

W4: Treatment Facility Volume and Outcomes in Waldenstrom Macroglobulinemia

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Introduction: Waldenstrom macroglobulinemia (WM) is a rare disease accounting for only 1-2% of all hematologic malignancies and with an overall annual, age-adjusted incidence of approximately 3.5 to 5.5 cases per million-person years. With approximately 13,000 active hematologist/oncologists in the US, most of who are in the community oncology setting, it's estimated that a hematologist/oncologist will only diagnose a WM case approximately every 8 years. Therefore, the clinical experience of a general hematologist/oncologist in the management of WM is likely very limited compared to more prevalent malignancies. Previous studies in the setting of rare cancers suggest a correlation between higher volume of care and improved outcomes. Therefore, we explored the volume-outcome relationship in WM using the National Cancer Data Base (NCDB).

Methods: Patient-level data from the NCDB, a nationwide, facility-based, database covering approximately 70% of all newly diagnosed cancer cases in the US, was queried for all new WM cases diagnosed between 2004 and 2014. Only patients requiring treatment were included. Treatment facilities were divided into quartiles based on the average annual volume of newly diagnosed cases of WM seen. Cox regression was used to analyze the association between facility WM volume and survival, adjusted by demographics (sex, age, race), socioeconomic status (income, education, insurance type), geography (area of residence, treatment facility type, travel distance), comorbidity factors (Charlson-Deyo score), and year of diagnosis. Time-to-event analysis was calculated from frontline therapy initiation date using the Kaplan-Meier method and the log-rank test.

Results: A total of 3,732 patients with WM treated in 831 facilities were included. The median age at diagnosis was 70 years and 75% of the patients were treated within 20 miles from their residency zip code. Patient characteristics per treatment facility volume quartile are shown in table 1. The median annual facility volume was 1 new WM patient/year (range 0.1 to 21). The median follow-up from frontline treatment was 5 years.

The unadjusted median OS by facility volume was: Q1: 6.5 years (95% CI: 5.7-7.4), Q2: 7 years (95% CI: 6.3-8.2), Q3: 8.2 years (95% CI: 7.1-8.9), and Q4: NR (95% CI: 8.5-NR), $p < 0.0001$ (figure 1). The estimated 5-year OS by facility volume was: Q1: 56%, Q2: 61%, Q3: 64%, Q4: 71%, $p < 0.0001$.

Multivariate analysis including all variables showed in Table 1 demonstrated that facility volume was independently associated with all-cause mortality. Compared to patients treated at Q4 facilities, patients treated at lower-quartiles facilities had a higher incremental risk of death (Q3 hazard ratio [HR], 1.07 [95% CI: 0.88 to 1.29] $p = 0.46$; Q2 HR, 1.34 [95% CI: 1.11 to 1.63] $p = 0.002$; Q1 HR, 1.52 [95% CI: 1.23 to 1.88] $p < 0.0001$).

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Conclusion: Our results suggest that a volume-outcome relationship exists in WM as patients treated initially at higher-volume facilities had a lower risk of mortality. Although differences in the underlying disease biology, referral patterns after initial therapy, or cumulative treating-physician experience could not be assessed, these potential biases would only underestimate the magnitude of the volume-outcome relationship reported.

Table 1. Characteristics of Patients According to Treatment Facility Volume Quartile

	Q1	Q2	Q3	Q4	p value
Patients/year, n	<0.5	0.5-1	1-2	> 2	
Facilities, n (%)	419 (50)	253 (31)	111 (13)	48 (6)	
Patients, n (%)	800 (21)	1,123 (30)	963 (26)	846 (23)	
Age, median (range)	70 (30-90)	70 (29-90)	71 (26-90)	70 (28-90)	0.38
Sex, male (%)	57	61	62	59	0.19
Race (%)					0.06
White	92	92	93	94	
African-american	7	6	6	4	
Native-american	0.2	0	0.1	0.3	
Asian	1.8	2	0.9	1.7	
Comorbidity index (%)					0.01
Charlson Score 0	79	80	80	84	
Charlson Score 1	16	15	15	13	
Charlson Score ≥2	5	5	5	3	
Residence (%)					<0.001
Metro	77	82	85	86	
Urban	21	15	14	13	
Rural	2	3	1	1	
Median Annual Household Income (%)					<0.001
≥\$46,000	28	38	40	46	
\$35,000-\$45,999	31	28	27	28	
\$30,000-\$34,999	24	23	20	18	
<\$30,000	17	11	13	8	
Education (%)					<0.001
High	15	10	11	7	
Middle-2	28	21	20	18	
Middle-1	36	37	35	34	
Low	21	32	34	41	
Insurance Status (%)					<0.001
Private Insurance	27	34	32	40	
Government Insurance	66	62	64	56	
No Insurance	4	2	2	3	

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	Other	3	2	2	1	
Treatment Facility (%)						<0.001
Academic		18	35	55	84	
Non-academic		82	65	45	16	
Distance to Treatment Facility (%)						<0.001
> 20 miles		18	21	26	39	
9-20 miles		26	26	27	23	
4-9 miles		25	26	25	22	
< 4 miles		31	27	22	16	
Year of Diagnosis (%)						0.13
2004-2008		35	34	31	35	
2009-2011		30	28	28	25	
2011-2014		35	38	41	40	

Figure 1. Overall Survival from Frontline Therapy Based on Facility Volume Quartile

