ELSEVIER

Blood 142 (2023) 4916–4917

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

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

Optimized Double-Unit Cord Blood Transplantation Mitigates Transplant-Related Mortality Resulting in High Progression-Free Survival in Adults with Hematologic Malignancies

Ioannis Politikos, MD[1,2], *Sean M. Devlin, PhD*[3], *Stephanie Chinapen*[2], *Sean Quach, BSc*[4], *Parastoo B. Dahi, MD*[5,6], *Boglarka Gyurkocza, MD*[6,7], *Ann A. Jakubowski, MDPhD*[8], *Esperanza B. Papadopoulos, MD*[6,7], *Doris M. Ponce, MD MS*[6,9], *Roni Tamari, MD*[7], *Andromachi Scaradavou, MD*[10], *Juliet N Barker, MBBS*[1]

[1] Department of Medicine, Weill Cornell Medicine, New York
[2] Adult Bone Marrow Transplantation Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York
[3] Department of Biostatistics and Epidemiology, Memorial Sloan Kettering Cancer Center, New York, NY
[4] Memorial Sloan Kettering Cancer Center, New York
[5] Adult Bone Marrow Transplant Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY
[6] Department of Medicine, Weill Cornell Medical College, New York, NY
[7] Adult Bone Marrow Transplantation Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY
[8] Memorial Sloan-Kettering Cancer Ctr., New York, NY
[9] Adult Bone Marrow Transplantation Service, Memorial Sloan Kettering Cancer Center, New York, NY
[10] Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY

Background : Double-unit cord blood transplantation (dCBT) with intermediate intensity conditioning (Cy50/ Flu150/ Thio10/ TBI400cGy) and cyclosporine-A (CSA)/ mycophenolate mofetil (MMF) graft-versus-host disease (GVHD) prophylaxis has been associated with high progression-free survival (PFS) in adult patients (pts) with hematologic malignancies (*Barker JN et al, Blood Advances 2020*). Now, our Center has investigated multiple refinements to further mitigate transplant-related mortality (TRM). Herein, we have analyzed transplant outcomes in these adult dCBT pts to establish an optimized dCBT platform.
Methods : Consecutive adult first allograft pts with high-risk hematologic malignancies who underwent first allografts with intermediate intensity dCBT between 3/2018-8/2022 were analyzed. Optimizations involved further refined unit selection placing highest priority on unit quality (i.e. optimized banking practices) & CD34+ cell dose over HLA-match, ensuring therapeutic (CSA) levels (> 250 ng/mL) by day 0, prompt treatment of pre-engraftment syndrome (PES) & letermovir prophylaxis in CMV seropositive pts from day +7. Also, we have investigated 2 strategies to mitigate acute graft-versus-host disease (aGVHD): pts early in the study period received CSA, MMF & tocilizumab (8 mg/kg on day -1) prophylaxis (**Toci Group**), whereas recent pts (**Recent Group**) received CSA/ MMF with prompt therapy of clinically diagnosed aGVHD.
Results : Of 74 patients (Table), 49 were in the **Toci Group**, & 25 in the **Recent Group**. Most pts were transplanted for acute leukemia (n = 55, 74%) & over half (n = 39, 53%) had non-European ancestry. Distribution of diagnoses, CMV serostatus, HCT-CI & graft characteristics were similar between the groups but **Recent Group** pts tended to be younger (38 vs. 47 years, p = 0.071).
Toci Group pts had delayed neutrophil recovery [engraftment incidence 94% (95%CI: 87-99) at a median of 25 days (range 16-40), one graft failure], but low rates of PES (n = 19, 39%). The day-100 incidence of grade II-IV & III-IV aGVHD were 69% (95%CI: 56-82) & 10% (95%CI: 2-19), respectively. One pt (false negative CMV-serostatus) who did not receive letermovir had CMV infection. One-year TRM was 16% (95%CI: 6-27) with a 1-year relapse rate of 6% (95%CI: 3-13). TRM was due to infection (n = 3), aGVHD (n = 3, 1 with concurrent COVID-19 infection), multiorgan failure (n = 2) & graft failure (n = 1). With a median follow-up of 47 months (range 28-62), the 1-year OS was 84% (95%CI: 73-94) & 1-year PFS was 78% (95%CI: 66-89).
By contrast, the engraftment incidence in **Recent Group** pts was 100% with a faster median neutrophil recovery of 19 days (range 11-36, p = 0.002) & all engrafted platelets at a median of 36 days (range 24-92). However, most **Recent group** pts developed PES [n = 20 (80%), p < 0.001] although this responded promptly to short course corticosteroids. Day 100 grade II-IV aGVHD was also higher [92% (95%CI: 81-99), p = 0.009], although grade III-IV aGVHD was low [8% (95%CI: <1-19)] & similar to tocilizumab pts. Day 100 incidence of CMV was 0%. With a median follow-up of 17 months (range 6-50), the 1-year

TRM in **Recent Group** pts is 0% with a 1-year relapse incidence of 13% (95%CI: 7-27). Consequently, the 1-year OS & PFS are high at 96% (95%: 89-99) & 87% (95%CI: 74-99), respectively (Figure).

Conclusions: Optimized dCBT with intermediate intensity conditioning, graft selection that prioritizes unit quality & CD34+ dose, CSA/ MMF prophylaxis with prompt therapy of PES & aGVHD, & letermovir CMV prophylaxis mitigates TRM in young & middle-aged adults. Thus, combined with relatively low relapse rates, the PFS & OS are high. Tocilizumab has been abandoned due to its notable association with delayed neutrophil engraftment & lack of survival advantage. Letermovir is highly effective completely preventing CMV infections & may contribute to the reduced aGVHD-related mortality recently (as compared to the pre-tocilizumab era), since avoidance of CMV antiviral therapy toxicities greatly facilitates aGVHD prevention & therapy. Given the rapid availability of cryopreserved unmanipulated CB grafts & frequent limitations of URD availability for minority populations, optimized dCBT is a highly attractive curative therapy for acute leukemias & other high-risk myeloid malignancies warranting prospective multi-center investigation.

Disclosures Politikos: *ExcellThera:* Other: Membership on Data and Safety Monitoring Board ; *Merck:* Research Funding. **Gyurkocza:** *Actinium Pharmaceuticals, Inc:* Research Funding. **Ponce:** *Evive Biotechnology:* Membership on an entity's Board of Directors or advisory committees; *Ceramedix:* Membership on an entity's Board of Directors or advisory committees; *Incyte Corporation:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Kadmon/Sanofi Pharmaceuticals:* Membership on an entity's Board of Directors or advisory committees. **Barker:** *Gamida Cell:* Consultancy; *New York Blood Center:* Consultancy; *Merck:* Research Funding.

Table. Demographics & Transplant Outcomes

	Toci (N = 49) CSA/MMF/Tocilizumab	Recent (N = 25) CSA/MMF	P-value
Demographics			
Median age (range)	47 years (27-60)	38 (23-61)	0.071
CMV seropositive, N (%)	31 (63%)	16 (64%)	0.99
Non-European ancestry, N (%)	27 (55%)	12 (48%)	0.627
HCT-CI 0-1 2 3+	 24 (49%) 8 (16%) 17 (34%)	 14 (56%) 6 (24%) 5 (20%)	0.415
Disease AML ALL MPAL MDS MPN/CML NHL	 22 (45%) 12 (24%) 3 (6%) 5 (10%) 3 (6%) 4 (8%)	 10 (40%) 5 (20%) 3 (12%) 5 (20%) 1 (4%) 1 (4%)	0.776
Median Cryo. TNC/kg x 10^7/unit (range) Median Cryo. CD34+/kg x 10^5/unit (range)	2.9 (1.5-7.5) 2.4 (1.0-7.7)	2.8 (1.7-5.0) 2.5 (0.9-4.7)	0.712 0.756
8-allele HLA-match	4/8 (3-6/8)	5/8 (3-6/8)	0.683
Outcomes			
Neutrophil Engraftment Median time (range)	94% (87-99) 25 days (16-40)	100% 19 (11-36)	0.002
Platelet Engraftment Median time (range)	94% (87-99) 35 days (17-57)	100% 36 (24-92)	0.742
Pre-Engraftment Syndrome, N (%) Median onset (range)	19 (39%) 13 days (7-16)	20 (80%) 10 (4-17)	0.001
Day 100 aGVHD, Grade II-IV Day 100 aGVHD, Grade III-IV	69% (56-82) 10% (2-19)	92% (81-99) 8% (<1-19)	0.009 0.752
Day 100 CMV infection	1 (2%)	0%	-
Day 100 TRM 1-year TRM	12% (3-21) 16% (6-27)	0% 0%	0.027
1-year Relapse	6% (3-13)	13% (7-27)	0.832
1-year OS	84% (73-94)	96% (89-99)	0.07
1-year PFS	78% (66-89)	87% (74-99)	0.10

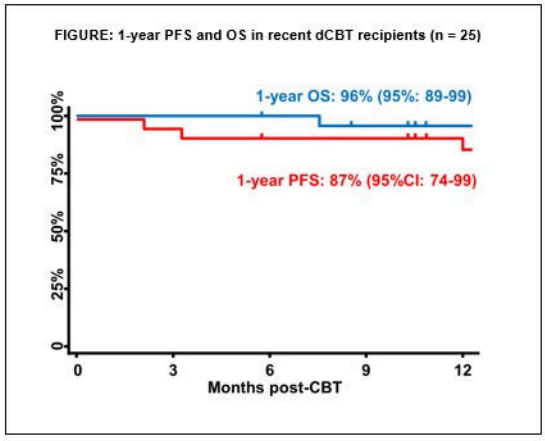

Figure 1

https://doi.org/10.1182/blood-2023-190528