

BACKGROUND

- ❖ Outcomes of patients with diffuse large B-cell lymphoma (DLBCL) and other high-grade B-cell lymphomas have improved with chemoimmunotherapy (CIT).
- ❖ Some patients are at an increased risk of developing secondary central nervous system (CNS) relapse, associated with a poor short term overall survival (OS) of less than 6 months.¹
- ❖ The incidence of secondary CNS relapse with DLBCL is approximately 5%. In patients with MYC, BCL-2, and/or or BCL-6 rearrangements this incidence may be as high as 50%.^{2,3}
- ❖ Intrathecal chemotherapy (ITC) or high-dose intravenous methotrexate (HD-MTX) has been used in these patients to decrease risk of CNS relapse. However, there is no consensus of which is the most appropriate prophylactic strategy.^{2,3}

PURPOSE

- ❖ The purpose of this study is to analyze the efficacy of ITC versus HD-MTX for the prevention of secondary CNS relapse in high-grade B-cell lymphoma patients.

METHODS

Study Design

- Single institution retrospective cohort study over 3 years
- Arm A: ITC
- Arm B: HD-MTX

Inclusion Criteria

- Age ≥ 18 years
- Diagnosed and histologically confirmed DLBCL or other high grade B-cell lymphomas
- Received either R-CHOP or DA-R-EPOCH as primary chemoimmunotherapy (CIT) regimen
- Had no CNS involvement at the time of diagnosis

OUTCOMES

Primary Outcome

- Incidence of secondary CNS relapse

Secondary Outcomes

- Progression free survival (PFS)
- Overall survival (OS)
- Rates of HD-MTX toxicity
- Delays in primary CIT regimen
- Cost of prophylaxis per cycle

RESULTS

Table 1. Baseline Characteristics

Baseline Characteristics	Arm A (N=11)	Arm B (N=11)
Gender, n (%)		
Male	5 (45.4)	7 (63.6)
Age, n (%)		
Median (range), years	61 (27-70)	63 (46-75)
65+	3 (27.3)	4 (36.4)
Ethnicity, n (%)		
Caucasian	3 (27.3)	3 (27.3)
Hispanic	5 (45.4)	5 (45.4)
Black	3 (27.3)	3 (27.3)
ECOG, n (%)		
0-1	11 (100)	8 (72.7)
2-3	0 (0)	2 (18.2)
4	0 (0)	1 (9.1)
HIV Diagnosis, n (%)		
Yes	4 (36.4)	1 (9.1)
DLBCL Staging, n (%)		
Stage I-II	4 (36.4)	0 (0)
Stage III-IV	7 (63.6)	11 (100)
High risk pathological features, n (%)		
BCL2, <i>myc</i> rearrangement	5 (45.4)	0 (0)
BCL 2, <i>myc</i> expression	2 (18.2)	4 (36.4)
None identified	4 (36.4)	7 (63.6)
Chemotherapy Regimen, n (%)		
R-CHOP	1 (9.1)	10 (90.9)
DA-R-EPOCH	10 (90.9)	1 (9.1)
CNS-IPI, n (%)		
0-1	3 (27.3)	1 (9.1)
2-3	7 (63.6)	0 (0)
4-6	1 (9.1)	10 (90.9)
NCCN-IPI, n%		
0-1	0 (0)	0 (0)
2-3	4 (36.4)	2 (18.2)
4-5	7 (63.6)	6 (54.5)
6-8	0 (0)	3 (27.3)

Table 2. Relapse Rates

Relapse Rates	Arm A (N=11)	Arm B (N=11)
CNS Relapse, n (%)		
Yes	2 (18.2)	2 (18.2)
Non-CNS Relapse, n (%)		
Yes	2 (18.2)	0 (0)

Figure 1. Progression Free Survival

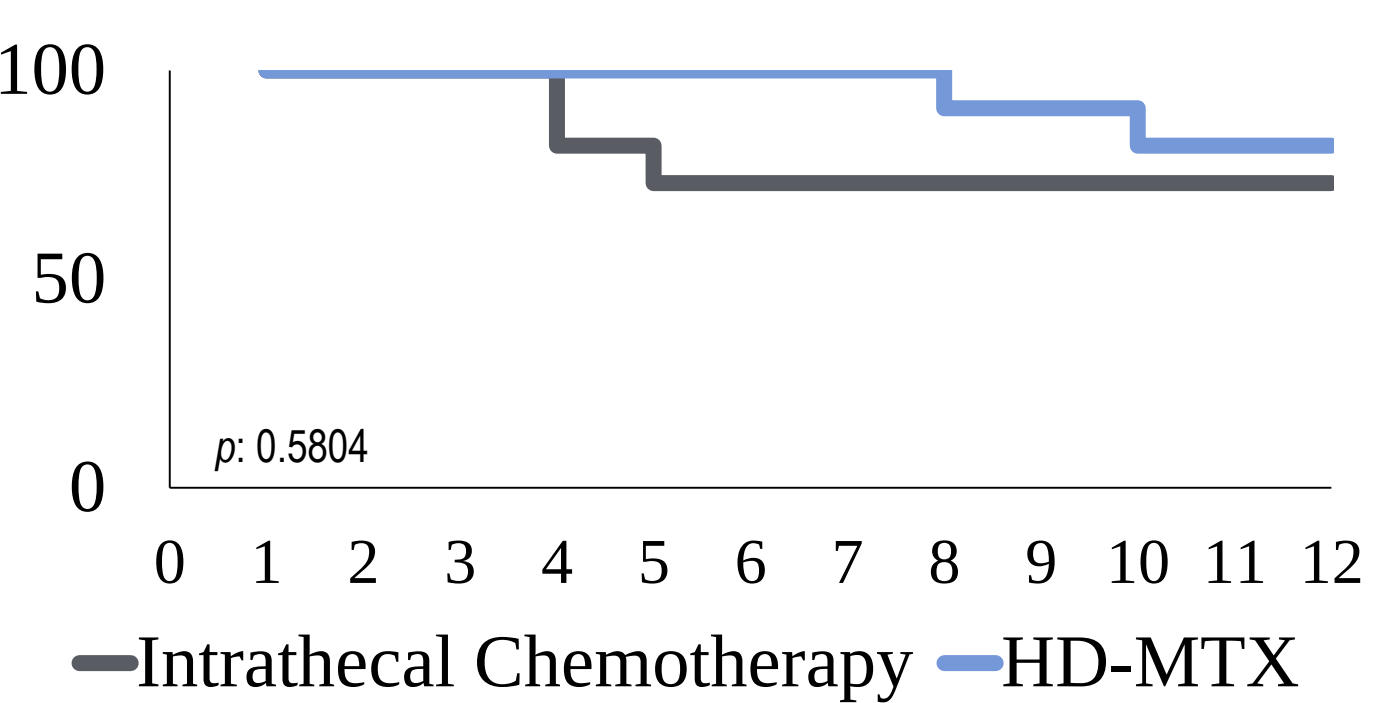


Figure 2. Overall Survival

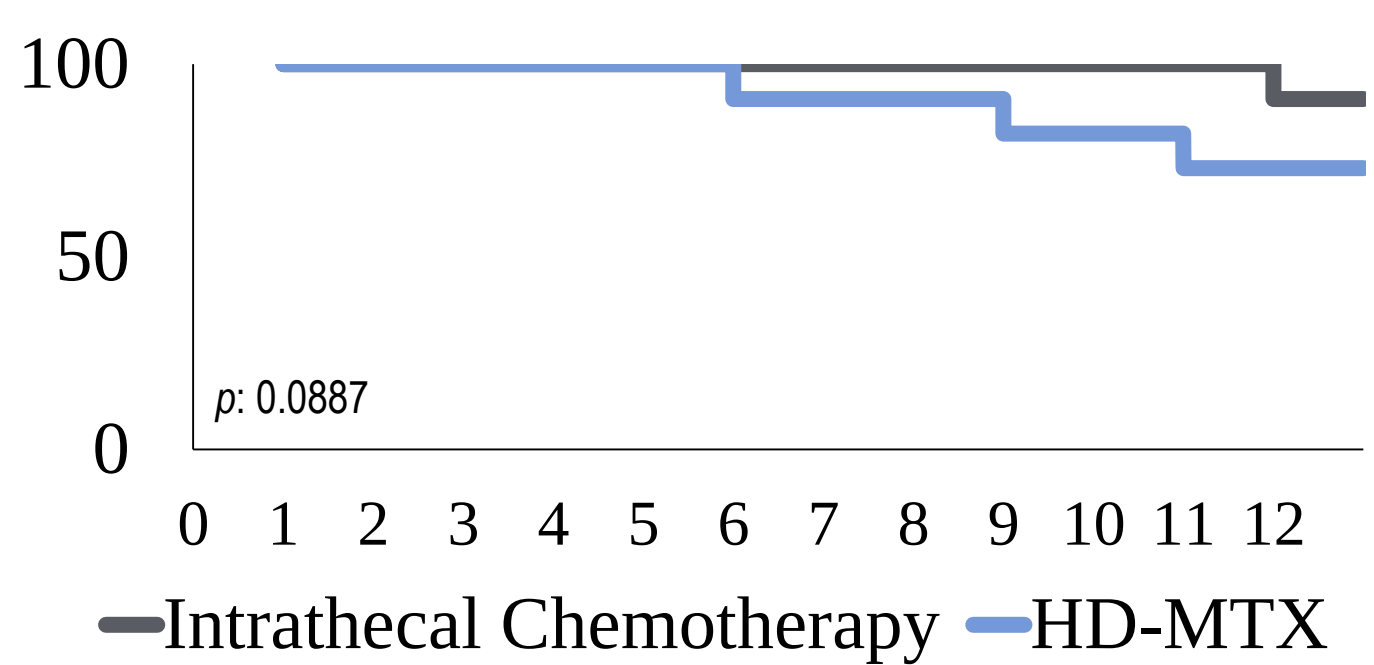


Figure 3. High-Dose Methotrexate Toxicity Rates

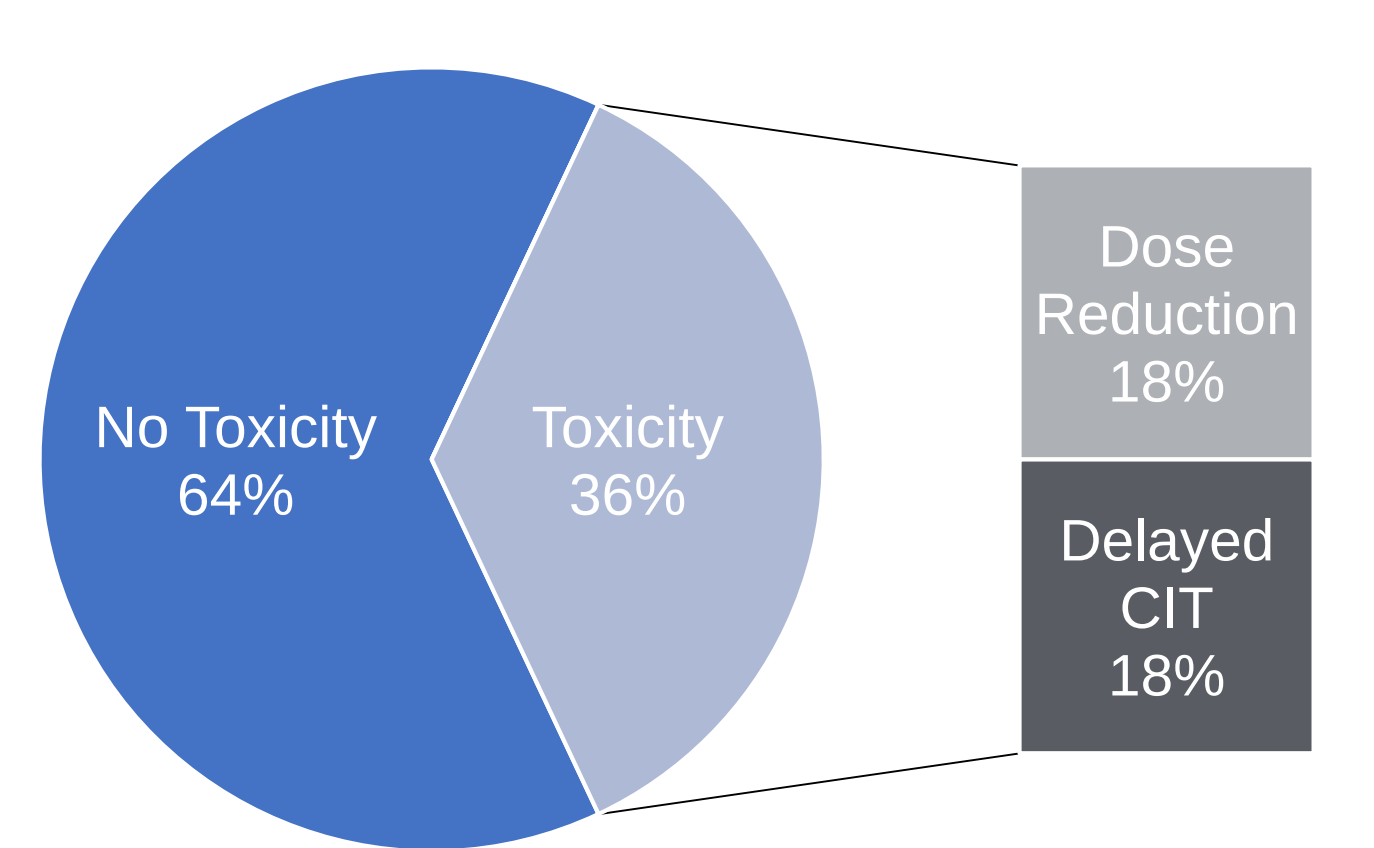
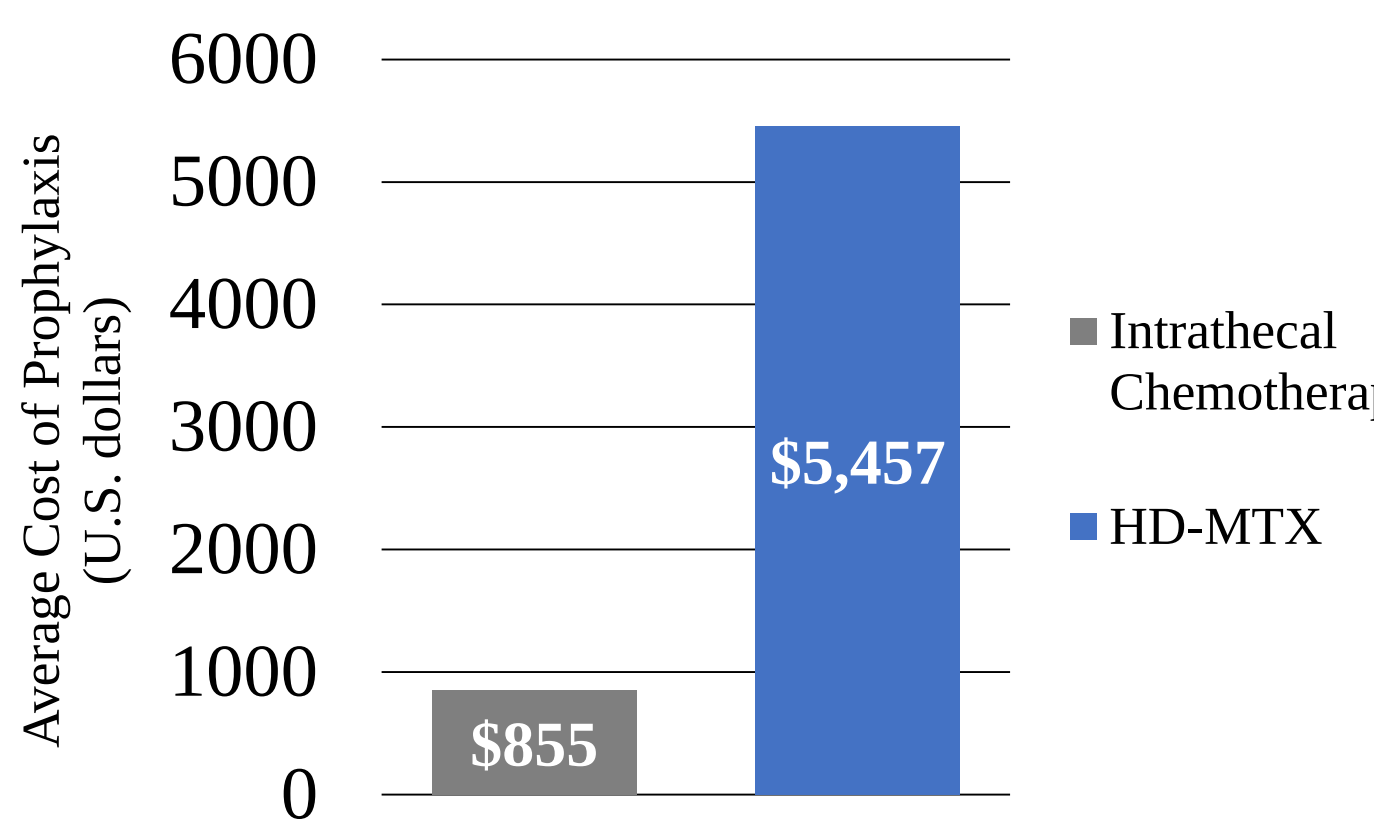


Figure 4. Average Cost of CNS Prophylaxis Regimen



DISCUSSION

- ❖ Patients that received ITC correlated with more utilization of DA-R-EPOCH for primary CIT regimen, whereas HD-MTX was more often utilized in combination with R-CHOP regimens.
- ❖ HD-MTX patients had higher CNS-IPI and NCCN-IPI scores, compared to patients receiving ITC.
- ❖ Secondary CNS relapse occurred in 4 patients (18.2%) out of the total 22 patients between both arms. Of note, 2 of these patients achieved only partial response (PR) to CIT and 2 patients had progressive disease (PD).
- ❖ In our study, rates of CNS relapse were higher than those reported in literature, but may be explained due to our patient population having higher CNS risk factors as reflected with their CNS-IPI and NCCN-IPI scores.
- ❖ Development of secondary CNS relapse occurred in 2 (18.2%) of patients in Arm A (ITC) and 2 (18.2%) in Arm B (HD-MTX), which was not statistically significant ($p=0.5804$).
- ❖ One year PFS was consistent between both arms at 72.7%.
- ❖ One year OS had a non-significant trend between both groups, 90.9% vs. 72.7%, ($p=0.0887$).
- ❖ Toxicity developed in 36% of high-dose methotrexate patients, with 3 cases being due to acute kidney injury and 1 case due to severe mucositis. Of these cases, 2 patients needed a dose reduction of high-dose methotrexate and 2 patients had delays in further cycles of primary CIT.
- ❖ HD-MTX was associated with a significantly higher cost of \$5,457 compared to \$855 with ITC, on average per cycle.

CONCLUSION

- ❖ There was no statistically significant difference in the development of secondary CNS relapse between ITC and HD-MTX.
- ❖ HD-MTX was associated with a significantly higher cost of care with the additional cost of supportive care, higher risk for toxicity, and delays of primary CIT.
- ❖ These findings are limited to small sample size and heterogeneity between both arms. Further prospective, randomized studies are needed to assess if CNS prophylaxis improved outcomes and which method of prophylaxis is more efficacious.

REFERENCES

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2. Schmitz et al. CNS International Prognostic Index: A Risk Model for CNS Relapse in Patients With Diffuse Large B-Cell Lymphoma Treated With R-CHOP. JCO 2016.
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DISCLOSURE

Authors of this presentation have nothing to disclose concerning financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.