Real-World Bruton Tyrosine Kinase Inhibitor Utilization and Clinical Outcomes among Patients with Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

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INTRODUCTION

- Bruton tyrosine kinase inhibitors (BTKis) are standard-of-care therapies for chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) in both the frontline and relapsed/refractory settings[1]
- The National Comprehensive Cancer Network has listed the second-generation BTKi acalabrutinib and next-generation zanubrutinib as preferred agents over the first-generation BTKi ibrutinib based on toxicity profiles[1]
- The aim of this study was to describe the characteristics and outcomes of patients with CLL/SLL treated with BTKis in the first-line setting in community oncology practices

METHODS

- US adult patients diagnosed with CLL/SLL who initiated treatment between January 1, 2020 and November 30, 2023 were identified using the Integra Connect PrecisionQ de-identified real-world database. Patients were followed until May 30, 2024
- This matched cohort study used structured and curated data in which patients who initiated zanubrutinib were matched at a 1:2 ratio based on age and sex with patients who initiated acalabrutinib
- Time to Discontinuation (TTD):
  - The index date was the initiation of BTKi in first line (1L)
  - The event date was the date of discontinuing BTKi or death
  - The censor date was last contact date or study end date, whichever occurred first
- Time to Next Treatment (TTNT):
  - The index date was the initiation of BTKi in 1L
  - The event date was the date of starting a second line of treatment or death
  - The censor date was last contact date or study end date, whichever occurred first
- Overall survival (OS) used the same index and censoring date, and the event date was the date of death
- TTD, TTNT, and OS were analyzed using Kaplan-Meier (KM) method adjusted for matched-set analyses
- Cox proportional hazards regression was used to obtain hazard ratios (HRs) and 95% confidence intervals (CIs). Matched-set (age and sex) adjusted HRs and 95% CIs were also reported

RESULTS

Baseline Demographics

- A total of 414 patients were included in the study, including 138 zanubrutinib patients matched with 276 acalabrutinib patients. Baseline demographics are shown in **Table 1**
- The median duration of follow-up was 12.7 (range 1.7, 53.0) months for all patients. The median duration of follow-up was 15.3 (1.7, 53.0) months for the acalabrutinib group and 10.9 (2.3, 32.2) months for the zanubrutinib group
- The median age for both groups was 76 (range 45, 89) years, and in both groups, 37.7% were female
- Baseline Eastern Cooperative Oncology Group (ECOG) status was similar between groups, with 63.4% of patients in the acalabrutinib group and 74.6% of patients in the zanubrutinib group having an ECOG status of 0 or 1 at index

Comorbidities at Baseline

- Cytopenias were the most frequent noncardiac comorbidities in both groups at baseline. Anemia was recorded for 38.0% and 44.9% of the acalabrutinib and zanubrutinib groups, respectively; thrombocytopenia was noted in 27.9% and 29 .0%, respectively; and neutropenia was noted in 9.4% and 10.1%, respectively (**Table 2**)
- Overall, 11.2% of patients in the acalabrutinib group and 14.5% of patients in the zanubrutinib group had a preexisting cardiac comorbidity. The most common baseline cardiac comorbidity in both groups was hypertension (**Table 2**)

Table 1. Baseline Patient Demographics

	Acalabrutinib (n=276)	Zanubrutinib (n=138)
Age at First-Line BTKi Initiation		
Median (range), y	76 (45, 89)	76 (45, 89)
Sex (n, %)		
Female	104 (37.7)	52 (37.7)
Male	172 (62.3)	86 (62.3)
Race (n, %)		
White	224 (81.2)	116 (84.1)
African American	14 (5.1)	8 (5.8)
Asian	2 (0.7)	0 (0.0)
Not documented/unknown/other	36 (13.0)	14 (10.1)
Ethnicity (n, %)		
Hispanic	5 (1.8)	3 (2.2)
Not Hispanic	186 (67.4)	92 (66.7)
Not documented/other	85 (30.8)	43 (31.2)
ECOG status at index (n, %)		
No. of patients with missing data (n, %)	82 (29.7)	23 (16.7)
ECOG 0	94 (34.1)	55 (39.9)
ECOG 1	81 (29.3)	48 (34.8)
ECOG 2+	19 (6.9)	12 (8.7)

BTKi, Bruton tyrosine kinase inhibitors; ECOG, Eastern Cooperative Oncology Group.

Table 2. Baseline Patient Comorbidities

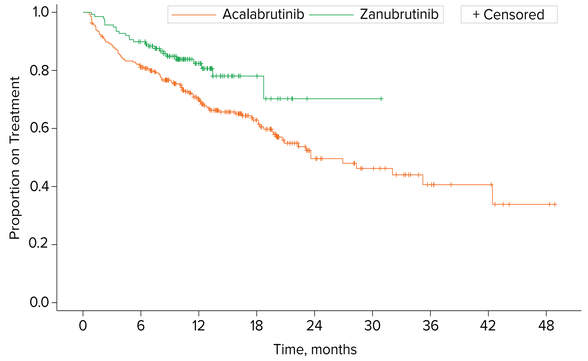
	Acalabrutinib (n=276)	Zanubrutinib (n=138)
Comorbidities (n, %)		
Anemia	105 (38.0)	62 (44.9)
Thrombocytopenia	77 (27.9)	40 (29)
Neutropenia	26 (9.4)	14 (10.1)
Renal disease	15 (5.4)	6 (4.3)
GI disease	9 (3.3)	5 (3.6)
Chronic pulmonary disease	6 (2.2)	2 (1.4)
Diabetes	6 (2.2)	7 (5.1)
GERD	2 (0.7)	4 (2.9)
Leukopenia	2 (0.7)	1 (0.7)
Cardiac comorbidities[a], (n, %)		
Any cardiac comorbidities	31 (11.2)	20 (14.5)
Hypertension	26 (9.4)	15 (10.9)
Atrial fibrillation	6 (2.2)	4 (2.9)
Congestive heart failure	1 (0.4)	3 (2.2)
Cardiotoxicity	1 (0.4)	0 (0.0)
Myocardial infarction	1 (0.4)	0 (0.0)
Cardiac arrhythmia	0 (0.0)	2 (1.4)
Left ventricular dysfunction	0 (0.0)	0 (0.0)

[a] 1-year baseline period.
GERD, gastroesophageal reflux disease.

TTD or Death

- The probability of remaining on treatment at 6 months and 12 months was higher for patients receiving zanubrutinib than for those receiving acalabrutinib (**Figure 1**)
  - 6 months: 80.7% (95% CI 75.5%, 84.9%) for acalabrutinib and 89.8% (95% CI 83.5%, 93.9%) for zanubrutinib; unadjusted HR (95% CI): 0.56 (0.31, 1.01), *P*=.05; adjusted HR (95% CI): 0.55 (0.30, 1.01), *P*=.06
  - 12 months: 68.8% (95% CI 62.6%, 74.2%) for acalabrutinib and 81.2% (95% CI 72.7%, 87.2%) for zanubrutinib; unadjusted HR (95% CI): 0.56 (0.35, 0.89), *P*<.05; adjusted HR (95% CI): 0.55 (0.34, 0.90), *P*<.05

Figure 1. Time to Discontinuation or Death



Acalabrutinib	276	216	142	81	35	24	11	7	2
Zanubrutinib	138	122	53	12	1	1	0		

Ongoing Treatment Probability (%, 95% CI)

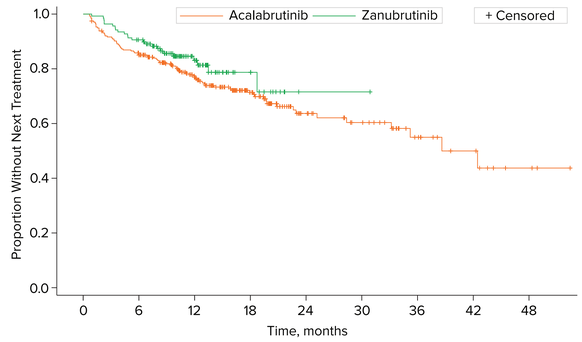
Acalabrutinib	80.7 (75.5, 84.9)	68.8 (62.6, 74.2)	62.9 (56.2, 68.9)	49.4 (40.7, 57.5)	46.0 (36.8, 54.7)	40.1 (28.9, 51)	40.1 (28.9, 51)
Zanubrutinib	89.8 (83.5, 93.9)	81.2 (72.7, 87.2)	78.3 (67.8, 85.7)	70.4 (50.3, 83.6)	—	—	—

CI, confidence interval.

TTNT or Death

- The probability of not receiving a subsequent treatment was numerically but not statistically significantly higher in the zanubrutinib group compared to the acalabrutinib group at both 6 and 12 months (**Figure 2**)
  - 6 months: 85.0% (95% CI 80.2%, 88.8%) for acalabrutinib and 90.1% (95% CI 83.9%, 94.1%) for zanubrutinib; unadjusted HR (95% CI): 0.74 (0.40, 1.36), *P*=.33; adjusted HR (95% CI): 0.68 (0.36, 1.33), *P*=.29
  - 12 months: 76.8% (95% CI 71.1%, 81.5%) for acalabrutinib and 82.0% (95% CI 73.5%, 87.9%) for zanubrutinib; unadjusted HR (95% CI): 0.74 (0.45, 1.21), *P*=.23; adjusted HR (95% CI): 0.68 (0.43, 1.19), *P*=.20

Figure 2. Time To Next Treatment or Death



Acalabrutinib	276	229	159	95	45	33	16	9	3
Zanubrutinib	138	123	55	13	1	1	0		

Probability Without Next Treatment (%, 95% CI)

Acalabrutinib	85 (80.2, 88.8)	76.8 (71.1, 81.5)	71.2 (64.8, 76.6)	63.5 (55.6, 70.3)	60.3 (51.6, 67.9)	54.6 (43.4, 64.6)	49.7 (35.7, 62.2)
Zanubrutinib	90.1 (83.9, 94.1)	82.0 (73.5, 87.9)	79.0 (68.4, 86.4)	71.8 (52.8, 84.3)	—	—	—

CI, confidence interval.

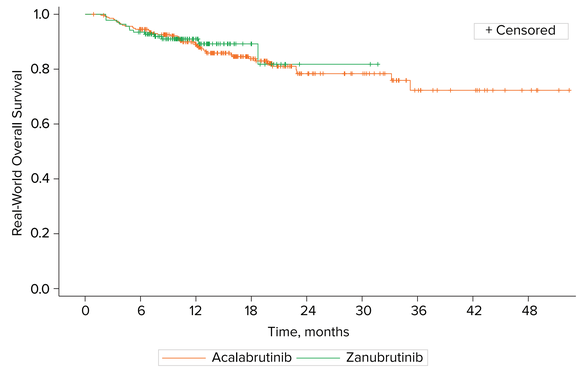
CONCLUSIONS

- This study describes the baseline demographic and clinical characteristics and outcomes of patients with CLL/SLL treated with BTKis in the first-line setting
- While zanubrutinib had shorter follow-up, patients were more likely to remain on first-line treatment at 6 and 12 months in the zanubrutinib group compared to patients in the acalabrutinib group
- Additionally, patients in the zanubrutinib group were less likely to require a subsequent treatment at 6 and 12 months compared to patients in the acalabrutinib group
- Further data curation and additional analyses are pending to understand the observed differences among BTKi utilization and outcomes in these patients with CLL/SLL

OS

- Median overall survival was not reached in either the acalabrutinib or zanubrutinib group (unadjusted HR [95% CI]: 0.89 [0.48, 1.65], *P*=.72; adjusted HR [95% CI]: 0.87 [0.58, 2.29], *P*=.68) (**Figure 3**)

Figure 3. Overall Survival



Acalabrutinib	276	252	183	106	53	40	19	13	5
Zanubrutinib	138	127	58	14	2	2	0		

LIMITATIONS

- This study is subject to the inherent limitation of a retrospective observational real-world database
- Zanubrutinib had shorter follow-up

REFERENCE

1. NCCN. Chronic lymphocytic leukemia/small lymphocytic leukemia. Version 1.2025. Published October 1, 2024.

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