

INPLASY PROTOCOL

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Support: KC201903

Review Stage at time of this submission: The review has not yet started.

Conflicts of interest:
None.

The efficacy and safety of different dosages of rituximab for adults with immune thrombocytopenia: a systematic review and meta-analysis

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Review question / Objective: To assess the efficacy and safety of different dosages of rituximab for immune thrombocytopenia. **PICO:** P (Patients): patients of any race, aged more than 18 years, and diagnosed with immune thrombocytopenia; I (Intervention): the use of rituximab in any dosage, with or without combination therapy; C (Comparison): non-rituximab treatment, or placebo; O (Outcome): efficacy and safety.

Condition being studied: Primary immune thrombocytopenia (ITP) is an autoimmune disorder characterized by immune-mediated peripheral platelet destruction, impaired platelet production, and an increased risk of bleeding.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 June 2020 and was last updated on 07 June 2020 (registration number INPLASY202060024).

INTRODUCTION

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dosage, with or without combination therapy; C (Comparison): non-rituximab treatment, or placebo; O (Outcome): efficacy and safety.

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impaired platelet production, and an increased risk of bleeding.

METHODS

Participant or population: Inclusion criteria: patients of any race, aged more than 18 years, and diagnosed with immune thrombocytopenia. Exclusion criteria: patients with secondary immune thrombocytopenia.

Intervention: The use of rituximab in any dosage, with or without combination therapy.

Comparator: Non-rituximab treatment, or placebo.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: Inclusion criteria: 1) Patient: any race, aged more than 18 years and diagnosed with immune thrombocytopenia. 2) Intervention: use of rituximab in any dosage, with or without combination therapy. 3) Comparison: non-rituximab treatment or Placebo. 4) Outcome: efficacy and safety outcomes. 5) Study type: randomized controlled trial. Exclusion criteria: 1) patients diagnosed with secondary immune thrombocytopenia; 2) trials without extractable data; 3) duplicate publications.

Information sources: We will search the following electronic databases for relevant information: MEDLINE(PuMed), EMBASE, the Cochrane Library, ClinicalTrials.gov, China National Knowledge Infrastructure (CNKI), Wanfang and Weipu (VIP) databases. Studies published between January 1990 and the present (8/6/2020) will be included, without language restrictions.

Main outcome(s): Platelet response: 1. CR (complete response: defined as a platelet count $\geq 100 \times 10^9/L$ measured on two occasions more than 7 days apart and the absence of bleeding. 2. OR (overall response): defined as a platelet count $\geq 50 \times 10^9/L$ more than 7 days apart and the

absence of bleeding; 3. PR (partial response): defined as a platelet count $\geq 30 \times 10^9/L$ or a greater than 2-fold increase in platelet count from baseline more than 7 days apart and the absence of bleeding.

Additional outcome(s): 1. The incidence of infection. 2. The incidence of significant bleeding. 3. The incidence of SAEs (serious adverse events).

Data management: Pilot testing of the data selection process will take place before the searches are conducted. Two reviewers (Mengjiao Hu and Yu Dong) will independently screen the titles and abstracts of the studies retrieved during the searches for eligibility, and those meeting the inclusion criteria will be selected for use in the review. Data will then be extracted from included studies, including: authors, publication year, the country where the study was conducted, funding sources, study ID, study design, study setting, participant demographics and baseline characteristics, details of intervention and control, outcomes and information for assessment of the risk of bias. If there is found to be missing data, we will attempt to contact the original authors of the studies in question to request the provision of the required information. Any discrepancies will be resolved by discussion.

Quality assessment / Risk of bias analysis: Two reviewers (Mengjiao Hu and Yu Dong) will independently assess the risk of bias of the included studies using the Cochrane risk of bias assessment instrument, which evaluates the following sources of bias: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. We will aim to minimize possible bias and strengthen the level of our results. In addition, publication bias will be assessed using funnel plots. Any discrepancies will be resolved through discussion, with a third reviewer, if necessary.

Strategy of data synthesis: Data will be synthesized using RevMan 5.3. Efficacy and safety (platelet response, incidence of significant bleeding, incidence of infection, and the incidence of SAEs) will be assessed by using relative risks (RR) with 95% confidence interval (CI). We will use χ^2 test and I^2 test to define the level of heterogeneity. If $I^2=50\%$ or $P<0.1$), we will try to explain its source by subgroup or sensitivity analyses. If the heterogeneity cannot be resolved, we will not perform a meta-analysis synthesis. Publication bias will be assessed using funnel plots.

Subgroup analysis: If the necessary data are available, subgroup analyses will be conducted for people treated with different doses of rituximab. In addition, if high levels of heterogeneity exist between the trials ($I^2\geq 50\%$ or $P<0.1$), the study designs and characteristics of the included studies will be analyzed, and we will try to explain the source of the heterogeneity by subgroup analysis or sensitivity analysis.

Sensibility analysis: Sensitivity analysis will be conducted to test the possible influence of the single studies and to explore the robustness of the result by eliminating possible extreme observations.

Language: English.

Country(ies) involved: China.

Keywords: ITP, rituximab, different dosages.

Contributions of each author:

Author 1 - Yu Dong.

Author 2 - Mengjiao Hu.