Zanubrutinib vs venetoclax+obinutuzumab in treatment-naive (TN) chronic lymphocytic leukemia (CLL)

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ABSTRACT

Background: Continuous zanubrutinib (zanu) efficacy has been evaluated in SEQUOIA (NCT03336333) in TN CLL/SLL, while fixed-duration venetoclax+obinutuzumab (VenO) was evaluated in CLL14 (NCT02242942). An unanchored matching-adjusted indirect comparison (MAIC) was conducted to compare survival (PFS and OS) and adverse events of interest (AEIs) between zanu (SEQUOIA) and VenO (CLL14).

Methods: The MAIC used study data with similar median follow-up periods (SEQUOIA, 62.67 mo; CLL14, 65.4 mo). Individual patient data of zanu were reweighted to match key patient characteristics of VenO. For the AEI analysis, incidence rates of infections, hematologic events, and treatment-emergent adverse events (TEAEs) leading to treatment (tx) discontinuation (dx) of zanu in SEQUOIA (n=351) and VenO in CLL14 (n=212) were compared.

Results: After applying matching adjustment to align with the patient characteristics of the VenO in CLL14 (N=216), the effective sample size for zanu in SEQUOIA was 163. Zanu had longer PFS ($HR_{PFS\text{-}INV}$=0.66 [95% CI: 0.44-0.97]; *P*=0.0351) and a trend for extended OS (HR_{OS}=0.89 [95% CI: 0.55-1.46]; *P*=0.6468). With a median tx duration of 23.9 mo with zanu vs 11.1 mo with VenO, the incidence of grade 3/4 infections (excluding COVID-19) was similar; grade 3/4 neutropenia, thrombocytopenia, and febrile neutropenia, and TEAEs leading to dx, were lower with zanu vs VenO (nominal *P*<.05 for all).

Conclusions: This MAIC suggested zanu had longer PFS and a trend for extended OS vs VenO. Hematologic toxicity rates and TEAEs leading to dx were also lower with zanu vs VenO.