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POSTER ABSTRACTS

723.ALLOGENEIC TRANSPLANTATION: LONG-TERM FOLLOW-UP AND DISEASE RECURRENCE

Trametinib Maintenance in Patients with RAS Mutated Hematologic Malignancy Undergoing Allogeneic Haematopoietic Stem-Cell Transplantation: A Retrospective Transplant Study

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Aim: The abnormal activation of MAPK signaling pathway plays an important role in the occurrence and development of leukemia. Whether MEK inhibitors can effectively reduce the recurrence of hematologic malignancy, We reviewed the efficacy and safety of trametinib maintenance in post-transplant patients with RAS mutations.
Methods: Our study retrospectively analyzed 61 hematologic malignities with RAS mutation who underwent allo-HSCT at Beijing Gaobo Boren Hospital between January 2018 and January 2023. Twenty-five patients received maintenance therapy with trametinib post-HSCT(trametinib group), and 36 patients did not receive any maintenance therapy (control group). Trametinib group and control group also achieved CR at 2 months post-HSCT.
Results: The diagnosed including AML (23, 37.7%), B-ALL (33, 54.1%), T-ALL (3, 5.0%), and 2 others (3.3%). Male: female = 29:32, The median age was 15 (1-68) years old. Before transplantation, 5 patients (8.2%) had extramedullary lesions and 16 patients (26.2%) had chromosomal abnormalities. The disease status before transplant was CR (42,68.9%),PR(6,9.7%),NR (13,21.3%) . 53 patients (86.9%) received second-line treatment. Fifteen cases (24.6%) were secondary transplants.
Donor type included haploidential (45, 73.8%), identical sibling (5, 8.2%), and unrelated (11, 18.0%). Myeloablative conditioning regimen with eitherTBI/fludarabine (33, 54.1%) based or busulfan/fludarabine (28, 45.9%) based were applied. There were no significant differences between the two groups in age, sex, extramedullary disease,central nervous leukemia, karyotype analysis, disease status, conditioning regimen, donor type,acute and chronic GVHD and acute GVHD grades.
The median follow-up time was 16.5 months (95%CI: 16.8-24.8 months), and the overall survival(OS) was 81.2% (95%CI: 68.6-89.1%). The disease-free survival (PFS) was 73.0% (95%CI: 59.7-82.5%). Trametinib group, the OS was 91.5% (95%CI: 70.0-97.8%), PFS was 88.0% (95%CI: 67.3-96.0%). Control group, the OS was 73.9% (95%CI: 55.9-85.6%), PFS was 65.8% (95%CI: 47.7-78.9%). Trametinib significantly improved the OS and DFS (P=0.044; P=0.041). In the trametinib group, 4 patients died after treatment, of which 3 died of relapse and 1 died of respiratory failure. In the non-trametinib group, 13 patients died, of which 6 died of relapse and 7 died of infection, stroke, GVHD and other causes. Trametinib treatment was initiated at a median of 94 days (range 63-178) at a median dose of 1 (range 0.5-2) mg daily.Trametinib was temporarily discontinued in 9 patients and dose modification in 12 patients because of side effects. mainly due to side effects including hematotoxicity in 5 patients, nosebleed in 4 patients, diarrhea in 1 patient, fatigue in 1 patient, and disease recurrence in 1 patient. The median modified daily dose was 0.5mg (range 0-1mg). Grade 2 AES occurred during the course of trametinib treatment, and no ≥ grade 3 AES was observed. The most common adverse events were neutropenia, anemia, thrombocytopenia, epistaxis, neutropenic fever, and fatigue, all of which were tolerable and reversible. No cardiorespiratory, renal, or neurotoxicity, or treatment-related deaths were observed. The median duration of trametinib maintenance therapy was 270 days (range 30-630 days).
Conclusions: In this study, We have observed that trametinib maintenance post-transplantation can significantly improve the prognosis of patients with RAS mutations.Trametinib can be used as maintenance therapy with different conditioning regiments post-HSCT, which does not increase the risk of GVHD and organ injury, and is safe and effective. Future prospective clinical trials with larger sample sizes are needed for further research.

Disclosures No relevant conflicts of interest to declare.

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