Real-World switching pattern, persistence, and associated healthcare resource utilization of Bruton Tyrosine Kinase Inhibitors for the Treatment of Mantle Cell Lymphoma in the United States

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Introduction: Mantle cell lymphoma (MCL) is an aggressive form of B-cell non-Hodgkin's lymphoma. While incurable, MCL can be controlled for a prolonged period of time, but typically becomes refractory or relapsed and requires additional treatment. Bruton tyrosine kinase inhibitors (BTKi) are approved for relapse/refractory MCL and recommended by the National Comprehensive Cancer Network (NCCN®); However, it is unclear how BTKi are being utilized and switched in the real-world patient populations. This study aimed to examine treatment patterns, persistence, and associated healthcare resource utilization of BTKi use in patients with MCL in the US.

Methods**:** A retrospective observational study was conducted using Symphony Integrated Dataverse (IDV®), a comprehensive, longitudinal, open-claims database and integrated Electronic Medical Record (EMR) data. Patients aged ≥18 years with ≥1 diagnosis for MCL and initiated a BTKi between 1/1/20 and 12/31/22 were included in the study. Patients were required to be continuously enrolled for 365 days leading up to the index date and ≥90 days following the index date (date of BTKi initiation).
The full patient history in the database was used to identify previous BTKi use and analyze switching patterns for each patient. Three mutually exclusive cohorts (ibrutinib, acalabrutinib, zanubrutinib) were developed based on first-initiated BTKi. Patients were followed until the end of the study period (3/31/23) or lost to follow-up. Treatment switching pattern, duration, persistence, time to discontinuation (TTD), and healthcare resource utilization (HCRU) were examined by each BTKi cohort. Treatment duration was defined as time from BTKi initiation to the end date of last BTKi prescription. TTD was defined as time from BTKi initiation to the end date of the BTKi prescription that had a gap of >60 days with a subsequent BTKi prescription. Treatment persistence was evaluated as the proportion of patients that were continually prescribed BTKi (≥80% proportion of days covered) across 30-day intervals. HCRU was measured by number of outpatient visits and inpatient services, per patient per month (PPPM), during the treatment regimen.

Results**:** BTKi switching patterns were analyzed for the 1,674 patients that initiated any BTKi therapy during study period (acalabrutinib [n= 697]; ibrutinib [n=693]; zanubrutinib [n=284]). Switching rates were 23.8% for ibrutinib, 5.6% for acalabrutinib, and 2.8% for the zanubrutinib cohort. In the ibrutinib cohort, the majority of patients switched to acalabrutinib (72.7%). Of those who switched from acalabrutinib, more than half (59.9%) switched to zanubrutinib. Of those who switched in zanubrutinib cohort, they were equally switched to ibrutinib and acalabrutinib (Table 1). Mean outpatient visits PPPM were 1.39 for patients who initiated with ibrutinib then switched to zanubrutinib, and 1.49 for those who switched to acalabrutinib. Mean inpatient services PPPM were 0.39 for patients who switched from ibrutinib to zanubrutinib, and 0.59 for those who switched to acalabrutinib. The 3 BTKi cohorts were similar across sociodemographic characteristics. The zanubrutinib cohort had higher median TTD (days) (188.5) compared to ibrutinib (161.5) and acalabrutinib (179), as well as higher median treatment duration (200) compared to ibrutinib (171) and acalabrutinib (194). Among MCL patients continuously enrolled for ≥ 360 days, zanubrutinib patients consistently had higher persistence

rates (p=0.0079. Figure 1). Persistence at 90-days was 66.9% for zanubrutinib compared to 56.3% for ibrutinib and 62.7% for acalabrutinib. After 360 days, zanubrutinib continued to have the highest persistence (16.9%) compared to ibrutinib (10.8%) or acalabrutinib (13.2%). Zanubrutinib had the least number of mean inpatient services PPPM (0.56) compared to ibrutinib (0.83) and acalabrutinib (0.71) and mean outpatient visits—zanubrutinib (1.53), ibrutinib (1.81), acalabrutinib (1.59).

Conclusions: This real-world study suggested that US patients with MCL receiving zanubrutinib showed longer treatment persistence, treatment duration and TTD, as well as lower switching rates and HCRU compared to those receiving acalabrutinib and ibrutinib.

Table 1. BTKi Switching Patterns Among MCL Patients

BTKi Users	**% BTKi users switched from initial BTKi to another BTKi**	**Subsequent BTKi that was switched to**
Ibrutinib (n=693)	23.8%	Acalabrutinib (72.7%)
		Zanubrutinib (27.3%)
Acalabrutinib (n=697)	5.6%	Ibrutinib (41.0%)
		Zanubrutinib (59.0%)
Zanubrutinib (n=284)	2.8%	Ibrutinib (50.0%)
		Acalabrutinib (50.0%)

Figure 1. 360-Day Treatment Persistence for MCL Patients