Survival Outcomes with Enfortumab Vedotin–Containing Regimens in Metastatic Urothelial Carcinoma: A Systematic Review and Meta-Analysis

Muhammad Ansab[1], Shree Rath[2], Ghazal Ishaque[3], Eiman Araib[4] , Iqra Khan[1], Umama Alam[5], Zain Sadiq[6], Nirmish Singla[7]

1 Services Institute of Medical Sciences, Pakistan; 2 All India Institute of Medical Sciences, India; 3 Shaheed Mohtarma Benazir Bhutto Medical College, Pakistan; 4 Dow University of Health Sciences, Pakistan; 5 Khyber Medical College, Khyber Pakhtunkhwa, Pakistan; 6 Quaid-e-Azam Medical College, Pakistan; 7 The Brady Urological Institute, Johns Hopkins University School of Medicine, Baltimore, USA.

Introduction

Metastatic urothelial carcinoma remains a highly lethal disease, particularly following progression on platinum-based chemotherapy and immune checkpoint inhibitors. Enfortumab vedotin (EV), a nectin-4–targeted antibody–drug conjugate, has shown encouraging activity in this setting, both as monotherapy and in combination with other agents. To systematically evaluate the efficacy and safety of Enfortumab Vedotin–containing treatment regimens, including monotherapy and combination therapies, in patients with metastatic urothelial carcinoma by analyzing survival outcomes, response rates, and treatment-related adverse events across published clinical trials.

Methods and Materials

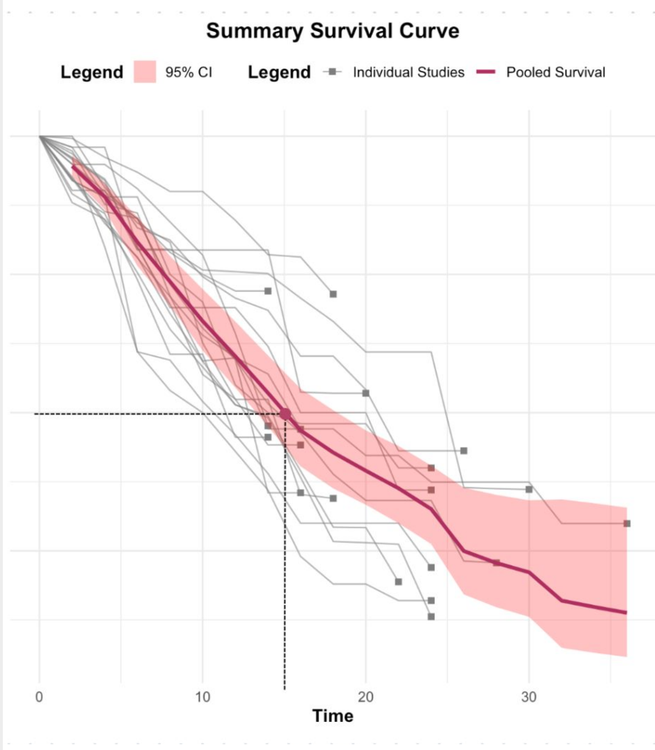
A systematic review and meta-analysis was conducted PubMed, Embase, and the Cochrane Library were searched till March 2025 for prospective clinical trials reporting survival outcomes of EV-based therapy. Summary survival curves were generated from pseudo individual patient data generated from published Kaplan–Meier curves for overall survival and progression free survival, and median OS and PFS were calculated, along with pooled OS and PFS at different time points. Secondary endpoints included objective response rate (ORR) and incidence of grade ≥3 treatment-related adverse events (TRAEs). Subgroup analyses were performed by regimen type (monotherapy vs. combination) and study phase.

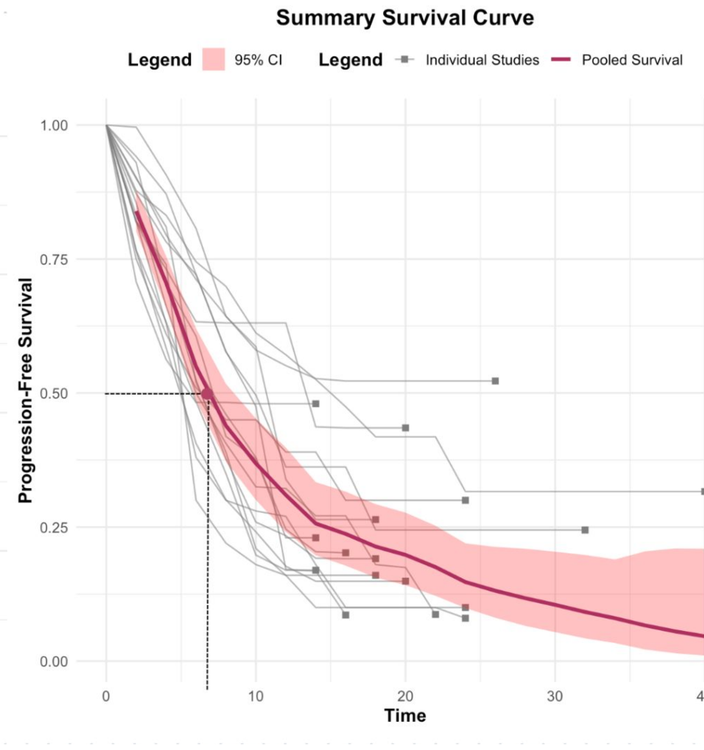
Results

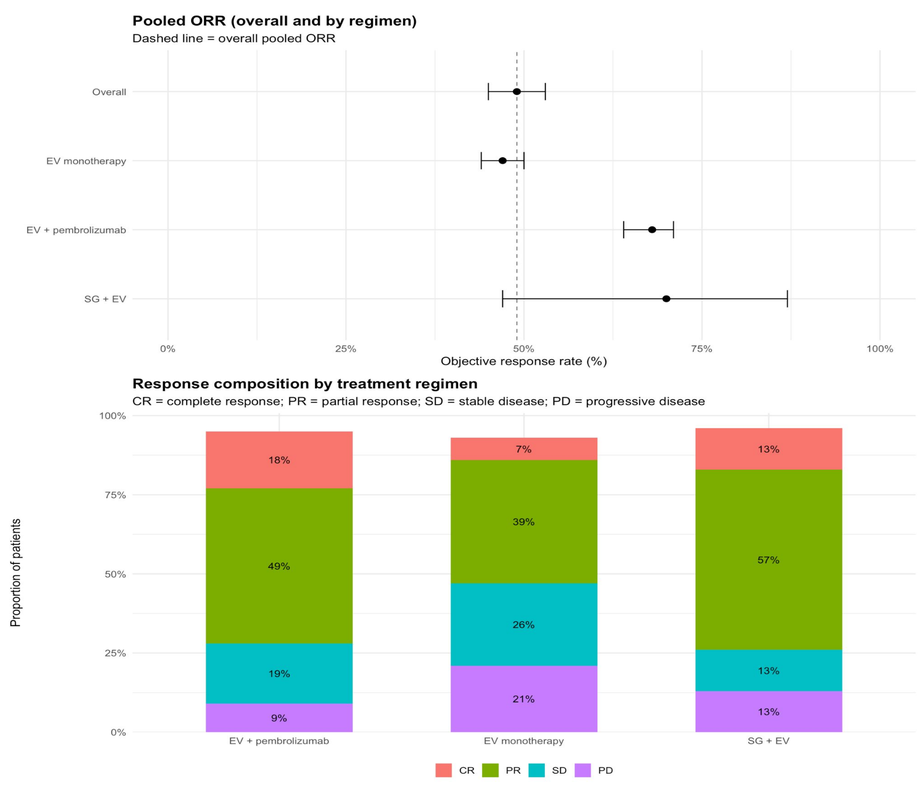
This meta-analysis included 3,770 patients with advanced urothelial carcinoma across 28 studies. Enfortumab vedotin (EV) monotherapy yielded a median overall survival (OS) of 14.9 months (95% CI: 12.74–17.07) and a median progression-free survival (PFS) of 6.9 months (95% CI: 5.77–8.29). Survival estimates declined steadily over time, with a 1-year OS rate of 59% and 2-year OS of 32%. When used in combination with pembrolizumab (EV + P), the median OS increased to 26.7 months and PFS to 13.1 months.

The pooled objective response rate (ORR) across 2,788 patients was 49% (95% CI: 45%–53%), with a complete response rate (CRR) of 8% and partial response rate (PRR) of 40%. EV + P showed the highest efficacy with an ORR of 68%, PRR of 49%, and CRR of 18%, outperforming both EV monotherapy and SG + EV combinations. Rates of stable disease (SD) and progressive disease (PD) were 25% and 19%, respectively, for EV monotherapy, while EV + P showed lower PD rates (9%).

Subgroup analyses by study design showed slightly higher response rates in prospective studies. Sensitivity analyses identified a few influential studies driving heterogeneity, but funnel plots were generally symmetrical, and replicability indices were high (97.5%–100%), supporting the robustness of findings.







Conclusion

EV-containing regimens demonstrate robust survival benefits and high response rates in patients with metastatic urothelial carcinoma, especially when combined with immune checkpoint blockade. These results support EV's integration into treatment paradigms and highlight the need for confirmatory randomized trials and biomarker-driven strategies to optimize outcomes.