ENFORTUMAB VEDOTIN OUTCOMES IN ADVANCED UROTHELIAL CANCER: REAL-WORLD DATA

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INTRODUCTION

Enfortumab vedotin in combination with pembrolizumab (EV-P) has become the standard first-line treatment for patients with locally advanced or metastatic urothelial carcinoma following the phase III EV-302/KEYNOTE-A39 trial, which demonstrated significant improvements in overall survival, progression-free survival and objective response rate compared with platinum-based chemotherapy. However, real-world populations are often older, have a greater burden of comorbidity and are underrepresented in clinical trials, particularly patients with upper tract urothelial carcinoma (UTUC). Consequently, there remains a need to evaluate the effectiveness and tolerability of EV-P in routine clinical practice

AIMS

- To evaluate real-world outcomes of patients with locally advanced or metastatic urothelial carcinoma treated with EV-P at the Royal Free London NHS Foundation Trust (RFL).

METHODOLOGY

Data Collection
Retrospective analysis was performed on patients with histologically confirmed locally advanced or metastatic urothelial cancer treated with EV-P at RFL

Time Frame
Data collected between June 2025 and June 2026

Statistical Analysis
Baseline demographic, radiological response and toxicity data was analysed.

PATIENT DEMOGRAPHICS

29 patients commenced treatment in the 12-month period

Median Age 75 years
(IQR: 69.6-80.2)

66% upper tract urothelial carcinoma (UTUC) vs. 33% bladder cancer

93% had metastatic vs 7% locally advanced disease.

RESULTS

22 Evaluable patients

77.3% Objective Response Rate (17/22; 95% CI 54.6-92.2%)

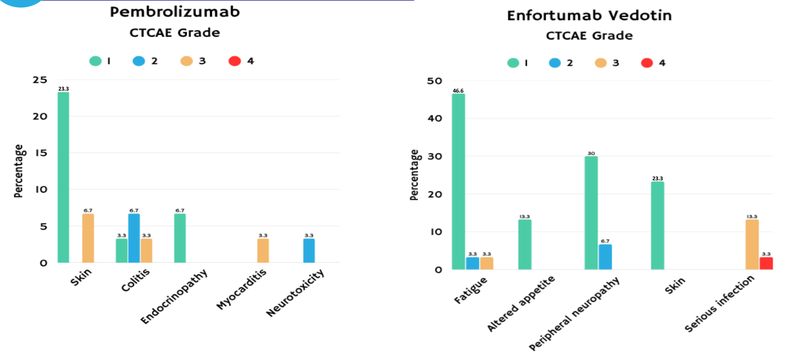
6 Complete responses (27.3%; 95% CI 10.7-50.2%)

- The longest duration on treatment at the time of data collection was 13 cycles.
- 22/29 patients had undergone at least 3 months or more of treatment and had a response scan.

Response	n/N	Rate (%)	95% CI (%)	EV302 trial (%)
Complete Response (CR)	6/22	27.3	10.7–50.2	29.1
Partial Response (PR)	11/22	50.0	28.2–71.8	38.7
Stable Disease (SD)	1/22	4.5	0.1–22.8	18.8
Progressive Disease (PD)	5/22	22.7	7.8–45.4	8.7

- 2 patients with complete or partial response have subsequently completed either cytoreductive surgery or consolidative radiotherapy in view of treatment-related toxicities necessitating discontinuation.

SUMMARY OF TOXICITIES



- 100% of patients reported treatment related adverse event of any grade
- Most adverse events were EV related toxicities graded 1-2 including fatigue, neuropathy, skin toxicity and appetite disturbance.
- No hyperglycaemia events were noted although this was common in the EV302 trial (5%)
- Grade 3 related toxicities (reported by 37% of patients) included serious infection, colitis, psoriasiform rash and myocarditis.
- Dose reductions due to treatment related adverse events occurred in 33.3% of patients, compared to 40.7% in the EV302 trial.

CONCLUSION

- In a real-world cohort characterised by older age , greater comorbidity and a higher proportion of upper tract disease, EV-P achieved an ORR of 77.3%, comparing favourably with the 67.7% ORR reported in EV-302.
- Complete Response rate of 27.3% was comparable to the 29.1% observed in EV-302.
- Despite the older age profile and higher burden of comorbidity within our cohort, the safety findings were broadly consistent with those reported in EV-302
- These early findings support the effectiveness and tolerability of EV-P in clinical practice.
- Two patients have become candidates for consolidative therapy with radiotherapy or surgery for local control. Both patient have had grade 3 toxicities making it difficult to continue EV-P. A further two patents have been referred for consideration.
- This is especially important in patients with UTUC where there is limited evidence base of neoadjuvant approaches and provides scope for further work into consolidative RT for locally advanced UTUCs
- Longer follow-up is required to better define survival outcomes and treatment durability in the real-world setting.

References:
Powles T, Valderrama BP, Gupta S, et al. Enfortumab Vedotin and Pembrolizumab in Untreated Advanced Urothelial Cancer. New England Journal of Medicine. 2024;390:875-888. doi:10.1056/NEJMoa2312117.