SEQUOIA 5-year follow-up in arm C: frontline zanubrutinib in patients with del(17p) and treatment-naive chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)

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ABSTRACT

Background: Zanubrutinib, a next-generation Bruton tyrosine kinase inhibitor is approved for CLL/SLL. Initial results from the SEQUOIA study (NCT03336333), demonstrated superior progression-free survival (PFS) with zanubrutinib vs bendamustine+rituximab (arms A and B) in patients with treatment-naive (TN) CLL/SLL without del(17p) and high overall response rate (ORR) and PFS benefit in patients with del(17p) (arm C). Here we report updated results in SEQUOIA arm C, in patients with del(17p), after approximately 5 years of follow-up (data cutoff: Apr 30, 2024).

Methods: Arm C is a nonrandomized cohort of SEQUOIA patients with del(17p) that received zanubrutinib. Investigator-assessed PFS, overall survival (OS), ORR, and safety/tolerability were evaluated. Adverse events (AEs) were recorded until disease progression or start of next-line therapy.

Results: Between Feb 2018-Mar 2019, 111 TN patients with del(17p) were enrolled to receive zanubrutinib. Median age was 71 years (range, 42-87), 79 (71%) were male, 67 (60%) were IGHV unmutated, and 47 (42%) had both del(17p) and *TP53* mutation. At a median follow-up of 65.8 months (range, 5-75), median PFS was not reached. The estimated 60-month PFS rate was 72.2% (62.4%-79.8%), or 73.0% (63.3%-80.6%) when adjusted for COVID-19. Median OS was also not reached. The estimated 60-month OS rate was 85.1% (76.9%-90.6%), or 87.0% (79.0%-92.1%) when adjusted for COVID-19. The ORR was 97.3%, and the complete response/complete response with incomplete hematologic recovery rate was 18.2%. Zanubrutinib treatment was ongoing in 62.2% of patients. Most common AEs of interest (AEI) included any-grade infection (82%), bleeding (60%) and neutropenia (19%). Grade ≥3 AEI included infection (33%), neutropenia (16%) and hypertension (8%).

Conclusions: In this 5-year SEQUOIA follow-up, the efficacy of zanubrutinib in patients with del(17p) was maintained and patients continue to demonstrate PFS benefits consistent with the randomized cohort of patients without del(17p). Additionally, with longer-term follow-up, no new safety signals were identified. This update, in the largest cohort of uniformly treated patients with del(17p), suggests that zanubrutinib remains a valuable frontline treatment option for patients with or without del(17p) CLL/SLL. Updated data will be available for the presentation.