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LBA87

EMBARK: Overall survival with enzalutamide in biochemically recurrent prostate cancer

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Background

The phase 3 EMBARK trial (NCT02319837) showed significant improvements in metastasis-free survival (MFS) and secondary efficacy endpoints with enzalutamide plus leuprolide (enza combo) and enzalutamide monotherapy (enza mono) vs leuprolide alone (LA). This analysis presents final overall survival (OS) data and other secondary efficacy outcomes from EMBARK.

Methods

Patients (pts) with high-risk biochemically recurrent prostate cancer (hrBCR), defined as a prostate-specific antigen (PSA) doubling time of ≤9 months, were randomised 1:1:1 to receive enza combo, LA, or enza mono. The primary endpoint was MFS for enza combo vs LA. OS, the time between randomisation and death from any cause, was an alpha-protected (final adjusted 2-sided alpha level of 0.0499) key secondary endpoint. Other secondary endpoints included MFS for enza mono vs LA, time to PSA progression, time to first use of new antineoplastic therapy, and time to first symptomatic skeletal event (SSE). Progression-free survival on first subsequent therapy (PFS2) was an exploratory endpoint. Survival data were collected every 12 weeks until final OS analysis, planned after 271 events. At final data cutoff (27 May, 2025), OS was compared between treatment groups with a 2-sided stratified log-rank test. Hazard ratios (HRs) were estimated by stratified Cox models. Pts without an OS event were censored at last contact.

Results

Enza combo reduced the risk of death by 40.3% vs LA (HR 0.597; 95% CI 0.444–0.804; P=0.0006). Enza mono reduced the risk of death by 17.0% vs LA, which did not reach statistical significance (HR 0.830; 95% CI 0.630–1.095; P=0.1867). Enza combo and enza mono both significantly prolonged time to first use of new antineoplastic therapy, time to first SSE, and PFS2 (Table). Safety findings were consistent with prior publications.

Conclusions

Enza combo reduced the risk of death vs LA by over 40%. This unprecedented survival advantage reinforces the MFS results and further supports enza combo as the standard of care for pts with hrBCR.Table: LBA87

Endpoint	Enza combo† (n=355)			Enza mono† (n=355)		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
OS‡§	0.597	0.444–0.804	0.0006‖	0.830	0.630–1.095	0.1867‖
First use of new antineoplastic therapy	0.374	0.287–0.489	<0.0001¶	0.570	0.450–0.721	<0.0001¶

Endpoint	Enza combo† (n=355)			Enza mono† (n=355)		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
First SSE	0.398	0.221–0.716	0.0015¶	0.493	0.283–0.857	0.0105¶
PFS2	0.563	0.420–0.755	<0.0001¶	0.761	0.581–0.998	0.0465¶

†LA (n=358) was the comparator. ‡Median follow-up time: enza combo, 94.2 months; LA, 94.0 months; enza mono, 93.8 months. §78.9% (95% CI, 73.9–83.1%), 69.5% (95% CI, 64.0–74.3%), and 73.1% (95% CI, 67.6–77.9%) of pts survived ≥8 years for enza combo, LA, and enza mono, respectively. ‖*P*<0.0499 was statistically significant. ¶Nominal *P*-value.

Clinical trial identification

NCT02319837.

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Disclosure

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