Real-world treatment utilization, sequencing and outcomes in mantle cell lymphoma: Emerging treatment patterns in the United States

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Introduction:

Mantle cell lymphoma (MCL) is a rare, aggressive B-cell non-Hodgkin lymphoma with poor prognosis and heterogeneous clinical outcomes. Despite expanded treatment options, there are limited data on utilization and sequencing of various regimens in the real-world patient population. This study aims to evaluate real-world treatment patterns and sequencing, assess clinical outcomes, and quantify healthcare resource utilization (HCRU) across lines of therapy (LOT) in treatment naïve (TN) and relapsed/refractory (R/R) MCL patients.

Methods:

A retrospective observational study using the Symphony Integrated Dataverse® identified patients who initiated MCL treatment between Jan 2020 to Apr 2025 (study period). Treatment regimens were categorized into 7 mutually exclusive groups: bendamustine (B)-based chemotherapy, R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone, with or without cytarabine), Bruton tyrosine kinase inhibitors (BTKi; covalent: zanubrutinib, acalabrutinib, ibrutinib, and non-covalent: pirtobrutinib), bortezomib (bort)-based, venetoclax (ven)-based, intensive chemotherapy (high-dose cytarabine, HyperCVAD (hyperfractionated cyclophosphamide, vincristine, adriamycin, and dexamethasone, etc.), and other regimens (CAR-T or others). Patient cohorts were defined by LOT, indexed on the day of treatment initiation and followed until end of study period or loss to follow-up. Patient demographics and clinical characteristics were examined at baseline. Treatment utilization was examined by index year and by LOT, in overall CLL and elderly (aged 65+) patients. Treatment sequencing was evaluated and visualized with Sankey plot across all LOTs. Time to discontinuation (TTD) and time to next treatment (TTNT) were calculated from the index to the end of the LOT, and to the start of the subsequent LOT, respectively. HCRU was reported as outpatient visits, inpatient services, and other medical services per patient per month (PPPM).

Results:

A total of 5,989 MCL patients initiated the first line (1L), 3,005 and 822 patients initiated the second line (2L) and the third and later lines (3L+), respectively. Mean age at baseline was 68.1 in 1L, 70.2 in 2L, and 70.8 in 3L+. Patients were primarily male (1L: 70.9%; 2L: 70.9%; 3L+:72.3%) and White/Non-Hispanic (1L: 62.4%; 2L: 64.6%; 3L+: 68.9%); Black/Non-Hispanic and Hispanic patients together accounted for 10% across all LOTs. B-based chemotherapy was commonly used regimen in 1L (47.6%), with higher utilization (51.4%) in elderly population (aged 65+). BTKi is predominant in 2L and 3L+ (49.9% and 42.1%, respectively). From 2020 to 2024, utilization of BTKi increased (1L: 6.9% to 23.9%; 2L: 45.4% to 60.9%, 3L+: 36.6% to 52.2%), while B-based chemotherapy utilization decreased across all LOTs (1L: 52.4% to 34.5%; 2L: 20.5% to 13.6%; 3L+: 11.2% to 6.2%). Mean TTNT was 15.6 months in 1L and 18.2 months in 2L. Among 1L B-based chemotherapy patients, 18.9% advanced to the next LOT, with 68.1% receiving BTKi. Among patients treated with BTKi and anti-CD20 in any LOT and advanced to the next LOT, 51.5% were treated with other BTKi (31.2% covalent BTKi and 20.3% non-covalent).

Overall HCRU remains substantial in MCL patients. Outpatient utilization PPPM was the highest for R-CHOP (1L: 3.77, 2L: 4.81, 3L+: 3.79) and B-based chemotherapy (1L: 2.97, 2L: 3.10, 3L+: 3.36), while lowest for BTKi patients (1L: 1.54, 2L: 1.70, and 3L+: 1.73). Inpatient PPPM rose from 0.28 PPPM in 1L to 0.34 in 2L and 0.39 in 3L+. The R-CHOP group consistently had the highest inpatient use across lines (1L: 0.46, 2L: 0.59, 3L+: 0.54 PPPM). Within elderly patients, outpatient utilization was significant higher in B-based chemotherapy vs. BTKi patients (1L: 2.93 vs 1.57; 2L: 3.05 vs 1.70; 3L: 3.34 vs 1.66, respectively).

Conclusions:

This real-world study found that a majority of MCL patients were treated with chemotherapy and/or immunotherapy in 1L, while BTKi use is predominant in R/R settings and increased across all LOTs. However, chemotherapy and/or immunotherapy were associated with the highest HCRU while BTKi were associated with the lowest HCRU. Notably, more than half of patients previously treated with BTKi and anti-CD20 therapies were subsequently treated with another covalent BTKi or a non-covalent BTKi, while approximately one-third received chemotherapy and/or immunotherapy, further emphasizing the need for novel therapeutic options in this heavily pretreated population.