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Blood 142 (2023) 4091–4092

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

508.BONE MARROW FAILURE: ACQUIRED

Avatrombopag in Combination with Immunosuppressive Therapy for Hepatitis-Associated Aplastic Anemia

Wenrui Yang[1], *Xin Zhao*[1], *Youzhen Xiong*[1], *Huihui Fan*[1], *Jianping Li*[1], *Lei Ye, MD*[1], *Li Zhang*[1], *Liping Jing, MD*[1], *Fengkui Zhang*[1]

[1] Anemia Therapeutic Center, Institute of Hematology and Blood Diseases Hospital, CAMS & PUMC, Tianjin, China

Hepatitis-associated aplastic anemia (HAAA) is an uncommon but distinct variant of aplastic anemia (AA), in which an episode of seronegative acute hepatitis precedes the onset of pancytopenia. Previous studies indicated that about only 20% of HAAA patients can get their hematologic partially restored after 3 months treatment with standard immunosuppressive therapy (IST). Recent studies have shown that adding thrombopoietin receptor agonist (TPO-RA) eltrombopag to standard IST can lead to a more, faster, and better hematologic responses. Nevertheless, eltrombopag is often associated with hepatic adverse effects, i.e., elevated transaminases and bilirubin, which maybe limit its use in patients with HAAA who have just experienced severe liver damage.

Avatrombopag is also a TPO-RA, which was approved for the treatment of thrombocytopenia in patients with chronic liver disease (CLD) and patients with chronic immune thrombocytopenia (ITP) by the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA). The pre-clinical studies indicated that avatrombopag can promote the hematopoietic and megakaryocyte progenitor cells proliferation and differentiation by the dose-dependence. These *in vitro* effects are similar to those of other TPO-RAs, including Eltrombopag. Theoretically, on the basis of adequate IST, avatrombopag can also promote hematopoietic recovery in patients with aplastic anemia just as Eltrombopag works. If this is true, then avatrombopag should be particularly suitable for HAAA due to its favorable hepatic adverse effect profile. Nevertheless, avatrombopag added to standard IST as first-line treatment for aplastic anemia could increase the rapidity and strength of hematologic response is still unknown. Herein, we retrospectively reviewed 8 consecutive cases of patients with hepatitis-associated aplastic anemia who were treated with avatrombopag plus IST regimen.

From September 2021 to December 2022, eight patients with hepatitis-associated aplastic anemia treated with avatrombopag in combination with standard IST were enrolled in this study. Among them, seven patients were diagnosed as VSAA and one SAA. The median age was 17 (9-20) years old and the median absolute neutrophil count was 0.09 (0.02-0.39) $\times 10^{9}$/L. The median time from onset of hepatitis to hematopoietic failure was 2 (0.5-5.5) months, and at the time of beginning of IST all the eight patients had their liver biochemical testing returns to normal. The karyocytes were normal in all patients. One patient presented positive PNH clone at the diagnosis of HAAA, with PNH clone size of 4.7%.

Avatrombopag was incorporated into day 1 of standard immunosuppressive therapy with p-ATG and cyclosporine for all the eight HAAA patients. The dose of avatrombopag was 40 mg/d at least 6 months. Dosage adjusting of avatrombopag was according to patient's platelet counts and adverse events. Encouragingly, four of the eight patients (50.0%) achieved hematologic response (HR) with two (20.0%) getting complete response (CR) at 3 months after IST and avatrombopag. Between 3 and 6 months after IST, the other two patient entered their hematologic responded. Then, six of eight (75.0%) patients got HR at 6 months, including 3 CR, 2 good partial hematologic response (GPR), and 1 partial response (PR). Unfortunately, one patient who was diagnosed as very severe HAAA, was without getting hematologic response and died at 118 days after treatment due to gastrointestinal infection.

We evaluate the side effects of avatrombopag and graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. No hepatic adverse events were observed in all the eight patients, that indicated avatrombopag may not increase the hepatic burden and is safe for HAAA. The median follow-up time was 371(118-665) days. Except for one patient who died within 6 months, six cases achieved hematologic response, with 4 CR and 2 GPR. There is no clonal evolution, i.e., MDS, AML, and PNH, was observed.

In conclusion, avatrombopag may be used as a safe and effective TPO-RA, added to IST for the treatment of hepatitis-associated aplastic anemia, which maybe improve the efficacy and the strength of hematologic response in HAAA.

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Disclosures No relevant conflicts of interest to declare.

https://doi.org/10.1182/blood-2023-179722

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