ASH 2026 Zanu vs Acala TN CLL Optum Abstract

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Abstract Guidelines

- **Abstract Body:** max. 4500 characters (including spaces)
- **New for 2026:** No tables or figures are permitted

Abstract Topic: 642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological

Abstract Title

Real-world treatment persistence and clinical outcomes among patients receiving first-line covalent Bruton tyrosine kinase inhibitors for chronic lymphocytic leukemia

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Introduction

Covalent Bruton tyrosine kinase inhibitors (cBTKi) are commonly used as first-line (1L) therapy for chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), where long-term disease control and sustained treatment benefit are important goals. Comparative real-world evidence evaluating treatment outcomes across currently used 1L cBTKi therapies remains limited. This study evaluated treatment persistence, time to next treatment (TTNT), and overall survival (OS) among patients initiating 1L cBTKi therapy.

Methods

This retrospective observational study used the US Optum claims database to identify adult patients (aged ≥18 years) with ≥2 entries of ICD codes for CLL/SLL diagnoses who initiated 1L cBTKi monotherapy (zanubrutinib [zanu], acalabrutinib [acala], or ibrutinib [ibr]) between 01/01/2020 and 09/30/2025; 1L start date was the index date. Eligible patients had continuous enrollment in health insurance (medical or pharmacy) for ≥3 months prior to the index date and were followed until disenrollment, death or the end of the study period (12/31/2025), whichever

occurred first. Baseline patient characteristics and outcomes were examined by each cBTKi. Kaplan-Meier methods were used to estimate time to treatment discontinuation (TTD), TTNT, and OS. TTD was defined as the time from treatment initiation to treatment discontinuation, defined by initiation of subsequent therapy, a treatment gap ≥120 days, or death. TTNT was defined as the time from the treatment initiation to the start date of a subsequent line of therapy or death. OS was defined as the time from the index date to death. A multivariable Cox proportional hazards model was used to estimate the hazard ratio (HR) of the outcomes of TTD, TTNT, and OS between zanu and acala or ibru, adjusting for age at index, sex, race, ethnicity, payer type, geographic region, Charlson Comorbidity Index, and index year. A subgroup analysis was conducted in elderly patients aged ≥65 years.

Results

A total of 9640 patients were included (zanu=2377; acala=3787; ibru=3476). Baseline characteristics were generally balanced across groups, although the age of patients receiving zanu trended higher than those receiving acala or ibru (median age, 74 vs 72 vs 71 years), with a higher proportion aged ≥65 years (80.3% vs 75.6% vs 73.3%). Median follow-up periods were 16 months for zanu, 22 months for acala, and 37 months for ibru.

Compared with acala and ibru, zanu demonstrated significantly longer TTD (adjusted HR 0.842 [95% CI 0.766–0.924], *P*=0.0003; adjusted HR 0.659 [95% CI 0.585–0.743], *P*<0.0001, respectively). Median TTD was 32.8 months for zanu versus 31.2 months for acala and 20.1 months for ibru. At 24 months, the estimated probabilities of remaining on treatment were 57%, 56%, and 46%, respectively.

Zanu was also associated with significantly longer TTNT than acala and ibru (adjusted HR 0.801 [95% CI 0.688–0.934], *P*=0.0045; adjusted HR 0.770 [95% CI 0.633–0.936], *P*=0.0088, respectively). Median TTNT was not reached for any treatment. At 24 months, the estimated probabilities of remaining free from next treatment were 84%, 82%, and 79%, respectively.

Zanu was associated with significantly longer OS than ibru and a trend toward longer OS than acala (adjusted HR 0.727 [95% CI 0.562–0.939], *P*=0.0148; adjusted HR 0.842 [95% CI 0.686–1.033], *P*=0.0983, respectively). Median OS was not reached for any treatment.

Results were generally consistent among patients ≥65 years. Compared with acala and ibru, zanu was associated with significantly longer TTD, TTNT, and OS. Median TTD was 30.3 months for zanu, 27.7 months for acala, and 18.1 months for ibru. Median TTNT and OS were not reached for any treatment.

Conclusions

In this real-world study of patients initiating 1L cBTKi therapy for CLL/SLL, zanubrutinib was associated with a lower risk of treatment discontinuation, longer TTNT, and improved OS compared with ibrutinib and acalabrutinib. Consistent findings among patients aged ≥65 years further support the effectiveness of zanubrutinib in a population representative of routine clinical practice. These results provide real-world evidence that zanubrutinib may offer more durable

treatment benefit and improved survival outcomes relative to other cBTKi therapies in the 1L setting. Additional follow-up is warranted to confirm the long-term durability of these findings.