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POSTER ABSTRACTS

508.BONE MARROW FAILURE: ACQUIRED

Efficacy, Safety, and Population Pharmacokinetics of Eltrombopag in Children with Different Severities of Aplastic Anemia

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OBJECTIVES: Eltrombopag (EPAG) was initially approved by the U.S. Food and Drug Administration (FDA) as first-line treatment, combined with standard immunosuppressive therapy, for patients older than two years old with severe aplastic anemia (SAA). However, the use of EPAG in children with different types of aplastic anemia (AA), especially non-severe AA (NSAA) has been limited. Therefore, we decided to investigate the efficacy, safety, and pharmacokinetics of EPAG in children with NSAA, SAA, and very severe AA (VSAA).
METHODS: A prospective, open-label, observational study was conducted at the Institute of Hematology and Blood Diseases Hospital, Tianjin, China. The efficacy including complete response (CR), partial response (PR), and no response (NR), as well as safety was assessed every three months after the start of treatment. A non-linear mixed-effects population pharmacokinetic (PPK) model was used to depict the pharmacokinetic profile of EPAG. We explored the exposure-response relationship of EPAG in patients with different types of AA. This study was registered at ClinicalTrials.gov (NCT03844360).
RESULTS: A total of 23 AA children with an average age of 7.9 (range of 3.0 - 14.0) years were enrolled in this study for efficacy, safety, and PPK analysis. Fifteen patients had a treatment response (5 had CR and 10 had PR). The response rate was 12.5% after 3 months, 50.0% after 6 months, and 100% after 12 months of treatment for patients with NSAA. For patients with SAA and VSAA, these response rates were 46.7%, 61.5%, and 87.5%. Hepatotoxicity occurred in one patient. Fifty-three blood samples were collected and analyzed to build the PPK model using allometric scaling with fixed exponents. Body weight significantly affected EPAG's apparent clearance and volume of distribution. The mean (range) of the area under the concentration-time curve from time zero to infinity (AUC_{∞}) was 316 (131 - 809) $\mu g \times h$ /mL. Twenty patients with genotypes were included in the genotype analysis. The apparent clearance of EPAG was significantly higher in allele-T carriers of adenosine triphosphate-binding cassette G2 (ABCG2) (rs2231142, G>T) (p=0.02). In patients with clinical response, children with NSAA exhibited lower AUC_{∞}, higher apparent clearance, and higher weight-adjusted apparent clearance than those with SAA or VSAA, although the differences were not significant.
CONCLUSIONS: This study enriched the efficacy and safety of EPAG in children with different types of AA. Body weight and *ABCG2* genotype significantly influence EPAG clearance. The results may support further individualized treatment of EPAG in children with AA.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: The use of eltrombopag (EPAG) treating children with acquired aplastic anemia in China is off-label but in-label in the US and EU. This study aimed to investigate the efficacy and safety of EPAG in children with different types of aplastic anemia and establish a population pharmacokinetic model to describe the pharmacokinetic behavior of EPAG, and to locate the physiological and genetic factors that might result in the variability of its exposure.

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