ELSEVIER

Blood 142 (2023) 6167–6169

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

## 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

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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 (Table1).
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%) | |
| Intermediate | 9 | (33.3%) | 4 | (40.0%) | 0 | (0.0%) | 0.518 |
| High | 14 | (51.8%) | 5 | (50.0%) | 5 | (83.3%) | |
| FLIPI2 – n, (%) | | | | | | | |
| Low | 4 | (14.8%) | 0 | (0.0%) | 0 | (0.0%) | |
| Intermediate | 6 | (22.2%) | 4 | (40%) | 1 | (16.6%) | 0.664 |
| 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%) | |
| PMR | 0 | (11.8%) | 1 | (10.0%) | 1 | (16.6%) | 0.329 |
| 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 1a

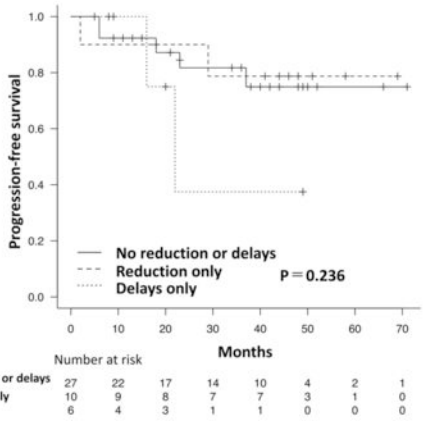


Figure 1b

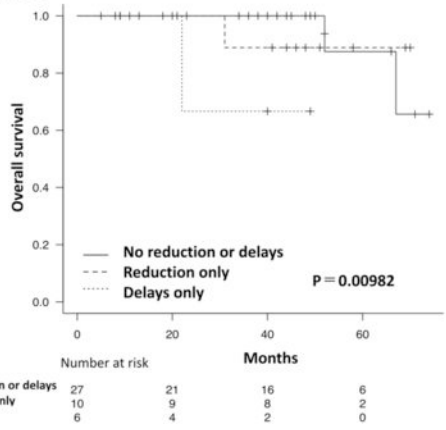


**Figure 1**

https://doi.org/10.1182/blood-2023-179228