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POSTER ABSTRACTS

732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

Allogeneic Hematopoietic Stem Cell Transplantation in Adolescents and Young Adults with Acute Lymphoblastic Leukemia - Retrospective Dual-Center Study

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Background: Adolescents and young adults (AYAs) with acute lymphoblastic leukemia (ALL) are treated with various chemotherapy regimens. Some patients undergo allogeneic hematopoietic stem cell transplantation (HCT) due to high-risk genetic characteristics, chemo-resistant disease (failure to achieve timely measurable residual disease (MRD) negative remissions, or relapse or refractory disease. There is paucity of data on outcomes of AYA ALL patients receiving HCT.
Methods: We performed a dual-center analysis of data from MD Anderson Cancer Center (MDACC) and Dana-Farber Cancer Institute (DFCI) to evaluate outcomes of AYA patients who received HCT for Philadelphia-negative (Ph ^{neg}) ALL and examined variables that might have an impact on these outcomes. We included all patients who received their first HCT between the ages of 15-40 years between the years 2010-2022. MRD status was evaluated using flow cytometry with a sensitivity of 0.01%. Acute and chronic graft versus host disease (GvHD) were classified according to consensus criteria. The primary endpoint was overall survival (OS), and secondary endpoints included progression rate and non-relapse mortality (NRM). Cox proportional hazards regression analysis was used to evaluate predictors of OS, and Fine and Gray regression for predictors of relapse and NRM. Competing risks were accounted for in analyses pertaining to progression and NRM.
Results: A total of 376 Ph ^{neg} ALL AYA patients were included in the analysis, 247 from MDACC and 129 from DFCI. The median age at transplant was 25 (range 15-40) years, 39 patients (10%) were aged ≤18 years at time of HCT and 251 (67%) were males.The majority had B-ALL (n=282, 75%), 42 (11%) had complex karyotype and 28 patients (7%) had translocation (4:11). Most patients received either pediatric-inspired (48%) or hyper- cyclophosphamide, vincristine sulfate, doxorubicin, dexamethasone (CVAD) based (42%) frontline induction regimens, and the median time from diagnosis to HCT was 11 (range 2-283) months. At transplant, most patients were in CR1 or CR2 (44% each); 63% of patients achieved MRD negativity prior to HCT. Most patients received an HCT from a matched unrelated donor (MUD) (33%) or a matched sibling donor (MSD) (32%), and most patients received myeloablative conditioning (MAC) (79%) (**Table 1**).

The cumulative incidence of grade 2-4 acute GvHD and grade 3-4 acute GvHD at 6 months was 37% (95% CI 33%-42%) and 13% (95% CI 10%-17%), respectively. The cumulative incidence of chronic GvHD at 3 years was 28% (95% CI 23%-33%), with most patients experiencing either mild (39%) or moderate (36%) chronic GvHD, and 25% had severe chronic GvHD.
For patients transplanted in CR1, CR2 and CR3/PD the estimated 3-year OS was 69% (95% CI 61%-77%), 53% (95% CI 44%-61%) and 29% (95% CI 16%-43%), respectively; the 3-year NRM rate was 9% (95% CI 5%-15%), 18% (95% CI 13%-25%) and 27% (95% CI 16%-43%), respectively; and the 3-year progression rate was 27% (95% CI 20%-35%), 36% (95% CI 29%-45%) and 48% (95% CI 36%-65%), respectively.
In multivariate analysis, HCT in CR3/PD was associated with inferior OS (HR 4.3, p<0.001) and higher NRM (HR 2.3, p=0.04, **Table 2**), however there was no difference in survival between HCT at CR1 vs. CR2 (p=0.3); >2 lines of therapy prior to HCT was associated with inferior OS (HR 1.8, p=0.004) and higher rate of progression (HR 1.9, p=0.008); HCT-CI>3 was associated with inferior OS (HR 1.6, p=0.01) and higher NRM (2.3, p=0.004); positive MRD status prior to HCT was associated with inferior OS (HR 1.9, p=0.004) and higher rate of progression (HR 3.3, p<0.001); use of bone marrow graft was associated with lower rate of progression (HR 0.6, p=0.02) and use of a matched donor (MSD/MUD) was associated with lower NRM (HR 0.5, p=0.01).
Conclusions: In this analysis of a large dual-center cohort of AYA Ph⁻ALL patients that received HCT, we found that patients transplanted in CR1 had the most favorable outcomes with 69% 3-year OS. Patients not in CR1/CR2, patients who received HCT after >2 lines of therapy and those with positive MRD pre-HCT had inferior OS on MVA. Although patients who received HCT at CR3/PD had inferior OS, an estimated one-third of patients were still alive at 3 years after HCT.

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Table 1. Patient characteristics

Parameter	N=376 n (%)	Parameter	N=376 n (%)
Gender		continued	
Male	251 (67)	MRD status at transplant	
Female	125 (33)	Negative	238 (63)
Age at transplant, years		Positive	55 (15)
≤18	39 (10)	Unknown	83 (22)
19-25	149 (40)	KPS	
26-30	81 (21)	90-100	239 (64)
31-35	54 (14)	≤80	103 (27)
36-40	53 (14)	Unknown	34 (9)
Histology		HCT-CI	
B-ALL	282 (75)	0-2	209 (56)
T-ALL	90 (24)	3	67 (18)
Other	4 (1)	4	47 (12)
Complex karyotype		>4	50 (13)
Yes	42 (11)	Recipient CMV status	
No	298 (79)	Negative	83 (22)
Unknown	36 (10)	Positive	278 (74)
Translocation 4:11		Unknown	15 (4)
Yes	28 (7)	Conditioning	
No	312 (83)	MAC	296 (79)
Unknown	36 (10)	RIC	79 (21)
Frontline regimen		Unknown	1 (0)
Hyper-CVAD	157 (42)	Donor type	
Pediatric	181 (48)	MSD	122 (32)
Adult/ Other	34 (9)	MUD	126 (33)
Unknown	4 (1)	Haplo/ MmSD	59 (16)
Time from diagnosis to transplant, months		CBT / MmUD	69 (18)
		Donor gender	
<6	95 (25)	Male	220 (59)
6-12	97 (26)	Female	154 (41)
12-24	65 (17)	Missing	2 (1)
>24	119 (32)		

Abbreviations: CBT=cord blood transplant, CMV= cytomegalovirus, CR=complete remission, CVAD= cyclophosphamide, vincristine sulfate, doxorubicin, dexamethasone, Haplo=haploidentical donor, HCT-CI=hematopoietic cell transplantation-specific comorbidity index, HCT=allogeneic hematopoietic stem cell transplantation, KPS=Karnofsky performance status, MAC=myeloablative conditioning, MmSD=mismatched sibling donor, MmUD=mismatched unrelated donor, MRD= minimal residual disease, MSD=matched sibling donor, MUD=matched unrelated donor, PD=progressive disease, RIC=reduced intensity conditioning

Table 2. Multivariate analysis

Parameter	Overall Survival		Progression		Non-relapse Mortality	
	Hazard Ratio (95% CI)	P value	Hazard Ratio (95% CI)	P value	Hazard Ratio (95% CI)	P value
Disease status at HCT						
CR1	1.0		1.0		1.0	
CR2	1.3 (0.8-2)	0.3	1.3 (0.8-2)	0.2	1.5 (0.7-3.0)	0.3
CR3 / PD	4.3 (2.1-8.7)[a]	<0.001	1.6 (0.8-2.9)	0.2	2.3 (1.04-4.9)	0.04
Number of prior lines of treatment						
≤2	1.0		1.0		-	-
>2	1.8 (1.2-2.8)[a]	0.004	1.9 (1.2-2.9)	0.008	-	-
Time from diagnosis to transplant						
<6 months	1.0		-	-	1.0	
≥6 months	1.6 (0.96-2.8)	0.07	-	-	1.8 (0.6-5.1)	0.3
HCT-CI						
≤3	1.0		-	-	1.0	
>3	1.6 (1.1-2.3)	0.01	-	-	2.3 (1.3-4.1)	0.004
MRD status at transplant						
Negative	1.0		1.0		-	-
Positive	1.9 (1.2-2.9)	0.004	3.3 (2.1-5.2)	<0.001	-	-
Recipient CMV status						
Negative	1.0		-	-	-	-
Positive	1.8 (1.2-3)	0.01	-	-	-	-
Graft Source						
Peripheral blood	-	-	1.0		-	-
Bone marrow	-	-	0.6 (0.4-0.9)	0.02	-	-
Cord blood			0.6 (0.3-1.2)	0.1		
Donor Gender						
Female	-	-	1.0		1.0	
Male	-	-	2.2 (1.4-3.3)	<0.001	0.5 (0.3-0.9)	0.02
Donor type						
Non-matched donor[b]	-	-	-	-	1.0	
MSD/MUD	-	-	-	-	0.5 (0.3-0.9)	0.01

Abbreviations: CMV= cytomegalovirus, CR=complete remission, HCT-CI=hematopoietic cell transplantation-specific comorbidity index, HCT=allogeneic hematopoietic stem cell transplantation, MRD= minimal residual disease, MSD=matched sibling donor, MUD=matched unrelated donor, PD=progressive disease.

[a] HR accounting for significant interaction effect between CR3/PD and number of prior treatment lines

[b] Includes mismatched sibling donor, mismatched unrelated donor, haploidentical donor, and cord blood transplant

Figure 1