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Editorial

CLL-IPI: A New and Improved Staging System for CLL

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Editorial

The Rai and Binet clinical staging systems, which rely on physical examination and blood counts, have represented for more than 40 years the basis for prognostication of Chronic Lymphocytic Leukemia (CLL). In recent years, insights into the genetic and molecular pathogenesis of CLL have led to the identification of new markers (e.g., IGHV mutational status, cytogenetic, mutations of TP53, NOTCH1, SF3B1, and BIRC3) that add complementary prognostic information to clinical staging. To date,

It has become challenging to know how best to combine different tests to predict outcome for individual patients. Several groups have attempted to develop prognostic scores which incorporate multiple prognostic markers into a single model. However, the use of these models has not been widely adopted in routine clinical practice due to their complexity and the fact that, in some cases, they are based on laboratory tests that are not widely available.

A recently published systematic review and meta-analysis recommend IGHV mutational status and FISH be performed in all newly diagnosed CLL patients "in those countries with the resources to do so" [1]. Both these tests are considered standard of care in the National Cancer Comprehensive Network (NCCN) guidelines, which are widely used as national guidelines for routine clinical practice in the U.S. Recently, an international consortium developed an international prognostic index for CLL (CLL-IPI) that integrates the major prognostic parameters " [2]. Data from eight phase 3 trials which included 3472 treatment-naïve CLL patients were analyzed to identify five independent prognostic factors: TP53 status (deletion or mutation, or both), IGHV mutational status, serum β2-microglobulin Concentration, clinical stage and age. The CLL-IPI Working Group used a weighted grading approach to generate a prognostic index which defines four risk groups (low, intermediate, high, and very high) with significantly different overall survival (OS) at 5 years [2].

Of note, in the CLL-IPINOTCH1 and SF3B1— two of the more than 40 recurrent mutations detected in CLL were not found to be independent prognostic factors.

The robustness of the CLL-IPI index in unselected cohorts of newly diagnosed patients with CLL has been confirmed in independent validation studies [3-5]. Although developed to predict overall survival, the CLL-IPI also predicts TTFT with accuracy not inferior to other recently developed tools specifically designed to predict this endpoint. Therefore all centres treating CLL patients should been courage to integrate the five parameters forming the CLL-IPI as part of the routine diagnostic workup and to report the CLL-IPI risk categories for stratifying patients in clinical trials.

In conclusion, the CLL-IPI score, based on the use of five widely employed parameters represents a step forward in CLL prognostication, easily applicable in daily clinical practice. The ultimate clinical impact of the CLL-IPI in the management of early stage CLL patients should be determined in large, well-designed, prospective clinical trials including randomized trials evaluating the benefit of early intervention for high-risk early stage patients. In addition, the prognostic effectiveness of CLL-IPI needs to be reconsidered in the era of BCR-inhibitors and BCL-2 antagonists to determine if these drugs will be able to overcome the shorter survival likelihood among cases with higher risk disease according to CLL-IPI.

References

1. Parikh SA, Strati P, Tsang M, West CP, Shanafelt TD. Should IGHV status and FISH testing be performed in all CLL patients at diagnosis? A systematic review and meta-analysis. Blood. 2016; 127: 1752-1760.
2. International CLL-IPI working group. An international prognostic index for patients with chronic lymphocytic leukaemia (CLL-IPI): a meta-analysis of individual patient data. Lancet Oncol. 2016; 17: 779-790.
3. Molica S, Shanafelt TD, GiannarelliD, Gentile M, Mirabelli R, Cutrona G, et al. The chronic lymphocytic leukemia international prognostic index predicts time to first treatment in early CLL: Independent validation in a prospective cohort of early stage patients. Am J Hematol. 2016.
4. Gentile M, Shanafelt TD, Rossi D, Laurenti L, Mauro FR, Molica S, et al. Validation of the CLL-IPI and comparison with the MDACC prognostic index: analysis of 1364 newly diagnosed patients. Blood. 2016.
5. da Cunha-Bang C, Christiansen I, Niemann CU. The International prognostic Index for patients with chronic lymphocytic leukemia (CLL-IPI) applied in a population-based cohort. Blood. 2016.

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