Bendamustine and Bortezomib-Containing Regimens Produce Higher Response Rates and More Durable Responses Versus Cyclophosphamide-Based Therapy in Frontline Waldenstrom Macroglobulinemia

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Introduction

Waldenstrom macroglobulinemia (WM) is an incurable IgM-secreting lymphoplasmacytic lymphoma. Primary therapy for symptomatic WM patients often consists of combination therapy with an alkylating agent or proteasome inhibitor with rituximab. However, randomized studies comparing these treatment regimens are lacking in WM patients.

Methods

- We retrospectively searched our database for WM patients who received primary therapy with bendamustine-rituximab (Benda-R), bortezomib-dexamethasone-rituximab (BDR), or cyclophosphamide-dexamethasone-rituximab (CDR) between 2005 and 2016.
- Pertinent clinical data were collected.
- Response was assessed based on current criteria.
- Univariate and multivariate regression models were fitted to evaluate the association between clinical variables and response.
- Time to events was estimated using the Kaplan-Meier method.
- The Cox regression method was used to fit univariate and multivariate models for progression-free (PFS) and overall survival (OS).
- P<0.05 was considered statistically significant.

Results (I)

Table. 1 Patients Characteristics

	Benda-R (n=57)	BDR (n=87)	CDR (n=38)	p-value
Age >65 years	36 (63%)	32 (37%)	19 (50%)	0.01
Male sex	35 (61%)	53 (61%)	20 (53%)	0.64
Hemoglobin ≤11.5 g/dl	23 (40%)	27 (31%)	10 (26%)	0.32
Platelets ≤100 K/ul	9 (16%)	7 (8%)	2 (5%)	0.20
Serum B2M >3 mg/l	39 (64%)	43 (49%)	16 (42%)	0.02
IgM >4,000 mg/dl	21 (37%)	62 (71%)	15 (39%)	<0.001
Marrow ≥50%	33 (58%)	38 (45%)	17 (45%)	0.29
Lymphadenopathy	25 (44%)	15 (17%)	14 (37%)	0.001
Splenomegaly	18 (32%)	6 (7%)	2 (5%)	<0.001
MYD88 L265P mutation	17 (89%)	23 (88%)	13 (100%)	0.60
CXCR4 mutations	10 (53%)	11 (42%)	7 (54%)	0.71
IPSSWM				
Low risk	20 (35%)	45 (52%)	24 (63%)	0.006
Intermediate risk	17 (30%)	30 (35%)	7 (18%)	
High risk	20 (35%)	11 (13%)	7 (18%)	
Best response				
Complete response	11 (19%)	9 (11%)	2 (5%)	0.37
Very good PR	14 (26%)	20 (24%)	14 (37%)	
Partial response	28 (49%)	40 (48%)	16 (42%)	
Minor response	2 (4%)	6 (7%)	2 (5%)	
No response	2 (4%)	8 (10%)	4 (11%)	
Received maintenance	35 (61%)	55 (65%)	26 (68%)	0.79

Results (II)

Figure 1. PFS Benda-R, BDR, CDR

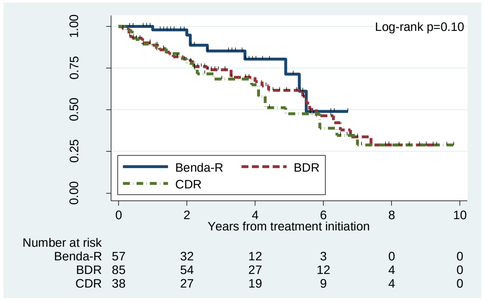
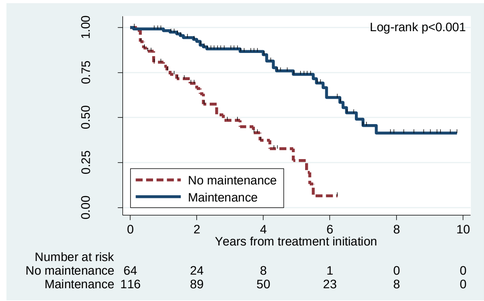


Figure 2. PFS maintenance R



PFS MVA	HR	95% CI	P-value
Benda-R	0.2	0.1-0.5	<0.001
BDR	0.6	0.3-1.0	0.05
Maintenance R	0.1	0.06-0.2	<0.001

Results (III)

Figure 3. OS Benda-R, BDR, CDR

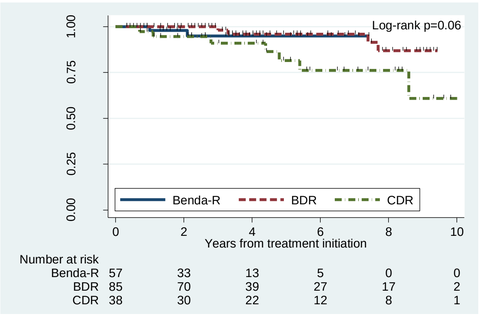
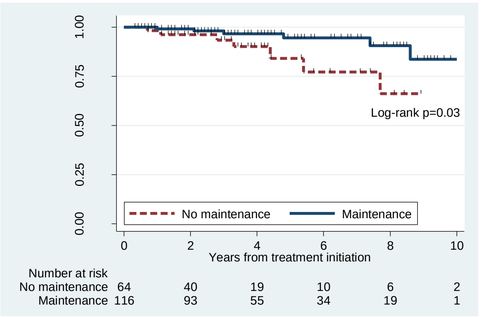


Figure 4. OS maintenance R



OS MVA	HR	95% CI	P-value
BDR	0.2	0.04-0.6	0.006
Maintenance R	0.2	0.05-0.6	0.006

Conclusions

- Primary therapy with Benda-R, BDR, and CDR produces high response rates and durable PFS in patients with WM.
- The risk of progression is lower in patients treated with Benda-R and BDR when compared to CDR.
- There is a trend towards a better OS in patients treated with BDR versus CDR.
- Maintenance rituximab is associated with both major and deep responses to therapy as well as superior PFS and OS.

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