Pooled safety analysis of zanubrutinib monotherapy in Asian patients with B-cell malignancies

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**Background:** In patients (pts) with B-cell malignancies, continuous treatment with the first-generation Bruton tyrosine kinase inhibitor (BTKi) ibrutinib is often limited due to toxicities that may be associated with inhibition of off-target kinases. Zanubrutinib is a potent and selective next-generation BTKi designed to maximize BTK occupancy and minimize off-target effects. Here, we present the pooled safety analysis of 406 Asian pts treated with zanubrutinib.

**Methods:** A post hoc pooled safety analysis of Asian pts from 10 clinical trials of zanubrutinib was performed. The analyses included pts with CLL/SLL, MCL, WM, FL, DLBCL, and MZL. Treatment-emergent adverse events (TEAEs) were summarized using MedDRA preferred terms and adverse events of special interest (AESIs) using pooled terms. Rates of TEAEs, exposure-adjusted incidence rates, and prevalence over time of AESIs were assessed.

**Results:** The analyses included 406 Asian pts (median age, 61 yrs) treated with zanubrutinib monotherapy. Median exposure to zanubrutinib was 25.0 mo, with 38.7% of pts receiving treatment ≥36 mo. Zanubrutinib discontinuation due to any TEAE occurred in 10.6% of pts; TEAEs leading to dose reduction occurred in 7.4%. Most common nonhematologic TEAEs of any grade were upper respiratory tract infection (38.2%), pneumonia (26.4%), and rash (21.2%). Pneumonia (16.0%) and anemia (8.1%) were the most common grade ≥3 TEAEs. Serious TEAEs occurred in 43.8% of pts, with pneumonia (14.5%) being the only serious TEAE in ≥10% of pts. Prevalence of AESIs tended to remain constant or decrease with longer follow-up. There were no cases of grade ≥3 atrial fibrillation and flutter. Deaths attributed to TEAEs occurred in 4.9% of pts, with most (2.0%) due to infections. Cardiac disorder–related deaths were 1.0% (n=4).

**Conclusions:** Zanubrutinib AEs were mild-to-moderate in severity and tended not to lead to treatment discontinuation. Prevalence of AESIs generally reduced over time without emergence of new safety signals. The overall safety profile in the present analysis remains largely consistent with previous reports for zanubrutinib, supporting its use as an appropriate long-term treatment option for Asian pts with B-cell malignancies.