INPLASY PROTOCOL

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Corresponding author:
Yin Liu

liuyin0706@126.com

Author Affiliation:
Henan Cancer Hospital,Affiliated Cancer Hospital of Zhengzhou University.

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None declared.

Efficacy and Safety of Thrombopoietin Receptor Agonists in Adults with Immune Thrombocytopenia: A Systematic Review and Network Meta-analysis

Liu, Y[1]; Fu, J[2]; Wang, X[3]; Zhang, S[4].

Review question / Objective: **To establish a clinically relevant ranking of the efficacy and safety of Thrombopoietin Receptor Agonists (TPO-RAs) for adults (≥18 years old) with Immune thrombocytopenia (ITP).**
Condition being studied: **Only one study compraed the efficacy and safety of Thrombopoietin Receptor Agonists (TPO-RAs), but it did not include other disease related thrombocytopenia, as well as not include hetrombopag.**
Information sources: **Medline, PubMed, Embase, web of science, CHKD-CNKI, CINAHL, WANFANG, and the Cochrane Library.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 December 2021 and was last updated on 11 December 2021 (registration number INPLASY2021120054).

INTRODUCTION

Review question / Objective: **To establish a clinically relevant ranking of the efficacy and safety of Thrombopoietin Receptor Agonists (TPO-RAs) for adults (≥18 years old) with Immune thrombocytopenia (ITP)**

Condition being studied: **Only one study compraed the efficacy and safety of Thrombopoietin Receptor Agonists (TPO-**

RAs), but it did not include other disease related thrombocytopenia, as well as not include hetrombopag.

METHODS

Participant or population: Male or female patients (≥18 years old) with Immune thrombocytopenia (ITP)

Intervention: Avatrombopag, lusutrombopag, eltrombopag, romiplostim, hetrombopag, recombinant human thrombopoietinAvatrombopag, lusutrombopag, eltrombopag, romiplostim, recombinant human thrombopoietin.

Comparator: Placebo; indirect comparison.

Study designs to be included: published randomized controlled trial.

Eligibility criteria: The inclusion criteria include:(1) Patients were adults (≥18 years old) with Immune thrombocytopenia (ITP); (2) Studies were published randomized controlled clinical trials, comprising any of the following interventions: avatrombopag, lusutrombopag, eltrombopag, romiplostim, hetrombopag, recombinant human thrombopoietin, or in combination with other drugs.(3) Studies revealed at least one of the following three outcomes: the number of patients who achieved platelet response (platelet counts ≥30 or 50 × 10^9 / L) as originally defined by each study, therapy-related serious adverse events, and incidence of bleeding episodes.The exclusion criteria include:(1) Studies were reviews, meeting summaries, letters, etc.) (2) There was missing or incomplete information on the trial;(3) Patients with diseases related to the blood systemThe inclusion criteria include:(1) Patients were adults (≥18 years old) with Immune thrombocytopenia (ITP); (2) Studies were published randomized controlled clinical trials, comprising any of the following interventions: avatrombopag, lusutrombopag, eltrombopag, romiplostim, recombinant human thrombopoietin, or in combination with other drugs.(3) Studies revealed at least one of the following three outcomes: the number of patients who achieved platelet response (platelet counts ≥30 or 50 × 109 /L) as originally defined by each study, therapy-related serious adverse events, and incidence of bleeding episodes.The exclusion criteria include:(1) Studies were reviews, meeting summaries, letters, etc.)(2) There was missing or incomplete information on the trial;(3) Patients with diseases related to the blood system.

Information sources: Medline, PubMed, Embase, web of science, CHKD-CNKI, CINAHL, WANFANG, and the Cochrane Library.

Main outcome(s): Platelet response (platelet counts ≥30 or 50×109 /L) during therapeutic or observational period.

Additional outcome(s): Incidence of any or severe bleeding events; Incidence of Adverse Events

Quality assessment / Risk of bias analysis: GRADE system is used to assess quality, including: selection bias: random sequence generation; allocation concealment; performance bias: blinding of participants and personnel; detection bias: blinding of outcome assesment; attrition bias: incomplete outcome data; reporting bias: selective reporting.

Strategy of data synthesis: A network meta-analysis on random effects was performed virtually using the STATA software. Evidence from both direct (head-to-head trials) and indirect (using common comparators without actual head-to-head trials) comparisons was combined. Moreover, all treatment effects were measured as dichotomous data and presented as the summary of risk ratios with 95% confidence intervals. We also calculated the surface under the cumulative ranking curve(SUCRA) to determine the hierarchy of the efficacy and risk of severe AEs, where SUCRA values of 100% indicated the most effective treatment or the treatment with the highest risk of AEs, and values of 0% indicated the least effective or least risky treatment.

Publication bias was assessed using a funnel plot, Egger's test, and Begg's test.

Subgroup analysis: **None.**

Sensitivity analysis: **Analysis with/without low-quality studies.**

Country(ies) involved: **China.**

Keywords: **Immune thrombocytopenia; thrombopoietin receptor agonist; Efficacy; Safety; Network Meta-analysis.**

Contributions of each author:
Author 1 - Yin Liu.
Author 2 - Jianyong Fu.
Author 3 - Xiaoyang Wang.
Author 4 - Shaokai Zhang.