Extended follow-up of zanubrutinib-treated patients with Waldenström Macroglobulinemia from the ASPEN trial through LTE1

Authors: Kazuyuki Shimada,[1] Shirley D'Sa,[2] Meletios A. Dimopoulos,[3] Wojciech Jurczak,[4] Paula Marlton,[5] Stephen Mulligan,[6] Björn E Wahlin,[7] Magdalena Sobieraj-Teague,[8] Andrew W. Roberts,[9] Constantine S. Tam,[10] Jorge J. Castillo,[11] Heather Allewelt,[12] Radha Prathikanti,[12] Wai Y. Chan,[12] Tian Tian,[12] Jingjing Schneider,[12] Remus Vezan,[12] Stephen Opat[13]

Affiliations: [1]Nagoya University Hospital, Nagoya, Japan; [2]Centre for Waldenström's Macroglobulinemia and Associated Disorders, University College London Hospital Foundation Trust, London, UK; [3]General Hospital of Athens-Alexandra, Llisia, Greece; [4]Maria Sklodowska-Curie National Research Institute of Oncology, Kraków, Poland; [5]Princess Alexandra Hospital and University of Queensland, Brisbane, QLD, Australia; [6]Royal North Shore Hospital, Sydney, NSW, Australia; [7]Karolinska Universitetssjukhuset Solna, Solna, Sweden; [8]Flinders Medical Centre, Bedford Park, SA, Australia; [9]Peter MacCallum Cancer Centre and Royal Melbourne Hospital, Melbourne, VIC, Australia; [10]Alfred Hospital and Monash University, Melbourne, VIC, Australia; [11]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA; [12]BeiGene USA, Inc, San Mateo, CA, USA; [13]Lymphoma Research Group, School of Clinical Sciences at Monash Health, Monash University, Clayton, VIC, Australia

ABSTRACT

Background: The ASPEN study (BGB-3111-302; NCT03053440) evaluated zanubrutinib (zanu) in patients (pts) with *MYD88*-mutated (cohort 1, vs ibrutinib) and *MYD88*–wild-type (cohort 2) Waldenström macroglobulinemia (WM). Here, we report outcomes in zanu-treated pts from the ASPEN study with extended follow-up in the BGB-3111-LTE1 study (LTE1; NCT04170283).

Methods: Zanu-treated pts from ASPEN (cohorts 1 and 2) were included in this ad hoc analysis. LTE1 requirements included safety assessments every 3 mo and disease response assessments every 6 mo using modified IWWM-6 response criteria (Owen RG, et al. *Br J Haematol*. 2013;160:171-6).

Results: A total of 129 pts received zanu in ASPEN (cohort 1, n=101; cohort 2, n=28), and 75 pts enrolled in LTE1 after ASPEN. Median follow-up was 69.8 mo (range, 1.6-85.4), and median treatment duration was 63.3 mo (0.8-84.2). The overall response rate (minor response or better) was 96.1% in cohort 1 and 84.6% in cohort 2; the rate of very good partial response or better was 40.2% in cohort 1 and 30.8% in cohort 2 (n=26, confirmed *MYD88* wild type). Median duration of response was 55.7 mo (95% CI, 31.3-68.4) in cohort 1 and 41.1 mo (15.7-not estimable) in cohort 2. The 60-mo event-free rates for progression-free survival were 74.8% (64.5-82.5) in cohort 1 and 39.3% (20-58.1) in cohort 2 and for overall survival were 82.8% (73.5-89.1) in cohort 1 and 79.9% (56.4-90.8) in cohort 2. During LTE1 (n=75), grade ≥3 and serious treatment-emergent adverse events (TEAEs) occurred in 28% and 23% of pts, respectively. No pts experienced TEAEs leading to treatment discontinuation. Three pts (4%) had TEAEs leading to dose reduction, and 3 had TEAEs leading to death. No grade ≥3 or serious TEAEs by preferred term occurred in ≥5% of pts during LTE1.

Conclusion: With a median follow-up of 5.8 y, responses remained durable in pts with WM treated with zanu in the ASPEN study. The tolerability and safety profile of zanu remained favorable.