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

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ABSTRACT

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

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

Results: A total of 129 patients received zanubrutinib in ASPEN (cohort 1, n=101; cohort 2, n=28), and 75 patients enrolled in LTE1 after ASPEN. Median follow-up was 69.8 months (range, 1.6-85.4), and median treatment duration was 63.3 months (0.8-84.2). During LTE1 (n=72 [patients treated]), grade ≥3 and serious treatment-emergent adverse events (TEAEs) occurred in 29.2% and 23.6% of patients, respectively. No patients experienced TEAEs leading to treatment discontinuation. Three patients (4.2%) 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 patients during LTE1. The prevalence of most TEAEs of interest for BTK inhibitors, including atrial fibrillation and hypertension, decreased over time. 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 not yet reached in cohort 1 and was 41.1 months (15.7-not estimable) in cohort 2. The 60-month event-free rates for progression-free survival were 74.8% (64.5-82.5) in cohort 1 and 39.3% (20.0-58.1) in cohort 2 and for overall survival were 82.8% (73.5-89.1) in cohort 1 and 79.0% (56.4-90.8) in cohort 2. Durable responses were observed regardless of *CXCR4* and *TP53* mutation status.

Conclusion: With a median follow-up of 5.8 years, responses in patients with WM treated with zanubrutinib in ASPEN remained durable and deepened over time. The tolerability and safety profile of zanubrutinib remained favorable.