Lower doses of bendamustine are not associated with worse response depth in patients with Waldenström macroglobulinemia

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Background

Bendamustine-rituximab has been shown in a randomized clinical trial to be highly effective in treating patients with WM (Rummel *et al*, Lancet Oncol 2013). In that study, bendamustine was administered at a dose of 90 mg/m^2 IV for 6 cycles (total dose: 1080 mg/m^2). Recent studies have suggested that lower doses of bendamustine might be associated with similar efficacy. However, this has not been previously evaluated in WM.

Patients and Methods

In this retrospective study, we searched our database looking for previously untreated patients with WM who have received primary therapy with bendamustine and rituximab between 2008 and 2015. All patients met clinicopathological criteria for WM (Owen *et al*, Semin Oncol 2003), and had at least one indication for initiation of therapy (Kyle *et al*, Semin Oncol 2003). Pertinent clinical data were gathered. With regards to treatment, we calculated the total dose of bendamustine in mg/m^2 received during induction therapy. Response was assessed based on current criteria (Owen *et al*, Br J Haematol 2012). Logistic regression models were used to evaluate the relationship between bendamustine dose with response.

Results

Table 1. Baseline clinicopathological characteristics of patients.

Characteristic	Patients (N=48)
Age at WM diagnosis – yr	66 (44-95)
Hemoglobin – g/dL	10.4 (4.0-15.3)
Serum IgM – mg/dL	3,645 (356-9,610)
Platelet count – K/uL	207 (42-485)
Bone marrow involvement - %	50 (0-90)
Lymphadenopathy – no. (%)	21 (43)
Splenomegaly – no. (%)	14 (30)
IPSSWM score – no. (%)	
Low	12 (25)
Intermediate	14 (30)
High	22 (45)
Treatment criteria – no. (%)	
Anemia	27 (57)
Symptomatic extramedullary disease	11 (22)
Hyperviscosity	11 (22)
Peripheral neuropathy	5 (11)
Constitutional symptoms	4 (9)
Thrombocytopenia	2 (4)

Results

A total of 48 patients who received frontline bendamustine-based therapy were included in this analysis. The median time from WM diagnosis to initiation of treatment was 9 months (range 0-178). At best response, the ORR was 94% (19% CR, 31% VGPR, 42% PR, 2% MR, and 6% NR). The rate of major response (CR+VGPR+PR) was 92%, and the rate of deep response (CR+VGPR) was 50%.

Based on total bendamustine dose, patients were divided into 3 groups: 90 mg/m^2 days 1 and 2 for 6 cycles (1080 group; n=20), 90 mg/m^2 on days 1 and 2 for 4 cycles (720 group; n=18), and 70 mg/mg^2 on days 1 and 2 for 4 cycles (560 group; n=10). There was no difference in age, hemoglobin levels, platelet counts, serum IgM levels, beta-2 microglobulin levels, or IPSSWM scores between the 3 groups (Chi-square p>0.05 for all comparisons).

Table 2. Serum IgM responses stratified by bendamustine dose.

Bendamustine Dose (mg/m^2)	Overall Response Rate (%)	Major Response Rate (%)	Deep Response Rate (%)
1080	95	95	55
720	94	89	44
560	90	90	50
P-value	**1.00**	**0.82**	**0.93**

Table 3. Logistic regression analysis for response attainment.

Bendamustine Dose (mg/m^2)	Crude OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Major Response				
1080	Reference		Reference	
720	0.42 (0.03-5.08)	0.50	0.39 (0.03-5.21)	0.48
560	0.47 (0.03-8.46)	0.61	0.22 (0.01-5.28)	0.35
Deep Response				
1080	Reference		Reference	
720	0.65 (0.18-2.36)	0.52	0.65 (0.18-2.37)	0.51
560	0.82 (0.18-3.74)	0.80	0.70 (0.15-3.37)	0.66

Logistic regression analysis showed no relation between total bendamustine dose and attainment of major or deep response (p>0.05 in both models). After adjusting for maintenance rituximab, no relation between bendamustine dose and depth of response was observed (p>0.05 in both models). 26 patients (54%) received maintenance rituximab, while 22 patients (46%) have not.

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Results

Figure 1. Kaplan-Meier curve of progression-free survival.

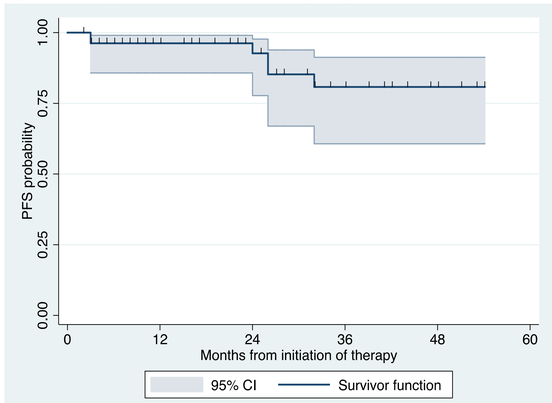
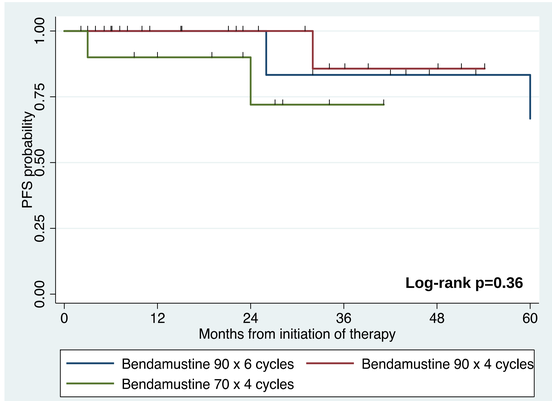


Figure 2. Kaplan-Meier curve of PFS for stratified by bendamustine dose.



Conclusion

Our study suggests that receiving a lower total bendamustine dose, administered concurrently with rituximab, does not negatively affect the attainment of major or deep response to therapy in previously untreated patients with WM.

Disclosures: The authors have no conflicts of interest to disclose.