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

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ABSTRACT

Background: In patients 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 patients treated with zanubrutinib.

Methods: A post hoc pooled safety analysis of Asian patients from 10 clinical trials of zanubrutinib was performed. The analyses included patients 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 pre-defined grouped terms. Rates of TEAEs and exposure-adjusted incidence rates of AESIs were assessed.

Results: The analyses included 406 Asian patients (median age, 61 years) treated with zanubrutinib monotherapy. Median exposure to zanubrutinib was 25.0 months, with 38.7% of patients receiving treatment ≥36 months. Zanubrutinib discontinuation due to any TEAE occurred in 10.6% of patients; 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 patients, with pneumonia (14.5%) being the only serious TEAE in ≥10% of patients. There were no cases of grade ≥3 atrial fibrillation and flutter. Deaths attributed to TEAEs occurred in 4.9% of patients, 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 only a minority lead to treatment discontinuation. The overall safety profile in the present analysis remains largely consistent with previous reports, suggesting that zanubrutinib is well tolerated in Asian patients with B-cell malignancies.