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ORAL ABSTRACTS

732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

A Multicenter Analysis of Allogeneic Transplant Outcomes in Patients with Philadelphia-like (Ph-like) Acute Lymphoblastic Leukemia (ALL)

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Background: Ph-like ALL is a high-risk subset of B-lineage ALL that responds poorly to standard chemotherapy regimens. While allogeneic hematopoietic cell transplantation (HCT) is routinely recommended for patients with Ph-like ALL, large multicenter data addressing its role is limited. Here, we conducted a multicenter study to evaluate the role of HCT in adolescent and young adult (AYA) and adult patients (pts) with Ph-like ALL and compare their outcomes to pts with Ph-pos and Ph-neg (non-Ph-like) ALL.

Methods: The study included pts (age ≥18) with B-lineage ALL who received HCT in first complete remission (CR1) at 3 academic centers (MD Anderson Cancer Center, City of Hope and Mayo Clinic) between 2006 and 2021. Pts were divided into 3 main subgroups: Ph-like, Ph-pos and Ph-neg ALL. Ph-like ALL cases were identified using cumulative data obtained by targeted RNA sequencing, conventional cytogenetics, FISH studies, whole genome chromosomal microarray and flow cytometry. Measurable residual disease (MRD) prior to HCT was measured using flow cytometry with a sensitivity of 0.01% for Ph-neg and Ph-like ALL, and with a PCR assay for *BCR::ABL1* for Ph-pos ALL. MRD-negativity was defined as <0.01%. Predictors of relapse were evaluated in univariate and multivariate analysis using Fine-Gray sub-distribution hazard models considering non-relapse mortality (NRM) as a competing risk.

Results: 673 patients were identified, 83 (12.3%) had Ph-like ALL, of which 73% had *CRLF2-alterations*. The remaining patients were classified either as Ph-pos (N=271, 40.3%) or Ph-neg ALL (N=319, 47.4%). Patients with Ph-like ALL were younger (median

age 40 years vs 48 and 46 years for Ph-pos and Ph-neg ALL, respectively, p=0.01), more likely to be of Hispanic ethnicity (69% vs 32% and 48% for Ph-pos and Ph-neg ALL respectively, p<0.001). Patients with Ph-like ALL were also more likely to have induction failure (24% vs 2% and 11% for Ph-pos and Ph-neg ALL, respectively, p=0.001). A summary of pts characteristics for each subgroup can be found in Table 1.

The median follow-up was 30, 52 and 48 months for patients with Ph-like, Ph-pos and Ph-neg ALL, respectively. In univariate analysis, 3-yr OS and PFS did not differ significantly (66% and 59% vs 59% and 54%, p=0.1) between patients with Ph-like and Ph-neg ALL, respectively. Similarly, the cumulative incidence of relapse was comparable between patients with Ph-like and Ph-neg ALL (22% vs 20%, respectively, p=0.7).

In contrast, the 3-yr OS (75%, p<0.001) and PFS (70%, p=0.001) were significantly higher and relapse rate significantly lower (12%, p=0.003) in pts with Ph-pos ALL compared with Ph-like or Ph-neg ALL (Figure 1). The inferior survival in patients with Ph-like and Ph-neg ALL was likely attributable to higher relapse rates (22% and 20% vs 12%, respectively, *p*=0.003) compared to Ph-pos ALL. Finally, the 3-yr NRM rate in patients with Ph-like ALL was comparable (20% vs 18% and 23%, respectively, p>0.1) to Ph-pos and Ph-neg ALL.

We confirmed that the relapse rate in patients with Ph-like ALL was comparable to the rate in pts with Ph-neg ALL (HR=1.02, 95% CI 0.6-1.8, p=0.9) on multivariate analysis (MVA). Ph-pos ALL was associated with a significantly lower relapse rate compared with Ph-neg ALL (HR=0.4, 95% CI 0.3-0.7, p<0.001). MRD positivity prior to allo-HCT was the only additional significant predictor for relapse on MVA (HR=2.9, 95% CI 1.8-4.7, p<0.001).

Conclusions: HCT appears to overcome the poor prognosis of patients with Ph-like ALL. Despite higher induction failure rates, patients with Ph-like ALL undergoing HCT in CR1 had similar outcomes to other Ph-neg ALL subsets. The impact of effective salvage therapy leading to MRD-negativity in CR1 in this group is under investigation and will be reported. Further studies are needed to assess the impact of different Ph-like alterations on HCT outcomes. Outcomes for patients with Ph-pos ALL are significantly better than other groups, likely due to the use of TKIs pre- and post-HCT.

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Table 1. Patient characteristics and treatment outcomes

Characteristics	Ph-like (N=83)	Ph-pos (N=271)	Ph-neg (N=319)
Age at allo-HCT, years			
Median (range) [IQRT]	40 (18-71) [28, 52]	48 (18-72) [36,58]	46 (18-77)
≤35	28 (34)	61 (22)	97 (30)
36-45	22 (26)	54 (20)	57 (18)
46-55	14 (17)	73 (27)	64 (20)
>55	19 (23)	83 (31)	101 (32)
Race (%)			
White	63 (76)	224 (83)	245 (77)
Black	0 (0)	9 (0.03)	7 (0.02)
Hispanic ethnicity (%)	57 (69)	87 (32)	152 (48)
Sex			
F	28 (34)	126 (46)	155 (49)
M	55 (66)	145 (53)	164 (51)
HCT-CI	2 (0-9) [1,4]	2 (0-9) [0,3]	2 (0-10)
≥3	34 (44)	89 (34)	120 (40)
Donor			
MRD	30 (36)	85 (31)	132 (41)
MUD	34 (41)	117 (43)	114 (36)
Haplo	13 (16)	31 (11)	48 (15)
Other	6 (7)	38 (14)	25 (8)
Cell source			
PB	65 (78)	240 (89)	257 (81)
BM	16 (19)	16 (6)	48 (15)
CBT	2 (2)	15 (5)	14 (4)
MRD prior to HCT			
Positive	7 (8)	48 (18)	40 (12)
Negative	69 (83)	126 (46)	215 (67)
Missing	7 (8)	97 (36)	64 (20)
Conditioning			
MAC	63 (76)	193 (71)	227 (71)
RIC/NMA	20 (24)	78 (29)	92 (29)
Induction chemo			
HCVAD	44 (53)	173 (64)	209 (66)
Pediatric regimens	30 (36)	41 (15)	73 (23)
ECOG	2 (2)	9 (3)	13 (4)
Other	7 (8)	47 (17)	23 (7)
Response to induction			
Yes	63 (76)	260 (98)	281 (89)
No	20 (24)	6 (2)	34 (11)

Table 1 (cont): Univariate Outcomes			
Median OS (months)	54	Not reached	87
Median PFS (months)	43	Not reached	62
%OS - 3 years	66% (53-75)	75% (69-80)	59% (53-64)
%PFS - 3 years	59% (47-70)	70% (64-75)	54% (48-60)
%Relapse - 3 years	20% (13-32)	12% (9-17)	22% (18-27)
%NRM - 1 year	14% (8-25)	13% (9-17)	16% (13-21)
%NRM - 3 years	20% (13-32)	18% (14-24)	23% (18-28)

Figure 1: Overall Survival

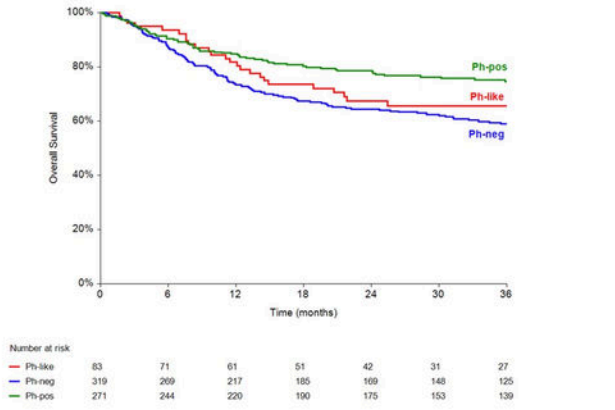

Figure 1

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