

**Novel  $\beta$ -lactam antibiotics versus other antibiotics for treatment of complicated urinary tract infections: A systematic review and meta-analysis**

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**ADMINISTRATIVE INFORMATION****Support** - None.**Review Stage at time of this submission** - Preliminary searches.**Conflicts of interest** - The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this protocol.**INPLASY registration number:** INPLASY202440054**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 April 2024 and was last updated on 30 May 2024.**INTRODUCTION**

**Review question / Objective** Participants: adult patients had to be diagnosed with cUTI. Intervention: The experimental group had to be treated with novel  $\beta$ -lactam antibiotics. Comparators: The control group had to be treated with other antibiotics. Outcome: clinical response, microbiological response, adverse effect, serious adverse effect, all cause mortality. Study design: randomized controlled trials (RCTs).

**Condition being studied** Due to the rapid emergence and dissemination of antimicrobial resistance, some patients with complicated urinary tract infections (cUTIs) are left with limited therapeutic options, which may lead to progression of the disease to more severe stages, including Extended-spectrum  $\beta$ -lactamase (ESBL)-producing and multidrug-resistant organisms (MDROs). Therefore, there is an urgent need to find new

treatment options. In recent years, some novel antibiotics, such as cefiderocol, novel  $\beta$ -lactam and  $\beta$ -lactase inhibitor, Sulopenem, Tebipenem Pivoxil Hydrobromide, have been treated for the infection caused by MDRO, including cUTIs. There is a controversy about whether the novel  $\beta$ -lactam antibiotics are better than other antibiotics. We conducted this systematic review and meta-analysis to explore the efficacy and safety of novel  $\beta$ -lactam antibiotics for patients with cUTI.

**METHODS**

**Participant or population** Adult patients had to be diagnosed with cUTI.

**Intervention** The experimental group had to be treated with novel  $\beta$ -lactam antibiotics.

**Comparator** The control group had to be treated with other antibiotics.

**Study designs to be included** Randomized controlled trials (RCTs).

**Eligibility criteria** (1) Participants: adult patients had to be diagnosed with cUTI.(2) Intervention: The experimental group had to be treated with novel  $\beta$ -lactam antibiotics.(3) Comparators: The control group had to be treated with other antibiotics.(4) Outcome: clinical response, microbiological response, adverse effect, serious adverse effect, ACM.(5) Study design: randomized controlled trials (RCTs).

**Information sources** Two authors searched PubMed, Embase, and Cochrane Central Register of Controlled Trials independently, studies including the efficacy and safety of novel  $\beta$ -lactam antibiotic for treatment patients with cUTIs. The following search terms were used:“urinary tract infection\*”, “UTI”,“bacteriuria”,“pyuria”, “pyelonephritis”,“ceftazidime/avibactam”, “ceftolozane/tazobactam”, “meropenem/vaborbactam”,“imipenem/cilastatin/relebactam”, “cefepime/tazobactam”, “ceftaroline/avibactam”, “cefepime/zidebactam”, “cefepime-enmetazobactam”, “Meropenem/nacubactam”, “Cefiderocol”, “Sulopenem”, “Tebipenem Pivoxil Hydrobromide”.

**Main outcome(s)** Clinical response, including clinical response at test of cure (TOC), clinical cure rate at the end of treatment (EOT).

**Additional outcome(s)** microbiological response, AEs, serious AEs,ACM.

**Quality assessment / Risk of bias analysis** Cochrane risk of bias.

**Strategy of data synthesis** Relative risk (RR) and 95% confidence intervals (CI) were calculated for dichotomous variables with the DerSimonian-Laird random effects model. Cochran's Q statistic (significance level,  $P < 0.01$ ) and  $I^2$  statistic were to evaluated of heterogeneity. Publication bias was assessed using funnel plots. Review Manager 5.4 was used for this meta-analysis.

**Subgroup analysis** Subgroup analyses were according to antibiotic type, infection type in clinical response, antibiotic type in microbiological pathogens, events type.

**Sensitivity analysis** Sensitivity analysis was undertaken to ascertain the results of the meta-analysis by excluding each individual study.

**Country(ies) involved** China.

**Keywords** novel;  $\beta$ -lactam antibiotics; complicated urinary tract infections; systematic review;meta-analysis.

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