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P1281 LIQUID BIOPSY PROVIDES COMPLEMENTARY INFORMATION TO TISSUE BIOPSIES FOR THE MOLECULAR CLASSIFICATION OF DLBCL PATIENTS

Topic: 20. Lymphoma Biology & Translational Research

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Background: Diffuse large B-cell lymphoma (DLBCL) displays a high degree of molecular heterogeneity and may be classified into molecular clusters harboring specific lesions and therapeutic vulnerabilities. To date, DLBCL molecular clusters are identified on the tissue biopsy and do not consider mutations deriving from different anatomical compartments.

Aims: The aim of this study is to evaluate the potential contribution of liquid biopsy to the identification of DLBCL molecular clusters.

Methods: A multicenter cohort of newly diagnosed DLBCL provided with circulating tumor DNA (ctDNA) from the plasma and with genomic DNA (gDNA) from the lymph node (LN) biopsy represented the basis of this study. The LyV4.0 CAPP-Seq assay that comprised a panel of 59 genes relevant to B-cell malignancies was used. The LymphGen tool v1.0 was utilized for cluster analysis.

Results:

The cohort included 77 newly diagnosed DLBCL patients treated with R-CHOP. After a median follow up of 27.1 months, the 36-month PFS and OS were 62.0% and 79.5%. Mutation analysis identified at least one somatic non-synonymous mutation in 92.2% (71/77) of patients in the LN biopsy and in 87.0% (67/77) in the ctDNA. Higher levels of ctDNA (≥2.5 log hGE/mL) were associated with a significantly worse PFS (p=0.025) and OS (p=0.004). Mutation analysis of different compartments, i.e. lymph node and plasma, allowed to identify mutations with potential clinical impact, that otherwise would have been missed by analyzing only one compartment. In particular, *GRHPR* (p=0.035) and *SGK1* (p=0.039) mutations identified only on the liquid biopsy, and *MYC* mutations identified only on the LN biopsy (p=0.021) were associated with a shorter PFS. Based on the mutational landscape identified in each compartment, DLBCL were analyzed with the LymphGen tool, that allows the cluster assignment in approximately 40-50% of DLBCL. In our cohort, 46.5% (33/71) of cases were assigned to a specific molecular cluster on the LN biopsy and 40.3% (27/67) on the liquid biopsy. Interestingly, one case was classified as EZB on the LNF biopsy and as MCD on the ctDNA (Fig. 1A). In all other cases, if not unclassified, the cluster identified on the ctDNA reflected the cluster identified on the LN biopsy. The combination of mutational data from LN and ctDNA improved DLBCL assignment to a specific cluster, thus classifying 48.7% (36/74) of cases. Two patients were assigned to two different clusters and defined as genetically composite. From a clinical perspective, by combining mutational data from the LN and from ctDNA, patients belonging to the BN2 and ST2 clusters showed a favorable outcome with a 36-month PFS of 100% compared to 62.3% for patients belonging to the MCD or EZB clusters (p=0.040) (Fig. 1B-C).

Image:

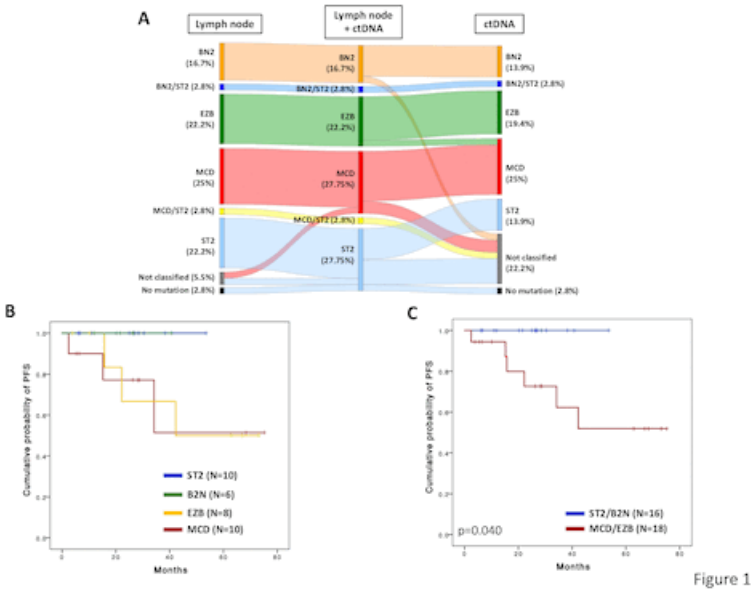

Figure 1

Summary/Conclusion: The combination of mutational data from the LN biopsy and from the liquid biopsy provides complementary information for the molecular classification and prognostic stratification of newly diagnosed DLBCL patients.