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Real-world treatment patterns, clinical, and economic outcomes following covalent Bruton tyrosine kinase inhibitor (cBTKi) therapy in patients with mantle cell lymphoma (MCL) in the United States

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Introduction: An important evidence gap remains in treatment patterns after cBTKi exposure in MCL, particularly as patients (pts) transition to emerging therapies, cellular therapy, or other systemic regimens. Limited real-world data are available on post-cBTKi treatment use, treatment duration, subsequent therapy, and associated economic burden. This study characterized post-cBTKi treatment patterns, time to treatment discontinuation (TTD), next line of therapy (LOT) sequencing, healthcare resource utilization (HCRU), and total cost of care among pts with MCL in routine clinical practice.

Methods: This retrospective observational study used the Optum Clinformatics Data Mart Database to identify adults with MCL from 01/2020-09/2025. Eligible pts were aged ≥18 y, had ≥3 mo of continuous follow-up, received a cBTKi in any LOT, and initiated a post-cBTKi regimen. Pts were followed until disenrollment, death, or end of the study in December 2025, whichever occurred first. Baseline demographics and clinical characteristics were summarized descriptively. Post-cBTKi regimens were categorized as pirtobrutinib-based, venetoclax-based, lenalidomide-based, chimeric antigen receptor T-cell therapy (CAR T), chemoimmunotherapy (CIT), or other regimens. Outcomes were not assessed in the other regimens group because of treatment heterogeneity. TTD was defined as the time from post-cBTKi regimen initiation to treatment discontinuation or death, whichever occurred first. LOT sequencing was estimated using time-to-next treatment Kaplan-Meier analyses and reported as the probability of pts receiving the next LOT at 6 and 12 mo. HCRU and total cost of care were assessed for all-

cause medical and pharmacy visits during the treatment period. Costs were adjusted to 2025 US dollars using the medical care Consumer Price Index.

Results: Among 15,165 pts with MCL identified in Optum, 4764 (31.4%) had prior cBTKi exposure in any LOT (1L: 24.0%; 2L: 56.4%; 3L: 14.8%); 342 pts met the eligibility criteria and initiated a post-cBTKi regimen. Median age was 73 y, 79.0% were aged ≥65 y, 74.9% were male, 74.6% had Medicare coverage, and median Charlson Comorbidity Index was 3.0 (range, 2.0-5.0). CAR T recipients were relatively younger with a median age of 64 y. Pirtobrutinib-based therapy was the most common post-cBTKi regimen (59.9%; n=205), followed by other (17.5%; n=60), venetoclax-based (7.9%; n=27), lenalidomide-based (7.0%; n=24), CIT (5.2%; n=18), and CAR T (2.3%; n=8) regimens. Median follow-up was 8.4 mo overall and ranged from 6.4 mo for pirtobrutinib-based therapy to 15.1 mo for lenalidomide-based regimens. Median TTD was short across regimens: 4.9 mo overall, 5.3 mo for pirtobrutinib- and venetoclax-based regimens, 6.8 mo for lenalidomide-based regimens, and 4.7 mo for CIT. At 6 mo, the estimated probability of receiving the next LOT was 24.5% overall, including 27.8% with pirtobrutinib-based, 33.3% with venetoclax-based, 17.6% with lenalidomide-based, 28.2% with CIT, and 0.0% with CAR T regimens. At 12 mo, the estimated probability of receiving the next LOT was 39.9% overall, including 44.0% with pirtobrutinib-based, 66.0% with venetoclax-based, 33.5% with lenalidomide-based, 38.5% with CIT, and 20.0% with CAR T regimens. CAR T was associated with the highest HCRU and total cost of care, with 100% of pts having ≥1 hospitalization and a median total cost of care of $306,495. Pirtobrutinib-, venetoclax-, and lenalidomide-based regimens and CIT were also associated with substantial median total costs of care during treatment, ranging from $97,419 to $137,371.

Conclusions: In this real-world analysis in pts with MCL treated after cBTKi exposure, pirtobrutinib-based therapy was the predominant post-cBTKi regimen, whereas use of venetoclax-based, lenalidomide-based, CIT, and CAR T regimens was limited. Median TTD was considerably short across post-cBTKi regimens, suggesting limited treatment durability in routine clinical practice. The estimated probability of receiving next LOT within 12 mo was substantial, particularly with venetoclax- and pirtobrutinib-based regimens; among CAR T recipients, the estimated probability was 20% despite the small sample size. CAR T recipients had the highest HCRU and total cost of care, with other post-cBTKi regimens also associated with substantial cost burden. These findings highlight the continued unmet need for durable, less resource-intensive treatment options after cBTKi therapy in relapsed/refractory MCL.