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Blood 142 (2023) 1216–1217

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

311.DISORDERS OF PLATELET NUMBER OR FUNCTION: CLINICAL AND EPIDEMIOLOGICAL

Effect of Hetrombopag Combined with Rhtpo in Patients with Severe Immune Thrombocytopenia

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Background:
Severe Immune Thrombocytopenia (ITP) is a life-threatening acquired hemorrhagic disease with dramatically decreased platelet number and clinical bleeding symptoms. Some patients with severe ITP did not respond to first-line treatment including steroids and Intravenous Immunoglobulin (IVIG). It was critical for them to use effective treatments to promote platelet and reduce the risk of fatal bleeding. Clinical practice guidelines have recommended the use of thrombopoietin receptor agonist (TPO-RA) as a second-line treatment for ITP. Recombinant human thrombopoietin (rhTPO) and hetrombopag are two distinct TPO-RAs with different mechanisms. As reported, there remains no study assessing the efficacy and safety of hetrombopag combined with rhTPO in the treatment of ITP. Therefore, the present study aimed to investigate the efficacy of hetrombopag plus rhTPO in Chinese patients with severe ITP, focusing on the short rather than the long-term efficacy, such as quickly increasing platelet count and significantly reducing bleeding, which would be more meaningful for severe patients whose platelet count $<10 \times 10^9$/L.

Methods:
This was a prospective, open-label, single-center study with a planned enrollment of 30 patients. The inclusion criteria were patients $\geq$ 18 years, diagnosed with primary immune thrombocytopenia, platelet count $<10 \times 10^9$/L, or bleeding score $\geq$ 5. Patients receiving other ITP drugs as maintenance therapy were eligible if previous glucocorticoid therapy doses were stable, and rituximab was used for at least 2 months and other immunosuppressants were stable for at least 4 weeks. Patients who had received IVIG, avatrombopag, eltrombopag, or romiplostim within 2 weeks prior to enrollment were excluded. Histories of platelet transfusion one week before treatment were excluded. Hetrombopag was given at 5 mg/day for 28 days, while rhTPO was administered at 300 U/kg subcutaneously daily for 14 days. When PLT $> 100 \times 10^9$/L, rhTPO should be discontinued. When PLT $> 150 \times 10^9$/L, the dosage of hetrombopag was reduced to 2.5mg/day, and it would be discontinued if PLT $> 250 \times 10^9$/L. The primary endpoints were proportion of subjects with platelet count $\geq 30 \times 10^9$/L and at least doubled the baseline platelet count within 28 days. Secondary endpoints included bleeding score, incidence of thrombotic events, and adverse events (AEs).

Results:
As to July 27, 2023, a total of 20 patients were included in this study, with a median age of 36 years and a male proportion of 50%. Among them, 70% (14 cases) were newly diagnosed ITP patients. 50% of patients have received $\geq$ 1 line of previous treatment, of which 2 patients have received IVIG treatment and both have achieved CR (PLT $\geq 100 \times 10^9$/L). The baseline median platelet count was 5×10^9/L, and 95% (19 cases) of patients had active bleeding with a bleeding score of $\geq$ 1 point. The median duration for hetrombopag at dose of 5mg is 8.0 days, and rhTPO is 6.5 days. After combined treatment, the median time for platelet counts reached 30, 50, and 100×10^9/L was 4.5 days, 6 days, and 7 days, respectively. Among them, the median platelet count reached 103×10^9/L after 7 days treatment and 214.5×10^9/L after 15 days. Within 15 days of combined treatment, 15% (3 cases) of patients achieved partial platelet reaction (PLT $> 50 \times 10^9$/L, without bleeding), and 85% (17 cases) achieved complete platelet reaction (PLT $> 100 \times 10^9$/L, without bleeding). In terms of safety, two patients experienced liver function abnormalities, both of which were grade 1-2. One was related to treatment drugs, and the other was associated with underlying autoimmune liver disease. No thrombotic events occurred in all patients.

Conclusion:
This study innovatively explores the efficacy and safety of combination therapy with hetrombopag and rhTPO in the treatment of severe ITP. It is preliminarily confirmed that this combination therapy can effectively and quickly improve the early platelet response of ITP patients, avoid bleeding damage, and is expected to become a new treatment choice for severe ITP patients. We also look forward to the overall efficacy evaluation results of all patients after completing treatment in the future.

Disclosures No relevant conflicts of interest to declare.

https://doi.org/10.1182/blood-2023-182691