INPLASY PROTOCOL

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None declared.

Efficacy and safety of caplacizumab in the treatment of thrombotic thrombocytopenic purpura: a meta-analysis of systematic reviews based on high-quality randomized controlled trials

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Review question / Objective: **We conducted this meta-analysis to investigate the efficacy and safety of caplacizumab in patients with thrombotic thrombocytopeni purpura (TTP).**
Condition being studied: **Thrombotic thrombocytopenia purpura (TTP) is a potentially fatal disorder characterized by systemic microvascular thrombosis(1). According to the etiology, TTP can be divided into hereditary TTP and acquired TTP, and the latter can be divided into idiopathic TTP and secondary TTP according to whether the etiology is clear.**
Information sources: **The databases we searched were PUBMED, WEP OF SCIENCE, COCHRANE LIBRARY and EMBASE before March 5, 2022.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 May 2022 and was last updated on 27 May 2022 (registration number INPLASY202250149).

INTRODUCTION

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METHODS

Participant or population: Adult patients diagnosed with thrombotic thrombocytopenic purpura.

Intervention: Caplacizumab, a humanized bivalent single-domain nanobody, has been approved by the European Union and the U.S. Food and Drug Administration for the treatment of adult-onset TTP. It binds to the A1 domain of VWF and effectively inhibits the interaction with platelet GP特b-IX-V. Thereby limiting platelet adhesion and microvascular thrombus formation.

Comparator: The usual treatment of TPP.

Study designs to be included: Only randomized controlled trials (RCTs) will also be considered.

Eligibility criteria: Inclusion criteria include: a. Published researches on caplacizumab in the treatment of TTP; b. RCT experiments; c. The subjects of the study are humans; d. Literature published in English. Exclusion criteria include: a, in vitro experiments and animal experiments; b, too few samples（The number of samples in each group is less than 10 cases）; c, grey journal literature.

Information sources: The databases we searched were PUBMED、WEP OF SCIENCE、COCHRANE LIBRARY and EMBASE before March 5, 2022.

Main outcome(s): The primary outcome measure for this meta-analysis was time to platelet counts normalization.

Additional outcome(s): Additional outcome measures included days of plasma exchange, length of hospital stay, relapse, mortality, and major thrombotic events.

Quality assessment / Risk of bias analysis: The quality of the final included RCTs were assessed using the Cochrane Collaboration's risk of bias assessment tool. The Cochrane Risk of Bias Assessment Tool specifically evaluates the risk of bias from 7 items designed from the following 6 aspects:: (1) Selection bias(Random sequence generation, Allocation concealment)、(2) Performance bias (Blinding of participants and personnel)、(3) Detection bias (Blinding of outcome assessment)、(4) Attrition bias (Incomplete outcome data)、(5) Reporting bias (Selective reporting)、(6) Other bias. The researchers evaluated the RCT studies item by item, and the evaluation results were expressed as low risk, high risk, and unclear.

Strategy of data synthesis: Data were entered and analyzed by using STATA software. The original included studies used the weighted mean difference (WMD) in continuous outcomes (Platelet count normalization time, days of plasma exchange, and length of hospital stay) to evaluate the difference between the caplacizumab groups and control groups. The precision of the effect sizes was reported as 95% CIs. A pooled estimate of the WMD was computed by using the DerSimonian and Laird random effects model.For dichotomous variables such as relapse, mortality, and major thrombotic events, RR values and corresponding 95% confidence intervals were used. Statistical heterogeneity between the studies was assessed using the Q and I2 statistics. Values of I2 >50% and p<0.1 indicated high heterogeneity, the random effect model is used. when valuer of I20.1 indicated low heterogeneity, a fixed effect model is used. Due to the small number of included studies, it would be inappropriate to perform meta-regression and publication bias.

Subgroup analysis: We will conduct subgroup analysis based on follow-up time and drug dosage for those with large heterogeneity to explore the source of heterogeneity.

Sensitivity analysis: Sensitivity analysis was performed by sequential deletion tests to test the stability of the main results. That is, after the deletion of any one study, the combined results of the remaining literature are not significantly different from those that would have passed the sensitivity analysis if it had not been deleted.

Country(ies) involved: China.

Keywords: Caplacizumab; Thrombotic thrombocytopenic purpura; Meta-analysis.

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