Comparing Real-World Treatment Patterns and Outcomes of Zanubrutinib and Acalabrutinib in Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma at University of California Academic Health Centers

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CONCLUSIONS

- In this real-world (RW) study comparing treatment outcomes of zanubrutinib and acalabrutinib in patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), zanubrutinib was associated with a lower discontinuation risk than acalabrutinib
- Poorer clinical outcomes were linked to older age, minority race/ethnicity, more comorbidities, and lower socioeconomic status
- Further studies investigating the underlying cause of these differences are needed

INTRODUCTION

- The introduction of innovative therapeutic classes, such as Bruton tyrosine kinase (BTK) inhibitors, has led to a notable improvement in the outlook for patients with CLL/SLL[1-4]
- Randomized controlled trials have also demonstrated that newer BTK inhibitors, including zanubrutinib and acalabrutinib, offer more favorable toxicity profiles over first-generation ibrutinib for the treatment of CLL/SLL, making them the preferred choice[2,5,6]
- However, both clinical trial and RW evidence for treatment patterns and outcomes of zanubrutinib and acalabrutinib remains limited

Aim

- This study was conducted to compare treatment patterns and outcomes of zanubrutinib and acalabrutinib, as well as examine health disparities, in diverse RW populations to provide critical insights and inform clinical practice
- The study also sought to determine whether specific variables significantly influence the risk of treatment discontinuation across the patient population, helping to understand how individual predictors affect treatment outcomes

METHODS

Data Source and Study Population

- This multi-center, RW, retrospective cohort study included patients ≥18 years of age with CLL/SLL receiving zanubrutinib or acalabrutinib between January 1, 2021, and September 30, 2024, at one of six sites within the University of California Health system
- Patients were required to have at least one subsequent visit after the index date, considered the first date of treatment initiation with zanubrutinib or acalabrutinib as monotherapy, and before the end of the study period. Visits were defined as physical encounters with University of California Health, detected by vital signs records, treatment administration, or lab tests
- Patients were excluded from the study if they had received <3 months of follow-up after starting zanubrutinib or acalabrutinib (except for cases where patients died), were receiving zanubrutinib or acalabrutinib as part of a combination therapy, or if they participated in an interventional clinical trial after the index date

Study Design

- RW treatment patterns and outcomes, including time to discontinuation (TTD), time to next treatment (TTNT), and overall survival (OS), were evaluated using a multivariate Cox hazards model with inverse probability of treatment weighting for balancing covariates between groups. Covariates included age, sex, Charlson Comorbidity Index (CCI) groups (0, 1, 2, 3, 4+), line of therapy (LOT; 1 vs 2+), race, and area deprivation index (ADI)
- Study endpoints included unadjusted and adjusted hazard ratios (HRs) for TTD, TTNT, and OS

RESULTS

Patient Characteristics

- The study population comprised 505 patients with CLL/SLL, with an average age of 73 years (**Table 1**)
  - In total, 205 patients received zanubrutinib and 300 received acalabrutinib, with median follow-up times of 16.1 and 26.0 months, respectively
- Most patients were male (63%), and the largest ethnic group was White (76%), followed by Hispanic or Latino (4%), Asian (4%), and Black or African American (3%). Demographics and characteristics were mostly similar between the zanubrutinib and acalabrutinib groups. The median ADI was 3.0 (interquartile range [IQR]: 1-5) and was consistent across both treatment groups. Patients who received acalabrutinib had a numerically higher CCI score of 2.0 (IQR: 0-3) compared with 1.0 for patients who received zanubrutinib (IQR: 0-3)
- The majority of patients had not previously received a BTK inhibitor (68%), with a lower percentage of patients in the zanubrutinib group being BTK inhibitor naïve (65%) versus those who received acalabrutinib (70%)

Table 1. Demographic and Clinical Characteristics Among Patients With CLL/SLL

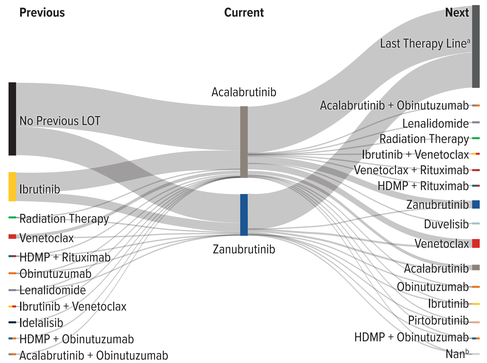
	Overall (N=505)	Zanubrutinib (n=205)	Acalabrutinib (n=300)	*P*-value[a]
Age, mean (SD)	72.7 (9.6)	73.3 (8.7)	72.4 (10.1)	.283
Gender, n (%)				1.000
Female	185 (36.6)	75 (36.6)	110 (36.7)	
Male	320 (63.4)	130 (63.4)	190 (63.3)	
Race, n (%)				.769
White	386 (76.4)	156 (76.1)	230 (76.7)	
Asian	19 (3.8)	<10 (4.9)[b]	13 (4.3)	
Black or African American	13 (2.6)	<10 (4.9)[b]	<10 (3.3)[b]	
Hispanic or Latino	22 (4.4)	10 (4.9)	12 (4.0)	
Other/Unknown	65 (12.9)	26 (12.7)	39 (13.0)	
ADI, median [IQR]	3.0 [1.0, 5.0]	3.0 [1.0, 5.0]	3.0 [1.0, 5.0]	.751
Missing, n	18			
CCI, median [IQR]	1.0 [0.0, 3.0]	1.0 [0.0, 3.0]	2.0 [0.0, 3.0]	.097
BTK inhibitor naïve, n (%)				.232
Naïve	344 (68.1)	133 (64.9)	211 (70.3)	
Not naïve	161 (31.9)	72 (35.1)	89 (29.7)	
Anti-HTN, n (%)	313 (62.0)	125 (61.0)	188 (62.7)	.771
Anticoagulant, n (%)	131 (25.9)	51 (24.9)	80 (26.7)	.729
Antiplatelet, n (%)	20 (4.0)	<10 (4.9)[b]	15 (5.0)	.224
LOT group, n (%)				.734
1	294 (58.2)	117 (57.1)	177 (59.0)	
2+	211 (41.8)	88 (42.9)	123 (41.0)	

[a]*P*-values from the comparisons between the zanubrutinib and acalabrutinib groups were calculated using Student's t-test for normally distributed continuous variables, the Mann–Whitney U test for non-normal continuous variables, and the Fisher's exact test for categorical variables. [b]The number of patients was fewer than 10. The exact number cannot be disclosed due to de-identification requirements to protect individual privacy.
HTN, hypertensive medications; SD, standard deviation.

Treatment Patterns

- The treatment transition patterns among patients receiving zanubrutinib or acalabrutinib are illustrated in **Figure 1**. Among patients who had a previous LOT, ibrutinib was the most common, while the subsequent therapy for those who advanced to the next treatment mostly consisted of venetoclax

Figure 1. Sankey Diagram of Therapy Line Transitions



[a]Patients who received zanubrutinib or acalabrutinib as their last therapy and did not have a next LOT. [b]Patients who received none of the therapies listed.
HDMP, high-dose methylprednisolone.

Comparative Survival Analysis

- The 12-month landmark TTD, TTNT, and OS rates were 73% (95% confidence interval [CI]: 65-79), 84% (77-88), and 92% (87-95) for zanubrutinib, and 57% (51-63), 80% (75-84), and 94% (90-96) for acalabrutinib, respectively (**Figure 2**)
- The median TTD was 14.8 (12.5-23.4) months for acalabrutinib and 30.1 (26.9-not estimable) months for zanubrutinib, while median TTNT and OS were not reached for both treatment groups
- Unadjusted Cox regression analyses indicated that zanubrutinib was associated with longer TTD than acalabrutinib (**Table 2**), which was also confirmed in adjusted analyses HR [95% CI]: 0.57 [0.44-0.74]). Unadjusted and adjusted TTNT and OS were not significantly different with either treatment

Table 2. Unadjusted and Adjusted Cox HRs for Zanubrutinib vs Acalabrutinib (TTD, TTNT, and OS)

	Zanubrutinib vs Acalabrutinib
Unadjusted Cox HR [95% CI]	
TTD	0.58 [0.43-0.78]
TTNT	0.80 [0.56-1.14]
OS	1.08 [0.59-1.95]
Adjusted Cox HR [95% CI]	
TTD	0.57 [0.44-0.74]
TTNT	0.81 [0.60-1.09]
OS	1.08 [0.65-1.78]

- Across the total patient population, multivariate regression modeling showed that Black or African American patients and Hispanic or Latino patients were associated with shorter TTD (HR [95% CI]: 2.65 [1.63-4.29], 1.81 [1.12-2.90]). Conversely, patients who received zanubrutinib (0.57 [0.44-0.74]) or had an index year of 2023 or later (0.66 [0.50-0.87]) had longer TTD (**Figure 3A**)
- Multivariate regression modeling similarly demonstrated that Black or African American patients were associated with shorter TTNT (2.46 [1.41-4.29]), in addition to LOT 2+ (1.60 [1.11-2.32]). Only government insurance was associated with longer TTNT (0.71 [0.55-0.91]) (**Figure 3B**)
- A higher ADI (1.12 [1.03-1.22]), advanced age (1.07 [1.04-1.10]), and a higher CCI score (1.09 [1.03-1.16]) were associated with shorter OS by the multivariate regression model analyses (**Figure 3C**)

Figure 2. Kaplan–Meier Curves for A) TTD, B) TTNT, and C) OS With Zanubrutinib vs Acalabrutinib

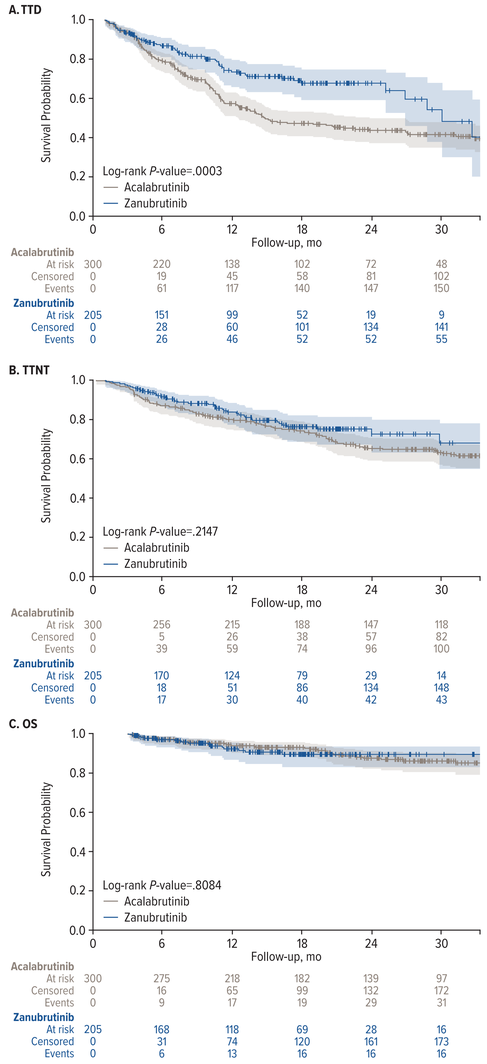
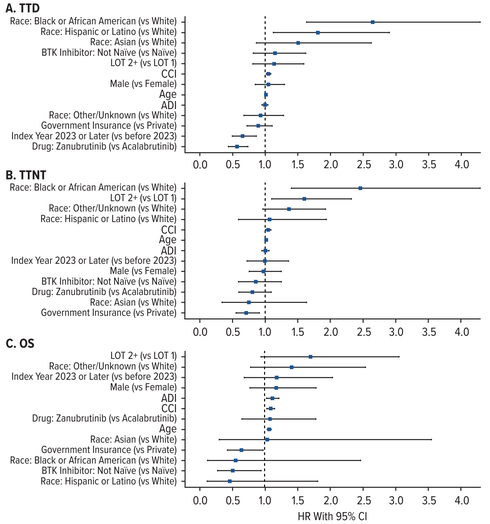


Figure 3. Multivariate Cox Regression Model Analyses for A) TTD, B) TTNT, and C) OS



For numeric variables (CCI, age, and ADI), HRs were reported for each increase of one unit of value.

DISCUSSION

- The results of this study suggested that clinical outcomes differed among patients with CLL/SLL receiving BTK inhibitors and were associated with race/ethnicity, age, and socioeconomic status
- These findings emphasize the need for further investigation into the underlying causes of these differences and the reasons for treatment discontinuation in patients receiving zanubrutinib versus acalabrutinib to guide clinical decisions and optimize CLL/SLL treatment strategies in diverse RW settings

Study limitations

- The limited sample size for some of the race/ethnicity subgroups may have reduced the ability to assess differences in treatment outcomes
- There is also potential for inconsistent data collection for patients accessing care outside of the University of California Health system sites
- General limitations with RW studies include their observational nature, leading to an inability to establish causal relationships between interventions and outcomes

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DISCLOSURES

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