(PB3747) COMPARISON OF EFFICACY BETWEEN POLA-R-CHP AND TUCIDINOSTAT-R-CHOP IN PREVIOUSLY UNTREATED PATIENTS WITH DOUBLE-EXPRESSOR DIFFUSE LARGE B-CELL LYMPHOMA: A MATCHING-ADJUSTED INDIRECT COMPARISON (MAIC)

Topic: 19. Large B cell lymphomas - Clinical

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Background

Double-Expressor Diffuse Large B-Cell Lymphoma (DE-DLBCL) is an intermediate-risk molecular subtype associated with poor prognosis. In the phase III POLARIX trial (NCT03274492), polatuzumab vedotin plus R-CHP (Pola-R-CHP) demonstrated superior progression-free survival (PFS) versus R-CHOP in previously untreated DLBCL, including DE subgroup. Similarly, tucidinostat (an HDAC inhibitor) combined with R-CHOP (Tuci-R-CHOP) showed promising efficacy in phase III DEB trial (NCT04231448) for untreated DE patients.

Aims

Given the absence of head-to-head trials, we conducted a MAIC to evaluate the comparative efficacy between Pola-R-CHP and Tuci-R-CHOP in previously untreated DE-DLBCL.

Methods

To adjust for cross-trial difference in the DE-DLBCL subgroup, an unanchored MAIC was performed. Individual patient data (IPD; N=115 global pts, N=35 Asian pts, N=15 Chinese pts) from the Pola-R-CHP arm of POLARIX were reweighted to match the aggregate data (AgD; N=211) of the Tuci-R-CHOP arm of DEB trial. Matching variables included gender, International Prognostic Index, and bulky disease. IPD for Tuci-R-CHOP were reconstructed from published Kaplan–Meier curves (Zhao et al. ASH 2025) using the algorithm by Liu et al. (2021), achieving high accuracy as confirmed by root mean square error and mean/max absolute error. The primary endpoint was PFS, secondary endpoint included CRR, OS, and EFS. Reweighted treatment effects are reported as hazard ratios (HR) for time-to-event outcomes and odds ratios (OR) for CRR, with 95% confidence intervals (CIs) and p-values.

Results

In the global DE population, after weighting, the effective sample size (ESS) was 114.2. Pola-R-CHP significantly improved CRR compared to Tuci-R-CHOP (84.0% vs 73.0%; p=0.019) and significantly improved overall EFS (HR=0.53; 95% CI: 0.36–0.77; p<0.001), with 24-month landmark rates of 77.6% vs 59.6%. The treatment also demonstrated favourable numerical trends in overall PFS (HR=0.67; p=0.054) and overall OS (HR=0.67; p=0.114), with corresponding 24-month snapshot estimates of 78.1% vs 69.5% and 88.9% vs 81.3%, respectively.
Asian and Chinese subgroups analyses demonstrated efficacy signals consistent with the global results. In the Asian subgroup (ESS=32.3), Pola-R-CHP showed favourable trends across all endpoints, including CRR (OR=1.27) and overall EFS (HR=0.69). In the Chinese subgroup, despite a limited sample size (N=15), the MAIC weighting achieved a high ESS retention rate of 97.3% (ESS=14.6), indicating strong baseline comparability. Pola-R-CHP achieved a numerically higher CRR (92.1% vs 73.0%). Notably, no deaths occurred in the Pola-R-CHP Chinese cohort (24-month OS: 100%), contrasting with the 81.3% rate in the comparator arm. Kaplan–Meier inspection indicated that survival in the Chinese and Asian subgroups was consistent with the results observed in the global analysis.

Summary/Conclusion

This analysis provides the first comparative evidence between Pola-R-CHP and Tuci-R-CHOP in untreated DE-DLBCL. The global analysis demonstrates that Pola-R-CHP offers statistically significant improvements in CRR and EFS, with consistent favourable trends in PFS and OS. Limitations include cross-trial heterogeneity, ethnic differences, and small Asian/Chinese sample sizes. Nevertheless, efficacy signals were consistent across global, Asian, and Chinese subgroups. Collectively, these data support Pola-R-CHP as a highly effective first-line treatment option for this molecular subtype.

Efficacy	Category	Tuci-R-CHOP at 2025 ASH	A Tuci-R-CHOP reconstruction data*	B Weighted Pola-R-CHP Global subgroup	Weighted OR/HR A vs. B	C Weighted Pola-R-CHP Asian subgroup	Weighted OR/HR A vs. C	D Weighted Pola-R-CHP Chinese subgroup#
Effective Sample Size (ESS)		211	211	114.2		32.3		14.6
Median follow up time (month)		44.9	44.9	72.9				48.2
CRR		73.0% (66.6%, 78.5%)	73.0% (66.6%, 78.5%)	84.0% (76.7%, 89.4%)	OR=1.949 (1.116, 3.402) P=0.019	77.4% (60.9%, 88.3%)	OR=1.268 (0.513, 3.132) P=0.607	92.1% (68.4%, 98.4%)
PFS	Median/M	NR (NE, NE)	NR (NE, NE)	78.1 (NE, NE)	HR=0.669 (0.444, 1.006)	78.1 (33.3, NE)	HR=0.868 (0.465, 1.619)	NR (20.2, NE)
	24M Rate	69.3% (61.7%, 75.6%)	69.5% (61.9%, 75.9%)	78.1% (69.4%, 84.6%)	P=0.054	69.9% (50.7%, 82.8%)	P=0.657	71.6% (44.1%, 88.2%)
OS	Median/M	NR (NE, NE)	NR (NE, NE)	NR (NE, NE)	HR=0.670 (0.407, 1.101)	NR (78.1, NE)	HR=0.686 (0.300,1.569)	NR (NE, NE)
	24M Rate	81.4% (75.3%, 86.1%)	81.3% (75.3%, 86.1%)	88.9% (82.0%, 93.3%)	P=0.114	86.2% (69.0%, 94.2%)	P=0.372	100.0% (100.0%, 100.0%)
EFS_{eff}	Median/M	NR (35.3, NE)	NR (27.4, NE)	78.1 (NE, NE)	HR=0.526 (0.359, 0.770)	78.1 (33.3, NE)	HR=0.688 (0.366, 1.219)	NR (20.2, NE)
	24M Rate	60.3% (53.0%, 66.9%)	59.6% (52.2%, 66.2%)	77.6% (68.9%, 84.1%)	P=0.001	69.9% (50.7%, 82.8%)	P=0.188	71.6% (44.1%, 88.2%)

* Individual patient data for the Tuci-R-CHOP arm were reconstructed from published Kaplan–Meier curves presented at ASH 2025, and minor discrepancies were assessed and deemed acceptable.
# The Chinese subgroup results are presented descriptively due to the limited sample size, but the landmark analysis findings are consistent with the Asian and global populations

Image. The weighted efficacy comparative analysis between Pola-R-CHP vs. Tuci-R-CHOP