Comparing real-world treatment patterns and outcomes of zanubrutinib and acalabrutinib in CLL/SLL at University of California academic health centers

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ABSTRACT

Background: Newer BTK inhibitors zanubrutinib (ZANU) and acalabrutinib (ACA) are preferred over first-generation ibrutinib for chronic lymphocytic leukemia (CLL) treatment due to better toxicity profiles shown in randomized controlled trials. However, real-world (RW) evidence for treatment outcomes of ZANU and ACA remains limited. Comparing treatment outcomes of ZANU and ACA in diverse RW populations can provide critical insights to inform clinical practice.

Methods: This multi-center, RW, retrospective case-controlled study included adult patients receiving ZANU or ACA between 2021 and 2024 within the University of California Health system. RW treatment patterns and outcomes, including time to discontinuation (TTD), time to next treatment (TTNT), and overall survival (OS), were evaluated using a multivariate Cox proportional hazard model with inverse probability of treatment weighting for balancing covariates between groups. Study endpoints included unadjusted and adjusted hazard ratios (HR) for TTD, TTNT, and OS.

Results: This study included 505 patients with a mean age of 73 years (SD: 9.6). 300 received ACA, and 205 received ZANU, with a median follow-up time of 26.2 months. Baseline characteristics indicated 63% male, 76% White, 4% Hispanic or Latino, 4% Asian, and 3% African American (AA). Median Area Deprivation Index (ADI) was 3 (interquartile range: 1-5). The 12-month landmark TTD, TTNT, and OS rates were 74% (95% CI: 67-80), 84% (77-89), and 94% (89-96) for ZANU, and 55% (49-60), 79% (74-83), and 94% (90-96) for ACA, respectively. The median TTD was 14.0 (11.3-18.2) months for ACA and 30.1 (26.9-inf) months for ZANU, median TTNT and OS were not reached for both. Adjusted analysis indicated that patients receiving ZANU were associated with a longer TTD compared with ACA (HR [95% CI]: 0.41 [0.34-0.51]). Higher ADI (1.10 [1.01-1.19]), advanced age (1.07 [1.04-1.10]), and a higher Charlson Comorbidity Index score (1.11 [1.05-1.17]) were associated with shorter OS. AA patients were associated with shorter TTNT (HR [95% CI]: 2.55 [1.47-4.42]) and treatment discontinuation (2.64 [1.63-4.27]).

Conclusions: In this RW study, ZANU was associated with a lower discontinuation risk than ACA. Poorer survival outcomes were linked to older age, more comorbidities, lower socioeconomic status, and AA patients faced higher risks of treatment discontinuation. These findings emphasize the need for further investigation into underlying causes to guide clinical decisions and optimize CLL treatment strategies in diverse RW settings.

		ZANU vs ACA HR [95%CI]
Unadjusted Cox	TTD	0.52 [0.39-0.70]
	TTNT	0.80 [0.56-1.14]
	OS	1.07 [0.59-1.94]
Adjusted Cox	TTD	0.41[0.34-0.51]
	TTNT	0.81[0.63-1.04]
	OS	1.23[0.80-1.88]

CI, confidence interval; TTD, time to discontinuation; TTNT, time to next treatment; OS, overall survival.