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POSTER ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Higher CD34+ Cell Doses Correlate with Reduced Incidence of Relapse and Better Event-Free Survival after KIR-Ligand Mismatch Cord Blood Transplantation for Childhood Acute Myeloid Leukemia

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Introduction

In children with acute myeloid leukemia (AML), hematopoietic stem cell transplantation (HSCT) is an important treatment, and cord blood units from unrelated donors provide a well-established source of stem cells for HSCT. The main advantages of using cord blood include rapid availability, allowance of greater HLA disparities due to a relatively low risk of severe graft-versus-host disease (GVHD), and possibly a greater graft-versus-leukemia (GVL) effect. Killer cell immunoglobulin-like receptors (KIRs) are the main receptors on natural killer cells that play an important role in GVL after HSCT. Previous studies on the effects of KIR-ligand (KIR-L) incompatibility in unrelated cord blood transplantation (CBT) for leukemia have resulted in conflicting results, and in some studies, this has led to an increased incidence of acute GVHD. Furthermore, the impact of KIR-L mismatch on outcomes in children with AML remains poorly understood.

In this study, we explored the association of KIR-L incompatibility and other clinical factors with patient outcomes in children with AML who received CBT.

Methods

Data were collected from the Transplant Registry Unified Management Program sponsored by the Japanese Society for Transplantation and Cellular Therapy and the Japanese Data Center for Hematopoietic Cell Transplantation. The patients were selected according to the following criteria: (1) *de novo* non-M3 AML, (2) age < 16 years and CR1 or CR2 at the time of receiving HSCT, (3) no prior HSCT, and (4) HSCT performed between 2000 and 2021. Patients without information on survival and disease recurrence or those with Down syndrome were excluded. KIR-L mismatch in the graft-versus-host direction was defined as lacking a donor KIR-L group (HLA-C1, C2, Bw4, or A3/A11) in a recipient. A myeloablative conditioning regimen was defined as total-body irradiation (TBI) at > 8 Gy, melphalan at > 140 mg/m^2, or busulfan at ≥ 9 mg/kg. All other regi-

mens were analyzed as reduced-intensity conditioning regimens. Adverse cytogenetics were defined as previously described [Creutzig et al. Blood, 2012].

Results

A total of 299 patients were included. The median age at HSCT was 5 years (range, 0-15), and the median follow-up period for survivors was 7.2 years (range, 0.1-22.4). The median total nucleated cell and CD34+ cell doses were 6.7 x 10^7/kg (range 0.01-12.3) and 1.9 x 10^5/kg (range 0.01-59.4), respectively. The study cohort consisted of 240 patients in the KIR-L match group and 59 patients in the KIR-L mismatch group. The background characteristics of these two groups did not differ significantly, except for a trend indicating that the KIR-L mismatch group received CBT more recently ($p = 0.063$).

The cumulative incidence rates of neutrophil recovery at Day 42 were 93.3% (95% CI, 89.3-95.9%) and 91.5% (95% CI, 80.0-96.5%) ($p = 0.980$), and the cumulative incidence rates of platelet engraftment at 6 months were 91.5% (95% CI, 87.1-94.5%) and 89.8% (95% CI, 77.9-95.5%) ($p = 0.314$) for the KIR-L match and mismatch groups, respectively. The cumulative incidence rates of grade II-IV acute GVHD at Day 100 were 40.9% (95% CI, 34.6-47.1%) and 40.7% (95% CI, 28.0-52.9%) ($p = 0.709$), whereas those of chronic GVHD at one year after transplantation were 15.6% (95% CI, 11.2-20.6%) and 15.9% (95% CI, 7.8-26.6%) ($p = 0.914$) for the KIR-L match and mismatch groups, respectively.

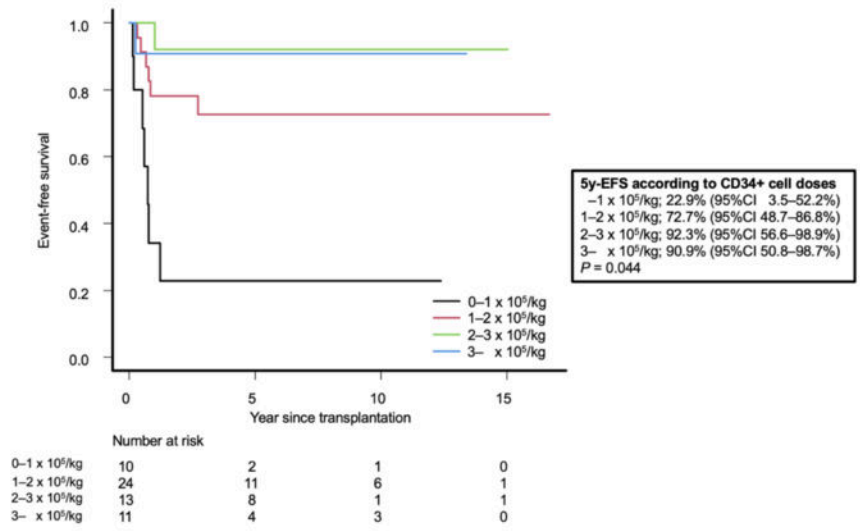
In univariate analyses, the 5-year event-free survival (EFS) was 70.1% (95% CI, 63.6-75.6%) for the KIR-L match group and 72.9% (95% CI, 59.0-82.8%) for the KIR-L mismatch group ($p = 0.609$). Stratification by CD34+ cell doses showed a significant correlation between higher CD34+ cell doses and better EFS in the KIR-L mismatch group (Figure 1), attributed not only to reduced nonrelapse mortality but also to a lower incidence of relapse. In multivariate analysis of EFS, KIR-L mismatch with high CD34+ cell doses (> the median doses) was identified as an independent favorable prognostic factor (Table 1; hazard ratio = 0.21, $p = 0.037$).

Conclusion

Our study demonstrates that higher CD34+ cell doses were associated with a lower relapse rate and better EFS in KIR-L mismatch CBT for childhood AML. This finding is noteworthy, as previous literature has primarily emphasized the role of higher CD34+ cell doses in reducing nonrelapse mortality. Our results suggest that higher CD34+ cell doses are also crucial for achieving a high GVL effect in the context of KIR-L mismatch CBT.

Disclosures No relevant conflicts of interest to declare.

Figure 1. Event-free survival according to CD34+ cell doses among patients receiving KIR-ligand mismatch CBT.



Abbreviations. KIR, killer cell immunoglobulin-like receptors; CBT, cord blood cell transplantation.

Table 1. Multivariate analysis of event-free survival.

Factor	Hazard ratio	*p* value
KIR match-CD34 low	ref	
KIR mismatch-CD34 low	1.51 (0.79–2.88)	0.233
KIR match-CD34 high	0.88 (0.51–1.51)	0.581
KIR mismatch-CD34 high	0.21 (0.05–0.92)	0.037
Age 0–4	ref	
Age 5–9	0.74 (0.41–1.35)	0.295
Age 10–15	0.67 (0.35–1.29)	0.213
Chemo-based MAC	ref	
TBI-MAC	2.18 (1.27–3.74)	0.005
RIC	0.71 (0.31–1.65)	0.429
HSCT year 2000–2009	ref	
HSCT year 2010–2021	1.16 (0.72–1.89)	0.578
CR1	ref	
CR2	1.36 (0.84–2.18)	0.224
Cytogenetics Favorable	ref	
Cytogenetics Intermediate	1.47 (0.74–2.91)	0.274
Cytogenetics Adverse	1.80 (0.82–3.96)	0.143
no grade II–IV acute GVHD	ref	
grade II–IV acute GVHD	1.04 (0.66–1.63)	0.860

Abbreviations. KIR, killer cell immunoglobulin-like receptors; MAC, myeloablative conditioning; TBI, total body irradiation; RIC, reduced-intensity conditioning; HSCT, hematopoietic stem cell transplantation; CR, complete remission; GVHD, graft-versus-host disease; ref, reference.

Figure 1

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