Impact of DA-R-EPOCH for High-Grade B-Cell Lymphoma Patients at the University of Michigan

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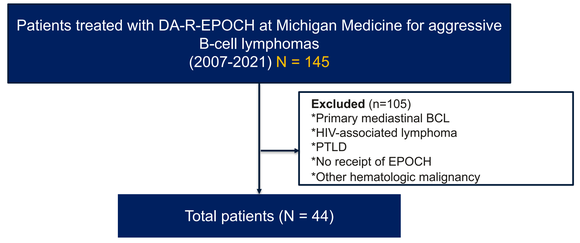
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Background

- High-grade B-cell lymphomas (HGBCL) are defined as those with c-MYC rearrangement along with either BCL-2 and/or BCL-6 translocations. Those with dual genetic insults are deemed double-hit lymphoma (DHL) and those with all 3 genetic rearrangements are triple-hit lymphomas (THL) [1].
- Typically outcomes among HGBCL patients are poor [2,3].
- Intensive regimens have been evaluated and our current institutional standard is dose-adjusted R-EPOCH (DA-R-EPOCH: rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin).
- The purpose of dose-adjustments of R-EPOCH is to enhance tumor-cell kill and maximize response [4].
- Whether dose-adjustments truly impact achievement and durability of responses remains unclear.
- Our study aims to investigate clinical characteristics and outcomes among HGBCL patients treated at the University of Michigan.

Study Design

- Single-center retrospective cohort study of DHL/THL patients who were treated with DA-R-EPOCH and seen at the University of Michigan between 2007-2021.
- Inclusion criteria: patients ≥ 18 years old, diagnosis of DHL/THL, and receipt of induction chemotherapy with DA-R-EPOCH.



Results

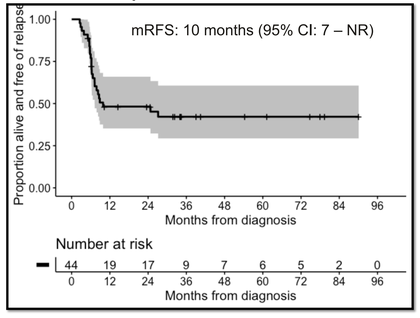
Baseline Characteristics	
Median age (range)	64 (34-80)
Median year of diagnosis	2018
	N; (%)
Male (%)	22; (50)
Ethnicity	
Non-Hispanic	40; (91)
Race	
Caucasian	39; (88.6)
ECOG (PS) ≤ 2	43; (98)
LDH	
< 1.5x ULN	24; (55.8)
1.5-3x ULN	12; (27.9)
> 3x ULN	7; (16.3)
R-IPI	
0	2; (4.7)
1-2	18; (41.9)
3-5	23; (53.5)

Disease Characteristics	
	N; (%)
CSF involvement	
Positive	2; (4.5)
Negative	24; (54.5)
Unknown	18; (41)
Bone marrow involvement	
Positive	7; (16)
Negative	14; (32)
Unknown	23; (52)
Stage III/IV disease	33; (75)
> 1 Extranodal Site	16; (36.4)
GCB Subtype	27; (96.4)
DHL	
BCL-2 rearrangement	37; (84.1)
BCL-6 rearrangement	17; (38.6)
THL	10; (22.7)
Transformed DLBCL	10; (22.7)

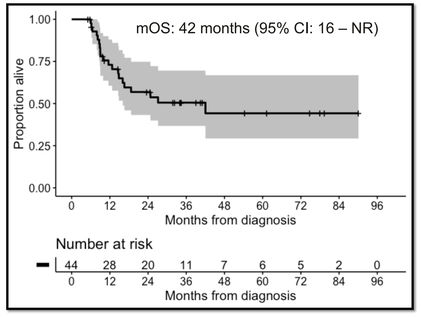
Univariable Associations

Variable	Estimated HR	95% CI
Stage III/IV vs I/II	1.181	0.391 – 3.567
Any dose escalations vs none	0.763	0.316 – 1.843
LDH within 1.5-3x ULN vs < 1.5x ULN	2.196	0.794 – 6.072
LDH > 3x ULN vs < 1.5x ULN	2.451	0.734 – 8.181
Per increase in highest dose level achieved	0.751	0.488 – 1.156

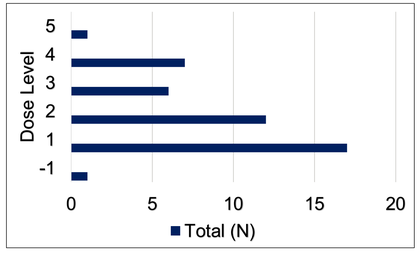
Relapse-Free Survival



Overall Survival



Highest Dose-Escalation of DA-R-EPOCH



Statistics

- Overall survival (OS) was defined as time from diagnosis to death or last follow-up. Relapse-free survival (RFS) was defined as time from diagnosis to relapse or death from any cause. Estimated with Kaplan Meier analysis.
- Overall response rate (ORR) defined as complete response (CR) + partial response (PR) after induction therapy.
- Descriptive statistics with univariate analyses performed for baseline characteristics using Cox proportional hazards model.

Conclusion

- Median OS for our HGBCL patients treated with DA-R-EPOCH was 42 months, higher compared to other studies [5].
- ORR was 73% across the cohort (95% CI: 58-84%) with 8 PR and 24 CR. Among those who attained CR, 63% maintained CR for > 2 years.
- Dose-escalation was defined as ≥ dose-level 2 which was performed in 59% of patients. Only 20% of patients were treated with ≥ dose-level 2 for ≥ 5 cycles.
- Factors such as stage III/IV disease, dose-escalation, and higher LDH levels did not significantly affect survival based on Cox regression analyses.
- Our study is limited by the small sample size and retrospective nature of data collection.
- Further investigation should be done to assess whether dose-escalations truly impact outcomes and whether attaining durable CR (> 2 years) affects survival. This correlation has been seen in DLBCL in that those who maintain remission for > 2 years are less likely to relapse.

References

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