Real-World Zanubrutinib Treatment Patterns in Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Among US Community Oncology Patients With Prior Acalabrutinib Therapy

PF618

Jing-Zhou Hou,[1] Rushir Choksi,[1] Gregory A. Maglinte,[2] Xiaoliang Wang,[2] Anna Rui,[3] Manasi Suryavanshi,[2] Beverly Chigarira,[3] Lindsay Aton,[3] Melissa Hagan,[2] Lisa Morere,[3] Rhys Williams,[2] Daniel A. Ermann[4]

[1]University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [2]BeOne Medicines Ltd, San Carlos, CA, USA; [3]IntegraConnect PrecisionQ, West Palm Beach, FL, USA; [4]University of Utah Huntsman Cancer Institute, Salt Lake City, UT, USA

CONCLUSIONS

- In US community oncology practices, most patients with CLL/SLL who switched from acalabrutinib to zanubrutinib did so within 1 year of initiating acalabrutinib, primarily due to toxicity
- For patients who switched to zanubrutinib, treatment duration was longer, and many remained on therapy through the end of follow-up
- Consistent with previous research, these real-world data from across the US demonstrate that zanubrutinib was well tolerated in patients with CLL who had received a prior Bruton tyrosine kinase inhibitor
- Overall, these outcomes suggest that zanubrutinib may be a valuable treatment option for patients with CLL/SLL who were previously treated with acalabrutinib

INTRODUCTION

- Bruton tyrosine kinase (BTK) inhibitors have demonstrated clinical efficacy in treating chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL).[1,2] Zanubrutinib is a highly specific and potent next-generation BTK inhibitor designed to maximize BTK occupancy and limit off-target kinase binding[3]
- Recent clinical data suggest that patients with CLL who were intolerant of ibrutinib or acalabrutinib and switched to zanubrutinib experienced continued or improved clinical benefit[4]
- Additionally, most of the intolerance adverse events with ibrutinib and acalabrutinib did not recur during zanubrutinib treatment[4]
- This study aimed to evaluate real-world characteristics, treatment duration, and reasons for treatment discontinuation in patients with CLL/SLL previously treated with acalabrutinib who later received zanubrutinib in United States (US) community oncology practices

METHODS

Data Source and Study Design

- This retrospective observational study included US adult patients with CLL/SLL who initiated acalabrutinib in any line of therapy (LOT) at any time between November 21, 2019, and November 30, 2024, and subsequently received zanubrutinib at any time through February 28, 2025. The index date was the start date of acalabrutinib therapy
- The study utilized structured electronic health data from the Integra Connect PrecisionQ de-identified real-world database, which contains electronic health records (EHRs) from >3 million de-identified cancer patients across >500 care sites
- Demographic and treatment characteristics were summarized using descriptive statistics
- The primary clinical outcomes of interest were treatment sequences, discontinuation rates, and reasons for discontinuation. A Sankey diagram was used to show BTK inhibitor treatment sequence. The Kaplan–Meier method was used to describe zanubrutinib time to treatment discontinuation or death
- The start of the BTK inhibitor sequence (Btx1) was defined as the first drug episode or prescription on the start date. The Btx was defined as any systemic therapy from the start of, and up to 60 days of, acalabrutinib mono- or combination therapy. Advancement to a new Btx sequence was based on the initiation of a new drug >60 days after initiation of a Btx, disease progression, or a treatment gap of ≥120 days. Switches from a covalent BTK inhibitor to another covalent BTK inhibitor within 60 days were not considered a treatment change and did not advance to a new Btx, even if due to disease progression

RESULTS

Baseline Demographics and Clinical Characteristics

- The baseline demographics and clinical characteristics of the 121 patients with CLL/SLL who initiated acalabrutinib and subsequently received zanubrutinib are shown in **Table 1**

Table 1. Baseline Demographic and Clinical Characteristics

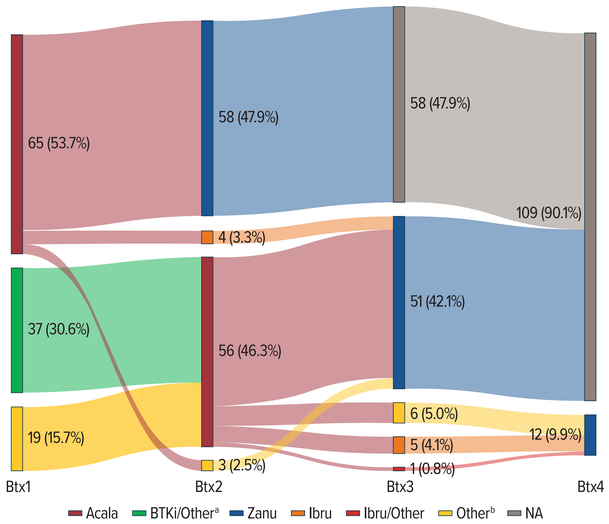
	Patients with CLL/SLL (N=121)
Median age (IQR) at index date, years	65 (59, 72)
Sex, n (%)	
Female	64 (52.9)
Male	57 (47.1)
Race, n (%)	
White	101 (83.9)
African American	5 (4.1)
Not documented/unknown/other	15 (12.4)
Ethnicity, n (%)	
Hispanic	1 (0.8)
Not Hispanic	93 (76.9)
Not documented/other	27 (22.3)
ECOG performance status at index date, n (%)	
No. of patients with missing data	38 (31.4)
0	45 (54.2)
1	34 (41.0)
2+	4 (4.8)
Time from diagnosis to acalabrutinib (years), n (%)	
0 to <1	24 (19.8)
1 to <2	9 (7.4)
2 to <3	15 (12.4)
3 to <4	8 (6.6)
4 to <5	5 (4.1)
5+	60 (49.6)

CLL, chronic lymphocytic leukemia; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; SLL, small lymphocytic lymphoma.

Treatment Patterns and Sequencing

- In most patients, acalabrutinib was initiated as first BTK inhibitor therapy (n=84, 69.4%) and the majority of patients received acalabrutinib as monotherapy (n=111, 91.7%)
- Of the 102 patients who switched directly from acalabrutinib to zanubrutinib, 74 (72.6%) received acalabrutinib as the first BTK inhibitor therapy after the start date and 28 (27.5%) received acalabrutinib as the second BTK inhibitor therapy or later
- After discontinuing acalabrutinib, 102/121 (84.3%) of patients switched directly to zanubrutinib, while the remaining 19/121 (15.7%) switched to one or more other systemic therapies before initiating zanubrutinib (**Figure 1**)
- The median duration of acalabrutinib therapy prior to zanubrutinib treatment was 5.6 months (interquartile range [IQR]: 2.1, 16.5). The median duration of zanubrutinib therapy after having received acalabrutinib was 10.7 months (IQR: 4.1, 18.8)

Figure 1. BTK Inhibitor Treatment Sequence



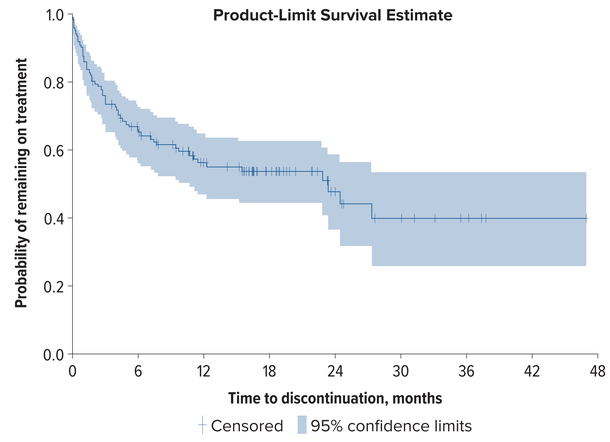
[a]35/37 patients received ibrutinib monotherapy or combination therapy.

[b]The other therapies included rituximab, bendamustine and rituximab, venetoclax, cyclophosphamide, cyclophosphamide and rituximab, or obinutuzumab.

Acala, acalabrutinib; BTK, Bruton tyrosine kinase; BTKi, Bruton tyrosine kinase inhibitor; Btx, BTK inhibitor line of treatment; Ibru, ibrutinib; NA, not available; Zanu, zanubrutinib.

- A total of 59/102 (57.8%) patients who directly switched from acalabrutinib remained on zanubrutinib at the end of the follow-up period
- Overall, 53/102 (52.0%) patients discontinued acalabrutinib within 6 months and 68/102 (66.7%) discontinued within 1 year

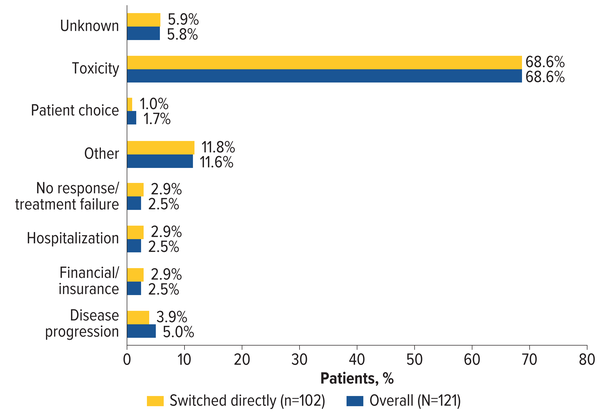
Figure 2. Time to Discontinuation of Zanubrutinib for Patients Who Initiated Acalabrutinib and Switched to Zanubrutinib



Treatment Discontinuation

- Of the 121 patients, the most common reason for discontinuation of acalabrutinib was toxicity (68.6%), followed by other/unspecified reasons (11.8%) and disease progression (3.9%) (**Figure 3**)
- A total of 43/102 (42.2%) patients who switched directly from acalabrutinib to zanubrutinib discontinued zanubrutinib at the time of data cutoff. The reasons for zanubrutinib discontinuation were toxicity (58.1%), other (7.0%) or disease progression (2.3%)

Figure 3. Reasons for Acalabrutinib Discontinuation Among Patients With CLL/SLL Who Switched From Acalabrutinib to Zanubrutinib



LIMITATIONS

- This study was subject to the inherent limitations of a retrospective, observational, real-world study based on data derived from EHRs, including missing, incomplete, inaccurate, or inconsistent documentation
- Data were sourced exclusively from the Integra network; information may not have been captured or may have been incomplete for patients who left the network or received care elsewhere
- The analysis could not control for the potential impact of concomitant medications or combination regimens on treatment discontinuation rates or reasons for discontinuation, however, because the majority of patients received acalabrutinib as monotherapy, the impact was comparatively small
- The evolving landscape of care over the study period potentially influenced treatment patterns, provider interactions, and outcomes

REFERENCES

1. Byrd JC, et al. *N Engl J Med.* 2014;371:213-223.
2. de Claro RA, et al. *Clin Cancer Res.* 2015;21:3586-3590.
3. Tam CS, et al. *Expert Rev Clin Pharmacol.* 2021;14:1329-1344.
4. Shadman M, et al. *Blood Adv.* 2025;9:4100-4110.

DISCLOSURES

JZH: Consulting: AstraZeneca; **RC:** Consulting: IntegraConnect PrecisionQ; **GAM:** Employment: BeOne Medicines Ltd; Stocks: Amgen, BeOne Medicines Ltd, CRISPR Therapeutics, Gilead; Advisory boards: BeOne Medicines Ltd, CRISPR Therapeutics; Support for attending meetings and/or travel: BeOne Medicines Ltd, CRISPR Therapeutics; **XW:** Employment: BeOne Medicines Ltd; Stocks: BeOne Medicines Ltds, Roche; **AR, BC, LA, LM:** Employee of IntegraConnect PrecisionQ and serve as paid consultants for BeOne Medicines Ltd; **MS, MH, RW:** Employment and Stocks: BeOne Medicines Ltd; **DAE:** Honoraria: AstraZeneca, Incyte; Consulting: AstraZeneca, BeOne Medicines Ltd.

ACKNOWLEDGMENTS

The authors thank the patients and their families, investigators, co-investigators, and the study teams at each of the participating centers. This study was sponsored by BeOne Medicines Ltd. Medical writing and editorial support was provided by Amiculum, supported by BeOne Medicines Ltd.

CORRESPONDENCE: Rushir Choksi, choksir@upmc.edu

Presented at the European Hematology Association (EHA) Congress 2026; June 11-14, 2026; Stockholm, Sweden