MADRID 2026 ESMO congress

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A phase II multicenter study of neoadjuvant disitamab vedotin combined with gemcitabine in MIBC patients with HER2 2 3+: Interim prognostic outcomes

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Background

Cisplatin-based neoadjuvant therapy for MIBC is limited by toxicity, especially in patients with renal dysfunction, neuropathy, or poor cardiac function. The HER2-ADC disitamab vedotin (RC48) has shown better efficacy and safety in advanced urothelial carcinoma. ADC plus immune checkpoint inhibitors also carry risks of immune-related AEs. We evaluated RC48 plus gemcitabine (GD) as neoadjuvant therapy for MIBC to explore a novel, tolerable regimen and report interim prognostic outcomes.

Methods

This non-randomized study (NCT05723991) enrolled T2-T4aNxM0 MIBC patients with predominant urothelial carcinoma, HER2 2+/3+, who were cisplatin-ineligible or refused cisplatin and planned RC+PLND. Patients received 3 or 4 cycles of GD (RC48 2 mg/kg d1, gemcitabine 1000 mg/m^2 d2, q2w). After neoadjuvant therapy, RC+PLND was performed within 4 weeks. Primary endpoint: pCR. Secondary: TRAEs, EFS.

Results

30 patients enrolled (mean 63±9 y; 28 male). 14 had stage >T2N0M0, 21 cisplatin-ineligible. 3 cycles: 13 pts; 4 cycles: 17 pts. Among the 3-cycle cohort, 10 patients ultimately underwent RC, 2 achieved clinical complete response (cCR), and 1 achieved clinical partial response (cPR). In the 4-cycle cohort, 14 patients underwent RC, 2 achieved cPR, and 1 achieved cCR. Post-RC pathology revealed an overall pCR rate of 62.5% (15/24): 40% (4/10) in the 3-cycle group and 78.6% (11/14) in the 4-cycle group. As of May 11, 2026, the median follow-up duration for all patients receiving GD was 27 months; median EFS was not reached. The 1-year, 2-year, and 3-year EFS rates were 92.4%, 88.0%, and 53.3%, respectively. Among patients who underwent RC as planned, the 1-year, 2-year, and 3-year EFS rates were 100%, 94.7%, and 73.7%, respectively. In patients who achieved pCR at RC, the corresponding EFS rates were 100%, 90.9%, and 77.9%. No grade >3 TRAEs were observed during neoadjuvant therapy. The most common TRAEs were elevated alanine aminotransferase (ALT, 40%), elevated aspartate aminotransferase (AST, 36.7%), decreased appetite (26.7%), limb numbness (26.7%), and alopecia (23.3%).

Conclusions

Neoadjuvant GD achieved high pCR rates and favorable EFS with good safety in HER2-positive MIBC.

Clinical trial identification

NCT05723991.

Legal entity responsible for the study

The authors.

Funding

Has not received any funding.

Disclosure

All authors have declared no conflicts of interest.

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