



## The 65th ASH Annual Meeting Abstracts

## POSTER ABSTRACTS

## 731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL

**Autologous Stem Cell Transplant in Fit Patients with Late Relapsed Diffuse Large B-Cell Lymphoma That Responded to Salvage Chemotherapy**

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**Background:** The new standard of care for fit patients with refractory or early relapse of diffuse large B-cell lymphoma (DLBCL) is chimeric antigen receptor T-cell (CAR-T) therapy. However, for patients with a relapse  $\geq 12$  months after completing frontline therapy, salvage chemotherapy followed by high-dose chemotherapy and autologous stem cell transplant (ASCT) remains the standard of care. There is a need to characterize such patients and their survival in view of the recent shift in treatment paradigm.

**Methods:** Patients with DLBCL that relapsed  $\geq 12$  months after R-CHOP or R-CHOP-like frontline therapy who underwent salvage therapy and ASCT at Mayo Clinic or University of Iowa between 07/2000 and 4/2020 were identified from institutional lymphoma and transplant databases. Clinical characteristics, treatment information, and outcome data were abstracted. Progression-free survival (PFS) and overall survival (OS) from the time of ASCT were analyzed using Kaplan-Meier method and Cox proportional hazards models. Statistical analyses were performed in JMP v15.

**Results:** A total of 158 patients with late relapsed DLBCL who underwent salvage chemotherapy and ASCT were identified. Baseline characteristics at relapse/ASCT are shown in Table 1. Median time from frontline therapy completion to 1st relapse was 26.4 months (range 12.0-152.4). Median age at relapse was 63 years (range 19-77), and 96 (61%) patients were male. A minority (3; 3%) had ECOG PS  $\geq 2$ . 43 (52%) patients had an elevated serum LDH level, 70 (65%) had advanced stage disease, and 12 (11%) had  $> 1$  extranodal involvement.

Median line of salvage therapy was 1 (range 1-3), and 17 (11%) patients required  $> 1$  line of salvage therapy. Best response before ASCT was complete response (CR) in 97 (61%) and partial response (PR) in 61 (39%). Median age at ASCT was 64 years (range 19-78). Median follow-up after ASCT was 91.5 months (95% CI 74.0-103.3). Median PFS and OS were 54.5 (95% CI 31.9-77.8) and 99.8 (95% CI 60.3-144.5) months, respectively. The 2-year PFS and OS rates were 64% (95% CI 56-71) and 81% (95% CI 74-87), respectively. No statistically significant difference in PFS was seen based on age at ASCT, sex, serum LDH, stage, or extranodal site involvement of  $> 1$  at relapse (Table 2). However, patients who required  $> 1$  line of salvage therapy, compared to those requiring 1 line of salvage therapy, had significantly inferior PFS (median 6.1 vs 61.8 months,  $P < 0.0001$ ) and OS (17.8 vs 111.7 months,  $P < 0.0004$ ). There was no statistically significant difference in survival in patients who achieved CR vs PR prior to ASCT, with a median PFS of 61.8 vs 37.8 months ( $P = 0.21$ ) and a median OS of 111.7 vs 78.3 months ( $P = 0.62$ ). Patients who achieved CR after 1 line of salvage therapy had the most favorable PFS and OS, with a median PFS of 65.6 vs 45.4 vs 6.1 vs 7.6 months ( $P = 0.0004$ ) and a median OS of 133.0 vs 88.9 vs 24.2 vs 17.6 months ( $P = 0.004$ ) in patients achieving CR after 1 line of salvage therapy vs PR after 1 line of salvage therapy vs CR after  $> 1$  line of salvage therapy vs PR after  $> 1$  line of salvage therapy, respectively (Table 2).

In multivariate Cox regression models adjusted for age at ASCT and sex, patients requiring  $> 1$  line of salvage therapy, compared to those who required 1 line of salvage therapy, had significantly inferior PFS with a hazard ratio (HR) of 3.25 (95% CI 1.82-5.78,  $P < 0.0001$ ) and OS with a HR of 3.50 (95% CI 1.86-6.60,  $P = 0.0001$ ). However, there remained no significant

difference in survival based on response status (CR vs PR) with a HR for PFS 0.78 (95% CI 0.52-1.17,  $P=0.23$ ) and OS 0.93 (95% CI 0.58-1.47,  $P=0.74$ ).

**Conclusions:** Survival after ASCT was excellent in patients with late relapsed DLBCL achieving CR after 1 line of salvage chemotherapy. Favorable survival outcomes were seen in patients who achieved PR after 1 line of salvage therapy. These data support the current clinical practice of ASCT consolidation in these patients. However, post-ASCT survival was poor in patients who required more than 1 line of salvage chemotherapy, despite achieving a satisfactory response to subsequent lines of salvage therapy. Alternative treatment strategies such as CAR-T therapy should be considered in such patients.

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**Table 1. Baseline variables at relapse, treatment pattern, and response to therapy of study patients (n=158)**

Summary	Number
Age at ASCT, median (range)	64 (19-78)
≤60	52 (33%)
>60	106 (67%)
Sex, male	96 (61%)
ECOG PS, ≥ 2	3 (3%)
LDH, elevated	43 (52%)
Stage, III-IV	70 (65%)
Extranodal involvement, >1	12 (11%)
First line salvage regimen	
Platinum or high dose cytarabine containing chemotherapy*	131 (83%)
Other strategies†	27 (17%)
Lines of salvage therapy, median (range)	1 (1-3)
1	141 (89%)
>1	17 (11%)
Response before ASCT	
CR	97 (61%)
PR	61 (39%)
Conditioning regimen	
BEAM	143 (91%)
Other regimens‡	15 (9%)

\* (R-) ICE; (R-) DHAP; RGDP; and (R-) ESHAP  
 † High dose methotrexate; hyper-CVAD; RCHOP; dose adjusted EPOCH-R; BR; R-GVP; and Vanderbilt Regimen  
 ‡ BCNU plus thiotepa; BVAC; bendamustine plus EAM; and CBV  
 Abbreviations: ASCT, autologous stem cell transplant; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; CR, complete response; PR, partial response

**Table 2. Univariate analyses of variables**

	Median PFS in months (95% CI)	P value	Median OS in months (95% CI)	P value
Age at ASCT		0.11		0.009
≤60	115.5 (40.0-144.5)		181.5 (115.5-181.5)	
>60	37.8 (25.7-61.4)		61.8 (50.4-99.8)	
Sex		0.34		0.69
Male	61.4 (29.0-117.1)		111.7 (61.8-181.5)	
Female	40.0 (25.7-72.6)		77.8 (49.5-NR)	
LDH at relapse		0.27		0.008
Normal	61.4 (27.3-NR)		NR (80.2-NR)	
Elevated	50.4 (18.2-133.0)		60.3 (31.9-NR)	
Stage at relapse		0.05		0.94
I-II	124.7 (50.4-NR)		126.2 (60.3-150.5)	
III-IV	45.3 (18.2-133.0)		88.9 (52.0-NR)	
Extranodal sites at relapse		0.76		0.47
≤1	61.4 (37.5-124.7)		111.7 (61.8-150.5)	
>1	59.3 (2.5-153.0)		77.8 (17.3-NR)	
Lines of salvage therapy		<0.0001		0.0004
1	61.8 (40.0-111.7)		111.7 (66.3-150.5)	
>1	6.1 (1.9-19.8)		17.8 (2.3-NR)	
Response before ASCT		0.21		0.62
CR	61.8 (32.1-117.7)		111.7 (57.0-181.5)	
PR	37.8 (13.0-77.8)		78.3 (51.5-150.5)	
Lines of salvage therapy and response status		0.0004		0.004
CR after 1 line of salvage	65.6 (52.0-128.5)		133.0 (59.3-181.5)	
PR after 1 line of salvage therapy	45.4 (13.1-78.3)		88.9 (57.1-NR)	
CR after >1 line of salvage therapy	6.1 (1.4-45.3)		24.2 (1.8-NR)	
PR after >1 line of salvage therapy	7.6 (1.2-NR)		17.6 (1.9-NR)	

Abbreviations: PFS, progression-free survival; OS, overall survival; ASCT, autologous stem cell transplant; LDH, lactate dehydrogenase; CR, complete response; PR, partial response; NR, not reached

**Figure 1**

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