2928 Bortezomib-Bendamustine-Dexamethasone in Patients with Relapsed/Refractory Multiple Myeloma (MM) Shows Marked Efficacy and Is Well Tolerated, but Assessment of PNP Symptoms Shows Significant Discrepancies Between Patients and Physicians

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Introduction: Bendamustine, an alkylating drug with purine like activities may exert synergistic activity in combination with bortezomib. Here we analyze the efficacy and tolerance of bortezomib-bendamustine-dexamethasone with particular focus on possible discrepancies between patient and physician assessed neuropathic symptoms.

Patients: 45 patients with relapsed/refractory MM have been enrolled. Median age: 64 years (range 40-86), male/female: 17/28, ISS stage I/II/III: 14, 16, and 15 patients, respectively. ECOG status 0/I/II: 25, 22, and 2 patients, respectively. Previous treatment lines: 1-2: 25, 3-4: 16, >4: 4 patients, respectively. Full data documentation for response evaluation (≥ 2 cycles) is available for 33 patients. Treatment regimen: Bendamustine 70 mg/m^2 day 1+4, Bortezomib 1.3 mg/m^2 days 1, 4, 8 and 11, Dexamethasone 20 mg on days 1, 4, 8 and 11, repeated every 4 weeks. For assessment of neuropathic sides effects the FACT-GOG/NTX self assessment instrument was used.

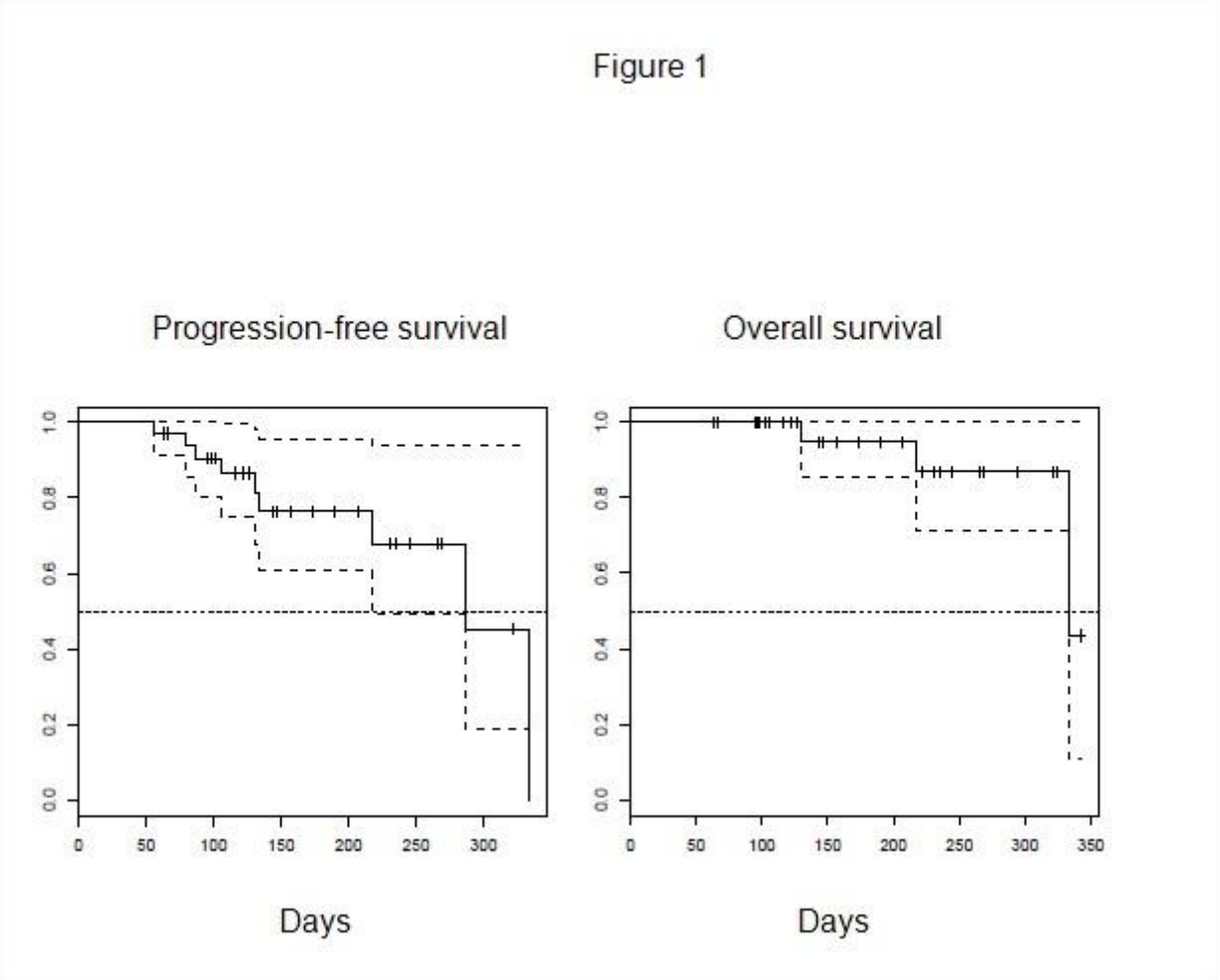
Efficacy: After a median follow up of 4.7 months, myeloma response (ORR: CR+VGPR+PR) was noted in 17 (51.5%) of the 33 evaluable patients. 5 (15% of) patients achieved CR, 2 (6%) VGPR, 10 (30%) PR; 10 (30%) MR, and 6 (18%) remained stable, while PD was noted in 6 (18% of) patients. Median time to response was 82 days. Responses were observed in 48.1% of patients previously exposed to bortezomib and in 47.1% pretreated with lenalidomide. Responses were seen in 53.8% of patients with high [ampl.1q21, del17p, t (4; 14)] and in 53.8% with standard risk (del13 or no aberration) cytogenetics. Median PFS is 9, 4 months; median overall survival is not reached at present (figure).

Tolerance: The regimen was well tolerated with low incidence of infections and gastrointestinal toxicities. Hematological toxicity remained stable from baseline to cycle

4, with G4 anemia, leucopenia and thrombopenia being recorded in < 5%. Patient self reported neuropathic symptoms at baseline were recorded as G1-2 in 57% and as G3-4 in 17%, respectively. This pattern remained stable from cycle 1 to 4. In contrast, physician assessed neurotoxicity G1-2 was documented in only 18% of patients at baseline. During the following 4 cycles physician assessed PNP remained constant in almost all patients with only 3 patients developing G3 PNP. G4 PNP was not reported.

Conclusions: The BBD regimen yielded a response rate of 52% and a PFS of 9.6 months in heavily pretreated myeloma patients. Substantial response rates were noted in patients pre-exposed to bortezomib (33.3%) and lenalidomide (36.4%) Patient self assessment of neuropathic symptoms revealed a much higher incidence of G1-2 and G3-4 symptoms than physician assessment. Physician assessment of neurotoxicity may underestimate neurologic symptoms associated with disease or neurotoxic treatment.

Figure 1



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Back to: 653. Myeloma - Therapy, excluding Transplantation: Poster II