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POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Ratio of Circulating CD8 + T Lymphocytes to M-MDSCs (CD8MMR): A Novel Prognostic Predictor for Treatment-Naïve DLBCL Patients

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Introduction:

CD8 + T lymphocytes are crucial in contemporary cell-and-immunotherapies as they can be functionally enhanced or manipulated. Monocytic myeloid-derived suppressor cells (M-MDSCs) are known for their intense immunosuppressive ability, and higher percentages of circulating M-MDSCs among peripheral-blood monocytes or white cells are associated with a worse prognosis. Recently, a low lymphocyte-to-monocyte ratio (LMR) has been linked to a poor prognosis in lymphoma patients. Consequently, we hypothesized that the ratio of circulating CD8 + T lymphocytes to M-MDSCs (CD8MMR) could be a novel and more precise predictor for the clinical outcomes of DLBCL patients before initiating treatment.

Methods:

This prospective, observational study enrolled 136 adults with treatment-naïve DLBCL from May 2019 to March 2023 in a tertiary medical center in Taiwan. Patients with primary CNS lymphoma or primary mediastinal B-cell lymphoma were excluded. Fresh peripheral blood samples were obtained to calculate the absolute counts of CD8 + T lymphocytes and M-MDSCs, defined as alive singlets with CD45 + CD3 + CD8 + and CD45 + CD15 - CD14 + CD11b + CD33 + HLA-DR $^{low/-}$ by flow cytometry, respectively. ROC analysis and AUC determined the cut-off values for LMR and CD8MMR.

Results:

For 136 treatment-naïve DLBCL patients, the median age was 70, with 61.8% being male. Among them, 37.5% were in stage IV, and 27.9% were classified as the germinal-center B-cell (GCB) subtype by IHC staining according to the Hans algorithm. Additionally, 43.4% were diagnosed with double expressor lymphoma (DEL). The IPI risk score distribution was as follows: 7.4%, 18.4%, 17.6%, 24.3%, 19.9%, and 12.5% were in scores 0, 1, 2, 3, 4, and 5, respectively. Of note, the median level of LMR was 2.17, the median level of absolute counts of circulating CD8 + T lymphocytes was 385/μL, the median level of absolute counts of circulating M-MDSCs was 102/μL, and the median level of CD8MMR was 3.56.

DLBCL patients with high-risk IPI had a significantly lower CD8MMR than patients with intermediate or low-risk IPI (1.34 vs. 4.51 vs. 7.82, $P_{H\ vs.\ L}$ = 0.001, $P_{H\ vs.\ I}$ = 0.060, $P_{I\ vs.\ L}$ = 0.082). DLBCL patients with the non-GCB subtype (2.75 vs. 5.63, P = 0.031) also demonstrated a significantly lower CD8MMR. Additionally, there were trends of lower CD8MMR in elderly patients > 70 (2.74 vs. 3.91, P = 0.209) and patients with DEL (3.33 vs. 4.65, P = 0.101).

After a median follow-up of 22.6 months for the 136 DLBCL patients, LMR was at first tested, and patients with LMR < 1.19 had significantly worse PFS (13.8 months vs. non-reach, Log Rank P = 0.004) and OS (non-reach vs. non-reach, Log Rank P = 0.019) than those with LMR ≥ 1.19. Next, we examined the CD8MMR, and patients with CD8MMR < 4.40 experienced significantly worse PFS (21.3 months vs. non-reach, Log Rank P < 0.001) and OS (non-reach vs. non-reach, Log Rank P < 0.001) compared to those with CD8MMR ≥ 4.40 **[Figure]**.

We subsequently conducted a multivariate Cox regression analysis to validate whether CD8MMR < 4.40 could serve as an independent predictor of poor prognosis **[Table]**. The results showed that "CD8MMR < 4.40" was confirmed as an independent prognostic factor for both PFS (HR = 2.747; 95% CI = 1.275 to 5.918; P = 0.010) and OS (HR = 3.669; 95% CI = 1.462 to 9.211; P = 0.006) after adjusting for confounding factors, including age, sex, IPI risk scores, bulky mass > 10 cm, non-GCB type, DEL, and LMR < 1.19.

In this study cohort, 106 (77.9%) patients received R-CHOP-like regimens as induction therapies, 25 (18.4%) patients received an R-EPOCH regimen, two (1.5%) patients received an R-HyperCVAD regimen, and three (2.2%) patients died before completing the first cycle of chemoimmunotherapy. Among the 106 DLBCL patients receiving R-CHOP-like regimens, 57 patients

showed CD8MMR < 4.40 and reported a significantly lower rate of complete remission (73.7% vs. 95.9%, $P = 0.006$) at the end of induction therapy compared to the 49 patients with CD8MMR $\geq$ 4.40. Furthermore, patients with CD8MMR < 4.40 had significantly worse PFS (17.4 months vs. non-reach, $P < 0.001$) and OS (non-reach vs. non-reach, $P < 0.001$) compared to those with CD8MMR $\geq$ 4.40.

Conclusion:

A low ratio of circulating CD8$^+$ T lymphocytes to M-MDSCs (CD8MMR) serves as a poor prognostic factor for both PFS and OS in treatment-naïve DLBCL patients. This finding warrants further investigation and highlights the possibility of risk-adapted strategies when treating DLBCL patients.

Disclosures No relevant conflicts of interest to declare.

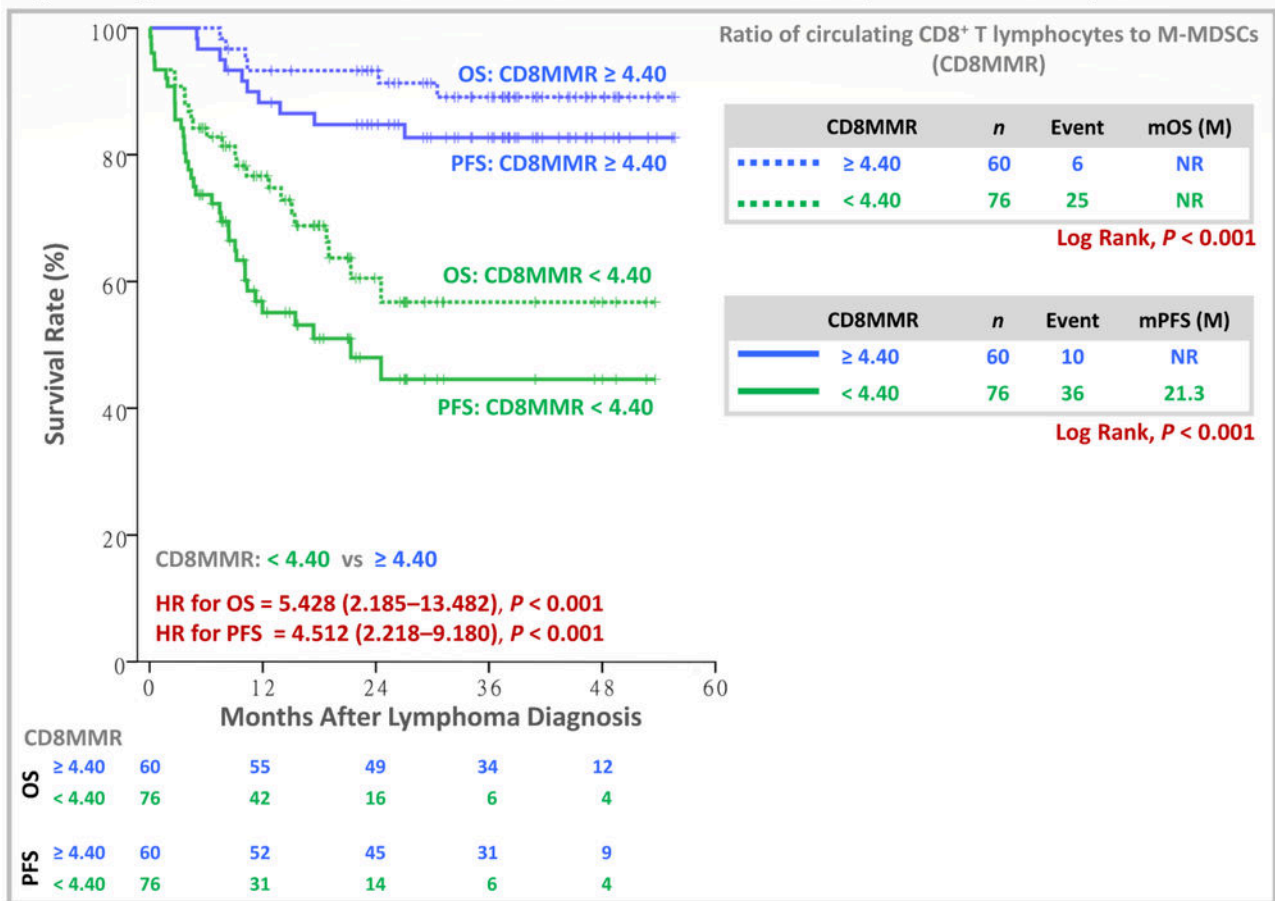Figure: Progression-free and overall survival in 136 treatment-naïve DLBCL patients stratified by CD8MMR

Table. Univariate and multivariate analyses of prognostic predictors in 136 treatment-naïve DLBCL patients

Clinical factors	Progression-free survival				Overall survival			
	Univariate		Multivariate [a,b]		Univariate		Multivariate [a,b]	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Age > 70	2.478 (1.336–4.596)	0.004	2.254 (1.206–4.214)	0.011	3.477 (1.553–7.782)	0.002	3.025 (1.348–6.786)	0.007
Female	1.056 (0.584–1.910)	0.857			1.388 (0.684–2.818)	0.364		
IPI risk								
➢ Low risk	1				1			
➢ Intermediate risk	7.345 (1.732–31.156)	0.007	6.289 (1.476–26.790)	0.013	5.952 (0.762–46.503)	0.089	4.418 (0.563–34.642)	0.157
➢ High risk	11.385 (2.668–48.591)	0.001	7.943 (1.827–34.533)	0.006	20.552 (2.756–153.238)	0.003	12.003 (1.588–90.702)	0.016
Bulky mass > 10 cm	0.576 (0.257–1.287)	0.179			0.626 (0.240–1.630)	0.337	–	–
Non-GCB type [c]	3.030 (1.284–7.154)	0.011	2.539 (1.022–6.312)	0.045	1.786 (0.732–4.357)	0.203		
Double expressor lymphoma	1.946 (1.086–3.489)	0.025			1.961 (0.959–4.007)	0.065		
LMR < 1.19 [d]	2.326 (1.278–4.236)	0.006			2.321 (1.126–4.784)	0.022		
CD8MMR < 4.40 [d]	4.512 (2.218–9.180)	< 0.001	2.747 (1.275–5.918)	0.010	5.428 (2.185–13.482)	< 0.001	3.669 (1.462–9.211)	0.006

[a] Multivariate Cox regression model (the backward stepwise method) included all available variables with P < 0.250.
[b] Age and sex were forced into the multivariate analysis because they may confound between-subject comparisons.
[c] Adopted immunohistochemistry stain according to the Hans algorithm.
[d] ROC analysis and AUC determined the cut-off values for LMR and CD8MMR.

Figure 1

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