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Enfortumab vedotin plus pembrolizumab (EV + P) as first-line (1L) treatment in recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC): Results from a cohort of the EV-202 trial

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Background

Patients (pts) with R/M HNSCC have a poor prognosis despite treatment advancements. P +/- chemotherapy is the standard of care for R/M HNSCC. EV, a nectin-4-directed ADC, demonstrated clinically meaningful activity as monotherapy in pts with heavily pretreated R/M HNSCC, with a confirmed objective response rate (cORR) of 23.9% and median duration of response (DOR) not reached (NR) after a median follow-up (f/u) of 9.3 months. EV-202 (NCT04225117) is an international phase 2 basket study evaluating the efficacy and safety of EV +/- P in various solid tumors. Here, we present primary results from cohort 9 (1L EV + P in R/M HNSCC).

Methods

Pts with R/M HNSCC, PD-L1 combined positive score (CPS) ≥1, ECOG PS 0–1 and no prior systemic therapy in R/M setting (systemic therapy completed >6 mo prior for locoregional disease allowed) were eligible. Pts received EV (1.25 mg/kg IV) on days 1, 8 and P (200 mg IV) on day 1 in 21-day cycles. Primary endpoint: investigator-assessed cORR (RECIST v1.1). Secondary endpoints: DOR, disease control rate (DCR), progression-free survival (PFS), overall survival (OS) and safety.

Results

41 pts were enrolled; 76% male, median age: 67 y, 27% had HPV+ disease, 39% had PD-L1 CPS 1-19 and 61% had CPS ≥20. At data cutoff (25 Feb 2025), median f/u was 11.0 mo (95% CI: 9.5, 12.1). Median number of treatment cycles was 6.0 for EV and 6.0 for P. cORR was 39.0% (95% CI: 24.2, 55.5) overall; 43.8% in PD-L1 CPS 1-19 and 36% in CPS ≥20. Complete response rate was 9.8%; DCR was 75.6% (95% CI: 59.7, 87.6); median DOR was NR; DOR rate at 6 mo was 81.7% (95% CI: 42.0, 95.4); median PFS was 5.1 mo (95% CI: 3.5, NE); and median OS is not yet mature. Grade ≥3 treatment-emergent adverse events occurred in 70.7% of pts; most commonly (>5%) fatigue (9.8%) and acute respiratory failure, dehydration, dysphagia, maculopapular rash, syncope and tumor bleeding (all 7.3%).

Conclusions

EV + P demonstrates promising clinical activity in 1L pts with PD-L1 CPS ≥1 R/M HNSCC with an encouraging antitumor response rate that met the protocol-defined efficacy threshold and was often durable. Safety profile was consistent with previous reports, reinforcing the manageable tolerability profile of EV + P.

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Legal entity responsible for the study

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Disclosure

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