Patterns of Treatment Utilization and Sequencing Across Lines of Therapy in Waldenström Macroglobulinemia (WM): Real-World Evidence from the United States

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Background

WM is a rare, incurable non-Hodgkin lymphoma with different treatment options available across successive lines of therapy (LOT). In the context of an evolving therapeutic landscape, there is limited real-world evidence detailing how treatment regimens are utilized and sequenced over time during the relapsing-remitting course of WM.

Aims

To evaluate real-world patterns of treatment utilization, sequencing, and associated healthcare resource utilization (HCRU) in WM.

Methods

A retrospective observational study was conducted using the US Symphony Integrated Dataverse® database to identify adults with ≥1 WM diagnostic code who initiated treatment 01/2020-08/2025. Patients were categorized into 8 mutually exclusive groups by treatment regimens: bendamustine-based chemotherapy (B/BR), rituximab-monotherapy (R-mono), other rituximab-combinations (R-combo, including R-cyclophosphamide, doxorubicin, vincristine, and prednisone [R-CHOP], and other combinations), Bruton tyrosine kinase inhibitor (BTKi; zanubrutinib, ibrutinib)-, bortezomib-, venetoclax-based regimens, and other regimens. Patient sociodemographic and clinical characteristics were analyzed in each group. Treatment utilization was analyzed overall, by year, and by LOT, with sequencing patterns visualized by Sankey diagram. All-cause HCRU during treatment (inpatient, outpatient, and other medical/hospital services) was examined and reported per-patient-per-year (PPPY).

Results

A total of 7583 patients with WM initiated first-line (1L) therapy. Of these, 2251 (29.7%) initiated second line (2L) therapy, and 976 (12.9%) initiated third or later LOT (3L+). BTKi was the most commonly used drug class across all LOTs, with zanubrutinib used most commonly, and with increasing frequency over time. 1L treatment utilization patterns (**Figure 1A**) showed that B/BR was the most commonly used regimen (27.1%), followed by R-mono (22.3%) and zanubrutinib (19.6%). In 2L and 3L+, R-mono was the most common regimen (19.9% and 20.3%, respectively), followed by BTKi. Treatment sequencing patterns (**Figure 1B**) suggest that in patients with WM who received 1L BTKi, B/BR was the most common subsequent treatment (42.7% after 1L zanubrutinib, 22.2% after 1L ibrutinib). Conversely, for patients who received 1L B/BR, BTKis were the most common 2L regimen (zanubrutinib 35.6%; ibrutinib 16.4%). In

patients who received 3L therapy after 2L zanubrutinib, 33.3% received B/BR and 30.0% received venetoclax, while after 2L ibrutinib, 50.0% were treated with either zanubrutinib (34.6%) or retreated with ibrutinib (15.4%), and 13.5% received B/BR. Substantial HCRU was observed across LOTs. Outpatient visits PPPY were lower for BTKi (zanubrutinib [1L: 12.0; 2L: 13.6; 3L+: 13.2]; ibrutinib [1L: 13.6; 2L: 15.2; 3L+: 16.0]) than for B/BR (1L: 33.7; 2L: 37.0; 3L+: 33.7), R-combo (1L: 42.3; 2L: 30.4; 3L+: 35.0), and R-mono (1L: 33.2; 2L: 32.2; 3L+: 32.6). Mean inpatient visits PPPY were lowest for both zanubrutinib (1L: 1.2; 2L: 1.0; 3L+: 1.6) and ibrutinib (1L: 1.7; 2L: 1.1; 3L+: 1.4), whereas the highest inpatient use was observed for venetoclax in 1L (4.7) and 3L+ (3.4) and 2L bortezomib (3.8).

Summary/Conclusion

In this real-world study, while BTKi was the predominant class across all LOTs, treatment sequencing frequently alternated between BTKi and B/BR-based regimens. These results shed light on current evolving WM treatment patterns and underscore the need for further studies to evaluate long-term outcomes to optimize treatment sequencing in real-world settings.

Figure 1A. Overall Treatment Utilization by LOT

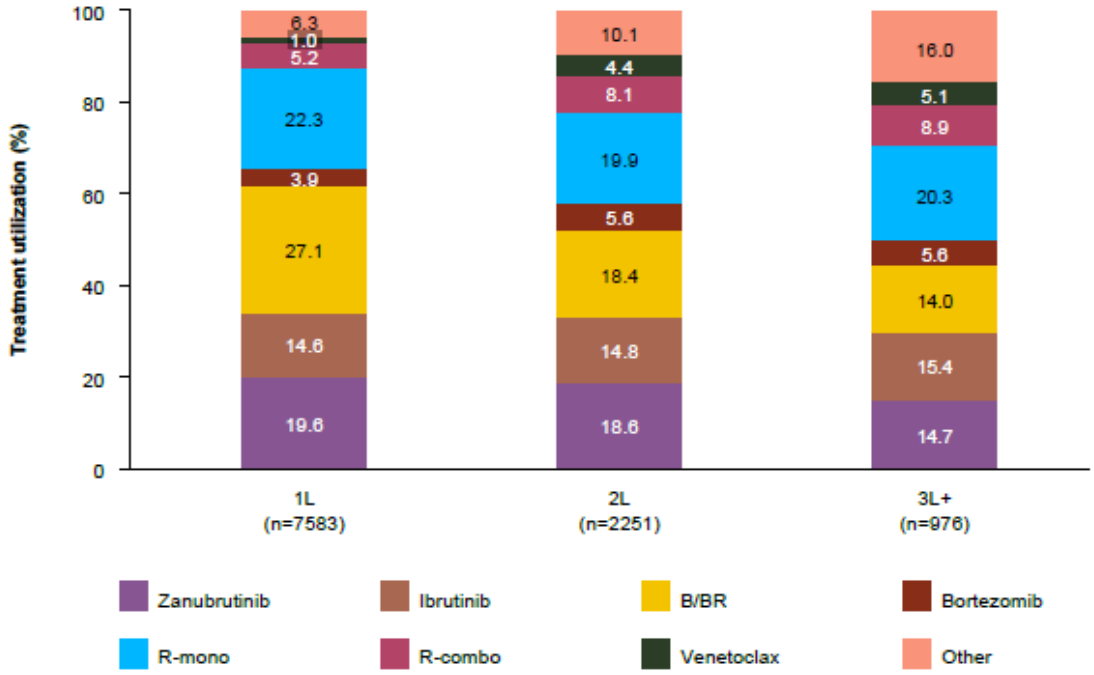

Figure 1B. Treatment Sequencing Pattern