ENFORTUMAB VEDOTIN-RELATED CUTANEOUS TOXICITIES IN PATIENTS WITH UROTHELIAL CARCINOMA:
A Systematic Review and Meta-analysis

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INTRODUCTION

Enfortumab vedotin (EV) is an antibody-drug conjugate, targeting nectin-4, that delivers microtubule-disrupting agentmonomethyl auristatin E (MMAE) to cancer cells. Cutaneous toxicities are associated with nectin-4 expression in the skin and have been reported in several clinical trials. Hence, we conducted a systematic review and meta-analysis to investigate EV-related cutaneous adverse events.

METHODS

We searched Pubmed, Cochrane and Embase databases for clinical trials (CTs) reporting the incidence of EV-related cutaneous toxicities in patients with locally advanced or metastatic urothelial carcinoma. Abstracts and observational studies were excluded. We pooled all-grade, grade ≥3, and severe cutaneous adverse -reactions (SCAR) and resented them as overall incidence rates and 95% confidence intervals (95% CI). Statistical analyses were performed using R software, and heterogeneity was evaluated through I2 statistics.

RESULTS

Of 1,047 reports, five CTs involving 751 participants met the inclusion criteria. Median age ranged from 64 to 75 years, and 75% (567) were male. The median follow-up of each study and median time to onset of skin toxicity varies from 10.2 to 16.4 and 0.42-0.95 months, respectively. The most frequent cutaneous TRAE was rash maculopapular, with an overall frequency of 40.25% (95% CI 30.21-50.29, I2 89%), and 5.31% (3.34-8.34, I2 40%) rate of grade 3 or higher. Alopecia was seen in 40.52% (95% CI 41.87-49.17, I2 11%) of patients, pruritus in 28.58% (22.21-35.94, I2 68%), and dry skin in 21.13% (17.06-25.87, I2 0%).

Six cases of bullous dermatitis, five of palmar-plantar erythrodysesthesia, and one case of Stevens-Johnson syndrome were reported.

Figure 1: Incidence of skin reactions any grade.

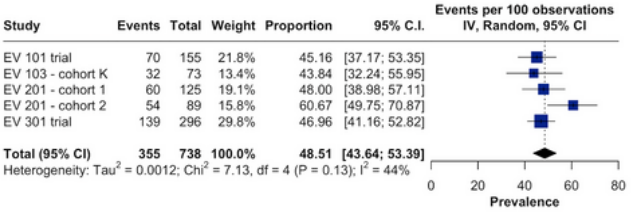


Figure 2: Incidence of rash maculopapular any grade.

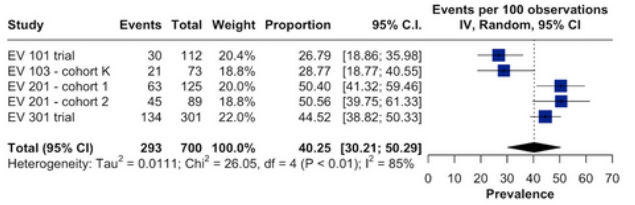


Figure 3: Incidence of rash maculopapular grade ≥3.

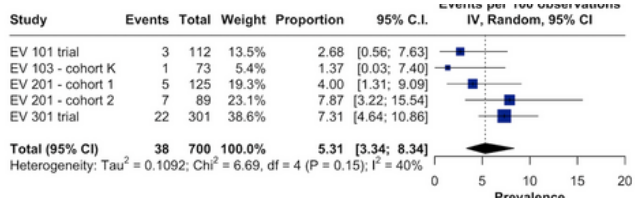
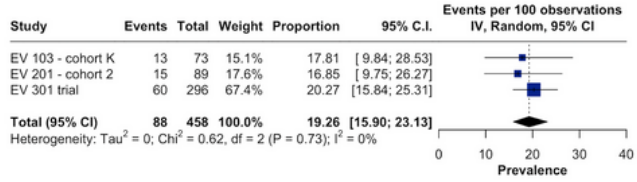


Figure 4: Incidence of severe cutaneous adverse reactions.



CONCLUSIONS

Despite the higher incidence of EV-related cutaneous toxicities, most cases were manageable with supportive care, dose reduction, and drug interruption. EV is an excellent drug for UC patients; therefore, understanding EV-related skin toxicities is paramount for comprehensive patient care.

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