Zanubrutinib treatment in patients with chronic lymphocytic leukemia or small lymphocytic lymphoma who were previously treated with another Bruton tyrosine kinase inhibitor in a US community oncology setting

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Introduction
Bruton tyrosine kinase inhibitors (BTKis) are considered safe and effective treatment for patients diagnosed with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). To date, few studies have examined the real-world treatment patterns of the second-generation BTKis in patients diagnosed with CLL/SLL. This study describes the demographic and treatment characteristics of patients initiating treatment on zanubrutinib after discontinuing treatment with another BTKi in a US community oncology setting. Of particular interest was the reason for the treatment change.

Methods
This was a retrospective observational study of patients diagnosed with CLL/SLL who initiated treatment with zanubrutinib following discontinuation of another BTKi in the US Oncology Network between January 2022 and September 2023. Among study eligible patients, a subset was randomly selected to undergo chart abstraction. Study data were captured from structured and unstructured fields of patient charts in the iKnowMed electronic health record. Descriptive analyses were conducted to evaluate patient demographics, clinical characteristics, and treatment patterns. Reasons for discontinuing the previous BTKi included documented adverse events (AEs), patient or physician preference, and disease progression.

Results
Among the 200 charts reviewed, 56 patients (28.0%) were identified as having been diagnosed with CLL/SLL, previously treated with a BTKi in any line of therapy, and subsequently initiated on zanubrutinib. Of these, 33 (58.9%) had been treated with ibrutinib and 23 (41.1%) with acalabrutinib. The median time from diagnosis was 84.6 months and median follow-up after zanubrutinib initiation was 4.7 months.

Baseline demographic characteristics included a mean age of 74.6 years, 71.4% were male, and for race 80.4% were White, and the remainder were Black, other, or not documented. ECOG status for patients with available data (n=21, 37.5%) was 0-1 and 2 for 81.0% and 19.0% of patients, respectively. The Charlson Comorbidity Index, assessed 6 months before and including the date of zanubrutinib initiation, showed a score of 0 in 78.6% of patients, 1-2 in 21.4%, and 3+ in 0%. Common comorbidities in the pre-index period included hypertension (35.7%), atrial fibrillation (19.6%), and other cardiovascular-related comorbidities (28.6%).

Documented reasons for treatment discontinuation from ibrutinib showed that 43.8% of patients discontinued due to AEs, 31.3% due to physician or patient preference, and 25.0% due to disease progression. For those discontinuing acalabrutinib, 91.3% of patients did so due to AEs, and 8.7% due to disease progression.

Conclusions

The results of this study suggest a real-world treatment strategy for patients diagnosed with CLL/SLL in the U.S. community oncology setting, who are no longer able to continue ibrutinib or acalabrutinib therapy, is to treat with zanubrutinib. For patients initially treated with the first-generation BTKi ibrutinib, the most common reason for discontinuation was adverse events. This was almost exclusively the reason for discontinuation of acalabrutinib therapy. A third of patients treated with ibrutinib discontinued due to physician or patient preference, likely reflecting changing patterns of care with alternative BTKi options. Progression of disease was the reason for discontinuation in a quarter of patients on ibrutinib and a smaller number on acalabrutinib. In this setting, this may reflect suboptimal initial BTKi therapy, as opposed to drug resistance. These findings provide important descriptive insights into the evolving treatment of patients diagnosed with CLL/SLL in the real-world community setting.