

ARTICLE



Fludarabine/busulfan versus busulfan/cyclophosphamide as myeloablative conditioning for myelodysplastic syndrome: a propensity score-matched analysis

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Myeloablative conditioning with fludarabine/busulfan (Flu/Bu4) prior to allogeneic hematopoietic stem cell transplantation (allo-HSCT) is effective for acute myeloid leukemia. However, the effectiveness of Flu/Bu4 for myelodysplastic syndrome (MDS) remains poorly understood. Therefore, we retrospectively analyzed nationwide registry data in Japan from 2006 to 2018 and compared transplant outcomes of adult MDS patients receiving Flu/Bu4 and busulfan/cyclophosphamide (Bu4/Cy) using propensity score (PS) matching. The primary endpoint was overall survival (OS). Among 2,482 MDS patients, 153 patients were assigned each to the Flu/Bu4 and Bu4/Cy groups. The 3-year OS rates were 52.7% (95% confidence interval [CI], 43.8–60.8%) and 49.5% (95% CI, 40.8–57.6%) in the Flu/Bu4 and Bu4/Cy group, respectively ($P = 0.548$). The 3-year progression-free survival ($P = 0.858$), the cumulative incidence of relapse ($P = 0.536$), and cumulative incidence of non-relapse mortality ($P = 0.684$) were not significantly different between the two groups. According to the findings of subgroup analyses, no patient had a favorable OS when using either of the two regimens. In conclusion, although our PS-matched cohort mainly comprised older patients who had a low hematopoietic cell transplantation-comorbidity index and low-risk disease status, Flu/Bu4 could be an alternative to Bu4/Cy for MDS patients prior to allo-HSCT.

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INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative treatment for myelodysplastic syndrome (MDS), but it is associated with severe toxicity [1, 2]. It was originally limited to younger patients who were eligible for myeloablative conditioning (MAC), such as busulfan/cyclophosphamide (Bu4/Cy) [3–5]. The introduction of reduced-intensity conditioning increased the number of elderly patients suitable for allo-HSCT [6–9]. In addition, a combination of fludarabine with myeloablative doses of busulfan (Flu/Bu4) was developed to reduce regimen-related toxicities and retain the anti-tumor activity of MAC [10, 11]. Many studies reported that Flu/Bu4 was effective for patients with myeloid malignancies [12–22]. Randomized controlled trials (RCTs) comparing Flu/Bu4 and Bu4/Cy in patients with acute myeloid leukemia (AML) reported fewer regimen-related toxicities with Flu/Bu4 and similar rates of relapse between the two regimens [17, 18].

However, the comparative effectiveness of Flu/Bu4 in MDS patients remains a matter of debate. Most previous studies focused on patients with AML and included few or no patients with MDS [12–19]. Although a single-center retrospective analysis of Flu/Bu4 focused on the outcomes of MDS patients, the Flu/Bu4 and Bu4/Cy arms had different patient background characteristics, such as age, sex, cytogenetic risk, and graft source [21]. Therefore, we retrospectively performed a nationwide propensity score (PS)-matched cohort study to compare the transplant outcomes between Flu/Bu4 and Bu4/Cy in MDS patients who had undergone allo-HSCT.

MATERIALS AND METHODS

Data collection and patient selection

This study was planned by the Adult Myelodysplastic Syndrome Working Group of the Japan Society for Hematopoietic Cell Transplantation and was approved by the Japanese Data Center for Hematopoietic Cell

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