a]RP2D safety population consists of participants in the all-treated population who received IV 3.5 mg D1, 18 mg D8, 300 mg D15, then 300 mg Q3W (Cohort 19) or Q6W (Cohorts 20 and 22). [b]n=173 (total), n=71 (IV), and n=44 (RP2D safety population). [c]All participants with >1 taxane regimen had both docetaxel and cabazitaxel, except 3 who had only docetaxel. AR, androgen receptor pathway inhibitor; D, Day; ECOG, Eastern Cooperative Oncology Group; IV, intravenous; Lu-177 PSMA RLT, lutetium Lu 177 vipivotide tetraxetan prostate-specific membrane antigen radioligand therapy; PS, performance status; PSA, prostate-specific antigen; Q3/6W; every 3/6 weeks; RP2D, recommended phase 2 dose; SC, subcutaneous.

Safety Profile of Pasritamig Was Favorable With Low Rates of Treatment-Related Adverse Events and Minimal Cytokine Release Syndrome



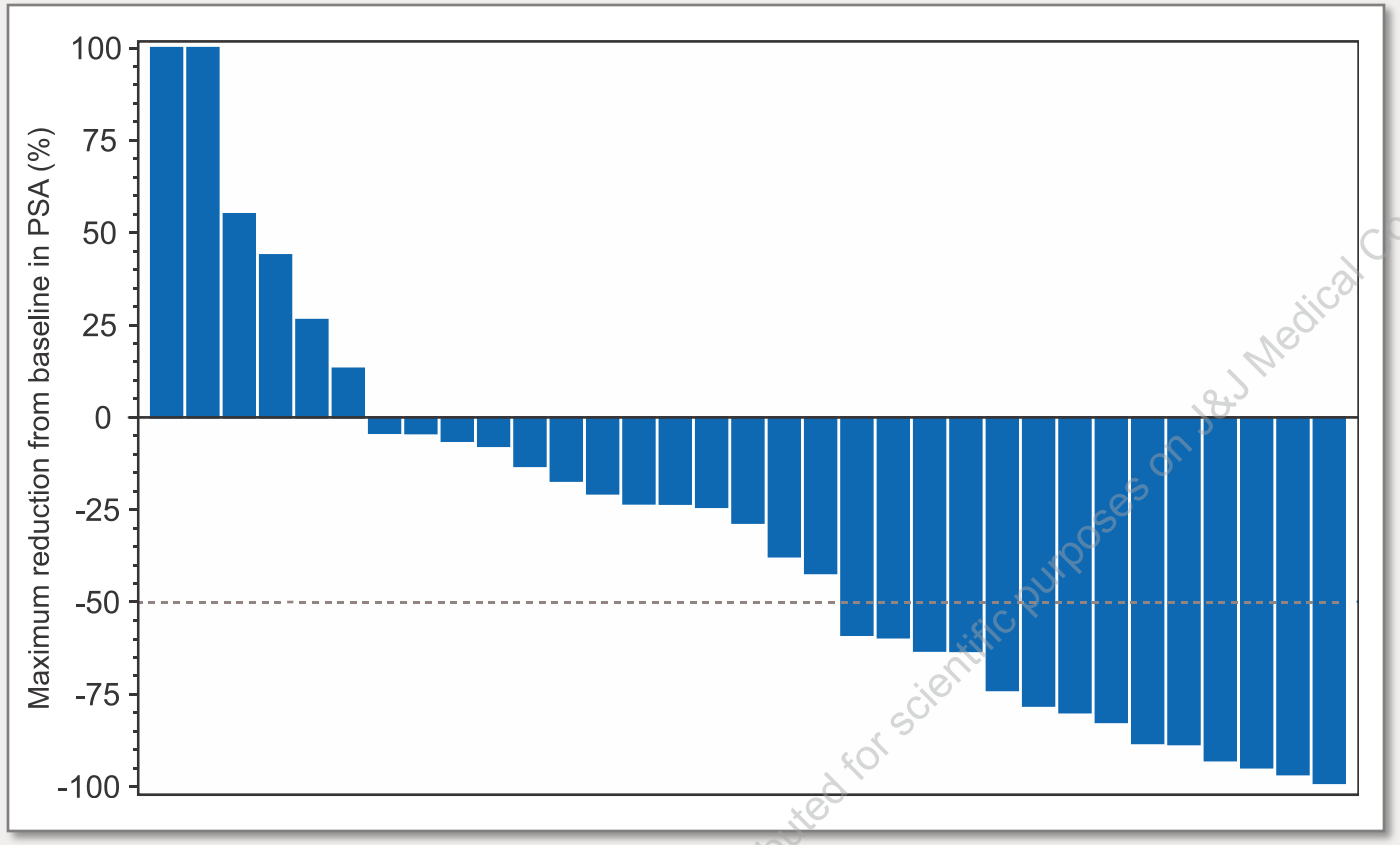
	All-Treated Population (SC/IV)	RP2D Safety Population (IV Only)
	N=174	N=45
Participants with ≥1 TRAE, n (%)	144 (82.8)	27 (60.0)
Serious TRAEs, n (%)	12 (6.9)	2 (4.4)[a]
Grade ≥3 TRAEs, n (%)	17 (9.8)	2 (4.4)
TRAEs leading to treatment discontinuation, n (%)	1 (0.6)	0

RP2D safety population (IV 3.5 mg D1, 18 mg D8, 300 mg D15 then Q3W/Q6W):

- **CRS** occurred in 4 pts (8.9%), **all Grade 1** (fever only) and **did not** require tocilizumab
- **IRRs** were seen **in 24.4%** of participants
  - Management was limited to mostly antipyretics; no steroid or tocilizumab was given
- **No** TRAEs led to treatment **discontinuation, dose reduction, ICANS, or death**
- The **only Grade 3** TRAEs were **transient** AST/ALT increases and neutropenia
- **No DLTs**[b]

Data cut-off March 7, 2025. Participants are counted only once for any given event, regardless of the number of times they experienced the event. [a]The serious TRAEs were both Grade 1 CRS hospitalized for observation. [b]1 DLT of transient Grade 3 ALT/AST increase occurred in the all-treated population after SC 50 mg step-up dose; recovered to Grade 1 in 8 days. ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRS, cytokine release syndrome; D, Day; DLT, dose-limiting toxicity; ICANS, immune-effector cell associated neurotoxicity syndrome; IRR, infusion-related reaction; IV, intravenous; RP2D, recommended phase 2 dose; SC, subcutaneous; TRAE, treatment-related adverse event.

Pasritamig Achieved Rapid and Deep Prostate-Specific Antigen Responses



RP2D efficacy population (IV 3.5 mg D1, 18 mg D8, then 300 mg Q6W):

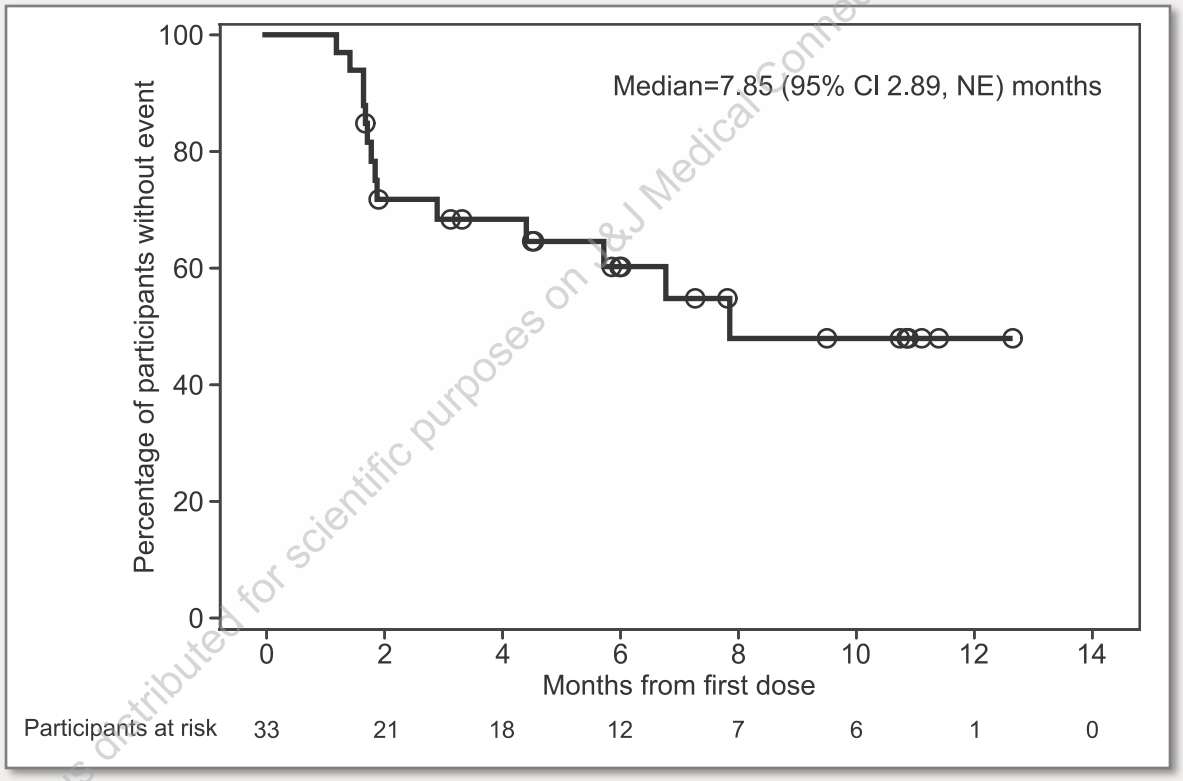
- **PSA decreases** were noted as early as initial step-up doses
- **14/33 (42.4%)** participants achieved **PSA50** at any time
  - **12/33 (36.4%)** participants achieved **confirmed PSA50**

- In the **all-treated population** with measurable disease at baseline (n=84/174), **ORR** was **8.3%** (7/84), not including **1 participant with a CR** who had non-measurable disease at baseline
  - Median (95% CI) **DOR** was **8.9** (3.6, NE) **months**

Data cut-off March 7, 2025. CR, complete response; D, Day; DOR, duration of response; IV, intravenous; NE, not estimable; ORR, overall response rate; PSA, prostate-specific antigen; PSA50, ≥50% decrease from baseline in PSA; RP2D, recommended phase 2 dose.

Responses to Pasritamig Were Durable With Promising Radiographic Progression-Free Survival

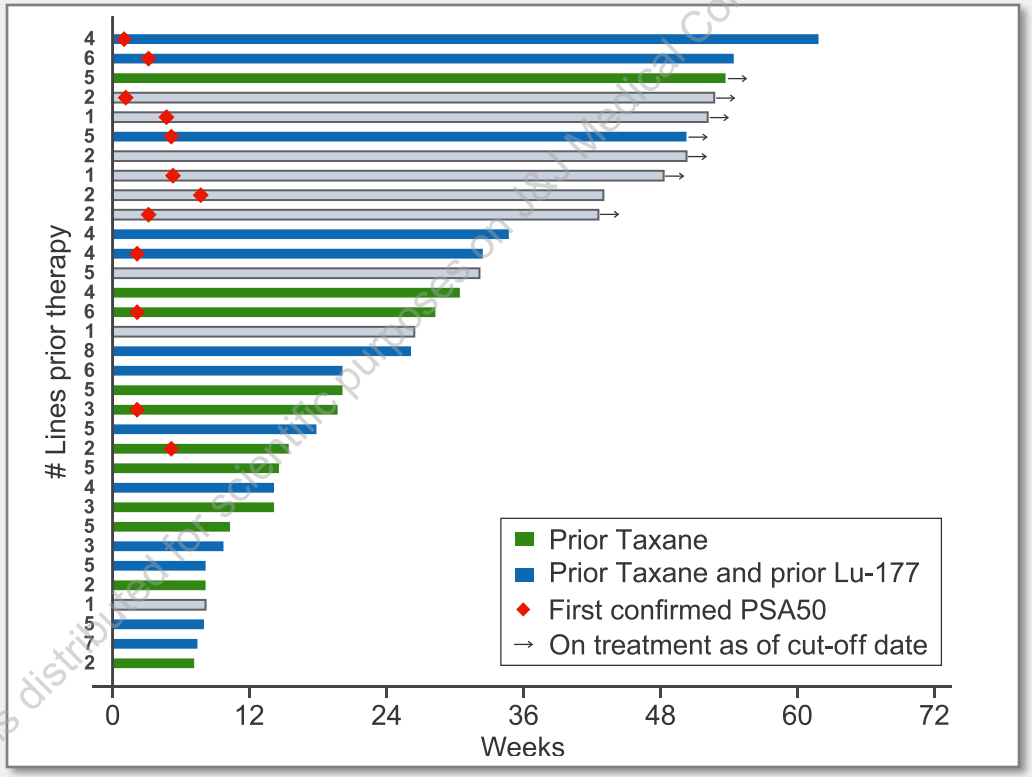
- In the **RP2D efficacy population**, median (95% CI) **rPFS** was **7.9** (2.9, NE) **months**



Data cut-off March 7, 2025. CI, confidence interval; Lu-177, lutetium Lu 177 vipivotide tetraxetan; NE, not estimable; PSA, prostate-specific antigen; PSA50, ≥50% decrease from baseline in PSA; PSMA, prostate-specific membrane antigen; rPFS, radiographic progression-free survival; RP2D, recommended phase 2 dose.

Responses to Pasritamig Were Durable With Promising Radiographic Progression-Free Survival

- **7/33 (21.2%)** participants were on treatment as of data cut-off
- **PSA50 responses** and **durable disease control** were observed **irrespective of prior treatment** with taxanes or PSMA-targeted radioligand therapy



Data cut-off March 7, 2025. CI, confidence interval; Lu-177, lutetium Lu 177 vipivotide tetraxetan; NE, not estimable; PSA, prostate-specific antigen; PSA50, ≥50% decrease from baseline in PSA; PSMA, prostate-specific membrane antigen; rPFS, radiographic progression-free survival; RP2D, recommended phase 2 dose.

Pasritamig (KLK2 x CD3) is a Promising New T-Cell Engager for Prostate Cancer

- **Pasritamig** demonstrated a **remarkable safety** profile
  - **Low rates** of **TRAEs** and **infrequent CRS** (only Grade 1) with no tocilizumab use
  - Safety of the **RP2D regimen** allowed for **outpatient dosing** on a **patient-friendly**, **every-6-week** schedule
  - Facilitates utilization of T-cell engagers in a **community oncology setting**
  - Safety and convenience of the **RP2D regimen** readily support monotherapy and combination therapy approaches
- Pasritamig achieved **durable responses** and **rPFS** that **compare favorably** to historical data in heavily pretreated participants with mCRPC[1,2]

Multiple pivotal studies of **pasritamig** are being developed

1. Sartor O, de Bono J, Chi KN, et al. Lutetium-177-PSMA-617 for metastatic castration-resistant prostate cancer. N Engl J Med 2021;385(12):1091-1103. 2. De Wit R, de Bono J, Sternberg CN, et al. Cabazitaxel versus abiraterone or enzalutamide in metastatic prostate cancer. N Engl J Med 2019;381(26):2506-2518. CRS, cytokine release syndrome; KLK2, human kallikrein 2; mCRPC, metastatic castration-resistant prostate cancer; rPFS, radiographic progression-free survival; RP2D, recommended phase 2 dose, TRAEs, treatment-related adverse events.

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These data are published in our simultaneous *J Clin Oncol* article