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Abstract 1624 Bendamustine, Bortezomib, and Rituximab in Patients with Previously Untreated Low Grade Lymphoma: A Phase II Trial of the Sarah Cannon Research Institute

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Background: Rituximab and bendamustine combination regimens have demonstrated high activity in non-Hodgkin's lymphoma (NHL). A phase III trial compared bendamustine plus R-CHOP as first-line treatment for follicular, indolent, and mantle cell lymphoma (Rummel ASH 2009). Bendamustine plus rituximab had an overall response rate of 94% and a complete remission rate of 40% compared to 94% and 31%, respectively, for R-CHOP. Phase III trials evaluating bendamustine plus rituximab as first-line therapy for patients (pts) with indolent and mantle cell lymphoma have shown equivalent or superior results when compared to R-CHOP or R-CVP as first-line treatment for indolent lymphoma. Bortezomib is a small molecule proteasome inhibitor that has shown substantial activity in multiple myeloma and lymphoma. Pre-clinical studies demonstrate significant synergy and/or ability to overcome resistance to a variety of current and investigational treatments for lymphoma. This trial evaluated the activity of bendamustine, bortezomib, and rituximab (BBR) in patients with previously untreated low-grade lymphoma.

Methods: Eligible patients had histologically-confirmed follicular center cell (FCC) lymphoma (grade 1 or 2), marginal zone lymphoma (MZL), small lymphocytic lymphoma (SLL), or lymphoplasmacytic lymphoma (LPL); lymph node biopsy containing CD20+ B-cells; Ann-Arbor Stage 2, 3, or 4 disease; no previous systemic treatment for lymphoma; bi-dimensional measurable disease with at least 1 lesion measuring > 2.0 cm in a single

dimension; ECOG PS 0-2. Treatment for all patients was given in 28-day cycles for a maximum of 6 cycles. Patients received rituximab 375 mg/m^2 IV on days 1, 8, and 15 of cycle 1 (cycles 2-6, rituximab only on day 1); bendamustine 90 mg/m^2 IV on days 1 and 2; and bortezomib 1.6 mg/m^2 IV on days 1, 8, and 15. Response evaluations were performed after cycle 3 and cycle 6. Patients were permitted to begin maintenance treatment with rituximab 6 months after completion of study treatment and after 6-month follow-up assessments have been conducted.

Results: Between 1/2010 and 11/2011, 55 patients were enrolled with a median age of 62 years (range 30-89). Fifty one percent were male, 85% stage III or IV. Diagnoses were: FCC, 38pts (69%); MZL, 8pts (15%); SLL, 5pts (9%) and LPL, 4pts (7%). The median follow-up is 13 months (range: 6-26). At the time of this analysis, 78% of pts had completed 6 cycles of BRR, and 56% had continued to maintenance rituximab. Two pts remain in the first 6 cycles of BRR. Five pts (9%) discontinued treatment due to toxicity (1pt G2 neuropathy, 1 pt G2 atrial fibrillation, 1 pt G3 pancreatitis, 1 pt G3 diarrhea, 1pt G2 rash). The remaining 5 pts discontinued prematurely (1pt death due to stroke, 1pt wound complication, 1 pt lost to follow-up, 2 pts off due to request). Objective response was achieved in 89% of pts; 26pts (47%) complete response, 23pts (42%) partial response, 2pts (4%) stable disease, and 4pts (7%) unevaluable at the time of this analysis. Related grade 3/4 hematologic toxicities were: neutropenia (25%), febrile neutropenia (2%), thrombocytopenia (5%), and anemia (4%). We observed no grade 4 treatment related non -hematologic adverse events, the most common grade 3 were neuropathy (9%), diarrhea (7%), fatigue (7%), constipation (5%), and rash (5%). Time-to-event data are immature and will be the subject of a later analysis. At the time of data cut-off, 3 pts (5.5%) had progressed or relapsed and 3pts (5.5%) had died.

Conclusion: BBR was well tolerated and produced high CR and OR rates. Toxicities including neuropathy were modest. Further study of this regimen in patients with previously untreated lymphoma is warranted.

Disclosures: Off Label Use: Off-label bendamustine and bortezomib in first-line treatment for lymphoma. **Boccia:** *Cephalon:* Research Funding.