Real-world zanubrutinib treatment patterns in CLL/SLL among a curated sample of US community oncology patients with prior acalabrutinib therapy

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ABSTRACT

Background

Bruton tyrosine kinase (BTK) inhibitors have demonstrated clinical efficacy in treating chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). Zanubrutinib is a highly specific and potent next-generation BTK inhibitor designed to maximize BTK occupancy and limit off-target kinase binding. In head-to-head trials, zanubrutinib was superior to ibrutinib (ALPINE trial; hazard ratio [HR]: 0.65; 95% confidence interval [CI]: 0.49-0.86), while acalabrutinib was noninferior to ibrutinib (ELEVATE-RR trial; HR: 1.00; 95% CI: 0.79-1.27) in patients with relapsed/refractory CLL. 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 (Shadman *Blood Adv.* 2025). Additionally, most of the ibrutinib and acalabrutinib intolerance adverse events did not recur during zanubrutinib treatment. There is limited real-world evidence describing the patient characteristics and treatment journey for patients with CLL/SLL who initiate acalabrutinib and subsequently receive zanubrutinib. This study describes the characteristics, treatment patterns, and reasons for discontinuation among patients who had previously discontinued acalabrutinib and changed to zanubrutinib in a real-world setting.

Methods

The IntegraConnect PrecisionQ database, which contains electronic health records from >3 million de-identified cancer patients across >500 care sites, was used to create a retrospective cohort of CLL/SLL patients who initiated and discontinued acalabrutinib and then initiated zanubrutinib between 11/21/2019 and 11/30/2024. Patients were followed through 2/28/2025. A medical record review was conducted to identify dates of treatment initiation and discontinuation and reasons for acalabrutinib and zanubrutinib discontinuation.

Results

A total of 806 patients initiated acalabrutinib and subsequently received another therapy; of these, 121 patients subsequently received zanubrutinib; 102 (84.3%) changed directly from acalabrutinib to zanubrutinib, and 19 (15.7%) changed from acalabrutinib to another therapy before initiating zanubrutinib. Of the 102 patients who changed directly from acalabrutinib to zanubrutinib, 74 (72.5%) received acalabrutinib in first-line and 28 (27.5%) received acalabrutinib in second-line or later. 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), and 59 (57.8%) patients remained on zanubrutinib at the end of the follow-up period. Overall, 53 (52.0%) patients discontinued acalabrutinib within 6 months and 68 (66.7%) discontinued within 1 year. The reasons for acalabrutinib discontinuation were toxicity (68.6%), other (11.8%), or disease progression (6.9%). A total of 43 (42.2%) patients who changed 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%).

Conclusion

In this real-world US community oncology setting, most zanubrutinib-treated patients with prior acalabrutinib therapy had discontinued acalabrutinib within 1 year. The primary reason for acalabrutinib discontinuation was toxicity. Consistent with previous research, real-world data from across the US have demonstrated that zanubrutinib was well tolerated and maintained effectiveness in patients with CLL who had received a prior BTK inhibitor.