P53 Expression Correlates with Worse Outcomes in a Cohort of Large B-Cell Lymphoma

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Background

- Identifying patients with aggressive large B-cell lymphomas (LBCL) at risk for relapse or refractory disease after first-line chemo-immunotherapy (CIT) remains an unmet clinical need
- Alterations in *TP53* are common in LBCL, yet their prognostic and therapeutic significance remains unclear in subtypes beyond diffuse large B-cell lymphoma (DLBCL)[1]
- Although prior studies have shown inferior CR rates, PFS, and OS in patients with *TP53*-mutated DLBCL, others suggest even worse outcomes in patients with other subtypes of LBCL[2,3]
- Research has indicated that p53 overexpression can serve as a surrogate marker for the presence of *TP53* alterations in DLBCL, providing a rapid and cost-effective diagnostic tool[4]
- This study attempts to determine the prognostic and predictive significance of p53 overexpression in a cohort of patients with LBCL treated with standard-of-care first-line CIT

Methods

- Patients with a diagnosis of LBCL managed at Medstar Georgetown University Hospital between 2015-2023 were retrospectively identified
- Patients were included if they had immunostaining for p53 performed or had FFPE blocks available for add-on testing
- Standard IHC with a DAKO mouse monoclonal antibody against p53 (clone DO-7) was performed
- Positivity was defined as ≥10% strong (3+) or ≥20% intermediate (2+) nuclear expression in tumor cells
- Collected data included demographics, WHO diagnosis, stage, IPI, COO, serum LDH, first-line treatment, and clinical outcomes
- Patient characteristics were compared using t-tests and chi-square tests, outcomes were analyzed using Kaplan Meier curves and log-rank testing, time-to-event analysis (PFS, OS) was modeled via Cox-regression hazards model

Results

Fig 1. Demographics and Clinical Characteristics

	p53⁺ (*n=35*)	p53⁻ (*n=70*)	Total (*n=105*)	p-value
Median age – yrs (range)	62 (34-90)	61 (23-85)	61 (23-90)	NS
Male sex – no (%)	19 (54)	38 (54)	57 (54)	NS
Stage 3-4 – no (%)	29 (83)	56 (80)	85 (81)	NS
IPI – no (%):				*p = 0.047*
<3	10 (29)	28 (40)	38 (36)	
≥3	17 (49)	22 (31)	39 (37)	
Unknown	8 (22)	20 (29)	28 (27)	
COO – no (%):				NS
GCB	14 (40)	30 (43)	44 (42)	
Non-GCB	20 (57)	36 (51)	56 (53)	
Not applicable	1 (3)	4 (6)	5 (5)	
Mean serum LDH (SD)	410 (14.4)	426 (14.9)	421 (14.7)	NS
Disease type – no (%):				
DLBCL	26 (36)	46 (64)	72 (69)	
HGBCL - NOS	4 (33)	8 (67)	12 (11)	
HGBCL – MYC/BCL2	0 (0)	3 (100)	3 (3)	
Transformed FL	3 (43)	4 (57)	7 (7)	
PMBCL	1 (17)	5 (83)	6 (6)	
GZL	0 (0)	2 (100)	2 (2)	
PCNSL	1 (33)	2 (67)	3 (3)	
Rearrangements – no (%):				
MYC single	0 (0)	1 (100)	1 (1)	
BCL2 single	5 (63)	3 (37)	8 (9)	
MYC and BCL2	0 (0)	3 (100)	3 (3)	

Yrs, years; NS, not significant; no, number; IPI, International Prognostic Index; COO, cell-of-origin classification; GCB, germinal center B-cell; LDH, lactate dehydrogenase; SD, standard deviation; DLBCL, diffuse large B-cell lymphoma; HGBCL, high-grade B-cell lymphoma; NOS, not otherwise specified; MYC/BCL2, with a MYC and BCL2 rearrangement; FL, follicular lymphoma; PMBCL, primary mediastinal B-cell lymphoma; GZL, gray-zone lymphoma; PCNSL, primary central nervous system lymphoma

Fig 2. Treatment Response

	p53⁺	p53⁻	p-value
First-line Treatment Response Overall cohort	(*n=33*)	(*n=56*)	*p < 0.01*
Complete response	18 (55)	48 (86)	
Partial response	11 (33)	4 (7)	
Progressive disease	4 (12)	4 (7)	
First-line Treatment Response HGBCL cohort	(*n=4*)	(*n=11*)	*p < 0.01*
Complete response	0 (0)	11 (100)	
Partial response	1 (25)	0 (0)	
Progressive disease	3 (75)	0 (0)	
60-month PFS, %	28.4	51.8	*p < 0.001*
60-month OS, %	54.5	73.4	*p < 0.01*

N, number; HGBCL, high-grade B-cell lymphoma; PFS, progression-free survival; OS, overall survival

Fig 3. Progression-Free Survival

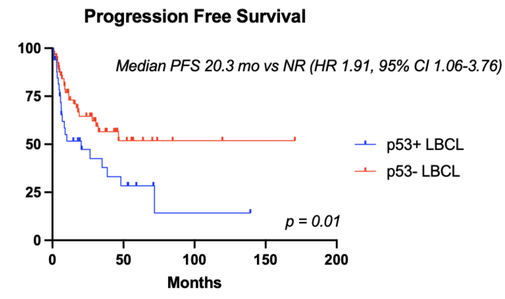
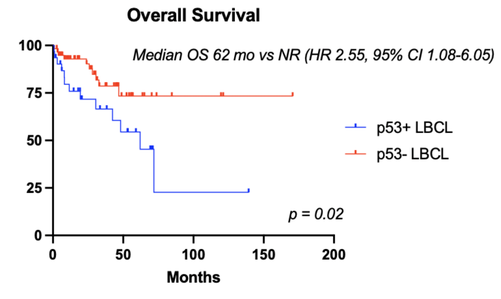


Fig 4. Overall Survival



Conclusions

- In a single-center cohort of 105 patients with newly diagnosed LBCL we found that 34% overexpressed p53
- p53 overexpression correlated with worse outcomes, including inferior CR rates, PFS, and OS
- Although limited data is available, patients with p53 positive HGBCL had especially poor outcomes
- Routine p53 IHC testing can provide prognostic and predictive information in patients with LBCL

Limitations and Next Steps

- Need for validation of p53 overexpression as a surrogate marker for the presence of *TP53* alterations in other subtypes of LBCL
- Heterogeneity of the LBCL category and limited inclusion of other subtypes than DLBCL
- Future research will focus on, and expand, the HGBCL cohort and integrate findings from genomic profiling

References

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