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POSTER ABSTRACTS

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

A Novel Post-Transplant Regimen for Selectively Promoting Unrelated Cord Blood Engraftment in Haploidentical-Cord Transplantation in Childhood Leukemia: A Single-Arm, Dual-Center Trial

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Background
Our previous studies indicated that complementary transplantation that was combined with a haploidentical peripheral blood stem cell (PBSC) transplant (haplo-SCT) and unrelated cord blood (UCB) transplant using a post-transplant cyclophosphamide (PTCy) regimen was applicable in children with acute leukemia. A better leukemia-free survival (LFS) was found in the UCB engraftment group, however, the engraftment of PBSC or UCB was unpredictable in the setting of complementary transplantation. Here, we conducted a prospective single-arm dual-center trial to investigate the effect of post-transplant cyclophosphamide plus fludarabine regimen for selectively promoting UCB engraftment in haploidentical-cord transplant.

Methods
This updated conditioning regimen was performed in two hospitals in China, including a total of eligible 78 pediatric patients who were enrolled from September 2019 to October 2022. The median follow-up was 24 months. This study is in progress. Meanwhile, 55 historically consecutive patients from December 2012 to June 2019 were included for comparison. The updated conditioning regimen (PT-Cy/Flu group) consisted of fludarabine (40mg/m ^{2}, d-5 to d-3 and d+3, d+4), busulfan (100mg/m ^{2}, d-6 to d-3), haplo-PBSC (d0), PTCy (50mg/kg, d+3, d+4) and UCB (d+6). The fludarabine was applied at d-6 to d-2 in the original conditioning regimen (PT-Cy group). In addition to PTCy, tacrolimus or cyclosporine and mycophenolate mofetil were administered as prophylaxis of GVHD. The primary aim was the UCB engraftment rate. In addition, the 2-year mid-term inspection included overall survival (OS), LFS, non-relapse mortality (NRM), graft-versus-host disease (GVHD)-free, relapse-free survival (GRFS), and cumulative incidence of acute and chronic GVHD.

Results
The characteristic of patients were shown in **Table 1**. In brief, 47 (60.3%) acute myeloid leukemia and 27 (34.6%) acute lymphoblastic leukemia pediatric patients were included. 64 (82.1%) patients achieved first complete remission (CR1) before SCT. The median of PBSC mononuclear cells was 20.0×10^8/kg and CD34$^+$ cells was 12.1×10^6/kg, while the median of CB total nuclear cells was 5.0×10^7/kg and CD34$^+$ cells was 1.8×10^5/kg. Eventually, 73 (93.6%) patients in the PT-Cy/Flu group achieved full UCB engraftment by short tandem repeat (STR) detection, while the UCB engraftment rate was 24 (43.6%) in the PT-Cy group ($p<0.001$). The OS of the PT-Cy/Flu group was 88.6% ± 4.0% (95%CI 81.2% - 96.7%), which was significantly higher than the PT-Cy group [60.0% ± 6.6% (95%CI 48.4% - 74.5%), $p<0.001$] **(Figure 1A)**. Of note, the LFS was markedly higher in the PT-Cy/Flu group compared to PT-Cy group [83.2% ± 4.3% (95%CI 75.2% - 92.0%) vs. 54.2% ± 6.8% (95%CI 42.4% - 69.2%), $p<0.001$] **(Figure 1B)**. However, there was no statistical difference in NRM between the PT-Cy/Flu and PT-Cy groups (7.7% ± 0.1% vs 12.7% ± 0.2%, $p=0.326$). Moreover, similar cumulative incidence of III-IV acute GVHD and severe chronic GVHD were found between groups **(Figure 1C, D)**. Finally, the GRFS of the PT-Cy/Flu was obviously better than the PT-Cy group [70.1% ± 5.9% (95%CI 59.5% - 82.5%) vs 39.4% ± 7.6% (95%CI 27.0% - 57.5%), $p=0.025$] **(Figure 1E)**.

Conclusion
These results suggested that the novel post-transplant cyclophosphamide plus fludarabine regimen can be considered as a strategy for selectively facilitating UCB engraftment and improving LFS in haploidentical-cord transplant in children with acute leukemia.

Disclosures No relevant conflicts of interest to declare.

Table 1. Characteristics of patients.

Characteristic		N=78
Age (years, mean (SD))		7 (4.5)
Sex (%)	Male	50 (64.1)
	Female	28 (35.9)
Diagnosis (%)	ALL	27 (34.6)
	AML	47 (60.3)
	Other leukemia	4 (5.1)
Remission pre-SCT (%)	CR1	64 (82.1)
	CR2	11 (14.1)
	CR3	1 (1.3)
	NR	2 (2.6)
PBSC (%)	HLA 8/10	5 (6.4)
	HLA 7/10	9 (11.5)
	HLA 6/10	17 (21.8)
	HLA 5/10	47 (60.3)
CB (%)	HLA 10/10	5 (6.4)
	HLA 9/10	14 (17.9)
	HLA 8/10	35 (44.9)
	HLA 7/10	22 (28.2)
	HLA 6/10	2 (2.6)
PBSC-MNC ($\times 10^8$/kg, median [IQR])		20.00 [20.00, 20.00]
PBSC-CD34 ($\times 10^6$/kg, median [IQR])		12.19 [7.35, 16.38]
CB-TNC ($\times 10^7$/kg, median [IQR])		5.03 [3.85, 7.00]
CB-CD34 ($\times 10^5$/kg, median [IQR])		1.80 [1.14, 2.50]
Engraftment (%)	CB	73 (93.6)
	PBSC	5 (6.4)
Neutrophil recovery time (days, median [IQR])		27.00 [24.00, 34.00]
Hemoglobin recovery time (days, median [IQR])		33.00 [21.75, 40.25]
Platelet recovery time (days, median [IQR])		36.00 [24.25, 45.50]

Figure 1. Main outcomes of this study.

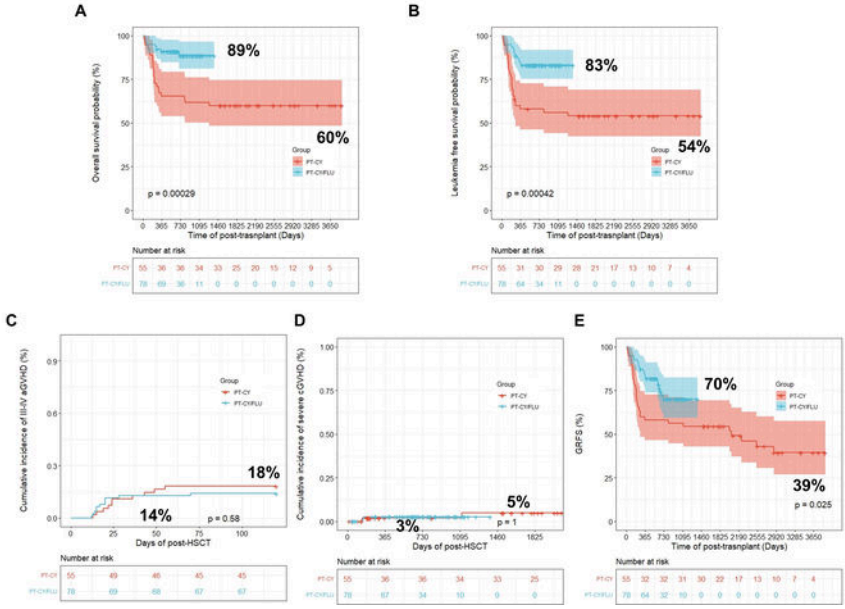

Figure 1

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