

Zanubrutinib is well tolerated and effective in acalabrutinib-intolerant patients with B-cell malignancies

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ABSTRACT

Objective: Previous results from the ongoing phase 2 study BGB-3111-215 (NCT04116437) showed that the BTK inhibitor (BTKi) zanubrutinib (zanu) was well tolerated in patients (pts) intolerant of ibrutinib (ibr) and/or acalabrutinib (acala). Here we report updated results with zanu in pts intolerant of acala.

Methods: Eligible pts with CLL/SLL, WM, MCL, or MZL intolerant of acala received zanu 160 mg twice daily or 320 mg once daily. Pts with disease progression on prior BTKis were excluded. Safety and efficacy, including recurrence of acala-intolerance events, were evaluated.

Results: As of May 1, 2024, 35 acala-intolerant pts received zanu (median zanu treatment duration: 14.8 mo; range, 0.1-43.8, median follow-up: 18.9 mo; range, 0.1-43.8; median acala cumulative exposure: 5.7 mo; range, 0.2-68.6). Median number of prior therapies was 2 (range, 1-6), and 14 pts (40%) had prior ibr; 24 pts remained on treatment. A total of 48 acala-intolerance events were reported (among 35 pts), most commonly arthralgia (7 events); myalgia (6); headache (5); rash (4); and diarrhea, fatigue, and hemorrhage (3 each). Thirty-three acala-intolerance events (69%) did not recur with zanu; 23 pts (66%) did not experience any event recurrence. Fifteen events (31%) recurred (8 lower grade; 7 same grade); 3 pts discontinued due to recurrence (myalgia, rash, and diarrhea; all same grade). Of 4 pts who experienced the same intolerance event with prior ibr and acala, 2 (atrial fibrillation, n=1; hemorrhage, n=1) did not have recurrence events with zanu and 2 (diarrhea, n=1; pain in extremity, n=1) had recurrence with zanu at lower grades (all grade 1). In 32 evaluable pts, the disease control rate was 93.8%: 13 pts (40.6%) had a best response of stable disease and 17 pts (53.1%) had better response.

Conclusions: Acala-intolerant pts can safely switch to zanu, with most intolerance events resolving or lowering in severity, with maintained or improved efficacy. Enrollment and follow-up are ongoing.