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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BACKGROUND

- 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
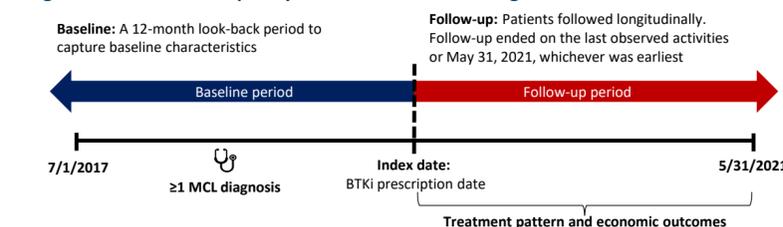
OBJECTIVES

- To examine clinical and sociodemographic characteristics of patients receiving BTKi
- To describe the treatment patterns and compliance by each BTKi
- To assess the costs and hospitalizations associated with each BTKi use in the real-world setting in the United States

METHODS

- **Study design:** Retrospective, observational study (Figure 1)
- **Data source:** 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
- **Study population:**
  - Adult MCL patients ≥1 BTKi prescription claim for 12 months
  - Index dateL: defined as the use of one of the BTKis of interest: ibrutinib, acalabrutinib, or zanubrutinib
- **Inclusion criteria**
  - Aged ≥18 years at index date
  - ≥1 diagnosis of MCL
  - ≥1 BTKi prescription claim
  - Patient should have ≥1 valid medical or prescription claim 12-month before and after the index date

Figure 1. Real-world frequency of risk assessment testing

Baseline: A 12-month look-back period to capture baseline characteristics

Follow-up: Patients followed longitudinally. Follow-up ended on the last observed activities or May 31, 2021, whichever was earliest

7/1/2017 — ≥1 MCL diagnosis — Index date: BTKi prescription date — 5/31/2021

Treatment pattern and economic outcomes

- **Treatment cohort:**
  - Patients were stratified into three cohorts based on their index BTKi (ibrutinib, acalabrutinib, and zanubrutinib)
- **Outcomes:**
  - Length of stay
  - Inpatient hospital charges
- Descriptive analysis was conducted to examine patient characteristics, treatment patterns, and economic outcomes by each BTKi
- **Treatment pattern:**
  - Treatment duration: The total number of days from the first day of a line of therapy to the last drug prescription date, plus days of supply for oral drugs of the therapy
  - Discontinuation: Treatment with BTKi was considered as discontinued when there was a gap of >60 days in medication supply
  - Compliance rate: Calculated as the ratio of actual number of days supply over possible number of days supply for each product

RESULTS

Demographic characteristics of MCL patients with BTKi treatment (Table 1)
- Among 30,199 patients with MCL identified, 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 than those in the acalabrutinib and ibrutinib groups
- 28.5% of acalabrutinib users were concurrently on proton pump inhibitors even though such concomitant use should be avoided
- More white patients were observed in the zanubrutinib and acalabrutinib users than in ibrutinib users
- The proportion of annual household income ≥$100K was higher in zanubrutinib group than those in either acalabrutinib or ibrutinib groups
- The proportion of those with a high school level of education or lower is higher in ibrutinib than that in acalabrutinib and zanubrutinib groups
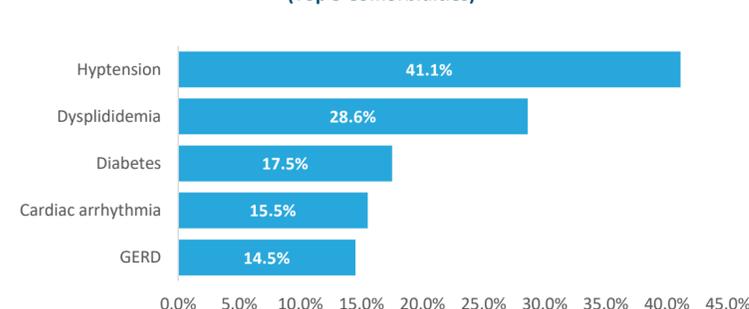
Table 1. Demographic Characteristics of MCL Patient Population

	Ibrutinib (N=1,242)	Acalabrutinib (N=485)	Zanubrutinib (N=67)
Age at index, Mean (SD)	71.4 (6.9)	71.6 (7.8)	73.8 (7.1)
Median (IQR)	64(64-74)	68(61-71)	71 (59-71)
Age≥65 years, n (%)	1,033 (83.2%)	398 (82.1%)	59 (88.1%)
Age≥75 years, n (%)	622 (50.1%)	243 (50.1%)	37 (55.2%)
Male, n (%)	917 (73.8%)	363 (74.9%)	45 (67.2%)
White, n (%)	856 (68.9%)	345 (71.1%)	50 (74.6%)
Annual household income distribution, n (%)			
<30k	182 (14.7%)	47 (9.7%)	5 (7.5%)
30K - 49.99K	169 (13.6%)	62 (12.8%)	9 (13.4%)
50K - 74.99K	211 (17.0%)	91 (18.8%)	10 (14.9%)
75K - 99.99K	180 (14.5%)	78 (16.1%)	9 (13.4%)
100K+	290 (23.4%)	127 (26.2%)	23 (34.3%)
Unknown	210 (16.9%)	80 (16.5%)	11 (16.4%)
Education distribution, n (%)			
High school graduate or Lower	270 (21.7%)	93 (19.2%)	12 (17.9%)
College	420 (33.8%)	179 (36.9%)	22 (32.8%)
Associate degree / Bachelor's degree or higher	349 (28.1%)	137 (28.3%)	22 (32.8%)
Unknown	203 (16.3%)	76 (15.7%)	11 (16.4%)

Clinical characteristics of MCL patients with BTKi treatment (Figure 2)
- The most common comorbidities at BTKi treatment initiation were hypertension, followed by dyslipidemia, diabetes, cardiac arrhythmia, and gastroesophageal reflux disease (GERD)

Figure 2. Baseline Comorbidities of MCL Patient Population with BTKi treatment (Top 5 Comorbidities)
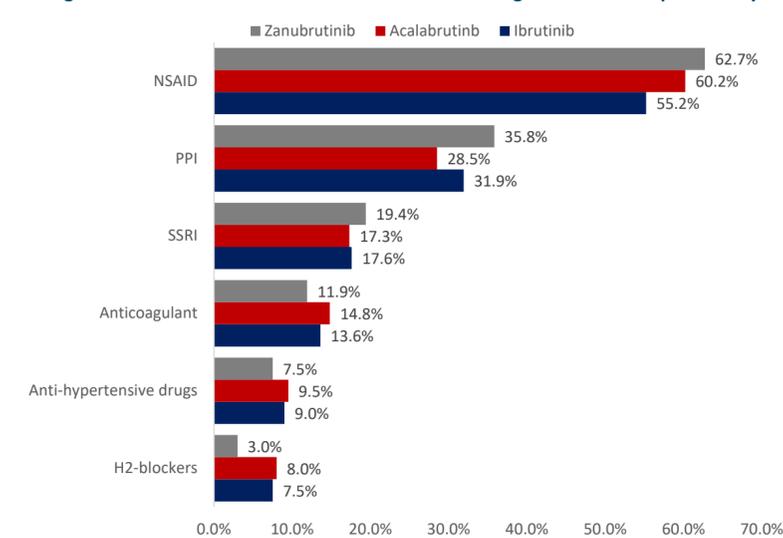

RESULTS

Clinical characteristics of MCL patients with BTKi treatment (Figure 3)
- NSAID and PPI are the 2 most common concomitant medications across the three BTKi drugs
- 28.5% of acalabrutinib users were concurrently on proton pump inhibitors even though such concomitant use should be avoided
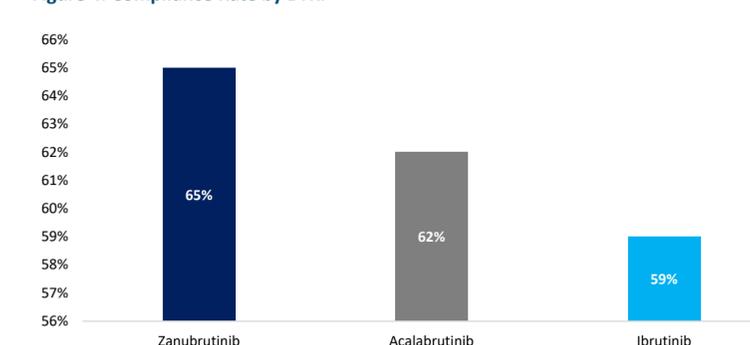
Figure 3. Baseline Concomitant Medication Use among MCL Patient Population by BTKi

BTKi treatment patterns
- **Switching:**
  - Among zanubrutinib users, 22% were switched from ibrutinib and 7% switched from acalabrutinib
  - Among acalabrutinib users, 21% were switched from ibrutinib
- **Line of therapy:**
  - 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)
- **Compliance:**
  - The compliance rate was higher in zanubrutinib group than acalabrutinib and ibrutinib groups (Figure 4)
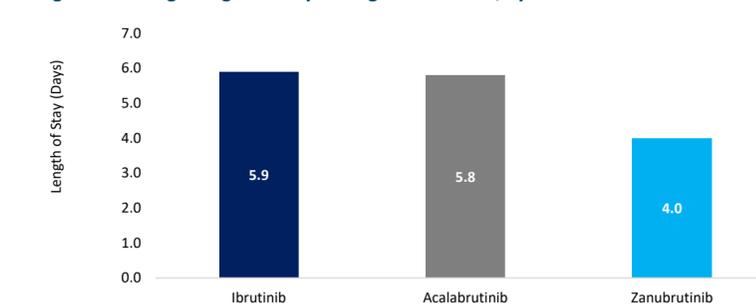
Figure 4. Compliance Rate by BTKi

RESULTS

Economic outcomes: Length of Stay (LOS)
- Overall, the average 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 than those in the ibrutinib and acalabrutinib groups (Figure 5)
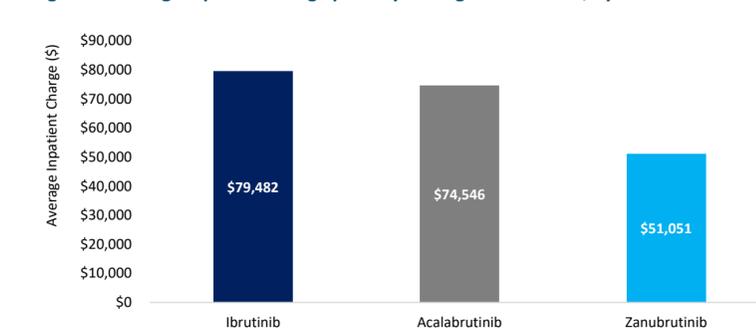
Figure 5. Average Length of Stay among MCL Patients, by BTKi

Economic outcomes: Inpatient charge per stay
- On average, the total submitted inpatient charge per stay is lower for patients in the zanubrutinib group than patients in the ibrutinib and acalabrutinib groups (Figure 6)

Figure 6. Average Inpatient charge per stay among MCL Patients, by BTKi

DISCUSSION

- Study results should be interpreted with consideration of limited sample size and follow-up periods due to disease rarity and data availability
- Study limitations were inherent to the use of claims databases in an observational study design
- Future studies are needed to further understand factors associated with treatment selection and outcomes

CONCLUSION

- 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 while used increasingly in the front-line settings
- Based on the 1-year follow-up period, the treatment adherence is better for zanubrutinib compared with the other two BTKis