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

Authors

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Background

Bruton tyrosine kinase (BTK) inhibitors are the standard of care for chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) in the first-line (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 only showed noninferiority to ibrutinib.

Aims

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. Here, we provide updates on the full cohort in these settings (~200 patients more than the previous report).

Methods

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. The probabilities of ongoing treatment and not advancing to next line of therapy (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.

Results

Six hundred patients were included in the study, including 200 zanubrutinib patients matched with 400 acalabrutinib patients. The median duration of follow-up was 13.4 (range 0.9, 53.3) months: 15.9 (0.9, 53.3) months for acalabrutinib and 11 (2.3, 32.2) months for zanubrutinib. The median age was 75 (interquartile range 67, 81) years and 36.5% were female in both groups. Baseline ECOG performance status was similar between groups, with 87.8% acalabrutinib patients and 87.5% zanubrutinib patients having an ECOG status of 0/1.

The ongoing treatment probability and the probability of not advancing to next LOT at 6, 12, 18, and 24 months were higher for zanubrutinib than acalabrutinib (Table). The adjusted HRs (95% CI) with acalabrutinib as the reference for ongoing treatment probability at 6 and 12 months were 0.51 (0.32, 0.80) and 0.51 (0.33, 0.74), respectively. The adjusted HRs (95% CI) for the probability of not advancing to next LOT at 6 and 12 months were 0.75 (0.40, 1.35) and 0.75 (0.43, 1.23), respectively. Median OS was not reached in either the acalabrutinib or zanubrutinib group.

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Conclusions

In this real-world comparative effectiveness analysis in 1L CLL/SLL, patients who received zanubrutinib were significantly more likely to remain on treatment compared with those who received acalabrutinib; they were also less likely to require the next LOT. Limitations include shorter follow-up time for zanubrutinib versus acalabrutinib.

Ongoing treatment probability and probability of not advancing to next line of treatment for patients on acalabrutinib or zanubrutinib

	1L, ongoing treatment probability, %		1L, probability of not advancing to next line of treatment, %	
Month	Acalabrutinib	Zanubrutinib	Acalabrutinib	Zanubrutinib
6	78.2	88.0	88.6	91.5
12	66.6	80.6	80.5	84.6
18	58.6	75.9	73.9	77.3
24	52.8	75.9	66.5	71.7

1L, first-line