## **INPLASY PROTOCOL**

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**Review Stage at time of this** submission: Completed but not published.

**Conflicts of interest:** None declared.

## **INTRODUCTION**

Review question / Objective: Based on the Meta-analysis of the efficacy and safety of different doses of tigecycline in the treatment of ventilator-associated pneumonia caused by multi-resistant bacteria.

Systematic evaluation and Meta-analysis of the efficacy and safety of different doses of tigecycline in ventilator-associated pneumonia caused by multiple resistant bacteria

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Review question / Objective: Based on the Meta-analysis of the efficacy and safety of different doses of tigecycline in the treatment of ventilator-associated pneumonia caused by multi-resistant bacteria.

Information sources: Using the way of keywords + free word in Cochrane library, Embase, PubMed, Chinese biomedical literature database, CNKI, literature retrieval in Chinese journal full text database, Wanfang, web database, Chinese search terms is: "teacycline, different doses, ventilator associated pneumonia", English search terms is: "Tigacycline, Drug-resistant bacteria, Ventilator-associated pneumonia", etc. The time limit for database construction is until December 2022. The search languages are in both Chinese and English.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 April 2023 and was last updated on 11 April 2023 (registration number INPLASY202340034).

> Condition being studied: Through Cochrane library, Embase, PubMed, Chinese biomedical literature database, CNKI, Chinese JP, WP, the database until December 2022. The searched literature was evaluated using Jadad quality score and Meta-analysis of literature data was performed using Stata software.

## **METHODS**

Participant or population: The study subjects were patients with ventilator-associated pneumonia caused by multi-drug-resistant bacteria, and the indicators reflecting the clinical effect and safety were taken as the observation indicators (such as treatment effect, adverse effects, etc.).

Intervention: All literature was assessed on the quality of the literature according to the literature Evaluation criteria of the Cochrane System Evaluator Manual and the modified Jadad scale.

Comparator: N/A.

Study designs to be included: Inclusion criteria: 1. All the included documents are randomized controlled experiments.2. The study subjects were patients with ventilator-associated pneumonia caused by multi-drug-resistant bacteria, and the indicators reflecting the clinical effect and safety were taken as the observation indicators (such as treatment effect, adverse effects, etc.).3. The treatments involved include different doses of tigecycline, placebo, etc.

Eligibility criteria: 1. Non-randomized controlled study.2. Incomplete data in the article and repeated published literature.3. Animal experiments, case reports, review, etc.

Information sources: Using the way of keywords + free word in Cochrane library, Embase, PubMed, Chinese biomedical literature database, CNKI, literature retrieval in Chinese journal full text database, Wanfang, web database, Chinese search terms is: "teacycline, different doses, ventilator associated pneumonia", English search terms is: "Tigacycline, Drug-resistant bacteria, Ventilator-associated pneumonia", etc. The time limit for database construction is until December 2022. The search languages are in both Chinese and English.

Main outcome(s): The included articles were tested for publication bias using

funnel plot and Egger's test, and none of the six articles had clinical efficacy as effect index (P> 0.05). A total of 6 articles reported the adverse effects of tigecycline in patients with ventilator-associated pneumonia caused by different doses of multiple resistant bacteria. Meta-analysis showed that there was no clinical heterogeneity or statistical heterogeneity between studies (I2=51%, P=0.10), a fixedeffect model was used to incorporate the effect size. The incidence of adverse effects in the observed group was not different from that of the control group [OR = 0.96,95% CI (0.61,1.50), P =0.85]. The included articles were tested for publication bias using funnel plot and Egger's test, and none of the four articles had adverse effects as effect indicators (P> 0.05).

Quality assessment / Risk of bias analysis: N/A.

Strategy of data synthesis: Statistical analysis was performed using Stata software, and the results of the included literature were tested for heterogeneity using Cochran's Q test, and the heterogeneity size passed the statistic I2representation.like I2With> 50% or P <0.05, indicating statistical heterogeneity among the literature, the random effect model incorporates the effect size; otherwise, the fixed effect model incorporates the effect size. The weighted mean difference (WMD), 95% confidence interval (95% CI) were used to represent the combined effect size of measurement data, the combined effect size of counting data used RR as the comprehensive effect, and 95% CI was used for interval assessment. Publication bias test was performed using funnel plot and Egger's test at test level  $\alpha = 0.05$ .

Subgroup analysis: N/A.

Sensitivity analysis: N/A.

Country(ies) involved: China.

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Keywords: tigecycline; drug-resistant bacteria; ventilator-associated pneumonia; Meta-analysis.

## **Contributions of each author:**

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Author 5 - Zhaoxu Cai.

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