Improved efficacy and safety of zanubrutinib vs ibrutinib in patients with relapsed/refractory chronic lymphocytic leukemia in China: a subgroup of ALPINE

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ABSTRACT

Objective: Zanubrutinib is an irreversible, potent, next-generation Bruton tyrosine kinase (BTK) inhibitor designed to maximize BTK occupancy across disease-relevant tissues with greater kinase selectivity and to minimize off-target inhibition. In a multinational, randomized, phase 3 study (ALPINE; NCT03734016), zanubrutinib was compared head-to-head with ibrutinib as a treatment for relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL; including small lymphocytic lymphoma [SLL]). In the predefined progression-free survival (PFS) final analysis, zanubrutinib demonstrated superior efficacy and a favorable safety profile vs ibrutinib (Brown et al. NEJM. 2022). Data from the prespecified subgroup of patients from China are reported here.

Methods: Patients with R/R CLL/SLL who had received ≥1 prior line of therapy and had measurable disease by imaging were randomized (1:1) to receive zanubrutinib 160 mg twice daily or ibrutinib 420 mg once daily until disease progression or unacceptable toxicity. Randomization included stratification

by geographic region (China vs non-China). Data from the subgroup of patients from China were descriptively analyzed.

Results: A total of 90 patients in China with R/R CLL/SLL (zanubrutinib, n=47; ibrutinib, n=43) were enrolled. Disease characteristics and baseline demographics were balanced between zanubrutinib and ibrutinib groups (age ≥65 years, 40% vs 37%, respectively; unmutated IGHV, 59.6% vs 62.8%; del17p/TP53 mutated, 34.0% vs 32.6%); median age was 60 and 61 years, respectively. Median number of prior therapies was 1. At a median follow-up of 25.3 months, PFS by independent review committee (IRC) was improved with zanubrutinib vs ibrutinib (hazard ratio [HR], 0.24; 95% CI, 0.09-0.64; nominal 2-sided P=.002), with 18-month landmark PFS rates of 88.9% vs 71.6%, respectively. Additionally, zanubrutinib was more favorable in patients with high-risk del17p/TP53 mutation (18-month landmark, 80.0% vs 64.3%; HR, 0.51; 95% CI, 0.12-2.13). ORR also favored zanubrutinib over ibrutinib by IRC (87.2% vs 76.7%; 95% CI, 0.93-1.38). The treatment discontinuation rate was lower with zanubrutinib (14.9%) vs ibrutinib (41.9%), with most discontinuations being due to progressive disease (6.4% vs 20.9%) and adverse events (AEs; 6.4% vs 14.0%). Rates of grade ≥3 AEs (64.4% vs 72.1%) and serious AEs (35.6% vs 51.2%) were lower with zanubrutinib vs ibrutinib. With zanubrutinib, 4 deaths (8.5%) were reported compared with 8 deaths (18.6%) with ibrutinib (HR, 0.45; 95% CI, 0.14-1.50).

Conclusion: Zanubrutinib showed improved PFS over ibrutinib in the ALPINE study in patients from China, including high-risk patients, consistent with results in the global population. A favorable safety profile was also observed in patients from China who received zanubrutinib vs ibrutinib, with lower rates of treatment discontinuations and serious AEs in patients with R/R CLL/SLL.