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POSTER ABSTRACTS

721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Efficacy and Safety of Hetrombopag in Promoting Platelet Engraftment after Allogeneic Hematopoietic Stem Cell Transplantation: A Prospective, Multicenter, Randomized Controlled Clinical Trial

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Background and Objective: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is widely used to treat hematological malignancies and non-malignant hematological diseases. However, the incidence of thrombocytopenia after transplantation is common, and within 60 days after HSCT, around 5-38% of patients experienced delayed platelet engraftment or persistent isolated thrombocytopenia. Thrombocytopenia after transplantation was significantly associated with life-threatening bleeding events and reduced overall survival rate. Previous studies have found that the biphenyl structure may have hepatotoxicity, Hetrombopag (TPORA) replaces it with a heterocyclic carboxyl group to reduce hepatotoxicity, which can also enhance the lipophilicity and improve the efficacy by report. Hetrombopag was proved safe and effective in treating ITP and aplastic anemia. The aim of this study is to evaluate efficacy and safety of Hetrombopag in promoting platelet engraftment after allo-HSCT.

Methods: Patients undergoing allo-HSCT were randomly grouped on day 3 after stem cell infusion. The experimental group treated with Hetrombopag 2.5mg/d or 5mg/d orally till platelet reconstitution, instead the control group was given thrombopoietin (TPO) 300U/kg/d. Platelet engraftment was defined as platelet count $\geq 20\times10^{9}$/L for consecutive 7 days without platelet transfusion. The primary endpoint is the time for platelet engraftment. The secondary endpoints include the time to granulocyte engraftment, platelet transfusion units, medical costs during hematopoietic reconstitution, and side effects.

Results:

Currently, 26 patients were enrolled in the Hetrombopag experimental group and 26 in the TPO control group. The median age of experimental group was 35 years (14-62 years), with 9 AML patients, 9 ALL, 5 MDS/MPN, 2 AA, and 1 MPAL. Among them, 12 received haplo-transplantation, and 14 underwent HLA-identical transplantation. The average number of transfused mononuclear cells (MNCs) was 8.6 (5.28-12.79) $\times10^{8}$/kg, and the average number of $CD34^{+}$ cells was 5.93 (2.39-9.37) $\times10^{6}$/kg. The mean time for granulocyte and platelet engraftment was 15.26±3.37 and 15.20±4.06 days respectively. Primary graft failure of platelet occurred in 1 patient (3.8%).

The median age of the control group was 36 years (19-63 years), with 12 patients diagnosed AML, 9 ALL, 2 MDS/MPN, 2 AA, 1 plasma cell leukemia, and 1 NKTCL. 19 of them received haplo-transplantation, while 7 receivedHLA-identical transplantation. The average numbers of transfused MNCs and $CD34^{+}$ cells were 9.05 (5.39-16.22) $\times10^{8}$/kg and 6.4 (1.96-10.45) $\times10^{6}$/kg respectively. The mean days of granulocyte and platelet reconstitution were 17.38±5.82 and 18.18±4.62 days, respectively. PGF occurred in 4 patients (15.4%). Compared with the control group, the experimental group had a significantly earlier engraftment of granulocytes (P=0.03) and platelets (P=0.01). During platelet reconstitution, the control group was transfused 6.87±3.93U of platelets and the experimental group was transfused less (3.92±3.45U, $P = 0.0009$). The medical cost of using TPO and Hetrombopag was 12555.39±5222.33 yuan in the control group and 2783.90±1020.04 yuan in the experimental

group ($P < 0.0001$). The above data are the interim analysis results of this study. Liver transaminases were elevated in 4/26 cases in the experimental group and 2 cases in the TPO group, after one week of drug administration; Different degrees of organ bleeding (digestive tract, urinary tract, etc.) occurred in 6 cases in the experimental group and in 9 cases in the control group. Notably, the above data are only interim analyses and the side effects may not only be due to the study medication, as allo-HSCT itself includes very complex factors.

Conclusion: Hetrombopag can safely promote rapid platelet engraftment, shorten the time difference between granulocyte and megakaryocyte reconstitution, reduce platelet transfusion, and decrease the economic burden of patients after allo-HSCT.

Keywords: Hetrombopag, Allo-HSCT, TPORA, Platelet engraftment.

Disclosures No relevant conflicts of interest to declare.

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