Outcomes with rituximab plus bendamustine (R-Benda), dexamethasone, rituximab, cyclophosphamide (DRC), and bortezomib, dexamethasone, rituximab (BDR) as primary therapy in patients with Waldenstrom macroglobulinemia (WM).

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Background:
Waldenstrom macroglobulinemia (WM) is a rare lymphoma for which scant comparative data exist to guide frontline therapy. Herein, we compare 3 commonly used regimens in WM: R-Benda, DRC, and BDR in frontline setting.

Methods:
Patients (Pts) with active WM seen at Mayo Clinic between 2000 & 2018 who received R-Benda, DRC or BDR as primary therapy were included in this retrospective study. Response rates were assessed by Consensus Criteria. All time to event analyses were performed from the frontline therapy, using Kaplan-Meier method.

Results:
The study included 172 pts with active WM (R-Benda, n=67, DRC, n=75, BDR, n=30).The median follow-up for the entire cohort was 3.7 years (y) (95% CI 3.7-3.0). Baseline characteristics, including IPSS, and time to frontline therapy from WM diagnosis were similar across the 3 cohorts. Clinically relevant endpoints are shown in the Table. Hematologic and non-hematologic toxicities were similar across the

3 groups. Grade 3 neuropathy requiring treatment discontinuation was encountered in 13% pts treated with BDR. 56 pts received subsequent salvage therapy [(10% in R-Benda arm, 44% in DRC arm, & 53% in BDR arm]; 29% pts in the R-Benda arm and 30% pts in DRC arm received a PI-based regimen while 69% pts in the BDR arm received alkylator-rituximab based therapy.

Conclusions:

Outcomes (MRR, TTNT and EFS) with frontline R-Benda are superior in comparison to frontline DRC or BDR in patients with WM. Clinically relevant endpoints are not significantly different with DRC vs. BDR. The toxicity profile across the 3 groups was comparable.

	R-Benda	DRC	BDR	p value R-Benda vs. DRC	p value R-Benda vs. BDR	p value DRC vs. BDR
ORR %	98	85	76	**0.01**	**0.004**	0.3
MRR %	96	60	52	**<0.0001**	**<0.0001**	0.5
EFS, median y, range	4.5 (3.7-NR)	4.3 (2.4-7)	1.4 (0.6-7)	**0.04**	**0.003**	0.1
TTNT, median y, range	NR (3.7-NR)	4.3 (3-7)	1.8 (0.8-NR)	**0.04**	**0.0015**	Print
3 y OS %	95	89	85	0.4	0.7	0.8

ORR: Overall response rate, MRR: Major response rate, EFS: Event (progression, toxicity or death that led to permanent discontinuation of therapy) free survival, TTNT: Time to next therapy, OS: Overall survival, NR: Not reached