Real-World Bruton Tyrosine Kinase Inhibitor Treatment Patterns, Compliance, Costs, and Hospitalizations in Patients with Mantle Cell Lymphoma in the United States

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Introduction: Mantle cell lymphoma (MCL) is a rare, aggressive, and incurable B-cell malignancy. MCL patients may initially respond well to frontline treatments; however, most will relapse or become refractory (r/r) to treatment. While there are real-world data available on the use of ibrutinib, the first Bruton tyrosine kinase inhibitor (BTKi) approved in 2013 for the treatment of r/r MCL, there is limited data on the more recently approved BTKis, acalabrutinib (approved in 2017) and zanubrutinib (approved in late 2019), primarily due to disease rarity and time lag of claims dataset. This study aimed to examine (1) clinical and sociodemographic characteristics of patients receiving BTKi, (2) treatment patterns and compliance by each BTKi, and (3) costs and hospitalizations associated with each BTKi use in the real-world setting in the United States.

Methods: A retrospective observational study was conducted using the patient longitudinal data between July 2017 and May 2021 from the Symphony Health's IDV® (Integrated Dataverse), a de-identified, open-source claims database. IDV captures and aggregates data from different data vendors and assigns a unique patient identifier to each claim through a proprietary patient matching process. Patients were considered to be active in the open-source database and eligible for the study if they have ≥ 1 MCL diagnosis and ≥ 1 BTKi prescription claim for two consecutive semesters (1 semester = 6 months) pre- and post- index date. The index date was defined as the use of one of the BTKis of interest: ibrutinib, acalabrutinib, or zanubrutinib. The BTKi groups were not mutually exclusive to capture the potential switching between groups. Descriptive analysis was conducted to

examine patient sociodemographic characteristics, comorbidities, concomitant medications, treatment patterns, costs, and hospitalizations in overall BTKi users, and by each BTKi. Treatment patterns were evaluated by frequency and duration of each BTKi use. Days of supplies and medication possession ratio were used to calculate persistency and compliance rates.

Results: Among 30,199 patients with MCL identified from the database, 3,821 MCL patients were on BTKi therapy, and the final study population consisted of 1,653 active patients with MCL and BTKi treatment. Patients in the zanubrutinib group were older (n=67, median age=78, 67.2% male) than those in either the acalabrutinib group (n=485, median age=74, 74.9% male) and ibrutinib group (n=1,242, median age=70, 73.8% male). Among zanubrutinib users, 22% were switched from ibrutinib and 7% switched from acalabrutinib, while 21% of acalabrutinib users were switched from ibrutinib. Over half of the ibrutinib use was in the frontline setting (68.4%) while the use of acalabrutinib and zanubrutinib was more in the r/r setting (68.9% and 80.6%, respectively). The most common comorbidities at BTKi treatment initiation were hypertension (41.1%), followed by dyslipidemia (28.6%), diabetes (17.5%), cardiac arrhythmia (15.6%), and gastroesophageal reflux disease (14.5%). However, 28.5% of acalabrutinib users were concurrently on proton pump inhibitors even though such concomitant use should be avoided. The compliance rate was higher in zanubrutinib group (65%) than acalabrutinib (62%) and ibrutinib (59%) groups. Overall, the average length of stay (LOS) is 5.9 days among MCL patients who used BTKi and had at least 1 hospitalization. Patients in the zanubrutinib group had a shorter LOS (4.0 days) than those in the ibrutinib (5.9 days) and acalabrutinib (5.8 days) groups (Figure 1A). On average, the total submitted inpatient charge per stay is lower for patients in the zanubrutinib group ($51,051) than patients in the ibrutinib ($79,482) and acalabrutinib ($74,546) groups (Figure 1B).

Conclusions: This study provides the first real-world evidence on patients with MCL treated with all currently available BTKis, zanubrutinib, ibrutinib and acalabrutinib. BTKis are largely being used in second-line plus settings. Future studies are needed to understand the

long-term outcomes of BTKi treatment as data matures.

Figure 1A. Average length of stay among MCL patients who were BTKi Users and had at least one hospitalization

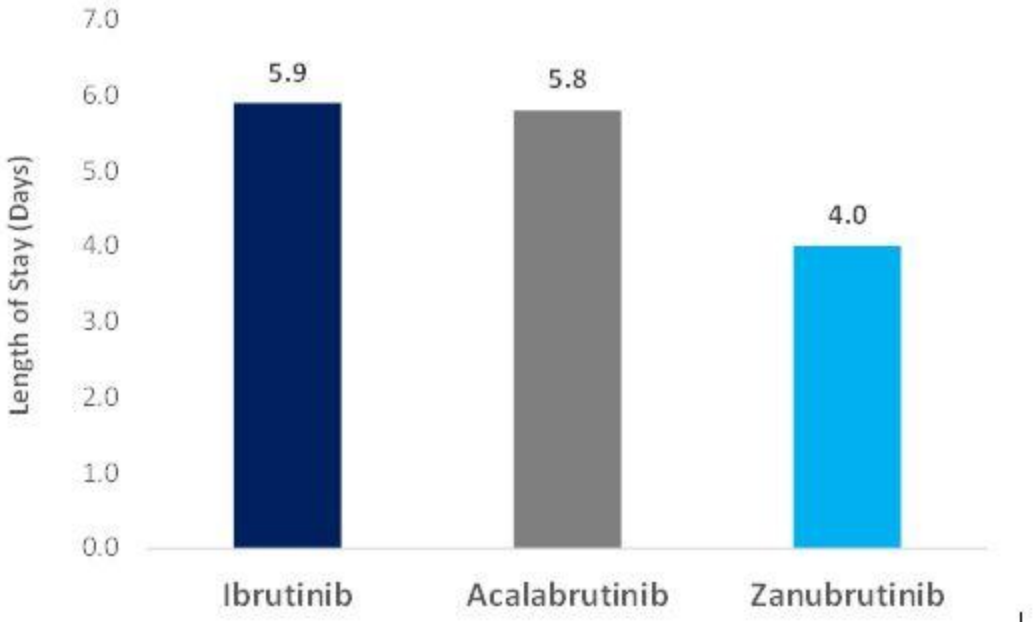

Figure 1B. Average inpatient charge per stay among MCL patients who were BTKi users and had at least one hospitalization