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ELEVENTH ANNUAL MEETING

Real-world outcomes of patients with double-hit lymphoma treated from 2013 to 2023 at the Royal Melbourne Hospital and Peter MacCallum Cancer Centre

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INTRODUCTION

- Double-hit lymphoma (DHL) (i.e., high-grade B-cell lymphoma with rearrangement of *MYC* plus *BCL2* and/or *BCL6* by FISH[1]) is associated with inferior prognosis compared with diffuse large B-cell lymphoma[2].
- Treatment with intensified regimens (e.g., dose-adjusted [DA]-R-EPOCH) has been suggested to improve progression-free survival, but not overall survival (OS)[3].
- Consolidative autologous stem cell transplant (ASCT) in first complete remission (CR1) may reduce risk of relapse[4,5].
- While conventional salvage regimens (e.g., R-ICE) are available for patients with relapsed/refractory (R/R) DHL, no standard-of-care currently exists in this setting[6] and data on CAR-T cell and novel antibody-based therapies are limited.

AIM

- To describe real-world outcomes of patients with DHL treated at our institutions over the past decade.

METHOD

- We retrospectively reviewed 64 consecutive patients with proven DHL treated at Royal Melbourne Hospital and Peter MacCallum Cancer Centre from June 2013 to March 2023.
- Baseline clinicopathologic variables, treatment, response and outcome data were collected.
- Kaplan-Meier method was used to estimate overall survival (OS).

RESULTS

- Median age at diagnosis was 61.5 (range, 33-98) years.
- 41 cases arose *de novo*; 23 were transformed from low-grade lymphoma (LGL) (follicular lymphoma, *n*=21; small lymphocytic lymphoma, *n*=1; MALT lymphoma, *n*=1).
- Initial treatment consisted of DA-R-EPOCH (*n*=29), R-CHOP (*n*=24), R-CODOX-M/R-IVAC (*n*=3), Pola-R-CHP combination therapy (*n*=2), R-ICE (*n*=2), R-HyperCVAD (*n*=1), obinutuzumab (G)-EPOCH (*n*=1), R-CHOP + tafasitamab (*n*=1), and steroids/cyclophosphamide (*n*=1).
- 20 received consolidative ASCT (17 in CR1, 3 in CR2); conditioning regimens were CBV (*n*=17), LACE (*n*=1), BEAM (*n*=1), and unknown (*n*=1).
- Response to DA-R-EPOCH was superior to R-CHOP with CR rates of 72% vs 58% with no significant benefit in OS (*p*=0.130).
- Among patients achieving CR with initial therapy (*n*=40), 5-year survival rates from date of diagnosis for patients who received frontline consolidative ASCT (n=17) and those who did not (n=23) were 82% and 64%, respectively (*p*=0.277).
- Of the 12 patients who received CAR-T (3 at first relapse, 9 at subsequent relapse), 2-year survival rate from date of CAR-T infusion was 73%.

Figure 1. Outcomes of patient cohort. (A) OS in patients achieving CR from date of diagnosis, stratified by ASCT at CR1. (B) OS of CAR-T treated patients from date of CAR-T infusion.

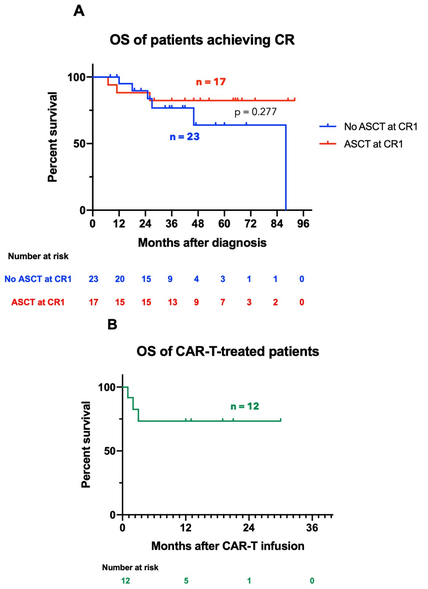


Table 1. Baseline characteristics of patient cohort at time of DHL diagnosis.

Baseline characteristic	DA-R-EPOCH (*n*=29)	R-CHOP (*n*=24)	Whole cohort (*n*=64)
Sex			
Male	20 (69%)	13 (54%)	39 (61%)
Female	9 (31%)	11 (46%)	25 (39%)
Age at diagnosis, median (range)	59 (44-73)	67.5 (33-85)	61.5 (33-98)
Histology			
DLBCL, *de novo*	21 (72%)	14 (58%)	41 (64%)
DLBCL, transformed from LGL	8 (28%)	10 (42%)	23 (36%)
FISH			
Double-hit	29 (100%)	20 (83%)	57 (89%)
Triple-hit	0 (0%)	4 (17%)	7 (11%)
Staging			
Limited stage (stage 1-2)	7 (24%)	3 (12.5%)	12 (19%)
Advanced stage (stage 3-4)	22 (76%)	21 (87.5%)	52 (81%)
Best response			
CR	21 (72%)	14 (58%)	40 (62.5%)
PR	6 (21%)	2 (8%)	11 (19%)
SD	1 (3%)	2 (8%)	3 (5%)
PD	1 (3%)	6 (25%)	10 (16%)
ASCT	13 (45%)	4 (17%)	20 (31%)
At CR1	10	3	17
At CR2	3	1	3
CAR-T	3 (10%)	6 (25%)	12 (19%)
Axicabtagene ciloleucel	1	4	7
Tisagenlecleucel	2	1	3
Rapcabtagene autoleucel	0	0	1
Allogeneic	0	1	1

CONCLUSIONS

- For patients with DHL, initial treatment with DA-R-EPOCH is associated with higher CR rates compared to R-CHOP.
- In our study, ASCT in CR1 was not associated with significant improvement in OS.
- CAR-T cell therapy may be an effective salvage option for patients with R/R DHL.

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