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

Funding Sources

This study is funded by BeOne Medicines Ltd

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 their widespread use, real-world evidence comparing therapy effectiveness is limited.

Aims

This US-based study compared the real-world effectiveness of zanu and acala monotherapy as first-line treatment for patients with CLL based on overall survival (OS) and time to next treatment (TTNT).

Methods

This retrospective analysis utilized the Komodo claims database between January 2015 and August 2025. Eligible patients were adults (aged ≥18 years) in the US with ≥2 diagnoses of CLL or SLL, who were treatment naïve for CLL and had an index claim for monotherapy with zanu (January 2023 to August 2025) or acala (November 2019 to August 2025). The index date was defined as the date of the first observed claim for the respective therapy. Patients were required to have continuous enrollment or activities within 1 year prior to and 3 months after the index date. Patients with evidence of clinical trial participation, prior CLL/SLL treatment, or a diagnosis of mantle cell lymphoma between January 2015 and the index date were excluded. Outcomes included OS (measured from index claim to all-cause mortality) and TTNT (measured from index claim to initiation of subsequent therapy or death). If death did not occur, patients were censored at the date of last activity or the enrollment end date. For OS analysis, Komodo data captured the death date, but not the cause of mortality. Survival analyses were conducted using Kaplan-Meier estimates and Cox proportional hazards models. Inverse probability of treatment

weighting (IPTW) was adjusted for age, sex, US region, treatment initiation year, and Charlson Comorbidity Index (CCI).

Results

Among 16,788 patients (zanu, n=5819; acala, n=10,969), median age was higher in zanu (73.3 years) than acala (71.8 years) cohorts. Most patients were male (acala, 62%; zanu, 59%), non-Hispanic white (acala, 73%; zanu, 72%), and the median CCI was 2 in both cohorts. Median follow-up was 12.8 and 16.4 months in zanu and acala cohorts, respectively. Median TTNT and OS were not reached for either cohort. With the unadjusted model, zanu had a longer TTNT (unadjusted hazard ratio [HR]=0.88; 95% CI, 0.79-0.97; *P*=.009) and OS (HR=0.72; 95% CI, 0.62-0.82; *P*<.001; **Table**). After IPTW adjustment, zanu was associated with a 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) compared with acala.

Summary/Conclusion

In this real-world analysis, zanu monotherapy demonstrated significantly longer TTNT and significantly improved OS compared with acala monotherapy in patients with CLL/SLL. These findings suggest that zanu may offer superior outcomes in the real-world setting.

Table. TTNT and OS Landmark Rates and HRs

		Zanu	Acala (ref)
TTNT	12 m, % (95% CI)	91.3 (90.4-92.0)	90.1 (89.4-90.7)
	18 m, % (95% CI)	88.3 (87.2-89.3)	86.8 (86.0-87.6)
	24 m, % (95% CI)	85.3 (83.8-86.6)	83.8 (82.9-84.6)
	Unadjusted HR (95% CI)	0.88 (0.79-0.97)	
	Adjusted HR (95% CI)	0.89 (0.80-0.98)	
OS	12 m, % (95% CI)	96.0 (95.4-96.5)	94.5 (94.0-95.0)
	18 m, % (95% CI)	94.2 (93.4-94.9)	92.0 (91.3-92.6)
	24 m, % (95% CI)	92.5 (91.3-93.5)	89.4 (88.7-90.1)
	Unadjusted HR (95% CI)	0.72 (0.62-0.82)	
	Adjusted HR (95% CI)	0.75 (0.65-0.86)	