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

The 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 treatment outcomes among patients with R/R MCL receiving zanubrutinib or acalabrutinib in real-world practice.

Methods

This is a retrospective, observational study of 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 were followed until Oct 31, 2025. Index date was the initiation of a 2L+ BTKi. Outcome measures included time to treatment discontinuation (TTD), time to next treatment (TTNT), and overall survival (OS). Event date was the date of discontinuing a BTKi or death for TTD, and the date of starting a subsequent line of treatment (LOT) or death for TTNT. The probabilities of not discontinuing treatment, not advancing to next LOT from zanubrutinib or acalabrutinib initiation, and OS were estimated using the Kaplan–Meier method.

Results

Overall, 93 patients 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 (range) follow-up was 17.3 (3.0-53.3) months for zanubrutinib and 20.2 (0.9-89.0) months for acalabrutinib. Median TTD was 17.8 months (95% confidence interval [CI] 14.7, not reached [NR]) for zanubrutinib and 9.6 months (95% CI 6.5, 15.4) for acalabrutinib (log rank P<.01). Primary reasons for discontinuation of zanubrutinib or acalabrutinib were toxicity (11.8% vs 11.0%), disease progression (6.5% vs 5.5%), and death (2.2% vs 4.4%). 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). Patients on zanubrutinib had a higher probability of not discontinuing treatment, not advancing to next LOT, and survival at 6, 12, and 18 months than those on acalabrutinib (Table).

Table: Real-World Effectiveness Outcomes

	TTD			TTNT			OS		
	6 m %	**12 m %**	**18 m %**	**6 m %**	**12 m %**	**18 m %**	**6 m %**	**12 m %**	**18 m %**
Zanu	80 (72, 89)	64 (54, 76)	49 (38, 63)	83 (75, 91)	66 (56, 77)	51 (40, 65)	93 (88, 99)	85 (77, 93)	75 (66, 87)
Acala (ref)	62 (52, 73)	44 (35, 56)	34 (25, 46)	67 (58, 78)	55 (45, 67)	45 (35, 57)	83 (75, 91)	77 (68, 86)	69 (59, 80)
Acala acalabrutinib, ***m*** months, ***ref*** reference, ***Zanu*** zanubrutinib									

Summary/Conclusion

In this real-world, comparative effectiveness analysis in R/R MCL, patients treated with zanubrutinib were more likely to remain on treatment, less likely to require subsequent LOT, and had better survival probability compared with those who received acalabrutinib. These findings are consistent with other real-world evidence suggesting improved outcomes for zanubrutinib over acalabrutinib. These data underscore the need for future studies evaluating long-term outcomes and optimization of sequencing strategies in real-world settings.