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**Clinical Outcomes Among Patients With Relapsed/Refractory Mantle Cell Lymphoma
Receiving Zanubrutinib or Acalabrutinib in Real-World Practice in the United States**

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Background

Second-generation Bruton tyrosine kinase inhibitors (BTKis), zanubrutinib and acalabrutinib, are established therapies for relapsed or refractory mantle cell lymphoma (R/R MCL). However, head-to-head trials are lacking.

Aims

To describe baseline characteristics and compare real-world treatment outcomes among patients with R/R MCL receiving zanubrutinib or acalabrutinib.

Methods

This retrospective, observational study included adult patients with R/R MCL initiating second-line or later (2L+) zanubrutinib or acalabrutinib treatment (Jan 1, 2018-Jul 31, 2025) in the US community oncology setting. Patients were identified using the Integra Connect PrecisionQ de-identified real-world database and followed through Oct 31, 2025. The index date was initiation of a 2L+ BTKi. Outcomes included time to treatment discontinuation (TTD), time to next treatment (TTNT), and overall survival (OS). Events were defined as BTKi discontinuation or death for TTD, and initiation of subsequent line of treatment (LOT) or death for TTNT. Kaplan-Meier method was used to estimate the outcome probabilities.

Results

Among 184 patients, 93 received zanubrutinib and 91 received acalabrutinib. Median age was 68 years; most patients were male (76.1%), non-Hispanic (77.2%), and White (84.2%). Median follow-up was 17.3 months for zanubrutinib and 20.2 months for acalabrutinib. Median TTD was significantly longer with zanubrutinib (17.8 months; 95% CI 14.7, not reached [NR]) than acalabrutinib (9.6 months; 95% CI 6.5, 15.4; log rank $P < .01$). Primary reasons for discontinuation included toxicity, disease progression, and death. Median TTNT was 18.2 months (95% CI 15.4, NR) for zanubrutinib and 15.4 months (95% CI 9.6, 26.6) for acalabrutinib (log rank $P = .15$). Median OS was NR (95% CI 30.0, NR) for zanubrutinib and 51.5 months (95% CI 41.7, NR) for acalabrutinib (log rank $P = .37$). At 6, 12, and 18 months, zanubrutinib was associated with higher probability of not discontinuing treatment, not advancing to next LOT, and survival.

Conclusion

In this real-world comparative effectiveness analysis, patients treated with zanubrutinib were associated with longer treatment and had better survival probability compared to acalabrutinib. These findings support that zanubrutinib has improved outcomes over acalabrutinib and underscore the need for future studies evaluating long-term outcomes and treatment sequencing in R/R MCL.