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Results from KEYNOTE-B49: A phase 3, randomized, double-blind study of pembrolizumab (pembro) vs placebo (pbo) plus chemotherapy (CT) in participants (pts) with HR+/HER2– advanced breast cancer (ABC)

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Background

After failure of endocrine-based therapy (ET), patients with HR+/HER2– ABC have poor outcomes. We report results of the phase 3 KEYNOTE-B49 (NCT04895358) study of pembro + CT vs pbo + CT in pts with PD-L1–positive HR+/HER2– ABC.

Methods

Pts with locally recurrent inoperable or metastatic HR+/HER2– ABC with PD-L1 CPS ≥1 who had prior ET and were candidates for first-line CT were randomized to pembro 200 mg or pbo Q3W for up to 35 cycles + CT (paclitaxel, nab-paclitaxel, liposomal doxorubicin, or capecitabine). The primary endpoint was PFS per RECIST v1.1 by BICR in pts with PD-L1 CPS ≥1. The key secondary endpoint was OS in pts with PD-L1 CPS ≥1. Following a protocol amendment, the sample size was reduced due to low PD-L1 prevalence.

Results

342 pts were randomized. Median age was 57 y; 99.4% of pts in the pembro + CT arm and 98.8% in the pbo + CT arm had prior CDK4/6i. At primary analysis (data cutoff, Sep 22, 2025; median follow-up, 29.1 mo), pembro + CT showed statistically significant improvement in PFS vs pbo + CT (HR, 0.74; 95% CI, 0.58–0.95; *P* = 0.0089; table). In pts with PD-L1 CPS ≥10, the HR for PFS (0.59; 95% CI, 0.35–0.98) favored pembro + CT (median [95% CI] PFS, 7.5 [4.2–10.3] mo in the pembro + CT arm and 4.4 [4.0–8.3] mo in the pbo + CT arm). At final analysis (data cutoff, Mar 16, 2026; median follow-up, 34.9 mo), PFS benefit was maintained (HR, 0.74; 95% CI, 0.58–0.95), but there was no significant difference in OS (HR, 1.04; 95% CI, 0.81–1.33; *P* = 0.6185; table). Grade ≥3 treatment-related AEs occurred in 37.6% in the pembro + CT arm and 32.7% in the pbo + CT arm; 11.2% and 5.4% discontinued treatment due to treatment-related AEs, respectively.

Conclusions

In pts with PD-L1 CPS ≥1 HR+/HER2– ABC, pembro + CT demonstrated a statistically significant improvement in PFS, indicating a 26% risk reduction, and a manageable safety profile. A numerical effect favoring pembro + CT for PFS was observed in pts with PD-L1 CPS ≥10. Table: LBA51

	Pembro + CT	Pbo + CT
Primary analysis for PFS		
PD-L1 CPS ≥1 ^a		

	Pembro + CT	Pbo + CT
Events, n/N	124/171	139/171
Median (95% CI), mo	6.7 (6.2–8.3)	6.0 (4.2–8.1)
HR (95% CI)	0.74 (0.58–0.95); <i>P</i> = 0.0089	
Final analysis for OS		
PD-L1 CPS ≥1 ^a		
Events, n/N	126/171	124/171
Median (95% CI), mo	21.0 (18.9–22.9)	22.2 (17.6–26.3)
HR (95% CI)	1.04 (0.81–1.33); <i>P</i> = 0.6185	

^aMultiplicity was controlled at α = 0.025 (1-sided)

Clinical trial identification

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