Abstract 766: Neoadjuvant treatment with disitamab vedotin plus perioperative toripalimab in patients with HER2-expressing muscle-invasive bladder cancer (MIBC) in the phase II RC48-C017 trial: updated results

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Background

- Disitamab vedotin (DV, a HER2-targeted antibody-drug conjugate with monomethyl auristatin E) in combination with toripalimab (a PD-1 inhibitor) has demonstrated significant and clinically meaningful improvement in both progression-free survival and overall survival (OS) in patients with untreated, HER2-expressing, advanced urothelial cancer (UC) in a phase III study.[1] However, its efficacy in the early-stage disease setting is not fully established.
- The RC48-C017 trial evaluated the efficacy and safety of the combination of DV and toripalimab in patients with HER2-expressing muscle-invasive bladder cancer (MIBC) in the perioperative setting. The previous analysis showed a pathological complete response (pCR) rate of 63.6% in the surgical patients, and manageable safety.[2]
- We report updated results with a longer follow-up (data cutoff date: August 14, 2025), including event-free survival, OS, and safety..

Methods

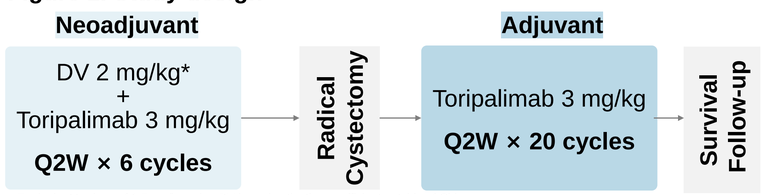
Study Design

- This was a single-arm, open-label, multicenter phase II trial (NCT05297552).

Key Eligible Criteria

- Histologically confirmed UC;
- MIBC at stage of cT2-T4a, N0-1, and M0;
- Eligible for radical cystectomy and pelvic lymph node dissection;
- HER2 expression of IHC 1+, 2+, or 3+ (assessed locally);
- ECOG performance status of 0 or 1.

Figure 1. Study design



*Equivalent to dose of 1.5 mg/kg using DV-based extinction coefficient outside of China.

Endpoints

- **Primary:** Pathologic complete response rate.
- **Secondary:** Pathological response rate; event-free survival (EFS); OS; adverse events.

Results

Patients

- A total of 47 patients were enrolled and treated; 33 underwent surgery.
- As of the data cutoff date, the median follow-up was 26.4 (95% CI: 24.4-28.2) months.

Table 1. Baseline characteristics

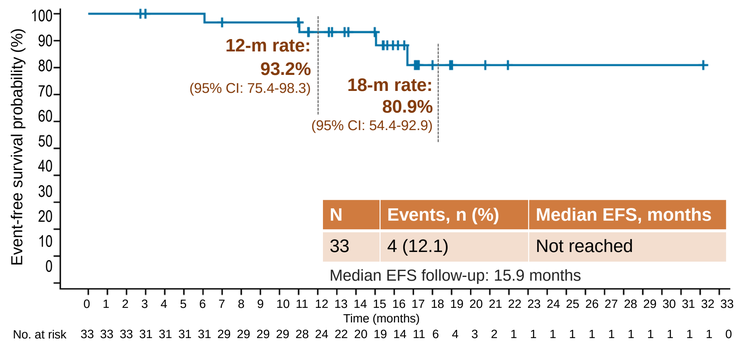
Characteristics	All patients (N=47)
Median age (range), years	64.0 (30, 82)
Male, n (%)	34 (72.3)
Histology, n (%)	
Pure UC / UC with other differentiation or variants	36 (76.6) / 11 (23.4)
ECOG performance status, n (%)	
0 / 1	25 (53.2) / 22 (46.8)
Baseline cTNM stage, n (%)	
cT2-4N0M0 / cT2-4aN1M0	39 (83.0) / 8 (17.0)
HER2 expression, n (%)	
IHC 1+ / 2+ / 3+	5 (10.6) / 27 (57.4) / 15 (31.9)
PD-L1 expression*, n (%)	
Negative / Not available	25 (53.2) / 9 (19.1)
Positive	13 (27.7)

*Assessed by PD-L1 IHC 22C3 pharmDx assay or Ventana SP263 PD-L1 IHC assay.

Efficacy

- The median EFS was not reached. At 12 and 18 months, the estimated EFS rate was 93.2% (95% CI: 75.4-98.3) and 80.9% (54.4-92.9), respectively, in the surgical patients, and was 91.0% (77.8-96.5) and 81.5% (64.3-90.9), respectively, in the total patients.
- The median OS was not reached; the 12- and 24-month OS rates were 95.7% (95% CI: 83.9-98.9) and 91.3% (95% CI: 78.6-96.7), respectively.

Figure 2. EFS in the patients with surgery



Results

Figure 3. EFS in all patients

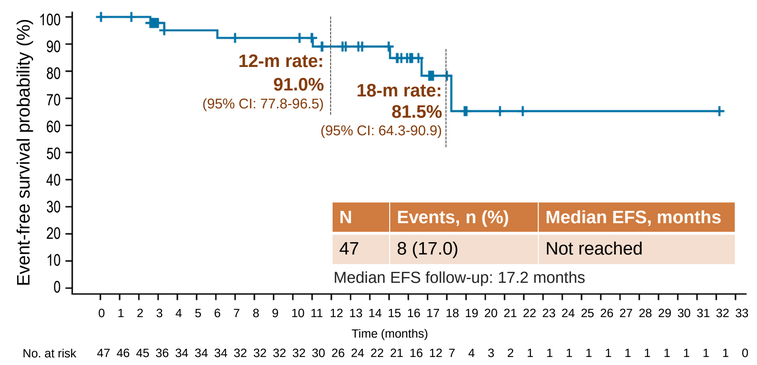
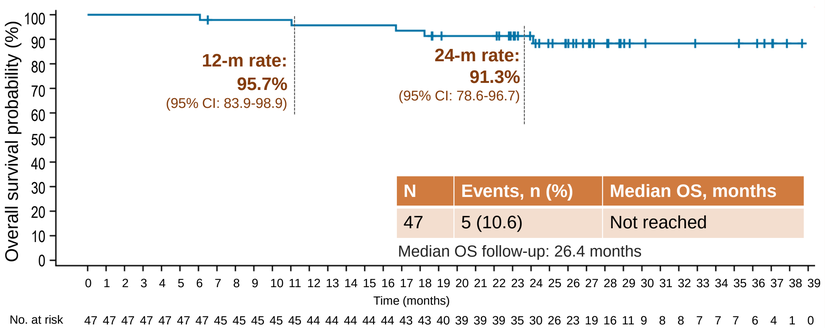


Figure 4. OS in all patients



Safety

- The overall safety profile was consistent with previous report, with no new safety signals observed.[2]

Conclusions

- These updated data demonstrated that the initial treatment response has translated into durable long-term disease control and survival, as reflected by the EFS and OS outcomes.
- This sustained treatment effect observed with neoadjuvant DV combined with perioperative toripalimab in patients with HER2-expressing MIBC warrants further evaluation in pivotal clinical studies.

REFERENCES:
1. Sheng X, et al. NEJM 2025; 393:2324-37. 2. Sheng X, et al. JCO 2025; 43(5):665.

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