Real-World Zanubrutinib Treatment Patterns in Mantle Cell Lymphoma Among US Community Oncology Patients With Prior Bruton Tyrosine Kinase Inhibitor Therapy

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CONCLUSIONS

- In the US community setting, most patients with mantle cell lymphoma (MCL) treated with zanubrutinib who had prior ibrutinib or acalabrutinib treatment discontinued ibrutinib or acalabrutinib within 1 year
- Real-world data from across the US have demonstrated the effectiveness of zanubrutinib in MCL after treatment with another Bruton tyrosine kinase (BTK) inhibitor
- Most patients changed from ibrutinib and/or acalabrutinib to zanubrutinib due to adverse events

BACKGROUND

- MCL is a rare and aggressive type of non-Hodgkin lymphoma
- Zanubrutinib, a next-generation BTK inhibitor, was developed to maximize efficacy and tolerability in patients by minimizing off-target binding
- The US Food and Drug Administration (FDA) has approved the next-generation BTK inhibitor acalabrutinib as a single agent and in combination with bendamustine and rituximab, and zanubrutinib for treating relapsed/refractory MCL[1,2]
- Ibrutinib, a first-generation BTK inhibitor, was voluntarily withdrawn in April 2023[3]
- Here, we evaluate the characteristics, treatment duration, and reasons for treatment discontinuation in patients with MCL previously treated with ibrutinib or acalabrutinib who later received zanubrutinib in the real-world US oncology setting

METHODS

- This retrospective observational study included US adult patients with MCL who initiated acalabrutinib or ibrutinib at any time between December 1, 2013, and November 30, 2023, and subsequently received zanubrutinib at any time through May 31, 2024. The index date was the start date of zanubrutinib treatment
- The study utilized structured electronic health data from the Integra Connect PrecisionQ de-identified real-world database
- Descriptive statistics were summarized to describe demographic and treatment characteristics
- Reasons for discontinuation were manually abstracted from medical chart notes among a subgroup of study patients whose electronic health records could be accessed by data abstractors

RESULTS

Baseline Demographics and Clinical Characteristics

- Of 879 identified patients with ibrutinib exposure, 59 (6.7%) changed to zanubrutinib. Of the 417 identified patients with acalabrutinib exposure, 31 (7.4%) changed to zanubrutinib
- Overall, the study included 80 unique patients who changed to zanubrutinib, including 21 patients with prior acalabrutinib, 49 patients with prior ibrutinib, and 10 patients with both prior acalabrutinib and ibrutinib
- Baseline demographics are shown in **Table 1**. Notably, more males were included than females in each group, and most patients were White
- Baseline clinical characteristics are shown in **Table 2**
- Most patients with previous ibrutinib exposure received ibrutinib in the first (42.4%) or second (52.5%) line of therapy (LOT), whereas patients with prior acalabrutinib exposure were more evenly distributed among the first (38.7%), second (25.8%), and third (25.8%) LOT (**Figure 1**)

Table 1. Baseline Patient Demographics

	Ibrutinib → Zanubrutinib (n=49)	Acalabrutinib → Zanubrutinib only (n=21)	Ibrutinib → Acalabrutinib → Zanubrutinib (n=10)
Median age (range) at index date, years	76 (52, 88)	76 (65, 88)	71.5 (48, 86)
Gender, n (%)			
Female	15 (30.6)	7 (33.3)	2 (20.0)
Male	34 (69.4)	14 (66.7)	8 (80.0)
Race, n (%)			
White	38 (77.6)	13 (61.9)	8 (80.0)
African American	0	1 (4.8)	0
Asian	0	0	0
Not documented/ unknown/other	11 (22.4)	7 (33.3)	2 (20.0)
Ethnicity, n (%)			
Hispanic	2 (4.1)	1 (4.8)	0
Not Hispanic	38 (77.6)	16 (76.2)	10 (100.0)
Not documented/ other	9 (18.4)	4 (19.0)	0

Table 2. Baseline Clinical Characteristics

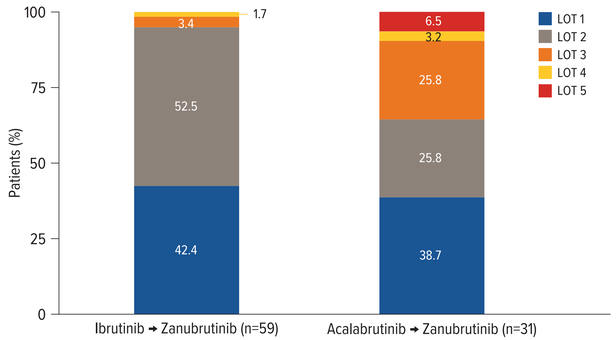
	Ibrutinib → Zanubrutinib (n=49)	Acalabrutinib → Zanubrutinib only (n=21)	Ibrutinib → Acalabrutinib → Zanubrutinib (n=10)
ECOG status at index, n (%)			
Patients with missing data	10 (20.4)	5 (23.8)	4 (40.0)
ECOG 0	15 (38.5)	3 (18.8)	0
ECOG 1	15 (38.5)	10 (62.5)	6 (100)
ECOG 2+	9 (23.1)	3 (18.8)	0
Time from diagnosis to BTK inhibitor initiation, n (%)			
<1 year	13 (26.5)	7 (33.3)	1 (10.0)
1 year	11 (22.4)	3 (14.3)	1 (10.0)
2 years	4 (8.2)	1 (4.8)	2 (20.0)
3 years	4 (8.2)	4 (19.0)	1 (10.0)
4 years	1 (2.0)	1 (4.8)	2 (20.0)
5+ years	16 (32.7)	5 (23.8)	3 (30.0)

ECOG, Eastern Cooperative Oncology Group.

Treatment Characteristics

- Most patients with previous ibrutinib exposure received ibrutinib in the first (42.4%) or second (52.5%) LOT, whereas patients with prior acalabrutinib exposure were more evenly distributed among the first (38.7%), second (25.8%), and third (25.8%) LOT (**Figure 1**)
- Overall, 71.0% of patients with prior ibrutinib and 90.4% with prior acalabrutinib initiated zanubrutinib as their subsequent therapy

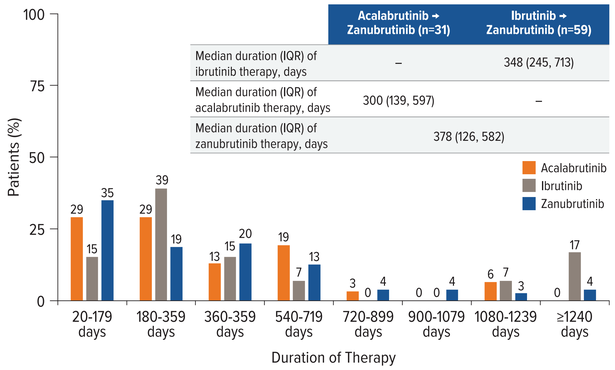
Figure 1. LOT Distribution of Patients Starting Ibrutinib or Acalabrutinib



10 patients are in both groups because they received both ibrutinib and acalabrutinib prior to zanubrutinib.

- The median duration of BTK inhibitor therapy is shown in **Figure 2**
  - Overall, 54% of patients with prior ibrutinib and 58% with prior acalabrutinib discontinued treatment within 1 year before initiation of zanubrutinib
  - The median (interquartile range [IQR]) duration of zanubrutinib treatment was 378 (126, 582) days, with 38 (47.5%) patients staying on zanubrutinib treatment at data cut off

Figure 2. Duration of BTK Inhibitor Therapy



- The majority of patients who discontinued other BTK inhibitors and changed to zanubrutinib did so due to adverse events (**Table 3**)

Table 3. Reasons For Discontinuation Among Patients Who Changed Directly From a BTK Inhibitor to Zanubrutinib

Reasons, n (%)	Ibrutinib → Zanubrutinib (n=24)	Acalabrutinib → Zanubrutinib only (n=13)	Ibrutinib → Acalabrutinib → Zanubrutinib (n=4)[a]
Adverse Events[b]	16 (66.7)	7 (53.9)	2 (50.0)
Progressive Disease	3 (12.5)	2 (15.4)	2 (50.0)
Others[c]	3 (12.5)	4 (30.8)	0
Unknown	**2 (8.3)**	**0**	**0**

Only curated data were considered for reasons for discontinuation. [a]Reasons for discontinuation of acalabrutinib reported. [b]Adverse events include toxicity, hospitalization, and worsening comorbidity. [c]Other includes patient lifestyle issues/convenience, financial/insurance, non-compliance, and other.

LIMITATIONS

- Structured data relies on medication order or prescription information and may be subject to misclassification of treatment start/end dates

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DISCLOSURES

RC: Consultant: IntegraConnect PrecisionQ; **GAM, XW, AL, RW:** Employment by BeOne Medicines and may hold stock or other ownership; **AR, BW, LM:** employment by IntegraConnect PrecisionQ; **J-Z H:** Consultant: AstraZeneca.

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