Real-World Bruton Tyrosine Kinase Inhibitor (BTKi) Treatment Patterns Among Patients with Chronic or Small Lymphocytic Leukemia (CLL/SLL) in US Community Oncology Practices

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Background: BTKis have become the standard-of-care therapies for both frontline (1L) and relapsed/refractory (2L) CLL/SLL, and recently the NCCN listed both second-generation BTKis, zanubrutinib and acalabrutinib, as preferred agents over the first-generation BTKi ibrutinib based on toxicity profile. The objective of this study was to assess real-world clinical characteristics, treatment patterns, and adverse events (AEs) among BTKi-treated patients with CLL/SLL.

Methods: This was a retrospective observational study of adult patients with CLL/SLL who initiated treatment between 01-Jan-2020 and 28-Feb-2023 in the community oncology setting across the US and were followed up through 31-May-2023. Included patients had to have at least 5 CLL/SLL visits or more CLL/SLL visits than non-CLL/SLL visits; all patients had to have 2 or more evaluation and management visits. The study included structured electronic health data from the Integra Connect-PrecisionQ de-identified real-world database. Descriptive analyses were conducted including all patients who received a BTKi, and a Kaplan-Meier analysis was performed for time-to-event outcomes.

Results: A total of 2650 patients who received a BTKi were included in the study (2465: BTKi 1L; 185: BTKi naïve in 1L with use of BTKi in subsequent lines). The median (range) age of patients in the 1L BTKi and BTKi-later line groups was 71 (35-89) and 74 (42-89) years, respectively, and most included patients were male (Table).

In 1L, 53.3% (n=1314/2465) were treated with ibrutinib, 43.3% (n=1068/2465) with acalabrutinib, and 3.4% (n=83/2465) with zanubrutinib. Among BTKi-later line patients, similar trends (45.9% [85/185] ibrutinib, 42.7% [79/185] acalabrutinib, 11.4% [21/185] zanubrutinib) were observed in 2L. The rates of cardiovascular AEs within the first 3 and 6 months of BTKi initiation were 10.1% (n=106/1048) and 13.4% (n=123/921) for patients treated with ibrutinib, 7.3% (n=56/767) and 9.8% (n=62/631) for acalabrutinib, and 7.3% (n=5/69) and 7.5% (n=3/40) for zanubrutinib, respectively.

More than 10% of ibrutinib-treated patients discontinued therapy and switched to a second-generation BTKi. The median time to treatment discontinuation (95% CI) in the 1L setting was 12.7 (11.7, 15.3) months for ibrutinib, 15.7 (12.0, 20.4) months for acalabrutinib, and 12.9 (10.3, NR) months for zanubrutinib. The proportion of patients continuing treatment at 6 and 12 months was higher with zanubrutinib (72.3% and 61.4%, respectively) compared to acalabrutinib (62.6% and 53.1%) and ibrutinib (62.3% and 51.9%). The median time to next treatment (TTNT) (95% CI) was not reached (NR) (12.6 months, NR) for those who received zanubrutinib in the 1L, while it was 31.3 (26.5, 35.5) months for ibrutinib and 35.8 (31.8, NR) months for acalabrutinib.

Conclusions: This study found that cardiovascular AEs at 6 months were higher among patients who received ibrutinib and acalabrutinib compared to zanubrutinib. While the study is limited by the smaller sample size and shorter follow-up period for the zanubrutinib group, the proportions of patients remaining on treatment were higher and the median TTNT was longer for patients who received zanubrutinib.

Table 1: Baseline Demographics and Clinical Characteristics of Patients Treated with BTKi			
	Ibrutinib (n=1314)	**Acalabrutinib (n=1068)**	**Zanubrutinib (n=83)**
Age			
Median (range), years	71 (35, 89)	72 (37, 89)	73 (40, 88)
Sex, n (%)			
Female	473 (36)	388 (36.3)	29 (34.9)
Male	834 (63.5)	665 (62.3)	53 (63.9)
Not documented/unknown/other	7 (0.5)	15 (1.4)	1 (1.2)
Race, n (%)			
White	797 (60.7)	676 (63.3)	53 (63.9)
African American	92 (7)	47 (4.4)	2 (2.4)
Asian	10 (0.8)	4 (0.4)	0 (0.0)
Not documented/unknown/other	415 (31.6)	341 (31.9)	28 (33.7)
Ethnicity, n (%)			
Hispanic	47 (3.6)	24 (2.2)	2 (2.4)
Not Hispanic	890 (67.7)	717 (67.1)	52 (62.7)
Not documented/other	377 (28.7)	327 (30.6)	29 (34.9)
Body mass index			
Patients with missing data, n (%)	185 (14.1)	155 (14.5)	10 (12)
Median (range), kg/m^2	28 (17, 63)	27 (15, 61)	27 (18, 63)
ECOG status at index, n (%)			
ECOG 0-1	798 (90.2)	639 (88.6)	52 (85.2)
ECOG 2+	87 (9.8)	82 (11.4)	9 (14.8)
Comorbidities, n (%)			
Chronic pulmonary disease	32 (2.4)	34 (3.2)	3 (3.6)
Diabetes without chronic complications	58 (4.4)	42 (3.9)	2 (2.4)
Diabetes with chronic complications	24 (1.8)	12 (1.1)	0 (0.0)
GERD	58 (4.4)	40 (3.7)	2 (2.4)
GI disease	103 (7.8)	86 (8.1)	5 (6)
Renal disease	51 (3.9)	54 (5.1)	0 (0.0)
Iron-deficient anemia	60 (4.6)	62 (5.8)	1 (1.2)
CV-related comorbidities, n (%)			
All CV comorbidities	211 (16.1)	178 (16.7)	10 (12)
Acute ischemic heart disease	2 (0.2)	1 (0.1)	0 (0.0)
Atrial fibrillation	42 (3.2)	37 (3.5)	3 (3.6)
Bleeding	1 (0.1)	3 (0.3)	0 (0.0)

Cardiac arrest	0 (0.0)	1 (0.1)	0 (0.0)
Cardiac arrhythmia	10 (0.8)	2 (0.2)	0 (0.0)
Cardiotoxicity	0 (0.0)	0 (0.0)	0 (0.0)
Hypertension	190 (14.5)	157 (14.7)	8 (9.6)
Myocardial infarction	7 (0.5)	10 (0.9)	0 (0.0)
Stroke	7 (0.5)	5 (0.5)	0 (0.0)
Ventricular tachyarrhythmia	3 (0.2)	1 (0.1)	0 (0.0)
Atrial flutter	7 (0.5)	8 (0.7)	0 (0.0)
Congestive heart failure	4 (0.3)	8 (0.7)	0 (0.0)
Ischemic stroke (cerebral infarction)	3 (0.2)	5 (0.5)	0 (0.0)
Left ventricular dysfunction	1 (0.1)	2 (0.2)	0 (0.0)
Ventricular tachycardia	0 (0.0)	1 (0.1)	0 (0.0)
Angina pectoris	4 (0.3)	0 (0.0)	0 (0.0)
Patients with at least 3 months of follow-up post BTKi initiation, n (%)*	1048 (79.7)	767 (71.8)	69 (83.1)
Patients with at least 6 months of follow-up post BTKi initiation, n (%)*	921 (70.1)	631 (59.1)	40 (48.1)
Duration of follow-up from BTKi initiation, months	19.1 (0.4, 41.5)	13.1 (0.1, 40.4)	7.4 (1.4, 26.6)
*Did not initiate another drug during this time period.			