Different prognostic impact of recurrent gene mutations in chronic lymphocytic leukemia depending on IGHV gene somatic hypermutation status: a study by ERIC in HARMONY

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Abstract: Recent evidence suggests that the prognostic impact of gene mutations in patients with chronic lymphocytic leukemia (CLL) may differ depending on the immunoglobulin heavy variable (IGHV) gene somatic hypermutation (SHM) status. In this study, we assessed the impact of nine recurrently mutated genes (BIRC3, EGR2, MYD88, NFKBIE, NOTCH1, POT1, SF3B1, TP53, and XPO1) in pre-treatment samples from 4580 patients with CLL, using time-to-first-treatment (TTFT) as the primary end-point in relation to IGHV gene SHM status. Mutations were detected in 1588 (34.7%) patients at frequencies ranging from 2.3-9.8% with mutations in NOTCH1 being the most frequent. In both univariate and multivariate analyses, mutations in all genes except MYD88 were associated with a significantly shorter TTFT. In multivariate analysis of Binet stage A patients, performed separately for IGHV-mutated (M-CLL) and unmutated CLL (U-CLL), a different spectrum of gene alterations independently predicted short TTFT within the two subgroups. While SF3B1 and XPO1 mutations were independent prognostic variables in both U-CLL and M-CLL, TP53, BIRC3 and EGR2 aberrations were significant predictors only in U-CLL, and NOTCH1 and NFKBIE only in M-CLL. Our findings underscore the need for a compartmentalized approach to identify high-risk patients, particularly among M-CLL patients, with potential implications for stratified management.

DOI: https://doi.org/10.1038/s41375-022-01802-y

Silvia; Scarfo, Lydia; Mattsson, Mattias; Davis, Zadie; Gogia, Ajay; Rani, Lata; Baliakas, Panagiotis; Foroughi-Asl, Hassan; Jylhä, Cecilia; Skaftason, Aron; Rapado, Inmaculada; Miras, Fatima; Martinez-Lopez, Joaquín; Zenz, Thorsten; et al (2023). Different prognostic impact of recurrent gene mutations in chronic lymphocytic leukemia depending on IGHV gene somatic hypermutation status: a study by ERIC in HARMONY. Leukemia, 37(2):339-347.
DOI: https://doi.org/10.1038/s41375-022-01802-y

CORRECTION OPEN

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Leukemia (2023) 37:504; https://doi.org/10.1038/s41375-023-01813-3

Correction to: *Leukemia* https://doi.org/10.1038/s41375-022-01802-y, published online 24 December 2022

In this article the author name Florence Nguyen-Khac was incorrectly written as Florence N'Guyen-Khac.

The original article has been corrected.

Published online: 12 January 2023