Interim Safety Analysis of Zanubrutinib in Japanese Patients With Mature B-Cell Malignancies

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Zanubrutinib (zanu) is a potent, irreversible Bruton tyrosine kinase (BTK) inhibitor designed to maximize BTK occupancy and minimize off-target kinase inhibition. We present the safety and pharmacokinetic profile (PK) of zanu assessed in patients (pts) with mature B-cell malignancies (BCMs) enrolled in an ongoing phase 1/2 study in Japan (BGB-3111-111; NCT04172246). In Part 1, safety, tolerability and PK of zanu were evaluated in pts with relapsed or refractory (R/R) mature BCMs who received zanu 160 mg orally twice daily. In Part 2, safety and efficacy of zanu was evaluated in pts with mantle cell lymphoma (MCL), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), and Waldenström macroglobulinemia (WM). As of 24 July 2021, 6 pts were enrolled in Part 1 (1 R/R MCL; 2 WM; 3 other non-Hodgkin lymphoma) and 40 pts were enrolled in Part 2 (8 R/R MCL; 13 CLL/SLL; 19 WM). Seven (15.2%) pts discontinued treatment (6 progressive disease, 1 investigator decision). Median follow-up time was 6.52 months (range: 0.6-17.8). Thirty-six (78.3%) pts experienced ≥1 adverse event (AE); most common all-grade AEs were platelet count decreased (13.0%), neutrophil count decreased (8.7%), and constipation (8.7%). Fourteen (30.4%) pts experienced grade ≥3 AEs; most common grade ≥3 AEs were neutrophil count decreased and neutropenia (both 6.5%). No pts in Part 1 experienced a dose-limiting toxicity. The PK of zanu was comparable to that of published data across ethnic groups. Preliminary safety data suggest that zanu was generally well tolerated in Japanese pts with mature BCM.