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Epstein-Barr virus DNA load in chronic lymphocytic leukemia is an independent predictor of clinical course and survival

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Abstract

The relation between Epstein-Barr virus (EBV) DNA load and clinical course of patients with chronic lymphocytic leukemia (CLL) is unknown. We assessed EBV DNA load by quantitative PCR at CLL presentation in mononuclear cells (MNC) of 220 prospective patients that were enrolled and followed-up in two major Institutions. In 20 patients EBV DNA load was also assessed on plasma samples. Forty-one age-matched healthy subjects were tested for EBV DNA load on MNC. Findings were validated in an independent retrospective cohort of 112 patients with CLL. EBV DNA load was detectable in 59%, and high (≥2000 copies/μg DNA) in 19% of patients, but it was negative in plasma samples. EBV DNA load was significantly higher in CLL patients than in healthy subjects (P < .0001). No relation was found between high EBV load and clinical stage or biological variables, except for 11q deletion (P = .004), CD38 expression (P = .003), and NOTCH1 mutations (P = .05). High EBV load led to a 3.14-fold increase in the hazard ratio of death and to a shorter overall survival (OS; P = .001). Poor OS was attributable, at least in part, to shorter time-to-first-treatment (P = .0008), with no higher risk of Richter's transformation or second cancer. Multivariate analysis selected high levels of EBV load as independent predictor of OS after controlling for confounding clinical and biological variables. EBV DNA load at presentation is an independent predictor of OS in patients with CLL.