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ORAL ABSTRACTS

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

Haploidentical Hematopoietic Cell Transplantation Combined with an Unrelated Cord Blood Unit for Adult Acute Myeloid Leukemia Results in Improved Survival Compared to Haploidentical Hematopoietic Cell Transplantation: Results of a Multicenter, Randomized, Phase III Trial

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Introduction

Haploidentical hematopoietic cell transplantation (haplo-HCT) is a potent treatment to improve the prognosis of acute myeloid leukemia (AML), but relapse and graft-versus-host disease (GVHD) related to dysregulation of alloreactivity are still the main causes of death posttransplantation. Cord blood graft usually has a promising graft-versus-leukemia effect with a lower cumulative incidence of GVHD. To improve the transplantation strategy, haplo-cord HCT combining haploidentical and unrelated cord blood (UCB) grafts (haplo-cord HCT) has been attempted. Previous studies showed significant improvement in prognosis in B-cell acute lymphoblastic leukemia or refractory acute leukemia patients with haplo-cord HCT compared to haplo-HCT. However, outcomes of haplo-cord HCT for AML patients are not yet clear. This is the first multicentric randomized trial designed specifically for the efficacy and safety of haplo-cord HCT for AML.

Methods

This is a multicenter, randomized, open-label, phase III study conducted in 5 centers in China (NCT03719534). Patients aged 18-60 years, diagnosed with AML (except for acute promyelocytic leukemia) with measurable residual disease, had an available haploidentical donor and were suitable for allotransplantation were enrolled. Patients were randomized 1:1 to receive UCB and haploidentical grafts infusion after Bu/Cy-based regimen or haploidentical graft infusion only after Bu/Cy-based regimen. The UCB unit, which had at least 3/6 matched HLA loci to the recipient and more than 1×10^4 $CD34^+$ cells/kg of recipient weight, was infused immediately after resuscitation and eight hours before the haploidentical graft infusion. The primary endpoint was 3-year overall survival (OS) and secondary endpoints included progression-free survival (PFS), cumulative incidence of relapse (CIR), and non-relapse mortality (NRM).

Results

From June 1, 2017, to June 30, 2021, 268 patients were enrolled (Table 1). With a median follow-up of 36.00 months, the 3-year OS was 80.5% (95% CI 73.7-87.9) in the haplo-cord HCT group and 67.8% (95% CI 60.0-76.5) in the haplo-HCT group, respectively (p=0.013, figure 1A). Haplo-cord HCT group showed favorable 3-year PFS and CIR than haplo-HCT group (PFS: 70.3%, 95% CI 62.6-78.8 vs. 57.6%, 95% CI 49.6-67.0, p=0.012; CIR: 12.1%, 95% CI 12.0-12.2 vs. 30.3%, 95% CI 30.1-30.4, p=0.024, figure 1B,C). The 3-year NRM was similar in the two groups (figure 1D).

Within two years posttransplantation, the most common grade 3-4 adverse events (AEs) in the haplo-cord HCT and haplo-HCT groups were infections (33.8% and 29.1%), acute GVHD (20.3% and 12.7%) and chronic GVHD (12.0% and 16.4%). AEs leading to death occurred in 8.3% of haplo-cord HCT and 14.9% haplo HCT patients.
Post- hoc analysis showed similar median levels of haploidentical chimerism in bone marrow (BM) between the two groups. However, UCB microchimerism was detected in the haplo-cord HCT patients by SNP-NGS in +1m posttransplantation (BM: 0.3%, IQR 0.04-1.6; peripheral blood: 0.06%, IQR 0.03-0.4) and its chimerism percentage decreased with time (figure 1E). Compared to haplo-HCT group, haplo-cord HCT group showed a faster cumulative incidence of neutrophil recovery (p=0.026, figure 1F) and a similar cumulative incidence of platelet recovery. Monitor of immune reconstitution showed a more rapidly increasing rate of T cells in the early period after transplantation in the haplo-cord HCT group (figure 1G). Improved recovery of Th2 (p=0.042), Th17 (p=0.047), Treg (p=0.045), and Tc2 (p=0.045) cells was observed in haplo-HCT group.

Conclusions

Coinfusion of a UCB unit in haplo-HCT can improve OS in AML patients without excessive AEs, and affect T-cell reconstitution pattern posttransplantation. Haplo-cord HCT could serve as a suitable therapeutic option for this patient population.

Disclosures No relevant conflicts of interest to declare.

	Haplo-cord HCT	Haplo-HCT
	N=134	N=134
Sex, male/female	75/59	73/61
Age, years	39.0 (30.0-45.0)	38.5 (29.0-48.8)
2017 ELN Risk Category		
Adverse	70 (52.2%)	56 (41·8%)
Intermediate	49 (36.6%)	56 (41·8%)
Favorable	6 (4.5%)	7 (5·2%)
Unknown	9 (6.7%)	15 (11.2%)
Detected at randomization		
Interval from diagnosis to randomization, months	5.0 (4·0-7·5)	5.50 (4.5-7.9)
Disease status		
CR1	90 (67.2%)	94 (70.1%)
CR2/CR3	26 (19.4%)	23 (17.2%)
PR/NR	18 (13.4%)	17 (12.7%)
Haploidentical hematopoietic cell source*		
BM	6 (4.5%)	2 (1.5%)
PB	68 (51.1%)	82 (61.2%)
Combination of BM and PB	59 (44.4%)	50 (37.3%)
Haploidentical grafts*		
Mononuclear cells, $\times10^8$/kg	9.48 (7.55-12.35)	10.20 (7.24-14.62)
CD34$^+$ cells, $\times10^6$/kg	4.03 (3.32-5.10)	4.17 (3.21-5.83)
Donnor type		
Parent	33 (24.8%)	34 (25.4%)
Offspring	69 (51.9%)	63 (47.0%)
Sibling	31 (23.3%)	37 (27.6%)
Donnor sex, male/female	89/44	95/39
Donnor age, years	29.0 (22.0-43.8)	27.0 (15.0-45.3)
Unrelated cord blood grafts*		
Mononuclear cells, $\times10^6$/kg	16·59 (1·73-31·71)	NA
CD34$^+$ cells, $\times10^4$/kg	4·60 (1·02-17·41)	NA

Table 1. Data are the median (IQR) or n (%).CR= complete response, PR=partial response, NR=nonresponse, BM=bone marrow, and PB=peripheral blood. *One haplo-cord HCT patient who withdrew informed consent and did not receive transplantation therapy was not included.

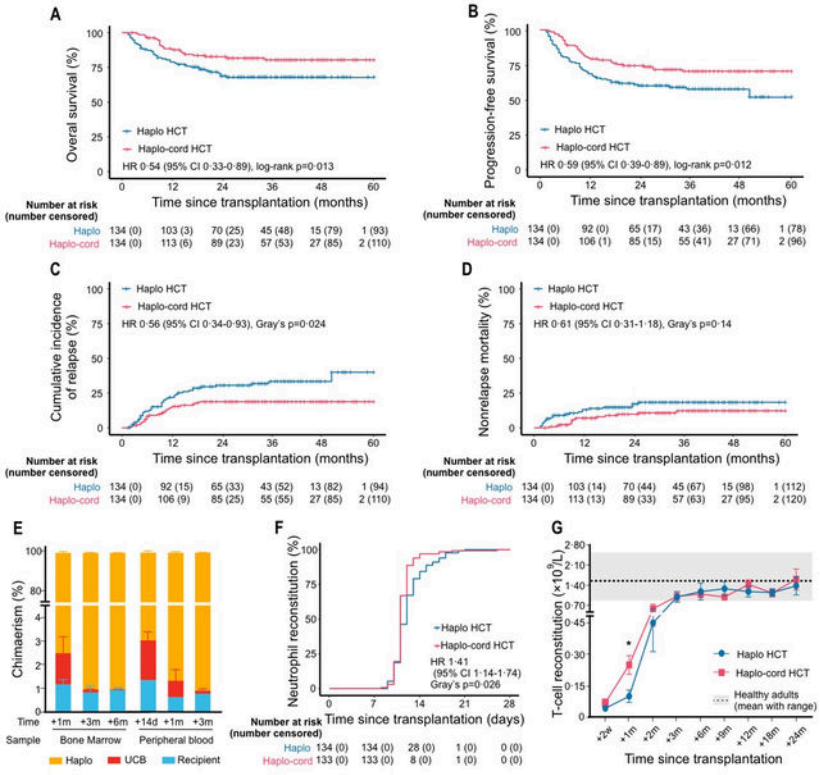

Figure 1. (A) Kaplan–Meier plots of overall survival. (B) Kaplan–Meier plots of progression-free survival. (C) Cumulative incidence curves of non-relapse mortality. (D) Cumulative incidence curves of the cumulative incidence of relapse. (E) Chimerism of recipient, haploidentical donor and unrelated cord blood unit in the haplo-cord group detected by SNP-NGS. (F) Cumulative incidence curves of neutrophil recovery. (G) T-cell reconstitution. *p<0.05.

Figure 1

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