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POSTER ABSTRACTS

731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL

Co-Expression of C-MYC/BCL2 Is Associated with Inferior Survival Outcomes in Relapsed/Refractory Diffuse Large B-Cell Lymphoma after Autologous Stem Cell Transplantation - a Nationwide Retrospective Analysis in Singapore

Jing Yuan Tan, MBBS[1], *Victor Ling Wei Teik*[2], *Cindy Krisnadi*[1], *Lawrence Cheng Kiat Ng*[1,3], *Melinda Si Yun Tan*[1,3], *Nicholas Francis Grigoropoulos*[1,3], *Shin Yeu Ong, MD*[1,3], *Chandramouli Nagarajan, MDMBBS,FRCP,FRCPath*[1,3], *Jeffrey Kim Siang Quek*[1], *Hein Than, MDFRCPath,MRCP*[4,3], *Joanne Shu Xian Lee, MBBS (UK), MRCP (UK), FRCPath*[2], *Esther Hian Li Chan, MBBS, MRCP, FRCPath*[2], *Lip Kun Tan*[2], *William Ying Khee Hwang, MBBS*[3,4], *Yeow Tee Goh, MBBS*[1,3], *Yeh Ching Linn*[3,1], *Liang Piu Koh*[2], *Aloysius Yew Leng Ho*[3,1], *Francesca Lorraine Wei Inng Lim*[3,1], *Michelle Limei Poon*[2], *Yunxin Chen*[3,1]

[1] Department of Hematology, Singapore General Hospital, Singapore, Singapore
[2] Department of Haematology-Oncology, National University Cancer Institute, Singapore, Singapore
[3] National Cancer Centre Singapore, Singapore, Singapore
[4] Department of Haematology, Singapore General Hospital, Singapore, Singapore

Introduction

Co-expression of C-MYC and BCL2 in diffuse large b-cell lymphomas (DLBCL), also termed double-expressor lymphomas (DEL), has been shown to be associated with poorer outcomes after standard R-CHOP induction therapy. Approximately 70% of DEL will relapse within 5 years. The subsequent traditional approach with potential for cure has been high dose chemotherapy followed by autologous hematopoietic stem cell transplantation (ASCT). Whilst factors such as remission status after front-line treatment and early relapse have been associated with poorer outcomes after ASCT, data are limited regarding significance of DEL status on survival outcomes post-ASCT. We retrospectively studied the prognostic impact of DEL status on outcomes in patients with relapsed or refractory (R/R) DLBCL who underwent ASCT.

Methods

This was a retrospective, nationwide study of adults patients, >18 years old, with R/R DLBCL who underwent autologous hematopoietic stem cell transplantation (ASCT) between 2010 and 2022 at the only 2 transplant centers in Singapore - Singapore General Hospital and National University Cancer Institute. Patients with double/triple hit lymphoma, defined as concurrent rearrangements of MYC and BCL2 and/or BCL6 by fluorescence in situ hybridization (FISH) analysis, were not included in this study. Patients with transformed indolent B-cell NHL (non hodgkin lymphoma), primary mediastinal B-cell lymphoma, primary CNS (central nervous system) lymphoma, or Richter transformation of chronic lymphocytic leukemia were excluded. Only patients that had available MYC and BCL-2 immunohistochemistry (IHC) were included in this study. Overall survival (OS) and progression free survival (PFS) were estimated using the Kaplan-Meier method. Cox proportional hazards regression models were used to assess associations between covariates of interest and OS or PFS.

Results

A total of 72 patients were included, 44 (61.1%) non-double expressor DLBCL (non-DEL) and 28 (38.9%) double expressor DLBCL (DEL). Patient demographics and disease characteristics at relapse were similar in both groups aside from a higher incidence of CNS involvement in the non-DEL group as compared to DEL group, 34.1% vs 10.7% (Table 1). Both groups achieved a >90% response (CR and PR) after second-line salvage chemotherapy as well as a >90% response post-transplant (CR and PR). Patients with DEL however were more likely to relapse post-transplant, 69.7% vs 40.9% ($p = 0.032$) and were also associated with increased odds of all-cause mortality, 60.7% vs 36.4% (p=0.043). This significance was maintained on multivariable analysis, HR 4.22 95% CI 1.20 - 14.84 (p=0.025) and HR 4.32 95% CI 1.10 - 17.15 (p=0.038) respectively. The median follow up for survivors were 42 months (range, 26 to 64 months) in the DEL patients and 60 months (range, 46 to 88 months) in the non-DEL patients. The 5-year PFS in patients with DEL was inferior to non-DEL patients, 23.3% vs 49.6% respectively, p=0.022. DEL patients were also associated with inferior 5-year OS, 40.2% vs 65.7%, p=0.041. In multivariable model, DEL status remained significantly associated with inferior PFS and OS. We also observed that patients with CNS involvement at relapse had inferior PFS and OS. Male gender and a less than complete metabolic response (CR) status prior to transplant, assessed on PET-CT, was also associated with inferior OS.

Conclusion

Co-expression of C-MYC/BCL2 was associated with inferior outcomes after ASCT in patients with R/R DLBCL. While ASCT has been the standard curative approach in the R/R setting, considerations for novel targeting therapies to achieve a deeper response prior to transplant or the upfront use of chimeric antigen receptor T-cell therapy at first relapse may be further explored in this high-risk subset of patients.

Disclosures Nagarajan: *BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *DKSH/Beigene:* Membership on an entity's Board of Directors or advisory committees; *Janssen:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: The Trial was supported by funding to IMF/AMN who were the sponsorswere the Sponsors; *Sanofi:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Astrazeneca:* Honoraria, Membership on an entity's Board of Directors or advisory committees.

Table 1: Demographics and clinical characteristics of non-DEL and DEL patients at relapse			
Characteristics	Non-DEL, no. (%)	DEL, no. (%)	P-value
Total	44	28	
Male Gender*	23 (52.3%)	17 (60.7%)	0.627
Subtype at diagnosis*			
Non-Germinal center	32 (72.7%)	23 (82.1%)	0.266
Germinal center	12 (27.3%)	5 (17.9%)	
Primary refractory or early relapse* (≤12 months)	20 (45.5%)	14 (50.0%)	0.810
Age ≥60 years*	16 (36.4)	12 (42.9)	0.582
Ann Arbor stage 3/4*	39 (88.6%)	20 (71.4%)	0.064
Sites of involvement			
Central nervous system*	15 (34.1%)	3 (10.7%)	0.022
Bone marrow*	9 (20.5%)	6 (40.0%)	0.573
sIPI*			
Low/Low-intermediate risk	26 (59.1%)	17 (60.7%)	0.545
Intermediate-high/High risk	18 (40.9%)	11 (39.3%)	
Disease status at time of transplant*			
CR	35 (79.5%)	19 (67.9%)	0.508
Not in CR	9 (20.5%)	9 (32.1%)	
Conditioning regimen			
BEAM	29 (65.9%)	24 (85.7%)	0.099
Thiotepa-based	15 (34.1%)	4 (14.3%)	
Response post-transplant			
CR/PR	43 (97.7%)	26 (92.9%)	0.334
Relapse post-transplant	18 (40.9%)	19 (69.7%)	0.032
PFS from transplant in months, median (IQR)	32 (8,109)	8 (3,31)	0.022
OS from transplant in months, median (IQR)	109 (23,109)	18 (10,62)	0.041
Mortality from any cause	16 (36.4)	17 (60.7)	0.043

DEL: Double expressor lymphoma; IQR: interquartile range; sIPI: second-line international prognostic index; BEAM: carmustine, etoposide, cytarabine, melphalan; CR: complete response; PR: partial response
*Variables that were included in multivariable analysis

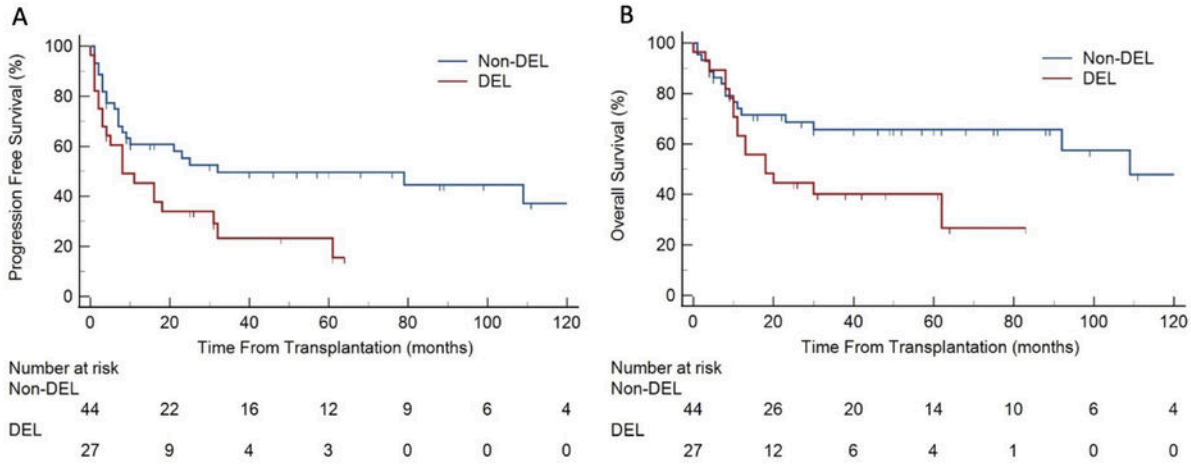

Figure 1: Graphs of (A) progression-free survival (B) overall survival after autologous stem-cell transplantation in patients with DEL compared with patients without DEL. DEL: double-expressor lymphoma

Figure 1

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