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Abstract 3647 Bendamustine + Rituximab (BR) Chemoimmunotherapy and Maintenance Lenalidomide in Relapsed/Refractory (R/R) Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL): A Wisconsin Oncology Network (WON) Study

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Introduction: BR chemoimmunotherapy was shown to have an overall response rate (ORR) of 59%, a median progression-free survival (PFS) of 14.7 months, and an acceptable toxicity profile in R/R CLL (Fischer K, et al. J Clin Oncol 2011). Given the single-agent activity of lenalidomide in R/R CLL/SLL, we hypothesized that maintenance lenalidomide after BR induction could improve PFS.

Methods: Thirty-four patients requiring therapy for R/R CLL/SLL were treated with bendamustine 90 mg/m^2 IV on days 1 & 2 and rituximab 375 mg/m^2 IV on day 1 every 28 days for a maximum of 6 cycles. Growth factor support was permitted. Patients achieving at least a minor response (objective improvement even if not meeting criteria for partial response) were eligible to proceed with 12 cycles of maintenance therapy with lenalidomide 5-10 mg/day orally given continuously in each 28-day cycle. Patients were

eligible if they had histologically proven CLL/SLL and had received >1 but ≤5 prior cytotoxic chemotherapy regimens (retreatment with an identical regimen was not counted as a separate treatment). The primary endpoint was PFS.

Results: Baseline characteristics include median age 67 (range 38-86), 25 men/9 women, 26 CLL/8 SLL, and median of 2 prior therapies (range 1-4). Cytogenetic profiling by FISH analysis was available in 22 patients (65%), with 11/22 demonstrating presence of 17p and/or 11q deletions. Twenty-five patients (74%) completed 6 cycles of induction BR. Two patients died from toxicities of pneumonia and heart failure during cycle 1; 7 patients received <6 cycles due to toxicities (n=4), progressive disease (n=2), and stable disease (n=1). Dose modifications were required in 14 (41%) patients, most commonly for neutropenia (12/14), thrombocytopenia (3/14), and weight loss/failure to thrive (3/14). Grade 3/4 toxicities were primarily hematologic, with neutropenia in 20 patients, anemia in 1, and thrombocytopenia in 7. Febrile neutropenia occurred in 4 patients. Infections with or without neutropenia were common; grade 2 infections in 16 patients, grade 3 in 7 patients. Grade 2 rash occurred in 4 patients. Eleven deaths have been observed, 7 events due to progressive disease (including 2 events of transformed lymphoma). Responses were evaluable in 31/34 patients. The ORR was 65%, with 6 complete (18%) and 16 partial (47%) responses. An additional 7 patients achieving stable disease were eligible to proceed to maintenance therapy. With a median follow up of 20.1 months, the median PFS and overall survival are 24.3 months and 27.9 months, respectively.

Conclusions: In our multicenter trial for patients with R/R CLL/SLL, the BR induction produced an ORR that is comparable to historical observations (65% vs 59%). However, the median PFS is longer (24.3 vs 14.7 months), suggesting maintenance lenalidomide may be contributing to an improved response duration. Based upon these promising results, we have initiated a successor study in which patients will receive lenalidomide plus rituximab maintenance after a BR induction.

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