The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Integrative Genomic and Transcriptomic Analysis Reveals Genetic Alterations Associated with the Early Progression of Follicular Lymphoma

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Background Follicular lymphoma (FL), the most common indolent lymphoma, is a clinically and genetically heterogeneous disease. However, the prognostic value of driver gene mutations and copy number alterations has not been systematically assessed.

Patients and Methods Here, we analyzed clinical-biological features of 415 FL patients to identify variables associated with disease within 24 months of first-line therapy (POD24). In addition, we applied whole exome sequencing (WES) to identify genomic alterations that predict POD24 based on 102 FL patients. Furthermore, we characterized the cellular and molecular heterogeneity within and across patients through bulk RNA sequencing and single-cell RNA sequencing.

Results POD24 occurred in 21% of evaluable FL patients. To further examine the effect of POD24 on OS, we used a 24-month landmark approach for Kaplan-Meier curve analysis. As expected, POD24 was related to poor OS, and the 3- and 5-year survival probabilities of patients in whom the disease progressed within the first 24 months were 89.2% (95% CI, 84.5-93.9) and 78.6% (95% CI, 70.4-86.8), respectively, compared with 98.5% (95% CI, 97.8-99.2) and 96.2% (95% CI, 95.0-97.4) in patients who were progression free at 24 months, respectively. Moreover, patients without progression at 24 months were more likely to exhibit a CR to front-line treatment (54% vs. 35%, P = 0.001) compared to the POD24 cohort. Patients with B symptoms, elevated lactate dehydrogenase and β2-microglobulin levels, unfavorable baseline haemoglobin levels, advanced stage, and high-risk FL International Prognostic Index (FLIPI) scores had an increased risk of POD24, with FLIPI being the most important factor in logistic regression. HIST1H1D, known as a driver mutation, was correlated with POD24. Gains of 6q22.2 (HIST1H1D) and 18q21.33 (BCL2) and loss of 1p36.13 (NBPF1) predicted POD24 independent of FLIPI. Integration of the four variants led to the identification of 76% of POD24 patients. Gene expression profiling of FL samples showed that the POD24 cohort was significantly enriched in the inflammatory response (mediated by interferon and tumor necrosis factor), cell cycle regulation (transcription, replication and proliferation) sets and PI3K-AKT-mTOR signaling. This result was further validated with transcriptome-wide information provided by RNA-seq at single-cell resolution.

Conclusion Our study, performed on a large cohort of FL patients, highlights the importance of distinctive genetic alterations and gene expression relevant to disease diagnosis and early progression.

Disclosures No relevant conflicts of interest to declare.