Development of a comprehensive prognostic index for patients with chronic lymphocytic leukemia.

In addition to clinical staging, a number of biomarkers predicting overall survival (OS) have been identified in chronic lymphocytic leukemia (CLL). The multiplicity of markers, limited information on their independent prognostic value, and a lack of understanding of how to interpret discordant markers are major barriers to use in routine clinical practice. We therefore performed an analysis of 23 prognostic markers based on prospectively collected data from 1948 CLL patients participating in phase 3 trials of the German CLL Study Group to develop a comprehensive prognostic index. A multivariable Cox regression model identified 8 independent predictors of OS: sex, age, ECOG status, del(17p), del(11q), IGHV mutation status, serum ?2-microglobulin, and serum thymidine kinase. Using a weighted grading system, a prognostic index was derived that separated 4 risk categories with 5-year OS ranging from 18.7% to 95.2% and having a C-statistic of 0.75. The index stratified OS within all analyzed subgroups, including all Rai/Binet stages. The validity of the index was externally confirmed in a series of 676 newly
diagnosed CLL patients from Mayo Clinic. Using this multistep process including external validation, we developed a comprehensive prognostic index with high discriminatory power and prognostic significance on the individual patient level. The studies were registered as follows: CLL1 trial (NCT00262782, http://clinicaltrials.gov), CLL4 trial (ISRCTN 75653261, http://www.controlled-trials.com), and CLL8 trial (NCT00281918, http://clinicaltrials.gov).