Blood Abstracts: 54th ASH Annual Meeting Abstracts; Vol. 120, Issue 21, 16 Nov 2012

Abstract 4047 Bendamustine, Bortezomib and Dexamethasone (BBD) As First-Line Treatment of Patients with Multiple Myeloma Who Are Not Candidates for High Dose Chemotherapy: Toxicity Comparison of Two Dose Schedules

Jesus G. Berdeja, MD[1,2], Michael R. Savona, MD, FACP[1,2*], James Essell, MD[1,3*], Patrick Murphy, MD[1,2*], Luis Chu, MD[1,4], Ralph V. Boccia, MD[5], Edward Arrowsmith, MD, MPH[1,6] and Ian W. Flinn, MD, PhD[1,2]

[1]Sarah Cannon Research Institute, Nashville, TN
[2]Tennessee Oncology PLLC, Nashville, TN
[3]Oncology Hematology Care, Inc, Cincinnati, OH
[4]Florida Cancer Specialists, Ft. Myers, FL
[5]Center for Cancer and Blood Disorders, Bethesda, MD
[6]Chattanooga Oncology Hematology Associates, Chattanooga, TN

Background: Despite significant advances, multiple myeloma is an incurable plasma cell disorder with an eventual fatal outcome. In newly diagnosed MM, combinations of bortezomib, steroids and alkylating agents, such as melphalan and prednisone, have achieved response rates in excess of 70% and have been established as a standard of care in patients (pts) who are ineligible for high dose chemotherapy. Bendamustine is a bi-functional alkylating agent with a purine-like benzimidazole ring effective as a single agent and in various combinations for the treatment of relapsed/refractory MM (Poenisch et al, 2007, Fenk et al, 2007). In this study, the combination of bendamustine, bortezomib and dexamethasone (BBD) was evaluated as a first-line therapy for patients with MM.

Methods: Patients with newly diagnosed active multiple myeloma who were not candidates for high-dose chemotherapy and met standard eligibility criteria with regards to renal, hepatic and hematologic function were enrolled. The original treatment schema (schema A) consisted of: bendamustine 80 mg/m2 IV on days 1, 4; bortezomib 1.3 mg/m2 IV on days 1, 4, 8, 11; and dexamethasone 40 mg on days 1, 2, 3, 4 with cycles repeating every 28 days. Patients had the option to continue on maintenance bortezomib. An interim analysis found this combination to be efficacious but relatively toxic. As a result the treatment schema was amended to the following (schema B): bendamustine 80 mg/m2 IV on days 1, 2; bortezomib 1.3 mg/m2 IV on days 1, 8, 15; and dexamethasone 20 mg on days 1, 2, 8, 9, 15, 16 every 28 days for a total of 8 cycles or 2 cycles beyond

documented CR, whichever occurred first. Again, patients had the option to continue maintenance bortezamib. Acyclovir or equivalent viral prophylaxis was recommended on schema A and became required on schema B. Responses were assessed using the IMWG criteria. AEs were assessed using the CTCAE Version 4.0. We report the results of an interim safety assessment of the amended BBD combination and compare the results to those seen with the original regimen.

Results: Treatment schema A accrued 18 patients between 5/2010 and 2/2011. Ten patients were accrued from 10/2011 and 4/2012 and treated on treatment schema B. The median ages of treatment schemas A and B were 75 and 72.5 respectively, with all other characteristics within expected distributions and no major differences between the groups. No grades 4 hematologic Adverse Events (AEs) were seen. Grade 3 hematologic AEs were similar in both arms seen in 33% of patients on treatment schema A and 40% of patients on treatment schema B. Grade 3/4 non-hematologic AEs were seen in 72% of patients on treatment schema A and 60% of patients on treatment schema B. Although the preliminary Serious Adverse Events (SAEs) were similar with 39% of patients on treatment schema A compared to 30% of patients on treatment schema B, a large proportion of patients on treatment schema A (39%) were unable to complete the study due to toxicity or related issues. The incidence and severity of neuropathy and herpes zoster infections were significantly different between the two schemas. Schema A had 72% of patients with any grade neuropathy, with 56% being grade 2 or worse while schema B had 40% of the patients with any grade neuropathy, all but one grade 1. Likewise, 44% of patients on the original treatment reported herpes zoster while there were no cases of herpes zoster reported for patients on the revised treatment schema. Thus far, the early response rates appear similar. Schema A had an ORR of 78% (56% >vgPR) while schema B had an ORR of 90% (40% >vgPR).

Conclusions: The combination of bendamustine, bortezomib and dexamethasone is feasible and efficacious in an elderly patient population. Using the revised schema, we were able to lower treatment toxicity without adversely impacting initial efficacy. Updated results will be presented at the meeting.

Disclosures: Off Label Use: Off-label use of Bendamustine in the treatment of Multiple Myeloma . **Chu:** *Millennium:* Research Funding; *Cephalon:* Research Funding.