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POSTER ABSTRACTS

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

Comparison of Myeloablative Conditioning with Cyclophosphamide and Total-Body Irradiation (Cy/TBI) Vs. Fludarabine, Melphalan, and Total-Body Irradiation (Flu/Mel/TBI) in Patients Undergoing Allogeneic Stem Cell Transplant for AML/ALL

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Background: Cyclophosphamide combined with total-body irradiation (Cy/TBI) has been widely used worldwide as the standard myeloablative conditioning (MAC) for allogeneic stem cell transplantation (allo-HCT), but there are concerns about the antitumor effects of CY, as well as side effects, including cardiotoxicity and mucosal toxicity. A few studies suggest that the addition of an anticancer agent to a Cy/TBI regimen may reduce recurrence rates, but comparative studies of Cy/TBI regimens versus other TBI regimens are scarce. Furthermore, the recent expansion of post-transplant cyclophosphamide as graft-versus-host disease (GVHD) prophylaxis has increased its utility for cyclophosphamide-free conditioning regimens. Our institution has extensive experience with cord blood transplantation for relatively elderly patients with high-risk leukemia and has worked to develop safer and more effective MAC regimens other than Cy/TBI. The purpose of this study is to examine the safety and efficacy of fludarabine and melphalan combined with total-body irradiation (Flu/Mel/TBI) regimen, which is widely used at our institution, compared to Cy/TBI.
Methods: We retrospectively analyzed adult acute leukemia patients who underwent allo-HCT between August 1994 to February 2023 at Toranomon Hospital. The inclusion criteria were as follows: a diagnosis of acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL), the first allo-HCT, and Cy (120mg/kg) /TBI (8-12Gy) or Flu (180mg/m ^{2}) /Mel (80-120mg/m ^{2}) /TBI (8-12Gy) as MAC regimen. We excluded patients who underwent haploidentical transplantation with post-transplant cyclophosphamide. The primary endpoint was the 5-year cumulative incidence of relapse, and the secondary endpoints were the 5-year cumulative incidence of non-relapse mortality (NRM), 5-year overall survival (OS), and relapse-free survival (RFS). OS and RFS were estimated by the Kaplan-Meier method and multivariate Cox proportional hazard models. The cumulative incidence of relapse and NRM were investigated with a competing risk analysis using Gray's test and multivariable Fine and Gray competing risk regression.
Results: A total of 198 patients were included in this study, comprising 101 patients treated with Cy/TBI and 97 treated with Flu/Mel/TBI. Patients who received Flu/Mel/TBI were of higher age (Median age: Cy/TBI 36 years vs. Flu/Mel/TBI 53 years, $p<0.01$), higher ECOG PS score (PS$\geq$1: 51.5% vs. 66.0%, p=0.044), fewer AML (49.5% vs. 22.7%, $p<0.01$), and more frequent CBT (45.5% vs. 76.3%, $p<0.01$). Disease status at HCT (CR1: 53.5% vs. 43.3%, p=0.154) and HCT-CI scores (HCT-CI$\geq$1: 35.6% vs. 44.3%, p=0.214) were not different between the two regimen groups. Regarding the primary endpoint, the 5-year cumulative incidence of relapse was significantly lower in Flu/Mel/TBI group (36.8% vs. 24.9%, p= 0.035). The cumulative incidence of NRM was not significantly different between the two groups (19.1% vs. 25.2%, p=0.345). In the multivariate analysis, conditioning with Flu/Mel/TBI was significantly associated only with a lower risk of relapse (HR: 2.817; 95%CI: 1.183-6.712; p=0.019). Regarding NRM, only disease status not in CR1 was associated with a higher risk (CR1 vs. non-CR1 HR: 2.21; 95%CI: 1.095-4.468; p=0.027). There was no significant difference in 5-year OS (Cy/TBI 48.1% vs. Flu/Mel/TBI 51.4%, p=0.604) and RFS (44.2% vs. 49.9%, p=0.24).
Conclusion: Despite older age and worse PS in the Flu/Mel/TBI group, Flu/Mel/TBI had a significantly lower 5-year cumulative relapse rate than Cy/TBI, with no significant difference in NRM. Our results suggest that Flu/Mel/TBI is a reasonable alternative to CY/TBI and may be a superior TBI-containing MAC regimen.

Disclosures No relevant conflicts of interest to declare.

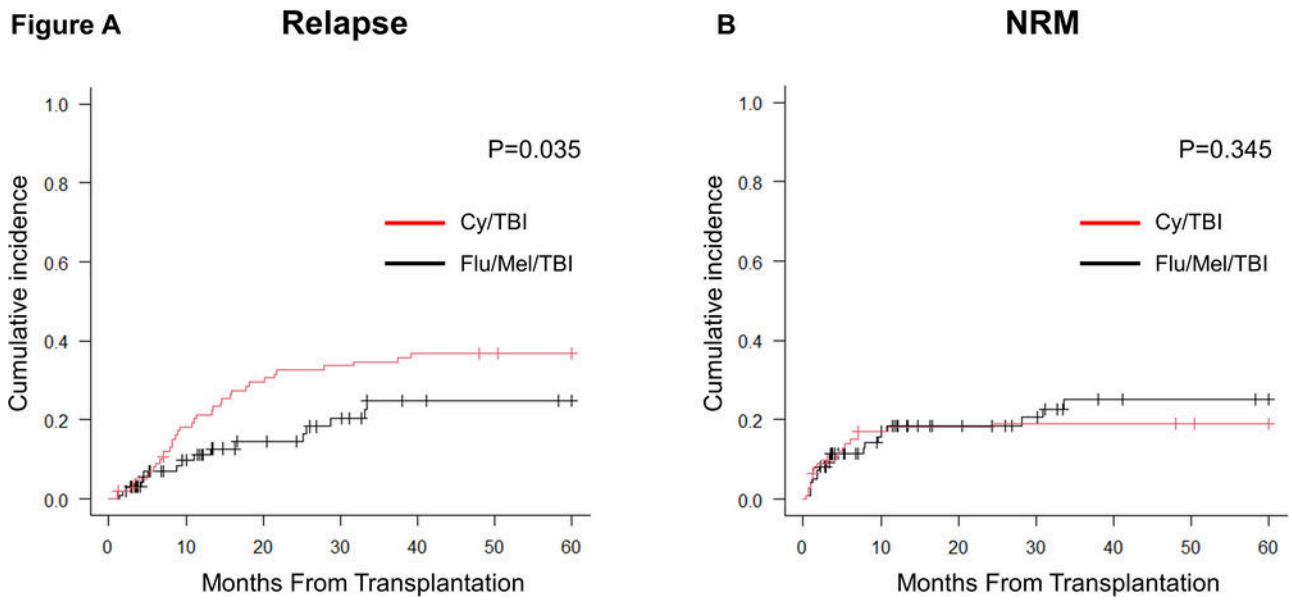

Figure 1

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