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The combination of rituximab, bendamustine, and cytarabine for heavily pretreated relapsed/refractory cytogenetically high-risk patients with chronic lymphocytic leukemia

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Abstract

Treatment of patients with B-cell chronic lymphocytic leukemia (CLL) relapsed/refractory (R/R) to conventional treatments is particularly challenging. The combination of bendamustine and cytarabine has demonstrated distinct and synergistic mechanisms of action in preclinical studies on cell lines and primary tumor cells of several B-cell lymphomas, including 17p deleted or TP53 mutated CLL. The efficacy of rituximab (375 mg/m(2) , Day 1), plus bendamustine (70 mg/m(2) , days 1-2), and cytarabine (800 mg/m(2) , Day 1-3; R-BAC), every 28 days for up to four courses, was evaluated in a pilot trial enrolling 13 patients with very selected high-risk R/R CLL. All patients (median age 60 years, range 53-74) had symptomatic Binet stage B or C active disease requiring treatment, were characterized by adverse cytogenetics (17p deletion, 11q deletion, or both), unmutated immunoglobulin heavy-chain variable region, and were heavily pretreated (1-5, median three previous lines). Overall, R-BAC was well tolerated with limited non-hematological toxicity. Major toxicities were transient Grade 3/4 neutropenia and thrombocytopenia in 84% and 85% of patients, respectively. Overall response rate (OR) was 84%, including complete and partial response in 38% and 46% of patients, respectively. Patients with 17p deletion had an OR of 78%. After a median follow-up of 17 months, median progression-free survival was 16 months while median overall survival (OS) was not reached (1-year OS: 75 ± 13%). R-BAC is an active regimen in R/R heavily pretreated high-risk patients with CLL, representing an option for the treatment of patients that are usually refractory to standard therapy.