A real-world comparison of treatment and survival outcomes with zanubrutinib and acalabrutinib monotherapy among patients with relapsed or refractory mantle cell lymphoma in the United States

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Background

Mantle cell lymphoma (MCL) is a rare and aggressive subtype of B-cell non-Hodgkin lymphoma that remains incurable. Bruton tyrosine kinase (BTK) inhibitors are an established standard of care for relapsed or refractory (R/R) MCL. However, comparative effectiveness data for different BTK inhibitors for R/R MCL are limited.

Aims

This study evaluated the real-world effectiveness of zanubrutinib (zanu) and acalabrutinib (acala) in United States (US) patients with R/R MCL based on overall survival (OS) and time to next treatment (TTNT).

Methods

A retrospective cohort study was conducted using Komodo health administrative claims data. Eligible patients were adults (aged ≥18 years) with ≥2 MCL diagnoses and continuous enrollment or activities within 1 year prior to and 3 months following the index date. Patients were required to initiate monotherapy with zanu (index period: November 2019 to August 2025) or acala (index period: October 2017 to August 2025) as a second-line or later (2L+) treatment, with index date defined as the first observed claim for zanu or acala. Patients with evidence of clinical trial participation, end-stage renal disease, or prior stem cell transplant were excluded. Outcomes included OS (time from index date to all-cause mortality) and TTNT (time from index date to subsequent therapy with an allowable gap of 120 days). If an outcome was not observed, patients were censored at the date of last activity or enrollment end date. 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

In total, 2219 patients (zanu, n=931; acala, n=1288) were eligible and included in the study. The mean age was higher in the zanu cohort (72.3 years; SD, 9.4) than the acala cohort (71.4 years; SD, 9.7). Most patients were male (zanu, 71%; acala, 75%), non-Hispanic white (zanu, 73%;

acala, 74%), and the mean CCI was 3.5 (SD, 3.2) and 3.6 (SD, 3.1) in the zanu and acala cohorts, respectively. Median follow-up was 14.8 and 18.2 months in zanu and acala cohorts, respectively. Median TTNT was 26.7 months for zanu and 20.8 months for acala. Median OS was not reached for zanu and was 60.6 months for acala. In the unadjusted model, zanu had a longer TTNT (hazard ratio [HR]=0.86; 95% CI, 0.76-0.97; *P*=.012) and OS (HR=0.74; 95% CI, 0.62-0.88; *P*<.001; **Table**). After IPTW adjustment, TTNT and OS favored zanu treatment (TTNT: IPTW-adjusted HR=0.86; 95% CI, 0.76-0.98; *P*=.025; OS: IPTW-adjusted HR=0.81; 95% CI, 0.68-0.98; *P*=.03).

Summary/Conclusion

In this real-world analysis of US health claims data, zanu monotherapy demonstrated significantly longer TTNT and improved OS compared with acala in patients receiving 2L+ therapy for MCL. These findings support zanu as an effective BTK inhibitor for R/R MCL.

Table. TTNT and OS Landmark Rates and HRs

		Zanu	Acala (ref)
TTNT	12 m, % (95% CI)	66.3 (63.0-69.4)	60.6 (57.8-63.3)
	18 m, % (95% CI)	58.3 (54.7-61.8)	53.8 (50.8-56.7)
	24 m, % (95% CI)	52.8 (48,9-56.6)	46.7 (43.7-49.8)
	Unadjusted HR (95% CI)	0.86 (0.76-0.97)	
	Adjusted HR (95% CI)	0.86 (0.76-0.98)	
OS	12 m, % (95% CI)	86.4 (83.9-88.6)	81.6 (79.3-83.7)
	18 m, % (95% CI)	81.1 (78.0-83.8)	74.8 (72.1-77.3)
	24 m, % (95% CI)	76.3 (72.7-79.6)	68.6 (65.6-71.4)
	Unadjusted HR (95% CI)	0.74 (0.62-0.88)	
	Adjusted HR (95% CI)	0.81 (0.68-0.98)	