Deepening of response after completing rituximab-containing primary therapy in patients with Waldenstrom macroglobulinemia

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Background

- Rituximab-containing regimens are commonly used for primary therapy in patients with symptomatic Waldenstrom macroglobulinemia (WM), and response is defined by decrease in serum IgM levels.
- We had observed that in a portion of WM patients who had completed rituximab-containing regimens as primary therapy, serum IgM kept decreasing after completing of therapy.
- We carried a retrospective cohort study aimed at describing the frequency of this phenomenon and identifying associated clinical factors.

Methods

- We included patients who had a clinicopathological diagnosis of WM and needed therapy based on criteria from the 2nd International Workshop for WM (IWWM) and received a rituximab-containing regimen as primary therapy.
- Responses were defined per criteria from the 6th IWWM. We stratified our analysis based on having received, or not, maintenance therapy after induction therapy.
- We gathered pertinent clinical data, including responses at the end of induction, at the end of maintenance and at the lowest serum IgM level after completion of induction or maintenance.

Results

- 179 patients were included; 57 (32%) received bendamustine and rituximab (benda-R), 86 (48%) bortezomib, dexamethasone and rituximab (BDR) and 36 (20%) cyclophosphamide, dexamethasone and rituximab (CDR) as induction therapy, and 117 (65%) received maintenance therapy.

Results

Table 1. Patients' characteristics

	No maintenance	Maintenance	p-value
Age, years	61 (30-86)	62 (33-87)	0.58
Male sex	39 (63%)	67 (57%)	0.53
Time to first treatment	0.6 (0.2-1.7)	0.5 (0.3-0.8)	0.31
Hemoglobin	10.9 (6-17.1)	10.6 (4-15.3)	0.94
Platelets	257 (42-485)	231 (17-528)	0.13
Beta-2-micro	3.2 (1.5-12.5)	2.8 (1.3-19.2)	0.11
BM involvem	40% (5-95%)	40% (3-95%)	0.68
MYD88	22/23 (96%)	30/34 (88%)	0.94
CXCR4	10/23 (43%)	18/34 (53%)	0.59
Base serum IgM	4,400 (155-10,020)	4,445 (289-8,100)	0.37
Regimen used			
Benda-R	21 (34%)	36 (31%)	0.82
BDR	30 (48%)	56 (48%)	
CDR	11 (18%)	25 (21%)	
End induction IgM	1,366 (114-7,108)*	969 (33-5,940)*	0.11
N cycles maintenance		6 (1-12)	
End maintenance IgM		528 (10-5,410)**	
Time to best response	0 (0-5.1)	0.5 (0-7.9)	
Best serum IgM	1,253 (11-7,108)**	384 (9-4,759)***	<0.001
Response end induction			
VGPR/CR	7 (11%)	16 (14%)	0.10
PR	31 (50%)	68 (58%)	
MR	10 (16%)	24 (21%)	
NR	14 (23%)	9 (8%)	
Response end maintenance			
VGPR/CR		40 (34%)	
PR		65 (56%)	
MR		11 (9%)	
NR		1 (1%)	
Best response			
VGPR/CR	13 (21%)	52 (44%)	<0.001
PR	29 (47%)	61 (52%)	
MR	6 (10%)	4 (3%)	
NR	14 (23%)	0 (0%)	

No maintenance

- 29/62 patients (47%) had lower IgM level after induction completed.
- 18/29 patients (62%) had >25% decrease in serum IgM after tx completed.
- Time to best response from end of induction: 1.6 years (0.2-5.1 years).

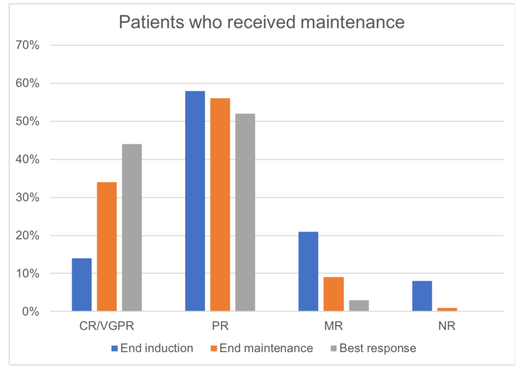
Maintenance

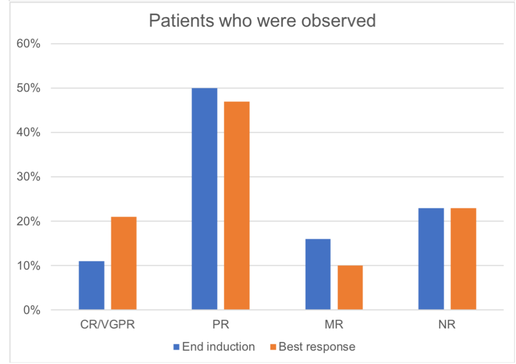
- 72/117 patients (62%) had lower IgM level after maintenance completed.
- 44/72 patients (61%) had >25% decrease in serum IgM after maintenance completed.
- Time to best response from end maintenance: 1.6 years (0.1-7.9 years)

Table 2. Logistic regression analysis on the odds of having deeper response after therapy complete

Variable	OR (95% CI)	p-value
Age 65+	1.10 (0.58-2.07)	0.76
Male sex	0.86 (0.46-1.60)	0.63
Hemoglobin <11.5 g/dl	0.44 (0.23-0.88)	0.02
Platelets <100 K/uL	1.00 (0.35-2.86)	1.00
Beta-2-micro >3 mg/l	0.66 (0.35-1.25)	0.21
BM involvement >50%	0.49 (0.26-0.93)	0.03
MYD88 mutation (n=57)	0.73 (0.11-4.78)	0.74
CXCR4 mutation (n=57)	0.33 (0.13-0.87)	0.03
Serum IgM >4,000 mg/dl	0.53 (0.29-0.99)	0.04
Maintenance	1.38 (0.72-2.67)	0.33
Benda-R vs. CDR	0.69 (0.30-1.63)	0.40
BDR vs. CDR	0.57 (0.26-1.27)	0.17

Figure 1. Categorical responses at the end of induction, end of maintenance and at best response





Conclusion

- A third of WM patients who receive primary therapy with rituximab-containing regimens experience deepening of response after completing therapy, with a median time to best response of 1.6 years.
- Low hemoglobin, high bone marrow burden, CXCR4 mutations and high serum IgM levels at primary therapy initiation associate with lower odds of response deepening.

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