Improved efficacy and safety of zanubrutinib versus ibrutinib in patients with relapsed/refractory chronic lymphocytic leukemia (R/R CLL) in China: A subgroup of ALPINE

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Introduction: Zanubrutinib is an irreversible, potent, next-generation Bruton tyrosine kinase (BTK) inhibitor designed to maximize BTK occupancy and minimize off-target inhibition. In a randomized phase 3 study (ALPINE; NCT03734016), zanubrutinib was compared head to head with ibrutinib as a treatment for R/R 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 in pts from China are reported here.

Methods: Patients (pts) 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 geographical region (**China vs non-China**). Data from the subgroup in pts from China were descriptively analyzed.

**Results:** A total of 90 pts 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 (aged ≥65 y [40% vs 37%]; unmutated IGHV [59.6% vs 62.8%]; del17p/TP53 mutated [34.0% vs 32.6%]) with a median age of 60 and 61 y, respectively. Median number of prior therapies was 1. At a median follow-up of 25.3 mo, 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 \(P = 0.002\)) with 18-mo landmark PFS rates of 88.9% vs 71.6% for zanubrutinib and ibrutinib, respectively (**Figure**). Additionally, zanubrutinib was more favorable in high-risk del17p/TP53 mutation (18-mo landmark 80.0% vs 64.3%; HR: 0.51; 95% CI 0.12-2.13). ORR also favored zanubrutinib over ibrutinib (87.2% vs 76.7%; 95% CI 0.93-1.38) by IRC. The treatment discontinuation rate was lower with zanubrutinib (14.9%) vs ibrutinib (41.9%) with most 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 to 8 deaths (18.6%) with ibrutinib (HR: 0.45; 95% CI 0.14-1.50).

**Conclusions:** Zanubrutinib showed improved PFS over ibrutinib in the ALPINE study in pts from China, including high-risk pts, consistent with that of the global population. A favorable safety profile was also observed in pts from China with zanubrutinib compared with ibrutinib, with lower rates of treatment discontinuations and serious AEs in patients with R/R CLL/SLL.
**Figure.** Kaplan-Meier Plot of PFS by IRC for the Subgroup in pts from China

No. of patients at risk

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Months from randomization

Progression-free survival probability, %