Z vs A Comp Effect CLL Encore Abstract

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Real-world treatment and survival outcomes for zanubrutinib and acalabrutinib monotherapy among treatment-naïve patients with chronic lymphocytic leukemia in the United States

Authors

Ryan Jacobs,[1] Manasi Suryavanshi,[2] Gregory Maglinte,[2] Divya Nagpal,[3] Nishit Jain,[3] Varun Gupta,[3] Qianhong Fu,[2] Rhys Williams,[2] Daniel A. Ermann[4]

Affiliations

[1]Atrium Health Levine Cancer Institute, Wake Forest University School of Medicine, Charlotte, NC, USA; [2]BeOne Medicines Ltd, San Carlos, CA, USA; [3]ZS Associates, Gurugram, Haryana, India; [4]Huntsman Cancer institute, University of Utah School of Medicine, Salt Lake City, UT, USA

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Background

Bruton tyrosine kinase (BTK) inhibitors are central to the management of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). Acalabrutinib (acala) was approved for CLL in the United States (US) in November 2019, followed by zanubrutinib (zanu) in January 2023. Despite widespread use, comparative real-world evidence remains limited.

Aims

To compare real-world effectiveness of zanu and acala monotherapy in patients with CLL based on overall survival (OS) and time to next treatment (TTNT).

Methods

This retrospective analysis used the Komodo claims database (January 2015-August 2025). Eligible patients were US adults (≥18 years) with ≥2 diagnoses of CLL/ SLL, treatment-naïve for CLL, and had an index claim for zanu (January 2023- August 2025) or acala (November 2019-August 2025) monotherapy. The index date was the first observed claim of therapy. Continuous enrollment or activities was required for ≥1 year pre-index and ≥3 months post-index. Patients with prior CLL/SLL treatment, mantle cell lymphoma, or clinical trial participation were excluded. Outcomes included OS (index to all-cause mortality) and TTNT (index to initiation of subsequent therapy or death). Patients were censored at date of last activity or end of enrollment. Kaplan-Meier method and Cox proportional hazard models were used. Inverse probability of treatment weighting (IPTW) adjusted for age, sex, US region, treatment initiation year, and Charlson Comorbidity Index (CCI) was used.

Results

Among 16,788 patients (zanu, n=5819; acala, n=10,969), median age was 73.3 years for zanu and 71.8 years for acala. Most patients were male (acala, 62%; zanu, 59%), non-Hispanic White (acala, 73%; zanu, 72%); median CCI was 2 in both cohorts. Median follow-up was 12.8 months (zanu) and 16.4 months (acala). Median TTNT and OS were not reached. In the unadjusted model, zanu had longer TTNT (unadjusted hazard ratio [HR]=0.88; 95% CI, 0.79-0.97; *P*=.009) and OS (uHR=0.72; 95% CI, 0.62-0.82; *P*<.001). After IPTW adjustment, zanu was associated with significantly improved OS (IPTW-adjusted HR=0.75; 95% CI, 0.65-0.86; *P*<.001) and TTNT (IPTW-adjusted HR=0.89; 95% CI, 0.80-0.98; *P*=.02).

Conclusion

In this real-world analysis, zanu demonstrated significantly longer TTNT and improved OS compared with acala in patients with CLL/SLL, suggesting improved outcomes for patients in the real-world setting.