Bendamustine + Rituximab as Treatment for Elderly Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma.

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Abstract

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Background: Current first-line immuno-chemotherapy for diffuse large B-cell lymphoma (DLBCL) is highly effective, curing 50–90% of patients, depending on staging and prognostic factors. Relapsed or refractory patients who are ineligible for transplant or who relapse after transplant generally have a poor prognosis. Aggressive salvage regimens for DLBCL are frequently intolerable and may involve hospitalization for this population of patients. Bendamustine (B) has demonstrated activity as a single-agent and in combination therapy for indolent lymphomas, however data about its activity in DLBCL and other aggressive lymphomas are limited. Based on the favorable toxicity profile and demonstrated synergy of bendamustine with rituximab (R), this study of combination BR is being conducted for subjects with relapsed or refractory DLBCL.
Methods: Patients who have failed at least one prior therapy and have at least one measurable lesion were given bendamustine (120 mg/m^2) on days 1 and 2, and rituximab (375 mg/m^2) on day 1 for up to six 28-day cycles. A Simon two-stage design was used (a=0.1,b=0.2,P_0=50%, P_1=70%), in which at least 8 of the first 15 patients enrolled achieved a complete or partial response to allow the study to continue until 43 patients in the modified intent-to-treat (MITT) population are evaluable for efficacy. The MITT cohort includes enrolled patients who have received at least one response evaluation. Safety is assessed weekly, and disease status measured by the Revised Response Criteria for Malignant Lymphoma is evaluated at completion of every two cycles, the first assessment at approximately eight weeks after enrollment.
Results: Enrollment in the trial is ongoing, with 43 subjects enrolled currently. These patients have a median age of 74 (range 54–90), ECOG status at baseline of 0 (n=18, 42%), 1 (n=23, 53%), and 2 (n=2, 5%), baseline R-IPI score very good/good (n=13, 30%) and poor (n=30, 70%) and have been administered a sum of 130 cycles, with a median of 3 cycles per subject. Efficacy data from 33 evaluable subjects to date (MITT population) demonstrate an ORR of 51.6% (CR: n=5, 15.2%; PR: n=12, 36.4%), with SD (n=7, 21.2%) and PD (n=9, 27.2%). Four patients are considered non-evaluable due to removal from the study prior to the first efficacy evaluation (three withdrew consent prior to cycle 1 and one progressed during cycle 1); four patients have yet to complete their first efficacy evaluations. Grade 3/4 treatment-related AEs include neutropenia (10), anemia (4), thrombocytopenia (4), leukopenia (3), hepatic failure (1), disseminated herpes zoster (1), diarrhea (1), elevated liver functions (1), mucositis (1), dehydration (1), anorexia (1), and weight loss (1). Grade 1/2 AEs have been consistent with treatment and anticipated co-morbidities of the DLBCL patient population.
Conclusions: Data from our ongoing trial suggest that BR may have a role in the treatment of relapsed/refractory DLBCL, particularly for older patients who are not candidates for transplant and who may not tolerate aggressive therapy associated with higher toxicity.
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