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Enfortumab Vedotin Plus Pembrolizumab Outcomes in Advanced Urothelial Cancer: Real-World Data

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Objective: Enfortumab vedotin plus pembrolizumab (EV-P) is the new standard first-line treatment with EV302/KeynoteA39 demonstrating OS, PFS and ORR benefit for locally advanced or metastatic urothelial carcinoma (la/mUC) compared with platinum-based regimes. We analysed real world data to review the impact of EV-P on patient age stratified outcomes.

Methods: Retrospective analysis was performed on patients with histologically confirmed la/mUC treated with EV-P at Royal Free London Trust (RFL) between June 2025 and June 2026. Baseline demographic, radiological response and toxicity data was analysed.

Results: 29 patients commenced treatment in the 12-month period. Median age was 75 years (IQR: 69.6-80.2) and 62% were male. Upper tract urothelial carcinoma (UTUC) accounted for 66% of cases. 93% had metastatic vs 7% locally advanced disease.

Longest duration on treatment was 11 cycles. ORR was 75.0% (15/20; 95% CI 53.3–88.8%), including 4 complete responses (CR) (20.0%; 95% CI 50.9–91.3%) and 11 partial responses (55.0%; 95% CI 31.5–76.9%). Stable disease occurred in 2 patients (10.0%; 95% CI 1.2–31.7%) and progressive disease in 3 (15.0%; 95% CI 3.2–37.9%). 2 patients with CR or near CR were referred for cytoreductive surgery in view of treatment-related toxicities necessitating discontinuation. At data cut-off, 4 patients died. Adverse effects are summarised in Table 1.

Table 1. Summary of Toxicities

CTCAE Grade	1	2	3	4
Enfortumab Vedotin				
Fatigue	46.6%	3.3%	3.3%	0
Altered appetite	13.3%	0	0	0

Peripheral neuropathy	30%	6.7%	0	0
Skin	23.3%	0	0	0
Serious infection	0	0	13.3%	3.3%
Pembrolizumab				
Skin	23.3%	0	6.7%	0
Colitis	3.3%	6.7%	3.3%	0
Endocrinopathy	6.7%	0	0	0
Myocarditis	0	0	3.3%	0
Neurotoxicity	0	3.3%	0	0

Conclusions: In a real-world cohort characterised by older age, median 75 vs 69 in EV-302, greater comorbidity and higher proportion of UTUC, EV-P achieved an ORR of 75% (vs 67.7% in EV-302). These early findings support the effectiveness and tolerability of EV-P in clinical practice, with patients becoming candidates for consolidative therapy for local control. This is especially important in UTUC patients, where there is currently limited evidence for neoadjuvant therapy.