



---

Year: 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

Mansouri, Larry ; Thorvaldsdottir, Birna ; Sutton, Lesley-Ann ; Karakatsoulis, Georgios ; Meggendorfer, Manja ; Parker, Helen ; Nadeu, Ferran ; Brieghel, Christian ; Laidou, Stamatia ; Moia, Riccardo ; Rossi, Davide ; Catherwood, Mark ; Kotaskova, Jana ; Delgado, Julio ; Rodriguez-Vicente, Ana E ; Benito, Rocío ; Rigolin, Gian Matteo ; Bonfiglio, 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

**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>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-239066>

Journal Article

Updated Version



The following work is licensed under a Creative Commons: Attribution 4.0 International (CC BY 4.0) License.

Originally published at:

Mansouri, Larry; Thorvaldsdottir, Birna; Sutton, Lesley-Ann; Karakatsoulis, Georgios; Meggendorfer, Manja; Parker, Helen; Nadeu, Ferran; Brieghel, Christian; Laidou, Stamatia; Moia, Riccardo; Rossi, Davide; Catherwood, Mark; Kotaskova, Jana; Delgado, Julio; Rodriguez-Vicente, Ana E; Benito, Rocío; Rigolin, Gian Matteo; Bonfiglio,

























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



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

Larry Mansouri, Birna Thorvaldsdottir , Lesley-Ann Sutton, Georgios Karakatsoulis, Manja Meggendorfer, Helen Parker, Ferran Nadeu , Christian Brieghel , Stamatia Laidou , Riccardo Moia , Davide Rossi, Mark Catherwood, Jana Kotaskova , Julio Delgado, Ana E. Rodríguez-Vicente , Rocío Benito , Gian Matteo Rigolin, Silvia Bonfiglio, Lydia Scarfo, Mattias Mattsson, Zadie Davis , Ajay Gogia, Lata Rani, Panagiotis Baliakas , Hassan Foroughi-Asl , Cecilia Jylhä, Aron Skaftason, Inmaculada Rapado, Fatima Miras, Joaquín Martínez-Lopez, Javier de la Serna , Jesús María Hernández Rivas, Patrick Thornton, María José Larráyo, María José Calasanz, Viktória Fésüs, Zoltán Mátrai, Csaba Bödör , Karin E. Smedby, Blanca Espinet , Anna Puiggros, Ritu Gupta , Lars Bullinger, Francesc Bosch, Bárbara Tazón-Vega, Fanny Baran-Marszak , David Oscier, Florence Nguyen-Khac, Thorsten Zenz , María Jose Terol, Antonio Cuneo, María Hernández-Sánchez , Sarka Pospisilova, Ken Mills , Gianluca Gaidano, Carsten U. Niemann , Elias Campo , Jonathan C. Strefford , Paolo Ghia , Kostas Stamatopoulos , and Richard Rosenquist 

© The Author(s) 2023

*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.



**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/>.

© The Author(s) 2023