Real-World Bruton Tyrosine Kinase Inhibitor Use and Clinical Outcomes Among Patients With Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

CLL-411

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CONCLUSION

- In this real-world comparative effectiveness analysis in first-line (1L) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), patients who received zanubrutinib were significantly more likely to remain on treatment compared with those who received acalabrutinib and were less likely to require the next line of therapy (LOT)

INTRODUCTION

- Bruton tyrosine kinase (BTK) inhibitors are the standard of care for CLL/SLL in 1L and relapsed/refractory (R/R) settings
- The next-generation BTK inhibitor zanubrutinib demonstrated superiority over the first-generation BTK inhibitor ibrutinib in treating R/R CLL, while the second-generation BTK inhibitor acalabrutinib showed noninferiority to ibrutinib[1,2]
- We previously reported that 138 patients treated with zanubrutinib were more likely to remain on treatment and less likely to require subsequent treatment compared with those treated with acalabrutinib in 1L CLL in community oncology practices (ASH 2024) in a 1:2 matched analysis[3]
- Here, we provide updates on the full cohort in these settings, including ~200 patients more than in the previous report

METHODS

Data Source and Study Design

- US adult patients diagnosed with CLL/SLL who initiated 1L 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 July 3, 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 treatment discontinuation (TTD) or time to next treatment (TTNT)
    - Index date was the initiation of a BTK inhibitor in 1L
    - Event date was the date of discontinuing a BTK inhibitor or death for TTD, and the date of starting a second-line treatment or death for TTNT
    - Censor date was last contact or study end date, whichever occurred first

Statistical Analyses

- The probabilities of ongoing treatment and not advancing to next LOT from zanubrutinib or acalabrutinib initiation and overall survival (OS) were estimated using Kaplan–Meier methods
- Hazard ratios (HRs) were estimated using Cox proportional hazard models, adjusted for matching set, del17p or *TP53* mutations, unmutated IGHV, and Eastern Cooperative Oncology Group (ECOG) performance status

RESULTS

Baseline Demographics and Characteristics

- The study included 600 patients, including 200 zanubrutinib patients matched with 400 acalabrutinib patients
- Baseline demographics and characteristics are shown in **Table 1**. No significant differences were noted for age at 1L BTK inhibitor start, gender, race, ethnicity, or ECOG status at index
- The overall median (range) duration of follow-up was 13.4 (0.9, 53.3) months: 15.9 (0.9, 53.3) months for acalabrutinib and 11.0 (2.3, 32.2) months for zanubrutinib

Table 1. Baseline Patient Demographics and Characteristics

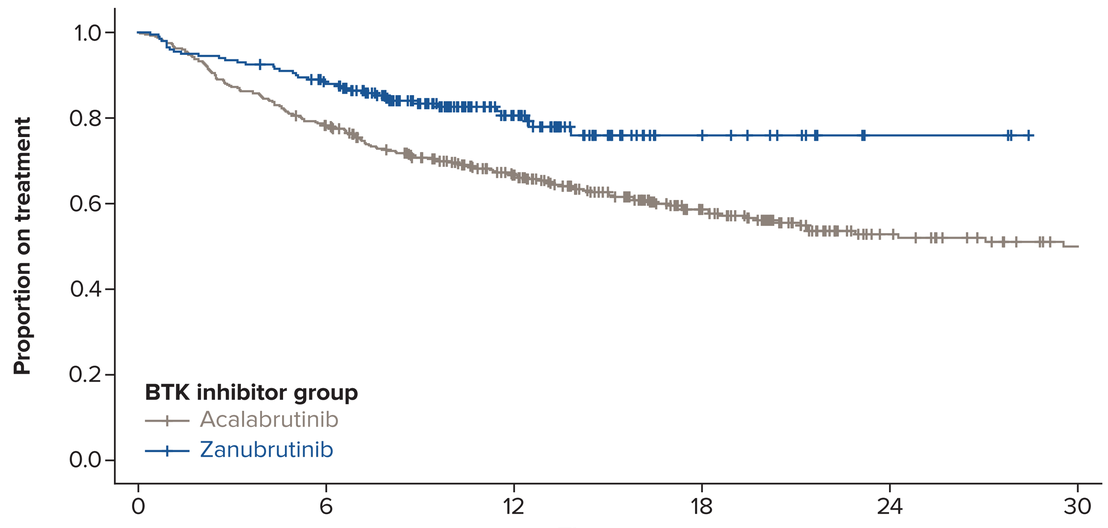
	Acalabrutinib (n=400)	Zanubrutinib (n=200)
Median age (IQR) at 1L BTK inhibitor start, years	75 (67, 81)	75 (67, 81)
Gender, n (%)		
Female	146 (36.5)	73 (36.5)
Male	254 (63.5)	127 (63.5)
Race, n (%)		
White	325 (81.3)	166 (83.0)
African American	22 (5.5)	13 (6.5)
Asian	3 (0.8)	1 (0.5)
Not documented/unknown/other	50 (12.5)	20 (10.0)
Ethnicity, n (%)		
Hispanic	7 (1.8)	3 (1.5)
Not Hispanic	273 (68.3)	134 (67.0)
Not documented/other	120 (30.0)	63 (31.5)
ECOG status at index, n (%)		
Missing data	121 (30.3)	41 (20.5)
ECOG 0	116 (41.6)	75 (47.2)
ECOG 1	129 (46.2)	64 (40.3)
ECOG 2+	34 (12.2)	20 (12.6)

IQR, interquartile range.

Treatment Characteristics

- The ongoing treatment probability (**Figure 1**) was higher at 6, 12, 18, and 24 months for patients on zanubrutinib compared with those on acalabrutinib
  - The adjusted HRs (95% confidence interval [CI]) with acalabrutinib as the reference for ongoing treatment probability were 0.51 (0.34, 0.78) at 6 months (*P*<.01) and 0.51 (0.34, 0.73) at 12 months (*P*<.01)

Figure 1. Time to Treatment Discontinuation (Probability of Ongoing Treatment)



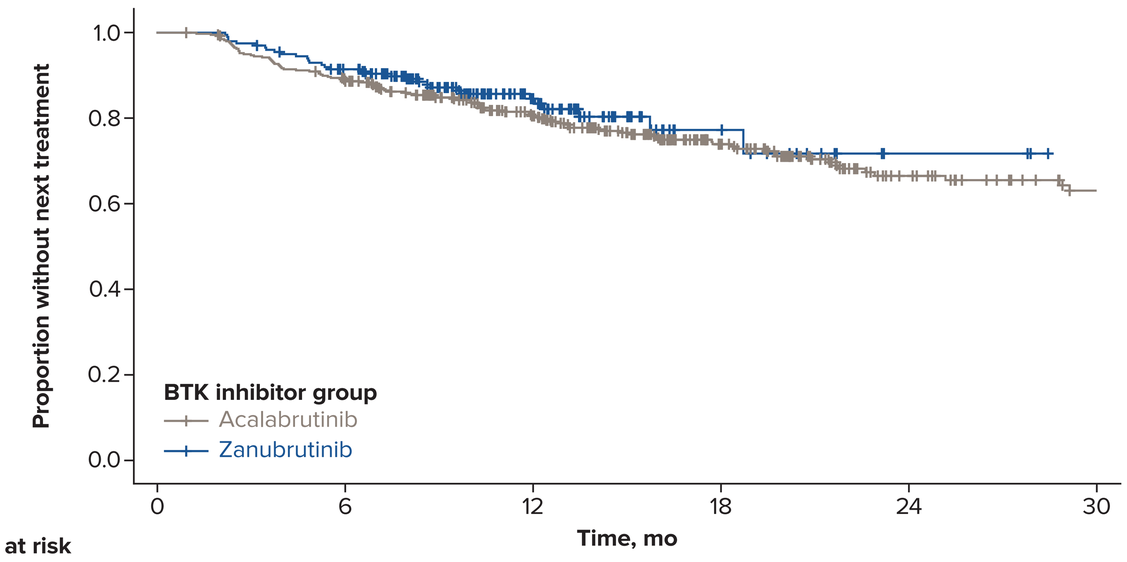
No. at risk

Acalabrutinib	400	311	217	122	64	46
Zanubrutinib	200	171	72	15	3	0

Treatment probability, % (95% CI)	6 mo	12 mo	18 mo	24 mo
Acalabrutinib (n=400)	78.2 (73.9, 82)	66.6 (61.7, 71.1)	58.6 (53.2, 63.6)	52.8 (46.8, 58.5)
Zanubrutinib (n=200)	88.0 (82.6, 91.8)	80.6 (73.7, 85.8)	75.9 (67.2, 82.6)	75.9 (67.2, 82.6)

- The probability of not advancing to next LOT (**Figure 2**) was higher at 6, 12, 18, and 24 months for patients on zanubrutinib compared with those on acalabrutinib
  - The adjusted HRs (95% CI; with acalabrutinib as the reference) for the probability of not advancing to next LOT were 0.73 (0.38, 1.33) at 6 months (*P*=.336) and 0.73 (0.41, 1.22) at 12 months (*P*=.291)

Figure 2. Time to Next Treatment (Probability of Not Advancing to Next LOT)



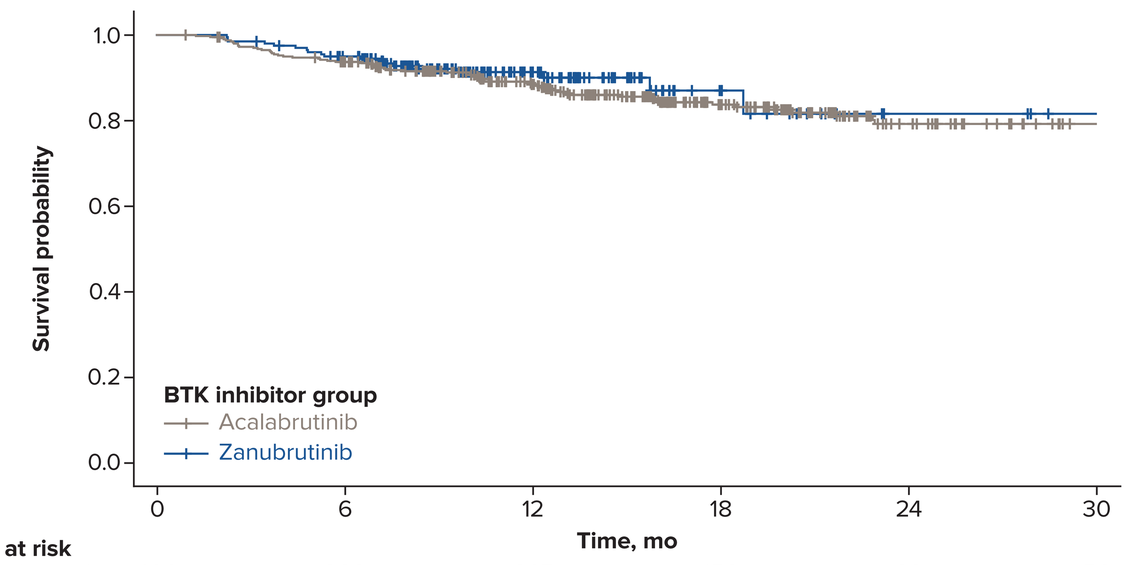
No. at risk

Acalabrutinib	400	344	245	140	73	50
Zanubrutinib	200	176	76	16	3	0

No next treatment probability, % (95% CI)	6 mo	12 mo	18 mo	24 mo
Acalabrutinib (n=400)	88.6 (85.1, 91.4)	80.5 (76.1, 84.2)	73.9 (68.8, 78.4)	66.5 (60.1, 72.2)
Zanubrutinib (n=200)	91.5 (86.6, 94.6)	84.6 (78.0, 89.3)	77.3 (66.6, 84.9)	71.7 (55.8, 82.7)

- Median OS was not reached in either the acalabrutinib or zanubrutinib group (**Figure 3**)

Figure 3. Overall Survival



No. at risk

Acalabrutinib	400	360	267	150	82	56
Zanubrutinib	200	184	81	18	4	1

Survival probability, % (95% CI)	6 mo	12 mo	18 mo	24 mo
Acalabrutinib (n=400)	93.7 (90.8, 95.7)	88.4 (84.7, 91.3)	83.7 (79.2, 87.4)	79.2 (73.4, 83.9)
Zanubrutinib (n=200)	95.0 (90.9, 97.3)	91.3 (86.2, 94.6)	87.0 (77.4, 92.7)	81.6 (65.0, 90.8)

LIMITATIONS

- Limitations of this study include shorter follow-up time for zanubrutinib compared with acalabrutinib

REFERENCES

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DISCLOSURES

J-Z H: Consultant: AstraZeneca; **GAM, XW, AL, RW:** Employment by BeOne Medicines Ltd and may hold stock or other ownership in BeOne Medicines Ltd; **AR, BW, LM:** employment by IntegraConnect PrecisionQ; **RC:** Consultant: IntegraConnect PrecisionQ.

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