

LBA56
Capivasertib (capi) + abiraterone (abi) vs placebo (pbo) + abi in patients (pts) with PTEN-deficient metastatic hormone-sensitive prostate cancer (mHSPC): Updated overall survival (OS) from CAPItello-281

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Background

In *de novo* mHSPC (also known as metastatic androgen pathway modulation-naïve/sensitive prostate cancer), PTEN deficiency is associated with poor prognosis despite current standard of care. CAPItello-281 (NCT04493853) met its primary endpoint showing a statistically significant radiographic progression-free survival (rPFS) benefit with capi + abi vs pbo + abi in PTEN-deficient *de novo* mHSPC (maturity: 39.3% rPFS; 26.4% OS). To provide more mature data, a descriptive analysis of efficacy, including OS (41.6% maturity), and safety for CAPItello-281 was conducted.

Methods

Pts with *de novo* mHSPC and PTEN-deficient tumours (defined as ≥90% of viable malignant cells with no specific cytoplasmic staining by immunohistochemistry [IHC]) received capi or pbo (1:1) + abi, pred and androgen deprivation therapy. OS was a descriptive alpha-controlled key secondary endpoint; rPFS was descriptive. Efficacy in post hoc exploratory PTEN deficiency (by IHC) subgroups and safety were also assessed.

Results

1012 pts received capi + abi (N=507) or pbo + abi (N=505). At this ad hoc data cutoff (DCO; 9 March 2026), the HR for OS was improved from the primary DCO and favoured capi + abi vs pbo + abi (41.6% maturity; HR 0.82 [95% CI 0.68, 0.99]; median OS 57.4 vs 46.5 mo; table). rPFS favoured capi + abi (52.6% maturity; 0.83 [0.70, 0.99]; 35.5 vs 26.0 mo). OS HRs at increasing PTEN-deficiency cutoffs (≥95%, n=814 to 100%, n=331) ranged from 0.76–0.74. With 17 mo additional follow-up, the capi + abi safety profile was consistent with the primary DCO.Table: LBA56

Overall population	Ad hoc DCO (9 Mar 2026)		Primary DCO (7 Oct 2024)	
	Capi + abi (N=507)	Pbo + abi (N=505)	Capi + abi (N=507)	Pbo + abi (N=505)
OS				
E, n (%)	421 (41.6)	267 (26.4)		
Median, mo (95% CI)	57.4 (47.0, NC)	46.5 (40.7, 53.2)	NC (42.5, NC)	NC (NC, NC)
HR (95% CI)	0.82 (0.68, 0.99)	0.90 (0.71, 1.15)		

Overall population	Ad hoc DCO (9 Mar 2026)		Primary DCO (7 Oct 2024)	
	Capi + abi (N=507)	Pbo + abi (N=505)	Capi + abi (N=507)	Pbo + abi (N=505)
<i>P</i>	0.044*	0.401		
rPFS				
E, n (%)	532 (52.6)	398 (39.3)		
Median, mo (95% CI)	35.5 (29.7, 40.5)	26.0 (22.4, 31.3)	33.2 (25.8, 44.2)	25.7 (22.0, 29.9)
HR (95% CI)	0.83 (0.70, 0.99)	0.81 (0.66, 0.98)		
<i>P</i>	0.033 (nominal)†	0.034		

*Descriptive OS analysis: alpha controlled, did not meet statistical significance; †Descriptive rPFS analysis, not formally tested. CI, confidence interval; E, events; HR, hazard ratio, NC, not calculable.

Conclusions

This descriptive analysis demonstrates an improved HR for OS vs the primary DCO and consistent rPFS benefit with capi + abi vs pbo + abi, addressing the poor outcomes and unmet need in PTEN-deficient *de novo* mHSPC. The safety profile of capi + abi remains consistent with primary DCO. Capi + abi represents a first-in-class targeted treatment for this population.

Clinical trial identification

NCT04493853.

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