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Title: Zanubrutinib Is Well Tolerated and Effective in Ibrutinib/Acalabrutinib-Intolerant Patients With Waldenström Macroglobulinemia

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The ongoing phase 2 study BGB-3111-215 (NCT04116437) investigated the next-generation BTK inhibitor zanubrutinib in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma, Waldenström macroglobulinemia (WM), mantle cell lymphoma, or marginal zone lymphoma, who were intolerant of prior ibrutinib and/or acalabrutinib and discontinued treatment. Patients received zanubrutinib 160-mg twice daily or 320-mg once daily. Safety and efficacy, including recurrence of ibrutinib/acalabrutinib intolerance adverse events with zanubrutinib treatment, were evaluated by investigators. As of May 1, 2024, 13 patients with WM had received zanubrutinib (ibrutinib only, n=9; acalabrutinib only, n=1; ibrutinib and acalabrutinib, n=3); median zanubrutinib treatment duration was 34.1 months (range, 6.5-46.0). Median age was 73 years (range, 58-87), median number of prior treatments was 2 (1-12), and median time on ibrutinib and acalabrutinib was 11.8 (0.9-73.7) and 3.4 (1.6-26.3) months. Twelve intolerance adverse events (63%; 12/19) from ibrutinib treatment and 7 (78%; 7/9) from acalabrutinib treatment did not recur with zanubrutinib. Of events that recurred, all were at the same grade (hypertension, hemorrhage, myalgia) or lower grade (diarrhea, arthralgia, fatigue, insomnia, nausea). Disease control rate was 100% (13/13). These data suggest that patients with WM who could not tolerate ibrutinib and/or acalabrutinib can safely and effectively switch to treatment with zanubrutinib.

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