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623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL**Retrospective Analysis of the Impact of Bendamustine Dose Reduction and Chemotherapy on the Outcomes of Follicular Lymphoma**

Yusuke Koba, MD¹, Kazuhiro Bandai, MD¹, Naoko Hiranuma, MD¹, Kensuke Fujiwara, MD¹, Takahito Kawata, MD PhD¹, Akira Tamekane, MD¹, Mitsumasa Watanabe, MD PhD²

¹ Department of Hematology, Hyogo Prefectural Amagasaki General Medical Center, Amagasaki, Japan

² Department of Hematology, Hyogo Prefectural Amagasaki General Medical Center, Amagasaki, Japan

Introduction

Follicular lymphoma (FL) is the most common indolent non-Hodgkin's lymphoma and primarily affects the elderly population. While bendamustine serves as a pivotal drug in standard therapy, it is often not administered as planned due to side effects, especially among the elderly. Clinical studies have shown that dose reduction and chemotherapy delays in the treatment of diffuse large B-cell lymphoma are associated with lower survival rates. However, few studies have analyzed the impact of bendamustine delays and dose reduction on the outcome of FL. Thus, the aim of our study was to clarify the effect of bendamustine dose reduction and chemotherapy course delay on treatment outcomes and to evaluate the effects of chemotherapy modification on FL.

Patients and Methods

This is a retrospective pooled analysis of previously untreated patients with FL who underwent consecutive bendamustine-based regimens at our institute. Patients receiving less than four courses of bendamustine-based regimens were excluded. Bendamustine dose reduction was defined as a cumulative dose reduction of at least 20% of the total prescribed dose. The total dose was defined as the sum of six cycles administered at 100% of the prescribed dose. Chemotherapy delays were defined as the total number of days of delay exceeding 21 days. The main goal of the study was to assess the impact of the chemotherapy scheme modification (dose reduction or delay) on progression-free survival (PFS) and overall survival (OS). The Kaplan-Meier method was used for single-variable survival data analysis. Differences in survival rate were determined using the log-rank test. Comparison among subgroups was performed using ANOVA for continuous covariates and Fisher's exact test for categorical variables.

Results

From January 2016 to June 2023, 43 untreated FL patients (23 females and 20 males) were started on rituximab-bendamustine (R-B) or obinutuzumab-bendamustine (G-B) at our institution. Median patient age was 69 years (range, 41-90 years) and the median follow-up time was 44 months (range, 5-74 months). Thirteen patients were treated with R-B, and 30 with G-B. Only one patient received obinutuzumab maintenance therapy due to the COVID-19 pandemic. Patients were divided into for three bendamustine delay/reduction groups. No bendamustine dose reduction or chemotherapy delays was observed in 27 patients (62.7%). The chemotherapy scheme was modified in 16 patients (37.2%): 10 patients (23.2%) experienced a bendamustine-only dose reduction and 6 patients (13.9%) experienced chemotherapy-only delays. None of the patients experienced both bendamustine dose reduction and delays. The main reasons for bendamustine dose reductions were the following: elderly/ frailty (60.0%), neutropenia (10.0%), thrombocytopenia (10.0%), and patient request (10.0%). The main reasons for chemotherapy delays were the following: patient request (33.3%), thrombocytopenia (33.3%), infection (16.6%), and skin rash (16.6%). Baseline characteristics were summarized in Table 1. The PFS of the three groups was comparable (Figure 1a). The OS of the group with chemotherapy delays was comparable to the group with no dose reduction or delay, while that of the group with dose reduction was inferior (Figure 1b). There were no differences in objective response rate (Table 1).

Conclusion

Our study showed that chemotherapy delays or bendamustine dose reduction did not adversely affect PFS, and only chemotherapy delays adversely affected OS. No clinically significant differences in PFS were observed among patients with chemotherapy delays, which could be attributed to insufficient statistical power. Our cohorts comprised a heterogeneous population, including patients treated with R-B and G-B. However, considering the lack of evidence regarding the optimal

dose intensity or chemotherapy interval for different populations, reducing the bendamustine dose may be a valid option for vulnerable patients.

Disclosures No relevant conflicts of interest to declare.

Table 1

	No reduction or delays (n = 27)		Reduction only (n = 10)		Delays only (n = 6)		P-value
Baseline characteristics							
Age – median, (range)	63	(41-81)	76	(49-90)	72.5	(63-82)	0.0421
Male gender – n, (%)	15	(55.5%)	3	(30.0%)	2	(33.3%)	0.366
Observation period (months) – median, (range)	44	(5-74)	47	(18-70)	21	(8-49)	0.0491
FLIPI – n, (%)							
Low	4	(14.8%)	1	(10.0%)	1	(16.6%)	0.518
Intermediate	9	(33.3%)	4	(40.0%)	0	(0.0%)	
High	14	(51.8%)	5	(50.0%)	5	(83.3%)	
FLIPI2 – n, (%)							
Low	4	(14.8%)	0	(0.0%)	0	(0.0%)	0.664
Intermediate	6	(22.2%)	4	(40%)	1	(16.6%)	
High	14	(51.8%)	6	(60%)	5	(83.3%)	
Unknown	3	(11.1%)	0	(0.0%)	0	(0.0%)	
Treatment							
Total number of days of delay – mean, (SD.)	4.77	(5.98)	6.00	(7.42)	31.66	(19.86)	0.03
Relative dose intensity of bendamustine – mean, (SD.)	100.00	(1.785)	71.04	(5.934)	98.19	(6.563)	<0.001
obinutuzumab-bendamustine therapy – n, (%)	19	(70.3%)	5	(50%)	6	(100.0%)	0.114
Transition to obinutuzumab maintenance therapy – n, (%)	1	(3.7%)	0	(0.0%)	0	(0.0%)	1
Response – n, (%)							
FDG-PET CMR	26	(96.2%)	8	(80.0%)	5	(83.3%)	0.329
PMR	0	(11.8%)	1	(10.0%)	1	(16.6%)	
SD	0	(5.9%)	0	(0.0%)	0	(0.0%)	
PD	1	(3.7%)	1	(10.0%)	0	(0.0%)	
Outcome							
2-year progression-free survival rate (95%CI)	0.817	(0.577-0.929)	0.900	(0.473-0.985)	0.375	(0.011-0.808)	0.236
2-year overall survival rate (95%CI)	1.000	(NA-NA)	1.000	(NA-NA)	0.667	(0.054-0.945)	0.00982

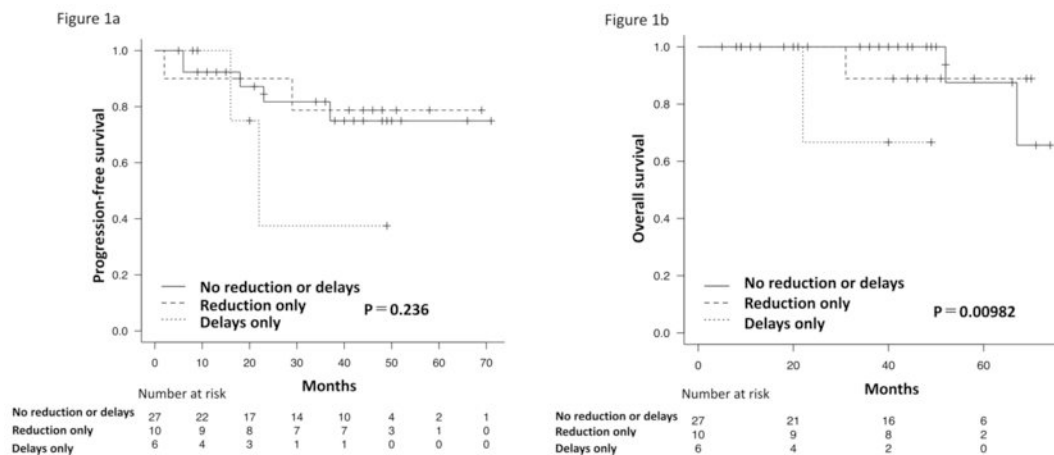


Figure 1

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