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637.MYELODYSPLASTIC SYNDROMES - CLINICAL AND EPIDEMIOLOGICAL

Recombinant Human Erythropoietin Combined with All-Trans Retinoic Acid and Testosterone Undecanoate in the Treatment of Anemia in Patients with Lower-Risk Myelodysplastic Syndromes: Updated Results of a Multicenter, Single-Arm, Prospective Trial

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[Background] More than 90% of low-risk MDS face refractory anemia and blood transfusion dependence for a long time. At present, recombinant human erythropoietin (EPO) is the main treatment, but the effective rate of single agent is 30%-40%, which seriously affects the quality of life of patients. Previous studies had shown that testosterone undecanoate could promote erythroid hematopoiesis and all-trans retinoic acid (ATRA) had the function of promoting blood cell differentiation in vitro. We previously reported that EPO combined with ATRA and testosterone undecanoate in the treatment of patients with low-risk MDS and demonstrated promising efficacy and safety in a prospective trial (Chen et al, ASH 2022). Here we present an updated analysis of efficacy and safety results in the ongoing study.
[Methods] In this multicenter, single-arm trial, patients with newly diagnosed lower-risk MDS based on the 2016 WHO classification and the Revised International Prognostic Scoring System (IPSS-R) from 3 different tertiary medical centers in China were included. Patients were received EPO (10000IU/day) plus ATRA (25mg/m 2/day) and testosterone undecanoate (80mg twice daily) for 3 months. The primary endpoint was overall hemoglobin response rate, defined as an increase in hemoglobin levels of $\geq$ 1.5g/dL from baseline in 2 or more consecutive assessments (2 weeks apart) and no red blood cell transfusions during this period. Response was assessed after completion of 3months. The data cut-off date was July 25, 2023.
[Results] As of July 2023, a total of 43 patients were enrolled, with a median age of 65 years, 24 males and 19 females, with median hemoglobin of 63 g/L, EPO concentration $>$ 500 IU/L in 18 patients, and the overall hemoglobin response rate of 65.1% (28/43). The hemoglobin response rates were 61.1% (11/18) in patients with EPO concentrations greater than $>$ 500 IU/L and 68.0% (17/25) in patients with EPO concentrations $\leq$ 500, which were not statistically different.
Among them, 112 known or putative mutational gene targets in hematologic malignancy were examined for mutations in 32 patients using a custom targeted next-generation sequencing (NGS) gene panel. The most frequent mutations were SF3B1 (15/32, 46.8%) and ASXL1 (8/32, 25.0%). The hemoglobin response rate was 80.0% (12/15) in patients with SF3B1 mutation and 37.5% (3/8) in patients with ASXL1 mutation, respectively.
Among 43 patients evaluable for safety analysis, the most common non-hematological adverse events were dry skin (17/43, 39.5%) and fatigue (12/43, 27.9%). No patients had disease progression during the treatment period.
[Conclusion]: This study showed that EPO combined with tretinoin and testosterone undecanoate regimen can effectively improve the anemia of lower risk MDS in approximately 65.1% of patients and is not affected by EPO concentration. It has the better efficacy in patients with SF3B1 mutation, but has worse efficacy in patients with ASXL1 mutation. It is worthy of further randomized controlled studies to verify the efficacy.

Disclosures No relevant conflicts of interest to declare.

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