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POSTER ABSTRACTS

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

Biomarker MSC-C5b-9-Guided Master Therapies for Resistant/Recurrent ITP: A Prospective, Randomized, Open-Label, Multicenter Trial

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Introduction:
Immune thrombocytopenia (ITP) is an acquired organ-specific autoimmune disorder and a common bleeding disorder that poses a considerable risk to human health. Steroids, as the first-line treatment, do not provide long-term relief. Our previous clinical trials have confirmed the efficacy and safety of all-trans retinoic acid (ATRA) in the treatment of ITP and identified that the biomarker MSC-C5b-9 may be a stratification marker for evaluating the efficacy of ATRA (Haematologica, 2019; Lancet Haematol. 2017; 2021). This research aims to develop a new treatment approach for steroid-resistant/recurrent ITP based on the marker MSC-C5b-9.

Method:
We conducted a prospective, randomized, open-label, multicenter trial to evaluate the efficacy and safety of ATRA combined with eltrombopag based on MSC-C5b-9 as a novel treatment for steroid-resistant/recurrent ITP. Following enrollment, all patients underwent bone marrow aspiration to assess MSC-C5b-9 levels. Subsequently, patients were randomly assigned in a 1:1 ratio to either the eltrombopag group or the eltrombopag + ATRA group. In both treatment groups, the initial dose of eltrombopag was 50 mg daily, with dose adjustments based on platelet levels. For patients assigned to the ATRA group, ATRA was given at a dose of 10 mg twice daily. Peripheral blood cell counts and adverse drug reactions were regularly monitored. The primary endpoint was the sustained response rate at 18 months after randomization, and secondary endpoints include Complete Remission, Partial Remission, Relapse rate, Early Response, Initial Response, Adverse Events, and Adverse Events graded using the National Cancer Institute Common Terminology Criteria (NCI CTCAE) v5.0 criteria. The study has been registered at clinicaltrials.gov. NCT05438875.

Result:
From March 2023 to July 2023, a total of 30 patients with steroid-resistant/recurrent ITP were enrolled in the study and randomized 1:1 to receive eltrombopag combined with ATRA (ATRA group, n=15, MSC-C5b-9 +6, -9) or eltrombopag alone (control group, n=15, MSC-C5b-9 +6, -9) in 5 centers, and all enrolled patients were included in the intention-to-treat (ITT) analysis. In the ATRA group, the median age was 38 years (range, 29-64), consisting of 8 male patients. In the control group, the median age was 44 years (range, 23-75), consisting of 9 male patients. There were no statistically significant differences observed in the baseline clinical characteristics between the two groups. There was no difference in the bleeding score and ECOG score between the two groups (P=0.717; P=1.000). The median platelet count was comparable between the ATRA group and the control group (17 (1-28) vs. 16 (2-26), P=0.850). Comorbidities at random, such as hypertension, were comparable between the two groups (26.7% (4/15) vs. 33.3% (5/15), P=1.000). Combined autoantibody abnormalities were compared between the two groups (6.7% (1/15) vs. 6.7% (1/15), P=1.000). The rate of Early Response in the ATRA group was higher than that in the control group, but the difference was not significant (73.3% (11/15) vs. 53.5% (8/15), P=0.256). As of July 29, 2023, a total of 24 patients had been enrolled for a duration exceeding 4 weeks. Similarly, the Initial Response rate was higher in the ATRA group, but no significant difference was observed between the two groups (84.6% (11/13) vs. 63.6% (7/11), P=0.357). Nevertheless, it is noteworthy that the 4-week CR rate in the ATRA group was higher than that in the control group (76.9% (10/13) vs. 36.4%

(4/11), P=0.045). What's more, the overall efficacy of the ATRA group was better than that of the control group. The mean platelet count at weeks 1, 2, 3, and 4 posttreatment, along with the mean maximum platelet count posttreatment, exhibited higher values in the ATRA group than in the control group; however, these disparities did not reach statistical significance (P=0.310; P=0.568; P=0.779; P=0.618; P=0.355). ATRA was well tolerated, and only one patient developed grade I dry mouth and headache, which improved after dose reduction. There was no difference between the ATRA and control groups in terms of medication adverse effects (13.3% (2/15) vs. 13.3% (2/15), P=1.000).

Conclusions:

Eltrombopag plus ATRA is an effective and well-tolerated approach for treating steroid-resistant/recurrent ITP. Eltrombopag plus ATRA can enhance patients' complete remission and is well tolerated.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: All-trans retinoic acid (ATRA), primarily used for the treatment of acne vulgaris.

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