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Titel des Beitrags:
Gene mutations and treatment outcome in chronic lymphocytic leukemia: results from the CLL8 trial.

Abstract:
Mutations in TP53, NOTCH1, and SF3B1 were analyzed in the CLL8 study evaluating first-line therapy with fludarabine and cyclophosphamide (FC) or FC with rituximab (FCR) among patients with untreated chronic lymphocytic leukemia (CLL). TP53, NOTCH1, and SF3B1 were mutated in 11.5%, 10.0%, and 18.4% of patients, respectively. NOTCH1(mut) and SF3B1(mut) virtually showed mutual exclusivity (0.6% concurrence), but TP53(mut) was frequently found in NOTCH1(mut) (16.1%) and in SF3B1(mut) (14.0%) patients. There were few significant associations with clinical and laboratory characteristics, but genetic markers had a strong influence on response and survival. In multivariable analyses, an independent prognostic impact was found for FCR, thymidine kinase (TK)≥10 U/L, unmutated IGHV, 11q deletion, 17p deletion, TP53(mut), and SF3B1(mut) on progression-free survival; and for FCR, age≥65 years, Eastern Cooperative Oncology Group.
performance status $\geq$ 1, 2-microglobulin $\geq$ 3.5 mg/L, TK $\geq$ 10 U/L, unmutated IGHV, 17p deletion, and TP53(mut) on overall survival. Notably, predictive marker analysis identified an interaction of NOTCH1 mutational status and treatment in that rituximab failed to improve response and survival in patients with NOTCH1(mut). In conclusion, TP53 and SF3B1 mutations appear among the strongest prognostic markers in CLL patients receiving current-standard first-line therapy. NOTCH1(mut) was identified as a predictive marker for decreased benefit from the addition of rituximab to FC. This study is registered at www.clinicaltrials.gov as #NCT00281918.