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
- NCCN Guidelines list the second-generation BTKis zanubrutinib and acalabrutinib as preferred agents over the first-generation BTKi ibrutinib based on toxicity profile[1]
- In the phase 3 ELEVATE-RR trial among high-risk patients with relapsed/refractory CLL, acalabrutinib was non-inferior to ibrutinib in terms of progression free survival[2]
- The phase 3 ALPINE study in relapsed/refractory CLL/SLL demonstrated superior PFS for zanubrutinib relative to ibrutinib, and zanubrutinib was associated with fewer adverse effects leading to discontinuation, including fewer cardiac adverse events and lower rate of atrial fibrillation[3]
- We investigated the clinical characteristics, treatment patterns, and adverse events (AEs) among BTKi-treated patients with CLL/SLL in the real-world setting

METHODS

Data Source

- IntegraConnect-PrecisionQ database of de-identified electronic health records, practice management, and claims data from 55 practices and over 1600 providers from the community oncology setting across the US

Patient Population

- ≥18 years old with CLL/SLL who initiated treatment between 1/1/2020-02/28/2023 with follow-up through 5/31/2023
- Patients had to have at least five CLL/SLL visits or more CLL/SLL visits than non-CLL/SLL visits; all patients had to have two or more evaluation and management visits

Data Analysis

- Descriptive analyses were conducted including all patients who received a BTKi
- Kaplan-Meier analysis was performed for time-to-event outcomes

Outcomes

- Demographics and baseline characteristics
- Cardiac AEs
- Time to next treatment (TTNT): the time from line of therapy (LOT) initiation to initiation of next LOT or death
- Time to treatment discontinuation or death (TTD): the time between treatment initiation and treatment discontinuation or death

RESULTS

Patient Demographics and Baseline Characteristics

Figure 1. Patient Disposition of CLL/SLL Patients Initiated On Treatment Identified During the Study Identification Period

1L, first line; BTKi, Bruton tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; SLL, small lymphocytic lymphoma.

Table 1. Demographics and Baseline Characteristics for 1L BTKi Patients

	Ibrutinib (n=1314)	Acalabrutinib (n=1068)	Zanubrutinib (n=83)
Age, median (range)	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)
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)

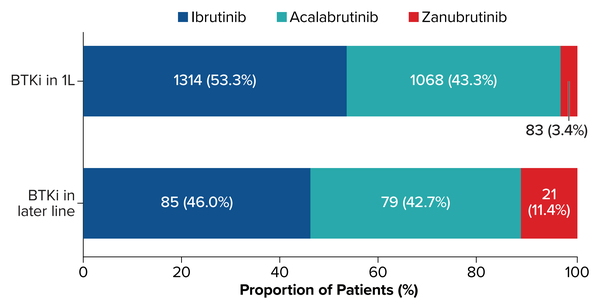
ECOG, Eastern Cooperative Oncology Group.

Table 1. Demographics and Baseline Characteristics for 1L BTKi Patients (continued)

	Ibrutinib (n=1314)	Acalabrutinib (n=1068)	Zanubrutinib (n=83)
Number of patients with follow-up post BTKi initiation*, n (%)			
3 months	1048 (79.7)	767 (71.8)	69 (83.1)
6 months	921 (70.1)	631 (59.1)	40 (48.1)
Duration of follow-up, months (95% CI)	19.1 (0.4, 41.5)	13.1 (0.1, 40.4)	7.4 (1.4, 26.6)
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)

BTKi, Bruton tyrosine kinase inhibitor; CV, cardiovascular; GERD, gastroesophageal reflux disease; GI, gastrointestinal.
*Did not initiate another drug during this time period.

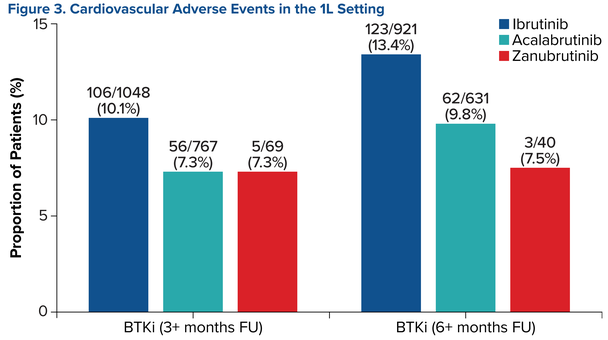
Figure 2. BTKi Utilization



1L, first line; BTKi, Bruton tyrosine kinase inhibitor.

- In 1L, 53.3% were treated with ibrutinib, 43.3% with acalabrutinib, and 3.4% with zanubrutinib. In later lines, somewhat similar trends were observed (ibrutinib 45.9%, acalabrutininb 42.7%, and zanubrutinib 11.4%). However, the proportion of patients using zanubrutinib was greater in subsequent lines than in 1L.

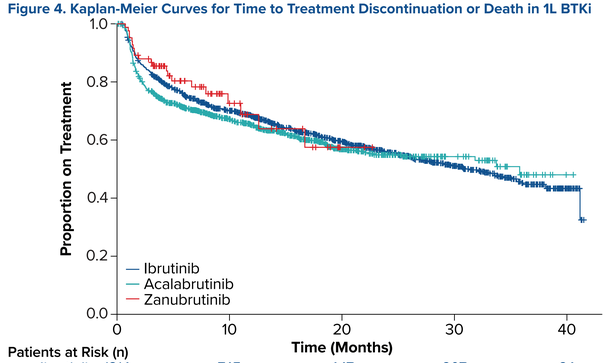
Figure 3. Cardiovascular Adverse Events in the 1L Setting



1L, first line; BTKi, Bruton tyrosine kinase inhibitor; FU, follow-up.

- Of patients with 3+ months of follow-up post BTKi initiation, the rate of cardiac AEs was highest in patients who initiated ibrutinib (10.1%), followed by acalabrutinib and zanubrutinib (both 7.3%)
- Differences between groups were more apparent for patients with 6+ months of follow-up
- More than 10% of ibrutinib-treated patients discontinued therapy and switched to a second-generation BTKi
- The proportion of patients who switched was similar among 1L ibrutinib patients who developed a cardiac AE (11.7%)

Figure 4. Kaplan-Meier Curves for Time to Treatment Discontinuation or Death in 1L BTKi



Patients at Risk (n)

Ibrutinib	1314	745	447	207	24
Acalabrutinib	1068	459	180	46	1
Zanubrutinib	83	22	2	0	

	Overall (N=2465)	Ibrutinib (n=1314)	Acalabrutinib (n=1068)	Zanubrutinib (n=83)
Discontinued/death n (%)	1266 (51.4)	738 (56.2)	501 (46.9)	27 (32.5)
Censored, n (%)	1199 (48.6)	576 (43.8)	567 (53.1)	56 (67.5)
TTD, median (95% CI), months	13.4 (12.1, 16.2)	12.7 (11.7, 15.3)	15.7 (12.0, 20.4)	12.9 (10.3, NR)
Treatment probability, % (95% CI)				
6 months	62.6 (60.7, 64.5)	62.3 (59.6, 64.8)	62.6 (59.6, 65.5)	72.3 (60.9, 80.9)
12 months	52.7 (50.6, 54.8)	51.9 (49.0, 54.7)	53.1 (49.8, 56.3)	61.4 (45.4, 74.1)
18 months	46.6 (44.3, 48.8)	45.3 (42.3, 48.2)	48.0 (44.4, 51.5)	49.2 (29.3, 66.3)
24 months	40.7 (38.2, 43.1)	38.9 (35.8, 42.0)	43.3 (39.3, 47.3)	–
30 months	36.6 (34.0, 39.3)	34.5 (31.3, 37.7)	41.4 (37.0, 45.8)	–
36 months	33.7 (30.7, 36.7)	31.8 (28.4, 35.3)	36.7 (29.0, 44.4)	–

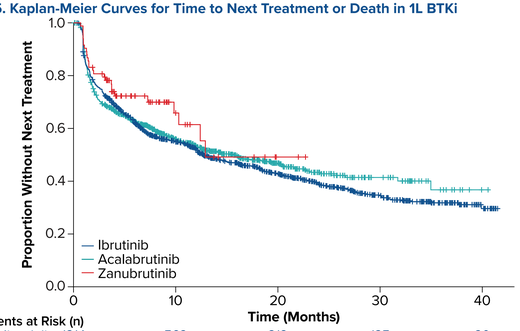
CI, confidence interval; NR, not reached; TTD, time to treatment discontinuation or death.

CONCLUSIONS

- This study found that cardiovascular AEs at 6 months were higher among patients who received ibrutinib and acalabrutinib as compared with zanubrutinib
- The proportions of patients remaining on treatment were higher and the median TTNT was longer for patients who received zanubrutinib

- The median TTD (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%)

Figure 5. Kaplan-Meier Curves for Time to Next Treatment or Death in 1L BTKi



Patients at Risk (n)

Ibrutinib	1314	562	312	135	20
Acalabrutinib	1068	364	141	36	1
Zanubrutinib	83	16	2	0	

	Overall (N=2465)	Ibrutinib (n=1314)	Acalabrutinib (n=1068)	Zanubrutinib (n=83)
NT/death, n (%)	962 (39.0)	546 (41.6)	395 (37.0)	21 (25.3)
Censored, n (%)	1503 (61.0)	768 (58.4)	673 (63.0)	62 (74.7)
TTNT, median (95% CI), months	31.8 (27.9, 35.5)	31.3 (26.5, 35.5)	35.8 (31.8, NR)	NR (12.6, NR)
No next treatment probability, % (95% CI)				
6 months	73.8 (71.9, 75.5)	75.5 (73.1, 77.7)	71.1 (68.3, 73.8)	80.3 (69.3, 87.8)
12 months	66.9 (64.9, 68.8)	68.1 (65.4, 70.7)	65.1 (62.0, 68.1)	68.8 (53.3, 80.1)
18 months	60.5 (58.3, 62.6)	61.5 (58.6, 64.3)	59.3 (55.8, 62.6)	57.5 (37.4, 73.3)
24 months	55.1 (52.7, 57.5)	55.7 (52.6, 58.8)	54.9 (50.9, 58.7)	–
30 months	51.3 (48.6, 54.0)	51.1 (47.7, 54.4)	54.3 (50.2, 58.2)	–
36 months	45.4 (42.0, 48.8)	45.2 (41.2, 49.2)	48.0 (40.0, 55.6)	–

CI, confidence interval; NR, not reached; NT, next treatment; TTNT, time to next treatment.

- The median time to next treatment (TTNT) (95% CI) was not reached (12.6, 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

LIMITATIONS

- In this study, patients receiving ibrutinib had a longer follow-up period opportunity vs acalabrutinib and zanubrutinib. Given the January 19, 2023 FDA approval of zanubrutinib CLL, the sample size for zanubrutinib in this study was smaller than ibrutinib and acalabrutinib with limited follow-up duration

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