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POSTER ABSTRACTS

621.LYMPHOMAS: TRANSLATIONAL-MOLECULAR AND GENETIC

Role of Circulating Tumor DNA As a Prognostic Biomarker in Patients with Diffuse Large B-Cell Lymphoma

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Introduction: Nearly 50-60% of the patients withDiffuse large B-cell lymphoma (DLBCL) can be cured by front line chemoimmunotherapy. Current risk stratification modalities include cell-of-origin (germinal center (GCB) or non-GCB (activated B-cell [ABC])) subtyping, use of the revised International Prognostic Index (R-IPI), Ki-67 proliferation index assessment, and cytogenetic aberration detection. However, a novel approach for molecular residual disease (MRD) detection and treatment monitoring is needed to improve patient outcomes.

Methods: A personalized and tumor-informed multiplex PCR assay (Signatera™ bespoke mPCR NGS assay) was used for the detection and quantification of ctDNA in a prospective clinical cohort of patients with DLBCL. Serial ctDNA testing was performed at various time points collected at the treating physician's discretion, including pretreatment (baseline), during first-line therapy, during and post-salvage therapy, at the end of treatment, and during surveillance, up to the last clinical follow-up. ctDNA clearance was defined as change in ctDNA status (positive to negative) from the pre-treatment time point to the subsequent time point. Event-free survival (EFS) was defined as the time elapsed since the initial ctDNA clearance or PET imaging, for those without ctDNA clearance, during which the patient did not experience progression, death or treatment with salvage therapy. EFS was censored at the last date of followup if the patient was alive and without an event. Overall survival (OS) was defined as the elapsed time after primary treatment until death from any cause. Univariate and multivariable models were analyzed using Cox proportional models.

Results: In this retrospective evaluation of commercial ctDNA testing in patients with stage I-IV DLBCL, a total of 50 patients (I:3, II:12, III: 4, and IV: 29;median age: 59 years) were analyzed. Patients were followed up for a median of 12.68 months (inter quartile range: 7.9-17.7 months). Of the 50 patients, 41 had pre-treatment (baseline) time points available and ctDNA was detected in 95% (39/41) of patients. Since the majority of the patients had stage IV disease, median ctDNA detection levels were observed to be high (overall median: 534 MTM/ml, range: 0-5957 MTM/ml; I median: 9.6 MTM/mL [range: 0.2-2822 MTM/mL], II median: 53 MTM/mL [range: 0.8-862 MTM/mL], III median: 368 [range: 2-940 MTM/mL], IV median: 1011 MTM/mL [range: 74-5958 MTM/mL]). Clearance of ctDNA at any point during first-line therapy was associated with improved outcomes (EFS, HR: 8.3, 95% CI: 2.56-27.0, $p<0.0001$ and OS, HR: 15.2, 95% CI: 1.53-149, $p=0.0021$), compared to patients who remained ctDNA-positive. Furthermore, 48% (13/27) of patients were found to clear their ctDNA upon the completion of the first cycle of treatment. On comparing baseline ctDNA levels with other clinicopathological risk factors, high ctDNA levels were observed to be strongly correlated with higher R-IPI scores (0-2 vs. 3-5; $p=0.0008$) and higher stage (I-II vs. III-IV; $p=0.0007$). Additionally, multivariate analysis determined that ctDNA clearance significantly outperformed all other clinicopathologic risk factors associated with EFS (HR: 48.8, 95% CI:1.2-2005, $p=0.04$). Finally, ctDNA clearance predicted complete response (CR)/no evidence of disease (NED) on average 95 days (range: 0-14.7 months) ahead of PET imaging or biopsy.

Conclusions: In this study utilizing a real-world cohort of patients with stage I-IV DLBCL, ctDNA clearance during first-line therapy was prognostic for EFS and OS and preceded clinical response. ctDNA testing in patients with DLBCL may enable personalized surveillance, intervention, and/or trial options, ultimately improving patient outcomes.

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