Real-World Switching Patterns, Persistence, and Associated Healthcare Resource Utilization of Bruton Tyrosine Kinase Inhibitors for the Treatment of Mantle Cell Lymphoma in the United States

Keri Yang,[1] Bijal Shah,[2] Mei Xue,[1] Wesley Furnback,[3] Kaitlyn Esselman,[3] Po-Ya Chuang[3]

[1]BeiGene, Ltd, Emeryville, CA, USA; [2]Moffitt Cancer Center, Tampa, FL, USA; [3]Real Chemistry, Inc, New York, NY, USA

BACKGROUND

- Mantle cell lymphoma (MCL) is an aggressive form of B-cell non-Hodgkin lymphoma[1,2]
- While incurable, MCL can be controlled for a prolonged period of time, but typically becomes refractory or relapsed and requires additional treatment[1,2]
- Bruton tyrosine kinase inhibitors (BTKi) are approved for relapsed/refractory MCL and recommended by the National Comprehensive Cancer Network (NCCN®)[3]; however, it is unclear how BTKis are being utilized and switched in real-world patient populations

OBJECTIVES

- This study aimed to examine treatment patterns, persistence, and associated healthcare resource utilization (HCRU) of BTKi use in patients with MCL in the United States (US)

METHODS

Data Source

- A retrospective observational study was conducted using the Symphony Integrated Dataverse, a comprehensive, longitudinal, open-claims database, and integrated Electronic Medical Record data

Inclusion Critieria

- Patients aged ≥18 years with ≥1 diagnosis for MCL who 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)

Cohorts

- Three mutually exclusive cohorts (ibrutinib, acalabrutinib, zanubrutinib) were developed based on initiated BTKi

Follow-Up

- Patients were followed until the end of the study period (3/31/23) or lost to follow-up

Study Outcomes

- Treatment switching pattern, duration, persistence, time to discontinuation (TTD), and 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

- BTKi switching patterns were analyzed for the 1674 patients that initiated any BTKi therapy during the 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 the zanubrutinib cohort, they were equally switched to ibrutinib and acalabrutinib (**Table 1**)

Table 1. BTKi Switching Patterns Among MCL Patients

BTKi Users (Initial BTKi in Patient History)	Switched to Another BTKi (%)	Subsequent BTKi (%)
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%)

BTKi, Bruton tyrosine kinase inhibitor.

Baseline Characteristics

- Of the 1674 patients initiating any BTKi during the index period, 1458 patients initiated their first BTKi during the index period. These patients were then divided into the mutually exclusive cohorts based on their specific BTKi at index
- There were 667 (45.7%) acalabrutinib patients, 509 (34.9%) ibrutinib patients, and 282 (19.3%) zanubrutinib patients
- Median follow-up was 392 days for acalabrutinib, 471 days for ibrutinib, and 340 days for zanubrutinib
- The 3 BTKi cohorts were similar across sociodemographic characteristics (**Table 2**)

Table 2. Baseline Demographics and Clinical Characteristics

Characteristic	Acalabrutinib (n=667)	Ibrutinib (n=509)	Zanubrutinib (n=282)
Sex, n (%)			
Male	460 (69.0)	376 (73.9)	196 (69.5)
Female	207 (31.0)	133 (26.1)	86 (30.5)
Age at index			
Mean (SD)	70.9 (8.0)	69.9 (8.1)	70.6 (8.1)
Median (IQR)	73 (65-77)	71 (64-77)	72 (65-78)
65+, n (%)	511 (76.6)	379 (74.5)	218 (77.3)
Payer type, n (%)			
Medicare	412 (61.8)	284 (55.8)	156 (55.3)
Commercial	213 (31.9)	183 (36.0)	112 (39.7)
Other	42 (6.3)	42 (8.3)	14 (5.0)
Prior lines of therapy			
Mean (SD)*	0.98 (0.56)	0.86 (0.64)	1.01 (0.58)
None, n (%)*	103 (15.4)	135 (26.5)	41 (14.5)
1L, n (%)	485 (72.7)	314 (61.7)	201 (71.3)
2L+, n (%)	79 (11.8)	60 (11.8)	40 (14.2)
CCI			
Mean (SD)	5.81 (3.72)	6.04 (3.94)	5.97 (3.75)
Median (IQR)	6 (4-8)	6 (3-8)	6 (6-8)

*P<0.05.
1L, first line; 2L, second line; CCI, Charlson Comorbidity Index.

- Baseline clinical characteristics were well balanced across the cohorts with only a significant difference in the mean number of prior line of therapies, which was highest for zanubrutinib
- Comorbidities present in the pre-index period are shown in **Table 3**

Table 3. Baseline Comorbidities

Comorbidities, n (%)	Acalabrutinib (n=667)	Ibrutinib (n=509)	Zanubrutinib (n=282)
Anemia	45 (6.8)	45 (8.8)	25 (8.9)
Atrial fibrillation	17 (2.6)	7 (1.4)	2 (0.7)
Cardiac arrhythmias	98 (14.7)	76 (14.9)	33 (11.7)
Bleeding	33 (5.0)	32 (6.3)	16 (5.7)
Cerebrovascular disease	18 (2.7)	13 (2.6)	10 (3.6)
Chronic pulmonary disease	54 (8.1)	46 (9.0)	23 (8.2)
Diabetes	81 (12.1)	58 (11.4)	38 (13.5)
Dyspnea	65 (9.8)	41 (8.1)	16 (5.7)
GERD	62 (9.3)	51 (10.0)	31 (11.0)
General fatigue*	48 (7.2)	33 (6.5)	34 (12.1)
GI disease	142 (21.3)	120 (23.6)	67 (23.8)
Heart failure	58 (8.7)	42 (8.3)	21 (8.5)
Hepatic disease	18 (2.7)	13 (2.6)	7 (2.5)
Hypertension	202 (30.3)	182 (35.8)	87 (30.9)
Myocardial infarction	17 (2.6)	16 (3.1)	7 (2.5)
Neutropenia	67 (10.0)	48 (9.4)	29 (10.3)
Renal disease	91 (13.6)	80 (15.7)	39 (13.8)
Soft tissue disorder	46 (6.9)	35 (6.9)	19 (6.7)

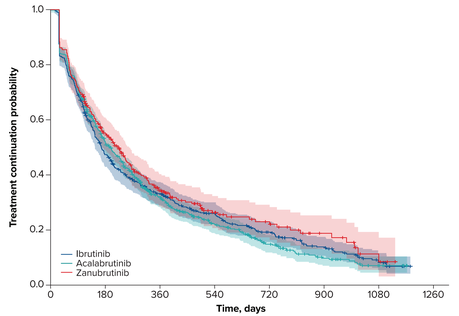
*P<0.05.
GERD, gastroesophageal reflux disease; GI, gastrointestinal.

- Baseline general fatigue was significantly higher in the zanubrutinib cohort compared with the acalabrutinib and ibrutinib cohorts
- There were no significant differences across the cohorts for the other comorbidities measured

Time to Discontinuation, Treatment Duration, and Persistence

- The zanubrutinib cohort had a higher median TTD (188.5 days) compared with ibrutinib (161.5 days) and acalabrutinib (179 days) (**Figure 1**), as well as a higher median treatment duration (200 days) compared with ibrutinib (171 days) and acalabrutinib (194 days)
- Among MCL patients continuously enrolled for >360 days, persistence rates were significantly different between the 3 BTKis (*P*=0.0079; **Figure 2**) and highest for zanubrutinib

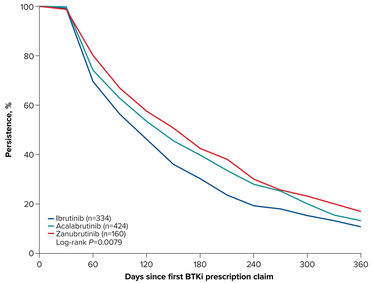
Figure 1. Time to Discontinuation



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

Figure 2. 360-Day Treatment Persistence



- Persistence at 90 days was 66.9% for zanubrutinib compared with 56.3% for ibrutinib and 62.7% for acalabrutinib
- After 360 days, zanubrutinib continued to have the highest persistence (16.9%) compared with ibrutinib (10.8%) or acalabrutinib (13.2%)

Healthcare Resource Utilization

- Zanubrutinib had the least number of mean inpatient services PPPM (0.56) compared with ibrutinib (0.83) and acalabrutinib (0.71) and mean outpatient visits: zanubrutinib (1.53), ibrutinib (1.95), acalabrutinib (1.59) (**Table 4**)

Table 4. HCRU

Resource	Acalabrutinib (n=667)	Ibrutinib (n=509)	Zanubrutinib (n=282)
All-cause, PPPM, mean (SD)			
Outpatient visits	1.59 (2.96)	1.95 (3.49)	1.53 (2.5)
Inpatient services	0.71 (3.84)	0.83 (4.02)	0.56 (2.21)
Other medical/hospital services	1.1 (2.39)	1.12 (2.44)	1.17 (2.4)

HCRU, healthcare resource utilization; PPPM, per patient per month.

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DISCLOSURES

KY: Employment: BeiGene, USA: current employment, equity holder in publicly-traded company. **BS:** Consulting: Adaptive Biotechnologies, BMS, Novartis, Pfizer, Amgen, Precision Biosciences, Kite, Jazz, Century Therapeutics, Deciphera, Autolus, Lily, Pepromene; Research funding: Incyte, Jazz, Kite, Servier; Travel, accommodations, and expenses: Celgene, Novartis, Pfizer, Janssen, Seagen, AstraZeneca, Stemline Therapeutics, Kite; Honoraria: Pharmacyclics/Janssen, Spectrum/Acrotech, BeiGene, Gilead Sciences. **MX:** Employment: BeiGene. **WF:** Employment: Real Chemistry; Stock or other ownership: Real Chemistry. **KE** and **P-YC:** Employment: Real Chemistry.

CORRESPONDENCE: Keri Yang, keri.yang@beigene.com

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