Navigating the post–covalent Bruton tyrosine kinase inhibitor landscape in mantle cell lymphoma: real-world insights on treatment patterns, discontinuation, and healthcare resource utilization

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Background: Covalent Bruton tyrosine kinase inhibitors (cBTKis) have become standard therapy for relapsed/refractory mantle cell lymphoma (MCL) and are rapidly advancing to the first-line setting. However, real-world evidence on clinical and economic outcomes following cBTKi therapy is limited.

Aims: To evaluate treatment patterns, time to treatment discontinuation (TTD), and healthcare resource utilization (HCRU) among patients with MCL previously treated with cBTKis

Methods: This retrospective observational study used claims data from the Symphony Integrated Dataverse (Jan 2020-Aug 2025) to identify adults with MCL who received a cBTKi in any line of therapy (LOT) and, following discontinuation, initiated another treatment. Post-cBTKi regimens were categorized as B-cell lymphoma 2 inhibitor (BCL2i), cBTKi, noncovalent BTK inhibitor (ncBTKi), chimeric antigen receptor T-cell therapy (CAR-T), chemo±immunotherapy (C±IT), and other. TTD and HCRU (outpatient/inpatient/other medical, reported per-patient-per-month [PPPM]), were assessed for regimens received post cBTKi.

Results: Of 10,519 total US patients with MCL, 571 were previously treated with cBTKis and received a subsequent therapy (median age, 72.0 years; ≥65 years, 77%; male, 74%; White non-Hispanic, 67%; Medicare, 62%). Regimens received in a subsequent LOT after cBTKi included cBTKis (38%), ncBTKis (32%), C±IT (11%), BCL2is (9%; monotherapy 7%), CAR-T (2%), and other (8%). Median TTD was longest with cBTKis (365 days), followed by ncBTKis (206 days), and shortest with BCL2is (140 days). Mean HCRU PPPM was lowest with cBTKis (outpatient, 1.21; inpatient, 0.20; other medical, 1.07) and highest with CAR-T (outpatient, 10.63; inpatient, 1.89; other medical, 1.55).

Summary/Conclusion: In this real-world analysis, patients with MCL who previously received cBTKis were most frequently re-treated with cBTKis, highlighting the need for novel treatment options in the post-cBTKi setting. TTD was greatest in patients who received cBTKis or ncBTKis and shortest in those treated with BCL2is. HCRU burden was lowest for patients who received cBTKis and highest for those treated with CAR-T. Further research, including an understanding of the reasons for re-exposure to cBTKis, is warranted to confirm these findings.

Table. TTD and HCRU by MCL Treatment Regimens Received Post cBTKi

Outcomes	All N=571	cBTKi n=215	ncBTKi n=182	C±IT n=62	BCL2i n=53	CAR-T n=12
Follow-up, median (IQR), days	294 (118-628)	414 (206-762)	189 (89-453)	330 (116-727)	256 (70-844)	412 (216-912)
TTD, median (95% CI), days	222 (181-281)	365 (278-460)	206 (173-304)	169 (112-183)	140 (100-315)	NA
HCRU, mean (SD), PPPM						
Outpatient	1.95 (2.82)	1.21 (1.61)	1.48 (2.19)	2.19 (2.65)	2.34 (2.70)	10.63 (5.05)
Inpatient	0.34 (0.91)	0.20 (0.67)	0.33 (0.75)	0.29 (0.82)	0.43 (1.22)	1.89 (1.89)
Other medical services	1.47 (2.62)	1.07 (1.93)	1.35 (2.54)	2.54 (3.59)	1.64 (2.82)	1.55 (1.70)

BCL2i, B-cell lymphoma 2 (BCL2) inhibitor; C±IT, chemo±immunotherapy; CAR-T, chimeric antigen receptor T-cell therapy; cBTKi, covalent Bruton tyrosine kinase inhibitor; HCRU, healthcare resource utilization; NA, not applicable; ncBTKi, noncovalent Bruton tyrosine kinase inhibitor; PPPM, per-patient-per-month; TTD, time to treatment discontinuation.