Bendamustine Combined with Rituximab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma.

Jeffrey Vacirca
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Abstract

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Background The diffuse large B-cell lymphomas (DLBCL) comprise 35% of all non-Hodgkins lymphomas (NHL) in the US and approximately 60% of aggressive NHL. Despite relatively effective first-line treatments (50-70% complete remission) consisting of immuno-chemotherapy (e.g. R-CHOP), chemo-radiotherapy, and transplant for younger high-risk patients, the majority of DLBCL patients suffer progression and require subsequent therapy. For patients with relapsed or refractory DLBCL who are not candidates for transplant, there are 10 or more combination regimens in clinical use. However, due to the limited efficacy of current salvage therapy, no standard treatment exists. Symptom control and delay of progression, with minimum treatment toxicity are important clinical objectives. The addition of rituximab (R) to chemotherapy has extended overall survival in DLBCL. Bendamustine (B), recently approved for relapsed or refractory NHL and chronic lymphocytic leukemia, has also demonstrated promising activity in aggressive NHL. We report initial results of a phase II clinical trial to evaluate the efficacy and safety of combination therapy using BR for patients with relapsed or refractory DLBCL.
Methods This open label, single arm trial is scheduled to enroll up to 54 DLBCL patients who have failed at least one prior therapy. Selection criteria include positive CD20 expression and at least one measurable lesion, according to the Revised Response Criteria for Malignant Lymphoma. BR are administered by intravenous infusion in 28 day cycles, with bendamustine (120 mg/m^2) given on day 1 and 2 and rituximab (375 mg/m^2) given on day 1, for up to six cycles. Safety endpoints are assessed weekly during treatment, and disease status/response is evaluated at baseline and at the completion of every two treatment cycles. A Simon two-stage design is employed, requiring ORR of $\geq$60% in the first 15 evaluable subjects.
Results At abstract submission, the intent-to-treat population included 17 subjects, (median age 74, range, 62-81). Patient ECOG status at baseline was: 0 (24%), 1 (35%), 2 (6%), data pending (35%). Data thus far include 36 total cycles administered (median 2 per patient). Efficacy is estimated from data received for the first 7 subjects. The overall response rate (ORR) is 57% (CR 0%, PR 57%), with SD (14%) and PD (29%). Three subjects were discontinued for treatment failure, and 1 withdrew consent prior to treatment. One grade 4 thrombocytopenia was reported. Grade 3 adverse events included 3 neutropenia, 1 anemia, 1 leukocytopenia, and 1 thrombocytopenia. No treatment-related serious adverse events have occurred.
Conclusions Combination therapy with BR is being studied as a treatment option for relapsed or refractory, CD20 positive DLBCL. Preliminary data suggest that BR is active and well tolerated. Analysis of the first 15 response-evaluable subjects is pending further treatment and accumulation of additional ORR data. This study is ongoing, and updated results will be presented.
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