Zanubrutinib vs bendamustine + rituximab (BR) in patients with treatment-naive (TN) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL): extended follow-up of the SEQUOIA study

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Aim: In SEQUOIA (NCT03336333), zanubrutinib displayed superior PFS vs BR in patients with TN CLL/SLL without del(17p); patients with del(17p) treated with zanubrutinib monotherapy showed similar outcomes. We report updated results from SEQUOIA (further 18 months of follow-up).

Method: Patients without del(17p) were randomized to receive zanubrutinib or BR; patients with del(17p) received zanubrutinib monotherapy. PFS, OS, ORR, and safety were evaluated. AEs were recorded until progression or start of next-line therapy.

Results: As of 31 October 2022, 479 patients without del(17p) were randomized to zanubrutinib (n=241) or BR (n=238). Median follow-up was 43.7 months (range, 0-60). Median PFS was not reached with zanubrutinib and 42.2 months with BR (HR, 0.30; 95% CI, 0.21-0.43). Estimated PFS rate at 42 months with zanubrutinib was 82.4%. PFS improved with zanubrutinib vs BR in patients with mutated *IGHV* (HR, 0.35; 95% CI, 0.19-0.64) and was sustained in patients with unmutated *IGHV* (HR, 0.23; 95% CI, 0.14-0.37). CR/CRi rates in patients without del(17p) were 17.4% (zanubrutinib) and 21.8% (BR). Median OS was not reached in either arm (HR, 0.87; 95% CI, 0.50-1.48); OS at 42 months was 89.4% (zanubrutinib) and 88.3% (BR). In 110 patients with del(17p), median follow-up was 47.9 months; 42-month PFS and OS rates were 79.4% and 89.5%, respectively, and the CR/CRi rate was 14.5%. Common causes of treatment discontinuation were AEs and progressive disease in those without (14.9% and 5.8%, respectively) and with del(17p) (13.5% each). Grade ≥3 AEs of interest included bleeding (5.8%, 1.8%), infection (23.8%, 22.0%), anemia (0.4%, 2.2%), thrombocytopenia (2.1%, 7.9%), and neutropenia (12.5%, 51.1%).

Conclusion: Extended follow-up SEQUOIA data showed that the efficacy and safety of zanubrutinib were maintained in patients without del(17p). Longer follow-up showed benefit in patients with mutated *IGHV.* Patients with del(17p) continued to demonstrate PFS benefit consistent with the randomized cohort.