NOTCH1, SF3B1, and TP53 mutations in fludarabine-refractory CLL patients treated with alemtuzumab: results from the CLL2H trial of the GCLLSG.

Abstract:
We studied the incidences, associations, and prognostic roles of NOTCH1 and SF3B1 mutations (NOTCH1(mut), SF3B1(mut)) as compared with TP53(mut) in fludarabine-refractory chronic lymphocytic leukemia (CLL) patients treated with alemtuzumab in the CLL2H trial. We found NOTCH1(mut), SF3B1(mut), and TP53(mut) in 13.4%, 17.5%, and 37.4% of patients, respectively. NOTCH1(mut) and SF3B1(mut) were mutually exclusive, whereas TP53(mut) were evenly distributed within both subgroups. Apart from correlation of SF3B1(mut) with 11q deletion (P = .029), there were no other significant associations of the mutations with any baseline characteristics or response rates. However, NOTCH1(mut) cases had a significantly longer progression-free survival (PFS) compared with wild-type cases (15.47 vs 6.74 months; P = .025), although there was no significant difference with overall survival (OS). SF3B1(mut) had no significant impact on PFS and OS. In multivariable analyses, NOTCH1(mut) was identified as an independent favorable marker for PFS. This clinical trial is registered at www.clinicaltrials.gov as