Real-world Treatment Patterns and Comparative Effectiveness of Bruton Tyrosine Kinase Inhibitors In Patients With Mantle Cell Lymphoma

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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
- Bruton tyrosine kinase inhibitor (BTKi) therapy first emerged in 2013 with ibrutinib, followed by acalabrutinib in 2017 and zanubrutinib, approved by the FDA in 2019 for R/R MCL
- BTKi therapies have not been comprehensively evaluated in real-world MCL patient populations

OBJECTIVE

- This study aimed to assess patient characteristics, treatment patterns and associated outcomes in real world BTKi-treated MCL patients

METHODS

Study Design

- Retrospective multicenter chart review

Data Source

- EMR data from the Cardinal Health Oncology Provider Extended Network

Study Population

- Aged ≥ 18 years at MCL diagnosis
- Initiated BTKi (ibrutinib, acalabrutinib, or zanubrutinib) therapy for the treatment of MCL between January 1, 2018, and March 31, 2021
- Baseline characteristics were assessed during a 12-month baseline period
- Patients were followed from index to last follow-up or death
- Index date: the use of any of the BTKi of interest
- Patients enrolled in clinical trials were excluded

Key Outcomes and Statistical Analysis

- Descriptive analyses were conducted to assess demographic/clinical characteristics, and MCL baseline features of MCL patients, BTKi treatment patterns, adverse events (AE), and response rates by BTKi
- Statistical comparisons across all three BTKi groups were performed
- Multivariable logistic regression was performed to assess factors associated with response and AE

RESULTS

Baseline Demographic Characteristics of BTKi-treated MCL Patient Population (Table 1)

- The study cohort consisted of 300 MCL patients (59% male; 69% white)
- Most (64%) patients were covered by Medicare, 34% had commercial insurance
- MCL patients were treated mainly by board-certified hematology/oncology physicians (82%)
- Patients in the zanubrutinib group were significantly older (median age=71, range=50-91) than patients in the ibrutinib (median age=69, range =39-87) and acalabrutinib (median age=70, range =51-86) groups

Table 1. Demographic characteristics of MCL patients at BTKi treatment initiation, by BTKi

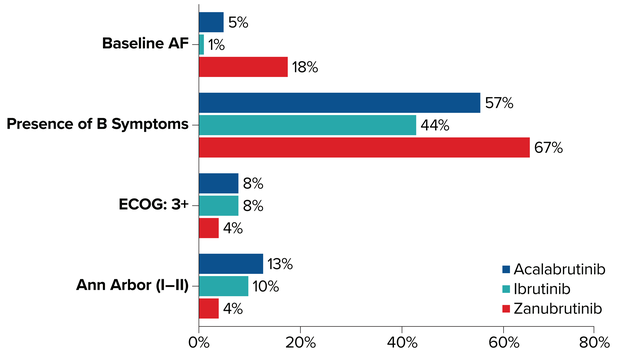
	Zanubrutinib N=100	Ibrutinib N=100	Acalabrutinib N=100	*P*-value
Age, years (median, min-max)				
At MCL diagnosis	70 (44-91)	66 (39-84)	68 (49-86)	0.02
At index BTKi	71 (50-91)	69 (39-87)	70 (51-86)	0.02
Sex, n (%)				
Male	51 (51%)	60 (60%)	65 (65%)	0.13
Female	49 (49%)	40 (40%)	35 (35%)	
Race, n (%)				
White	68 (68%)	72 (72%)	66 (66%)	0.70
Asian	12 (12%)	6 (6%)	12 (12%)	
Black/African American	17 (17%)	18 (18%)	19 (19%)	
Insurance, n (%)				
Medicare	65 (65%)	56 (56%)	71 (71%)	0.08
Commercial	36 (36%)	40 (40%)	26 (26%)	0.10
Medicaid	9 (9%)	6 (6%)	17 (17%)	0.04
US region, n (%)				
Northeast	32 (32%)	25 (25%)	31 (31%)	0.02
Midwest	8 (8%)	13 (13%)	22 (22%)	
South	29 (29%)	32 (32%)	33 (33%)	
West	31 (31%)	30 (30%)	14 (14%)	

Abbreviations: BTKi, Bruton Tyrosine Kinase inhibitor; MCL, mantle cell lymphoma.

Baseline Clinical Characteristics of BTKi-treated MCL Patient Population (Figure 1)

- Significantly fewer patients in the zanubrutinib group had baseline Ann Arbor stage I-II (4%) than ibrutinib (10%) or acalabrutinib (13%) at treatment initiation
- Significantly more zanubrutinib patients had presence of B symptoms (67%) than ibrutinib (44%) or acalabrutinib (57%) at baseline treatment initiation
- At BTKi initiation, significantly more patients in zanubrutinib group (18%) had history of atrial fibrillation than ibrutinib (1%) or acalabrutinib (5%)

Figure 1. Clinical characteristics and baseline features of MCL patients at BTKi treatment initiation, by BTKi



Abbreviations: AF, atrial fibrillation; ECOG, Eastern Cooperative Oncology Group.

BTKi Treatment Pattern

- BTKis were given mainly as monotherapy (93%) and second-line of therapy (86%)
- Most patients were started at an on-label BTKi dose
- In zanubrutinib patients, 160 mg BID was more common (64%) than 320 mg QD (31%)

Treatment Response and Safety Associated with BTKi

- Multivariable regression reported a significant association of age, gender, extranodal/splenic involvement, and timing of BTKi initiation with response and AE
- After adjusting for patient characteristics, there was a trend for lower odds of response to BTKi therapy among those treated with ibrutinib or acalabrutinib versus zanubrutinib
- There was a trend for increased odds of an AE among those treated with ibrutinib or acalabrutinib versus zanubrutinib

Table 2. Multivariable regression of treatment response and adverse events

	Response OR (95% CI)	AE OR (95% CI)
BTKi initiation (Ref= Zanubrutinib)		
Ibrutinib	0.75 (0.38, 1.47)	1.17 (0.61, 2.24)
Acalabrutinib	0.87 (0.45, 1.69)	1.52 (0.80, 2.87)
Age at index BTKi Initiation	**0.54 (0.31, 0.96)**	**2.52 (1.43, 4.47)**
Gender (Female vs. Male [Ref])	**0.91 (0.84, 0.98)**	0.96 (0.92, 1.01)
Duration of BTKi Therapy	1.00 (0.97, 1.04)	**0.96 (0.93, 0.99)**
Race (Non-white vs. White [Ref])	1.11 (0.63, 1.94)	1.44 (0.84, 2.46)
Ann Arbor stage (0/1 vs 2+ [Ref])	1.04 (0.57, 1.91)	0.70 (0.40, 1.22)
ECOG PS (0/1 vs 2+ [Ref])	0.31 (0.07, 1.44)	0.69 (0.27-1.72)
Splenic involvement (No vs. Yes [Ref])	**0.34 (0.19, 0.60)**	**0.49 (0.28, 0.86)**
Extranodal disease involvement (No vs. Yes [Ref])	**0.33 (0.16, 0.68)**	**0.31 (0.14, 0.68)**
Index BTKi line (1L vs. 2L+ [Ref])	0.73 (0.25, 2.16)	**0.26 (0.01, 0.70)**

Abbreviations: BTKi, Bruton tyrosine kinase inhibitor; CI, confidence interval; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; Ref, reference; OR, odds ratio

DISCUSSIONS

- This study provides the first real-world evidence on comparative effectiveness of ibrutinib, acalabrutinib, zanubrutinib in MCL patients
- Study limitations were inherent to the use of multicenter chart review study design and may not represent all patients diagnosed with MCL or treated with the drugs of interest or physicians treating these patients

CONCLUSIONS

- While patients treated with zanubrutinib were older and had more complex MCL baseline features at initiation, multivariable regression suggested a trend favoring zanubrutinib over ibrutinib or acalabrutinib for both response and AE
- Frontline initiation of BTKi therapy was also associated with improved tolerability
- Future real-world studies are needed to discern long-term outcomes

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