Meta-analysis investigating response rates of continuous bruton tyrosine kinase inhibitor (BTKi) monotherapies in the treatment of B-cell lymphomas (BCL)

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ABSTRACT

Introduction: BTKi monotherapy has led to improved patient outcomes in BCLs, including chronic lymphocytic leukemia (CLL), Waldenström macroglobulinemia (WM), marginal zone lymphoma (MZL), and mantle cell lymphoma (MCL). This meta-analysis aimed to compare response rates associated with BTKi monotherapy across BCLs in treatment-naive (TN) and/or relapsed and refractory (R/R) stages.

Methods: Trials reporting complete response (CR) rates or objective response rates (ORRs) for zanubrutinib, acalabrutinib, or ibrutinib monotherapies in patients with one of the BCLs were identified by systematic literature review. Response rates at similar follow-up time points (maximum 12-month difference) and longest available follow-up time points were pooled across all applicable studies. Odds ratios (ORs) comparing CR and ORR of zanubrutinib with those of the other 2 BTKis were calculated within each BCL indication and then meta-analyzed across all indications, using random effects models.

Results: The meta-analysis found zanubrutinib to be associated with statistically significant improvements in investigator-assessed CR and ORR vs acalabrutinib and ibrutinib across BCLs, using data with similar duration of follow-up. The pooled estimates of ORs (95% CI) for CR were 1.80 (1.03-3.13) for zanubrutinib vs acalabrutinib and 2.85 (1.16-7.04) for zanubrutinib vs ibrutinib. In R/R MCL, zanubrutinib demonstrated statistically superior efficacy over both acalabrutinib and ibrutinib for CR, with ORs (95% CI) of 3.33 (1.91-5.81) and 9.53 (5.45-16.66), respectively. In R/R MZL, zanubrutinib showed superior efficacy over ibrutinib for CR, with an OR of 3.32 (95% CI, 1.28-8.61). The pooled estimates of ORs (95% CI) for ORR were 1.59 (1.0003-2.53) for zanubrutinib vs acalabrutinib and 2.25 (1.40-3.61) for zanubrutinib vs ibrutinib. In TN CLL, zanubrutinib demonstrated statistically superior ORR (95% CI) over acalabrutinib (4.33 [1.68-11.15]) and ibrutinib (5.47 [2.47-12.12]). In R/R MCL and R/R MZL, zanubrutinib showed superior ORR over ibrutinib, with ORs (95% CI) of 2.23 (1.21-4.12) and 2.39 (1.18-4.85), respectively.

Conclusions: Zanubrutinib demonstrated significantly higher CR rates and ORRs compared to acalabrutinib and ibrutinib across BCLs. Findings are consistent with results of existing trials, which report higher rates of overall and complete response with zanubrutinib relative to other BTKis in certain BCLs.