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Sacituzumab Tirumotecan (sac-TMT) + Pembrolizumab (Pembro) in metastatic castration-resistant prostate cancer (mCRPC): Results from phase II MK-2870-002/SKB264-II-06 Study

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Background

Novel therapies are needed to improve outcomes in mCRPC. Sac-TMT (MK-2870/SKB264) is a TROP2-targeting ADC with a topoisomerase I inhibitor payload KL610023. We present results from Cohort D of the MK-2870-002/SKB264-II-06 study evaluating sac-TMT + pembro in participants (pts) with mCRPC.

Methods

Male pts aged ≥18 y with confirmed mCRPC and key eligibility criteria were enrolled: 1) PCWG-modified RECIST 1.1 measurable disease or detectable bone metastasis per PCWG guideline, 2) 1 or 2 prior next-generation hormonal agents but ≤1 chemotherapy regimen for mCRPC, 3) ECOG PS of 0 or 1. Pts received IV sac-TMT 4 or 5 mg/kg on days 1, 15, and 29 + IV pembro 400 mg on day 1 of each 42-day cycle until PD or unacceptable toxicity. Primary endpoints were dose-limiting toxicity (DLT), AEs, ORR per PCWG-modified RECIST 1.1, and PSA50 response rate; secondary endpoints included disease control rate (DCR), duration of response (DOR), and radiographic PFS (rPFS).

Results

Of 46 pts in Cohort D, 10 received sac-TMT 4 mg/kg + pembro and 36 received sac-TMT 5 mg/kg + pembro. More pts in the sac-TMT 5 mg/kg vs 4 mg/kg group received ≥3 prior lines of therapy (44% vs 0%, respectively) and prior docetaxel (64% vs 30%). By data cutoff (Nov 18, 2024), median (range) follow-up was 10.8 (10.1–11.3) mo for sac-TMT 4 mg/kg and 12.9 (11.0–17.9) mo for sac-TMT 5 mg/kg. No pts in either group had a DLT. Grade ≥3 treatment-related AEs (TRAEs) occurred in 5/10 pts (50%) with sac-TMT 4 mg/kg and 25/36 pts (69%) with sac-TMT 5 mg/kg. TRAEs led to discontinuation of any treatment in 1 pt (10%) and 7 pts (19%), to discontinuation of sac-TMT in 1 pt (10%) and 2 pts (6%), and to death in no pts and 1 pt (3%; sepsis), respectively. Efficacy shown in table.

Conclusions

Sac-TMT + pembro had encouraging antitumor activity with a manageable safety profile in pts with mCRPC, warranting further investigation of sac-TMT 4 mg/kg + pembro in this population.Table: 2421P

	Sac-TMT 4 mg/kg + Pembro n = 10	Sac-TMT 5 mg/kg + Pembro n = 36	Sac-TMT (4 mg/kg + 5 mg/kg) + Pembro n = 46
PSA50 response rate (95% CI),[a] %	40 (12.2–73.8)	36 (20.8–53.8)	37 (23.2–52.5)
rPFS, median (95% CI),[b] mo	NR (2.1–NC)	11.6 (8.9–NC)	12.6 (11.3–NC)
Pts with measurable disease at baseline	n = 4	n = 15	n = 19
ORR (95% CI),[b] %	75 (19.4–99.4)	40 (16.3–67.7)	47 (24.4–71.1)
DCR (95% CI),[b] %	100 (39.8–100.0)	87 (59.5–98.3)	90 (66.9–98.7)

NC, not calculated; NR, not reached; PCWG, Prostate Cancer Working Group; PSA, prostate-specific antigen. [a]Proportion of pts with a decrease in PSA from baseline ≥50% measured twice ≥3 wk apart. [b]Per PCWG-modified RECIST v1.1.

Clinical trial identification

NCT05642780.

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Legal entity responsible for the study

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Disclosure

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