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Disitamab vedotin (DV) plus toripalimab (T) versus chemotherapy (C) in first-line (1L) locally advanced or metastatic urothelial carcinoma (la/mUC) with HER2-expression

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Background

DV+T showed encouraging efficacy in patients (pts) with previously untreated or chemo-refractory HER2-unselected la/mUC in a phase 1b/2 trial, with better efficacy in those with HER2 expression (Zhou et al, Ann Oncol, 2024). Based on the data, RC48-C016, an open-label, multicenter, randomized phase 3 trial, was conducted to evaluate 1L treatment of DV+T vs C (gemcitabine+ cisplatin/carboplatin) in pts with HER2-expressing la/mUC in China.

Methods

Eligible pts with previously untreated, histopathologically confirmed, unresectable la/mUC expressing HER2 (centrally assessed as IHC 1+, 2+ or 3+) were randomized (1:1) to receive either DV+T or C with stratification factors of cisplatin eligibility (yes vs no), visceral metastases (yes vs no), and HER2 expression (IHC 1+ vs IHC 2+/3+). Tumors were assessed every 8 weeks by both blinded independent review committee (BIRC) and investigators per RECIST v 1.1. The dual primary endpoints were BIRC-assessed progression-free survival (PFS) and overall survival (OS). We report the results from the planned interim analysis of this study.

Results

A total of 484 pts were randomized (DV+T: n=243; C: n=241). Baseline characteristics were balanced between the two groups. As of Mar 31, 2025, the median follow-up for survival was 18.2 months. PFS was significantly longer in the DV+T group than the C group (median, 13.1 vs 6.5 months; hazard ratio [HR], 0.36; 95% confidence interval [CI], 0.28-0.46; P<0.0001). Prolonged OS was also observed with DV+T (median, 31.5 vs 16.9 months; HR, 0.54; 95% CI, 0.41-0.73; P<0.0001). The PFS and OS benefits were consistent across all the prespecified subgroups, including cisplatin eligibility status, visceral metastases status, and HER2 expression levels. The BIRC-assessed objective response rate was 76.1% and 50.2% in the DV+T and C groups, respectively. Investigator assessments of PFS and tumor response were aligned with BIRC. The safety profile of DV+T was more favorable than C (grade ≥3 treatment-related adverse events: 55.1% with DV+T and 86.9% with C).

Conclusions

DV+T significantly improved outcomes over C in pts with untreated HER2-expressing la/mUC.

Clinical trial identification

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Legal entity responsible for the study

RemeGen.

Funding

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Disclosure

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