Title: PRELIMINARY RESULTS OF THE PHASE 2 STUDY OF ZANUBRUTINIB IN PATIENTS WITH PREVIOUSLY TREATED B-CELL MALIGNANCIES INTOLERANT TO IBRUTINIB AND/OR ACALABRUTINIB

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Objectives: Many patients (pts) with B-cell malignancies require continuous treatment with Bruton tyrosine kinase inhibitors (BTKi). Adverse events (AEs) are a common reason for ibrutinib (ibr) or acalabrutinib (acala) discontinuation. The objective of the BGB-3111-215 trial is to assess the safety of zanubrutinib (zanu) and recurrence of AEs that led to prior BTKi intolerance in pts with B-cell malignancies. Initial data showed zanu was well tolerated, and here, we report additional preliminary results with a median follow-up of 4.2 months.

Methods: Pts meeting protocol criteria for intolerance to ibr, acala, or both (without documented progressive disease) were given zanu monotherapy (160 mg twice daily or 320 mg once daily). Recurrence of AEs that led to intolerance of prior BTKi and additional safety measures were assessed based on the Common Terminology Criteria for AEs v5.0. Investigators determined responses using disease status at study entry as baseline and established disease criteria.

Results: As of November 1, 2020 (data cutoff), 44 pts (n=34 chronic lymphocytic leukemia/small lymphocytic lymphoma, n=6 Waldenström macroglobulinemia, n=2 mantle cell lymphoma, n=2 marginal zone lymphoma) were enrolled, received ≥1 dose of zanu, and were analyzed for safety. The median age was 70.5 y (range, 49-91); median duration of treatment was 4.2 months (range, 0.1-12.6). The median number of prior regimens was 2 (range, 1-12). Regarding prior BTKi, 39 pts received ibr only, 4 received ibr and acala, and 1 received acala only. The median number of ibr- or acala-intolerant AEs per pt was 2 (range, 1-5). 83% of ibr- and 78% of acala-intolerant events did not recur on zanu. At cutoff, 43 pts remained on treatment; 1 withdrew consent due to zanu-unrelated grade 3 syncope. Overall, 34 pts (77.3%) reported any AE; most commonly reported AEs were myalgia (n=9; 20.5%), contusion (n=8; 18.2%), dizziness (n=7; 15.9%), fatigue (n=7; 15.9%), and cough (n=5; 11.4%). Grade ≥3 AEs were reported in 6 pts (13.6%), serious AEs in 1 pt (2.3%, febrile neutropenia and salmonella infection), AEs requiring dose interruptions in 6 pts (13.6%), and AEs leading to dose reduction in 2 pts (4.5%). No AEs led to zanu discontinuation. No deaths were reported. All efficacy evaluable pts (26/26 [100%]) maintained (10 [38.5%]) or achieved deepening (16 [61.5%]) of their response.

Conclusions: Zanu provided an additional treatment option after intolerance to other BTKi, demonstrating tolerability and sustained or improved efficacy. Updated results will be presented.