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Perioperative pembrolizumab (pembro) or enfortumab vedotin (EV) plus pembro in pts with muscle-invasive bladder cancer (MIBC) who are cisplatin-ineligible: Ad hoc analysis from KEYNOTE-905

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Background

Primary results of the phase 3 KEYNOTE-905/EV-303 study (NCT03924895) showed significantly improved event-free survival (EFS), overall survival (OS), and pathological complete response (pCR) with perioperative EV + pembro added to radical cystectomy vs cystectomy alone (control) in 344 concurrently randomized pts with MIBC who were cisplatin-ineligible or declining. Here, we report results for pembro or EV + pembro vs control.

Methods

Eligible pts had centrally assessed T2-T4aN0M0 or T1-T4aN1M0 MIBC and were ineligible for or declined cisplatin. The study initially randomized pts to perioperative pembro vs control; an EV + pembro arm was added in August 2020. EFS, pCR (pT0N0), and pathological downstaging (pDS; <pT2 and N0) were analyzed ad hoc in pts concurrently randomized to all 3 arms until randomization to the pembro arm was stopped in November 2022. No formal statistical testing was performed.

Results

This analysis included 255 pts (pembro: n=83; EV + pembro: n=85; control: n=87). As of June 6, 2025, median follow-up was 42.0 mo (range, 12.9–53.7). Median (95% CI) EFS was 28.7 mo (13.9–not reached [NR]) with pembro, NR (41.2–NR) with EV + pembro, and 15.7 mo (9.5–31.6) with control; at 2 yrs, an estimated 55.8%, 75.8%, and 41.0% of pts were event-free. EFS HR (95% CI) was 0.71 (0.47–1.07) for pembro vs control and 0.40 (0.25–0.65) for EV + pembro vs control. pCR rates (95% CI) were 25.3% (16.4–36.0) with pembro, 58.8% (47.6–69.4) with EV + pembro, and 10.3% (4.8–18.7) with control. pDS rates (95% CI) were 33.7% (23.7–44.9), 65.9% (54.8–75.8), and 14.9% (8.2–24.2), respectively. Treatment-emergent AEs occurred in 96% (gr ≥3, 70%) of pts in the pembro arm, 100% (gr ≥3, 69%) in the EV + pembro arm, and 63% (gr ≥3, 42%) in the control arm.

Conclusions

Ad hoc efficacy outcomes in KEYNOTE-905 favored EV + pembro vs control in pts concurrently randomized to all 3 arms, consistent with primary study results. Furthermore, EFS, pCR, and pDS in the pembro arm indicate activity of perioperative pembro in this setting. EV + pembro is the only FDA-approved perioperative regimen for pts with MIBC who are cisplatin-ineligible.

Clinical trial identification

KEYNOTE-905/EV-303. NCT03924895.

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Legal entity responsible for the study

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Disclosure

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