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Significance of zeta-associated protein (ZAP-70) and CD38 expression in chronic lymphocytic leukemia

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Chronic lymphocytic leukemia (CLL) is a disease with a highly variable clinical course; some patients never need treatment, while others require intensive treatment early after diagnosis. Some new prognostic factors, such as immunoglobulin variable heavy chain (IgVH) mutational status, zeta-associated protein (ZAP-70) and CD38 expression in leukemic cells were introduced to identify attenuated versus progressive types of CLL bearing the potential to facilitate risk-adapted treatment strategies. So, the aim of this work is to evaluate the clinical value of ZAP-70 and CD38 as predictors of disease progression. We assessed the expression of these markers by flowcytometry in 38 patients with CLL and correlated their levels with genetic abnormalities detected by fluorescence in situ hybridization (FISH) and the clinical outcome. We found that 18 patients (47.4 %) were positive for ZAP-70 (> or = 20%) and 16 patients (42.1%) were positive for CD38 (> or = 20%). Positive ZAP-70 and CD38 status were associated with an unfavorable clinical course including high leukocytic count, lymphocytosis, high lactate dehydrogenase (LDH) serum level, advanced disease stage, trisomy 12 and del (11q); negative ZAP-70 and CD38 status were correlated with del (13q). The treatment-free survival time was 30 months for ZAP-70-positive patients and 18 months for ZAP-70-nagative patients ($p < 0.01$). Combined analysis of ZAP-70 and CD38 yielded discordant results in 10 patients (26.3 %), whereas 16 patients (42.1%) were concordantly negative and 12 patients (31.6%) were concordantly positive for ZAP-70 and CD38 expression. Median treatment-free survival times in patients whose leukemic cells were ZAP-70+CD38+ was 27 months as compared to 100 months in patients with a ZAP-70(-)CD38(-) status. In patients with discordant ZAP-70/CD38 results, the median treatment-free survival time was 40 months. Thus, ZAP-70 and CD38 expression analyses provide complementary prognostic information and allow distinguishing the patients groups with the most favorable prognosis as well as those with the worst. The current findings suggest that both ZAP-70 and CD38 protein expression should be assessed in patients with CLL for the definition of prognostic subgroups.