

Efficacy and safety of meivrometostat (M) in combination with enzalutamide (E) in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC): Data from a phase 1 study

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Background: M is a potent and selective inhibitor of enhancer of zeste homolog 2. M 1250 mg twice daily (BID) on an empty stomach + E + androgen deprivation therapy showed improved outcomes vs E alone in pts with mCRPC, with a manageable adverse event (AE) profile, in the randomized, dose-expansion part of a phase 1 study (NCT03460977). We report efficacy and safety data from 2 pt cohorts (2A & 2C) who received M 875 mg BID with food + E.

Methods: Pts with mCRPC who received prior abiraterone and/or E (2A) or prior abiraterone (2C), ≤1 prior chemotherapy in any setting, with evidence of progression per modified Prostate Cancer Working Group 3 criteria were included. Primary endpoints were radiographic progression-free

survival (rPFS) per investigator assessment and safety. Secondary endpoints included objective response (OR) by RECIST 1.1 (for pts with measurable disease at baseline) and decline in prostate-specific antigen of $\geq 50\%$ from baseline (PSA₅₀).

Results: As of September 1, 2025, 29 pts had received M 875 mg BID with food + E (2A, n=15; 2C, n=14). Median (range) age was 74 (61–86) years in 2A and 73 (55–83) years in 2C. In 2A, 9 (60.0%) pts had received abiraterone and 9 (60%) pts had received E; in 2C, 14 (100%) pts received prior abiraterone and were E naive. Efficacy and safety outcomes for 2A and 2C are shown (Table). Six confirmed events (5 progressive disease, 1 death) were observed in 2A and 4 (all progressive disease) in 2C; median (90% CI) rPFS was 14.3 (2.0, not estimable [NE]) months in 2A and NE (6.2, NE) months in 2C. Confirmed PSA₅₀ (95% CI) was observed in 6 (40.0%) (16.3, 67.7) pts in 2A and 6 (42.9%) (17.7, 71.1) pts in 2C. In pts with measurable disease at baseline (2A, n=4; 2C, n=6), confirmed OR rate (95% CI) was 25.0% (0.6, 80.6; 1 partial response) in 2A and 16.7% (0.4, 64.1; 1 partial response) in 2C. For 2A+2C combined, most common treatment-emergent AEs (TEAEs) were diarrhea (48.3%), thrombocytopenia (48.3%), and decreased appetite (44.8%). Grade ≥ 3 TEAEs were observed in 41.3% pts (most common: thrombocytopenia, anemia, asthenic conditions, and hypokalemia). Grade ≥ 3 TEAEs considered related to M were reported in 31.0% pts. There were no treatment-related deaths.

Conclusions: M 875 mg BID with food + E shows promising outcomes in pts with mCRPC and a manageable AE profile. Further investigation of M + E in pts with mCRPC is warranted.

Table.

	2A (n=15)	2C (n=14)	2A + 2C (n=29)
Efficacy			
Median rPFS (90% CI), months	14.3 (2.0, NE)	NE (6.2, NE)	–
OR (95% CI), %	25.0 (0.6, 80.6)	16.7 (0.4, 64.1)	–
PSA ₅₀ (95% CI), %	40.0 (16.3, 67.7)	42.9 (17.7, 71.1)	–
Safety, n (%)			
Any TEAE	15 (100)	14 (100)	29 (100)
Grade ≥3	6 (40.0)	6 (42.9)	12 (41.4)
TEAE related to M	15 (100)	13 (92.9)	28 (96.6)
Grade ≥3	4 (26.7)	5 (35.7)	9 (31.0)

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