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Blood 142 (2023) 2721–2722

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

508.BONE MARROW FAILURE: ACQUIRED

Comparison between Hetrombopag and Eltrombopag Combined with IST As First-Line Treatment for Severe Aplastic Anemia

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Idiopathic aplastic anemia is a primary bone marrow failure disease that manifests with pancytopenia. Standard IST combined with eltrombopag (EPAG) is recommended as a first-line regimen for severe aplastic anemia patients who are ineligible for HSCT. HPAG is also a small molecule non-peptide TPO-RA developed in China, and the preclinical experiments have demonstrated that hetrombopag (HPAG) can promote the proliferation and differentiation of hematopoietic stem cells and the strength of stimulation was superior to eltrombopag. HPAG also can achieve hematological response for over 40% of IST-refractory SAA patients, and it was approved for use in IST-refractory SAA patients in China in 2021. Our previous report showed that as a first-line treatment, it could improve the HR and CR rate of SAA patients by 68.7% and 34.4% within 6 months, but there has yet to be a report on its efficacy compared to EPAG. Therefore, this study aims to evaluate the difference in early treatment efficacy of SAA patients with HPAG/EPAG combined with IST as first-line therapy.

A total of 109 patients were included in this study, with a median age of 38 years, 53 male and 56 female. Among them, 67 patients received treatment with HPAG combined with ATG+CSA, and 42 patients received treatment with EPAG combined with ATG+CSA. The median follow-up time for the HPAG group was 13.7 (8.1-19.6) months, with a median usage duration of 12 (9.4-14.5) months. For the EPAG group, the median follow-up time was 22.5 (9.9-30.5) months, with a median usage duration of 13.5 (7.8-18.7) months.

At 3 months, 34 (50.7%) cases in the HPAG group achieved HR, including 9 (13.4%) CR. In the EPAG group, 21 (50%) cases achieved HR, including 5 (11.9%) CR. The HR rates in the HPAG group after 3 months of IST were similar to those in the EPAG group, with no statistically significant difference (P=0.973). At 6 months, there were no differences in HR and CR between the HPAG and EPAG groups, 65.6% vs 73.8% and 31.3% vs 28.6%, respectively (P=0.494 and 0.452). The median time to first response in the HPAG group was similar to the EPAG group [3.7 (95% CI: 3.1-6) months vs 3.5 (95% CI: 3.2-6) months, P=0.79].

We further compared the efficacy of TPO-RA combined with IST in patients with different severity of disease. The results showed that the HR and CR of patients with VSAA at 3 and 6 months in the HPAG group were no different compared to that in the EPAG group (HR at 3 and 6 months, 22.2% vs 35.7% and 33.3% vs 57.1%, P=0.671 and 0.404, respectively; CR at 3 and 6 months, 11.1% vs 14.3% and 16.7% vs 28.6%, P=1.000 and 1.000, respectively). In the patients with SAA, the HR, and CR at 3 and 6 months in the HPAG group were comparable to that in the EPAG group (HR, 61.2% vs 57.1% and 77.6% vs 82.1%, P=0.883 and 0.557, respectively; CR, 14.3% vs 10.7% vs 36.7% vs 28.6%, P=1.000 and 0.486, respectively).

In the multivariable analysis, for all 109 patients, the acquisition of HR at 6 months was unrelated to TPO-RA types, and positively correlated with higher HGB and PLT levels and PNH positivity, while negatively correlated with disease severity and ALC levels. Baseline PLT levels were the only predictive factor for EPAG group patients to achieve HR 6 months after IST. The acquisition of HR in HPAG group patients after IST was negatively correlated with disease severity and ALC levels, and positively correlated with baseline PNH positivity.

Overall, both HPAG and EPAG have good safety profiles, and no patients discontinued treatment due to adverse drug reactions. Abnormal liver function is a concern for both drugs and changes in the main liver function indicators (AST, ALT, DBIL, IBIL) at 3 and 6 months after IST. Among them, significant increases in indirect bilirubin levels were observed in patients using EPAG at 3 and 6 months (P<0.001), while no significant increases in indirect bilirubin levels were observed in the HPAG group.

Overall, HPAG added to standard IST can provide SAA patients with similar efficacy to EPAG, while achieving deeper and faster hematological responses. Moreover, the hepatic safety of HAPG may be superior to EPAG. However, this study is a retrospective study with a small number of cases, and large-scale prospective clinical studies are still needed to verify the results.

Disclosures No relevant conflicts of interest to declare.

https://doi.org/10.1182/blood-2023-186123