Abstract:

PURPOSE: The phase II CLL2H trial evaluated safety and efficacy of subcutaneous alemtuzumab in patients with fludarabine-refractory chronic lymphocytic leukemia (CLL). Clinical and biologic markers were evaluated for their impacts on outcome. PATIENTS AND METHODS: One hundred nine patients were enrolled, and 103 received at least one dose of alemtuzumab. After dose escalation, alemtuzumab was administered subcutaneously at 30 mg three times weekly for up to 12 weeks. Response was assessed every 4 weeks during treatment and quarterly thereafter. RESULTS: The overall response rate was 34% (complete response, 4%; partial response, 30%). The median progression-free survival was 7.7 months, and the median overall survival (OS) was 19.1 months. Grades 3 to 4 neutropenia, thrombocytopenia, and anemia occurred in 56%, 57%, and 49% of patients, respectively. Grades 3 to 4 noncytomegalovirus and cytomegalovirus infections occurred in 29% and 8% of patients, respectively. Injection-site skin reactions were
generally mild. Efficacy did not vary significantly in subgroups defined by genetic parameters (in particular, in 17p deletion, 11q deletion, mutated TP53, and unmutated VH), but efficacy was inferior in patients with increased beta2-microglobulin (beta2-MG) and thymidine kinase (TK). In multivariate analysis of clinical and biologic variables, age, performance status, beta2-MG, and TK were independent prognostic factors for OS. CONCLUSION: Subcutaneous alemtuzumab appears as effective and safe as intravenous alemtuzumab in fludarabine-refractory CLL. Subcutaneous administration should be the preferred delivery route because of its efficacy, improved adverse effect profile, and cost savings. In contrast to chemotherapy-based therapy, alemtuzumab treatment overcomes the adverse prognostic impact of VH mutation status, TP53 mutation, and genomic aberrations.