INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Efficacy and safety of Enfortumab vedotin in the treatment of advanced urothelial carcinoma: A systematic review and meta-analysis

Wang, LB[1]; Shi, GY[2].

Review question / Objective: **This study aimed to investigate whether Enfortumab vedotin (EV) is suitable for patients with locally advanced or metastatic urothelial carcinoma and to perform a meta-analysis of its efficacy and safety.**
Eligibility criteria: **The study included randomized controlled trials, non-randomized controlled trials, case-control studies, cohort studies, and cross-sectional studies; subjects: (1) patients' age≥18 with histology confirmed locally advanced or metastatic urothelial transitional cell carcinoma (aka: bladder cancer, renal pelvic carcinoma, ureteral carcinoma, orurethral carcinoma), including patients with squamous differentiation or mixed cellularity, with an ECOG performance status of 2 or less; (2) unless considered as inappropriate for cisplatin-based chemotherapy, or the patient has failed at least one chemotherapy regimen for advanced disease, e.g., the patient has radiographic progression or relapse during or after PD-1/L1 inhibitor therapy or a platinum-based regimen; (3) Interventions: same dose of Enfortumab vedotin, 1.25 mg/kg.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 August 2022 and was last updated on 17 August 2022 (registration number INPLASY202280070).

INTRODUCTION

Review question / Objective: **This study aimed to investigate whether Enfortumab vedotin (EV) is suitable for patients with locally advanced or metastatic urothelial carcinoma and to perform a meta-analysis of its efficacy and safety.**

Condition being studied: **UC (Urothelial Carcinoma) which is a common malignant tumor of the urinary system with increasing incidence year by year can occur in any part covered by the urothelium, including renal pelvis, ureter, bladder, and urethra.Most of these urothelial carcinomas originate in the bladder,**

accounting for about 90%, About 20% of patients were initially diagnosed with MIBC (muscle-invasive bladder cancer), about 50% recurred within 2 years of surgery, and about 5% developed distant metastases at diagnosis. The prognosis of metastatic urothelial carcinoma is poor, the median overall survival (OS) is only about one year, and the patients with visceral metastasis are even worse. Clinically, metastatic urothelial carcinoma has always been a thorny problem for urologists. The standard treatment for mUC has been cisplatin-based chemotherapy with a 5-year survival rate of < 5%, and some patients suffer from renal insufficiency, heart failure, or with poor ECOG-PS (Eastern Cooperative Oncology Group-Performance Status) or other complications deemed inappropriate for cisplatin-based chemotherapy. With the exception of a few available for carboplatin chemotherapy, anti-programmed death 1 or anti-programmed death ligand 1 (PD-1/L1) are supplementary therapy, but currently clinical studies show that the objective response rate is still low.Enfortumab vedotin is an antibody-drug conjugate (ADC) which can selectively target on nectin-4, co-developed by Seattle Genetics and its partner Astellas, approved by the U.S. Food and Drug Administration (FDA) in November 2019 for the treatment of advanced or metastatic urothelial carcinoma previously treated with platinum-based chemotherapy or PD-1/PD-L1 inhibitors, and also was the first ADC approved for patients with urothelial carcinoma.

METHODS

Participant or population: Patients' age≥18 with histology confirmed locally advanced or metastatic urothelial transitional cell carcinoma (aka: bladder cancer, renal pelvic carcinoma, ureteral carcinoma, orurethral carcinoma), including patients with squamous differentiation or mixed cellularity, with an ECOG performance status of 2 or less.

Intervention: Enfortumab vedotin1.25 mg/kg was given as treat.

Comparator: There is no.

Study designs to be included: Non-randomized pilot studies and randomized case-control study.

Eligibility criteria: The study included randomized controlled trials, non-randomized controlled trials, case-control studies, cohort studies, and cross-sectional studies; subjects: (1) patients' age≥18 with histology confirmed locally advanced or metastatic urothelial transitional cell carcinoma (aka: bladder cancer, renal pelvic carcinoma, ureteral carcinoma, orurethral carcinoma), including patients with squamous differentiation or mixed cellularity, with an ECOG performance status of 2 or less; (2) unless considered as inappropriate for cisplatin-based chemotherapy, or the patient has failed at least one chemotherapy regimen for advanced disease, e.g., the patient has radiographic progression or relapse during or after PD-1/L1 inhibitor therapy or a platinum-based regimen; (3) Interventions: same dose of Enfortumab vedotin, 1.25 mg/kg.

Information sources: A comprehensive and systematic search was conducted for articles published before November 21, 2021 in PubMed, Embase, Web of Science.

Main outcome(s): The meta-analysis indicated that EV showed good efficacy and safety in the patient population of locally advanced or metastatic urothelial carcinoma. However, given the limited number of studies included in this article, more high-quality articles are still needed in the future to further explore the value of EV in ADC drugs and in combination with immunotherapy in advanced or mUC (metastatic Urothelial Carcinoma).

Quality assessment / Risk of bias analysis: The literature quality was assessed according to MINORS evaluation tool. Begg's test were used to detect publication bias.

Strategy of data synthesis: Meta-analyses were performed using Stata 15.0 software.

Subgroup analysis: No.

Sensitivity analysis: Meta-analysis was performed using a fixed model when there was no statistical heterogeneity among the results of each study (P≥10, I2≤50%); Meta-analysis was performed using a random model when when there was statistical heterogeneity (P50%).

Country(ies) involved: China.

Keywords: "Bladder cancer", "metastatic urothelial carcinoma", "advanced urothelial carcinoma", "antibody drug conjugate", "Enfortumab vedotin".

Contributions of each author:

Author 1 - Leibo Wang - Leibo Wang and Guanyu Shi conceived and designed the article and wrote the thesis.
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Author 2 - Guanyu Shi - Guanyu Shi conducted a feasibility analysis of the study.
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