ZANUBRUTINIB IN 13 ACALABRUTINIB-INTOLERANT PATIENTS (PTS) WITH B-CELL MALIGNANCIES

Mazyar Shadman, MD, MPH[1] Ian W. Flinn, MD, PhD[2] Edwin C. Kingsley, MD[3] Benjamin Freeman, MD[4] Moshe Y. Levy, MD[5] Jennifer Cultrera, MD[6] Charles M. Farber, MD[7] Arvind Chaudhry, MD, PhD[8] Ryan Porter, MD[9] Rocco Crescenzo, MD[10] Adam Idoine, PhD[10] Xiaoping Zhang, MD[10] Aileen Cohen, MD, PhD[10] Kunthel By, PhD[10] Jane Huang, MD[10] Jeff P. Sharman, MD[11]

[1]Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA, USA [2]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA [3]Comprehensive Cancer Centers of Nevada, Las Vegas, NV, USA [4]Summit Medical Group, Florham Park, NJ, USA [5]Texas Oncology-Baylor Charles A. Sammons Cancer Center, Dallas, TX, USA [6]Florida Cancer Specialists & Research Institute, Leesburg, FL, USA [7]Atlantic Hematology Oncology, Morristown Medical Center, Morristown, NJ, USA [8]Summit Cancer Centers, Spokane, WA, USA [9]SSM Health Dean Medical Group, Madison, WI, USA [10]BeiGene (Beijing) Co., Ltd., Beijing, China & BeiGene USA, Inc., San Mateo, CA, USA [11]Willamette Valley Cancer Institute & Research Center, Eugene, OR, USA

Objectives: Bruton tyrosine kinase inhibitors (BTKi) use is limited by adverse events (AEs), potentially due to off-target inhibition. The next-generation BTKi zanubrutinib was designed with minimal off-target binding to maximize tolerability. Results from the phase 2 study BGB-3111-215 (NCT04116437) showed that zanubrutinib was well tolerated in pts who discontinued ibrutinib and/or acalabrutinib due to AEs (*Blood* 2021;138[suppl 1]:1410). We report updated results of the recurrence and change in severity of AEs that led to acalabrutinib intolerance from cohort 2 of this ongoing multicenter study. **Methods**: Eligible pts with chronic lymphocytic lymphoma/small lymphocytic lymphoma (CLL/SLL), Waldenström macroglobulinemia (WM), mantle cell lymphoma (MCL), or marginal zone lymphoma (MZL) who met protocol-defined criteria for intolerance to acalabrutinib received zanubrutinib 160 mg twice daily or 320 mg once daily. Pts who progressed on prior BTKi therapy were excluded. Safety and efficacy, including recurrence of intolerance events from prior acalabrutinib, were evaluated. Investigators assessed responses every 3 cycles based on standard response criteria for each indication using parameters at study entry as baseline. **Results**: As of January 6, 2022, 13 pts received zanubrutinib in cohort 2 (9 CLL/SLL; 2 WM; 1 MCL; 1 MZL). Median age was 73 y (range, 51-83); median treatment duration was 9.2 mo (range, 0.5-16), with median follow-up of 12.9 mo (range, 0.8-16). Median number of prior therapies was 2 (range, 1-6); 8 (62%) pts received ibrutinib before acalabrutinib, with acalabrutinib as the most recent therapy. Ten pts remain on treatment and 3 discontinued treatment (myalgia, progressive disease, and withdrawal; 1 pt each). Twenty-two acalabrutinib-intolerance events were reported in 13 pts, most commonly arthralgia (4), myalgia (3), headache (2), and hemorrhage (2). Sixteen (73%) acalabrutinib-intolerance events did not recur on zanubrutinib, corresponding to 8 (62%) pts not experiencing any recurrence. Six events recurred (1 lower grade, 5 same grade, 0 higher grade; **Figure**) and 1 pt discontinued due to recurrence (myalgia; same grade). Three pts who experienced the same intolerance events (pain in extremity, diarrhea, and atrial fibrillation) on ibrutinib and acalabrutinib did not have a recurrence of those on zanubrutinib. Among the 10 pts on zanubrutinib with ≥90 days of follow-up, 80% achieved at least stable disease and 70% achieved a deepening of response. **Conclusions**: Zanubrutinib may be a viable therapeutic option for pts who are intolerant to acalabrutinib. With zanubrutinib, 80% of pts received clinical benefit, and 62% did not experience recurrence of their prior intolerance events. Enrollment and follow-up are ongoing.