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

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Background: Zanubrutinib is a next-generation Bruton tyrosine kinase inhibitor that is approved for 5 indications, including CLL/SLL. Initial results from the SEQUOIA study (NCT03336333), at a median follow-up of 26.2 months, demonstrated superior progression-free survival (PFS) by independent review with zanubrutinib vs bendamustine + rituximab (arms A and B) in patients with treatment-naive CLL/SLL without del(17p) as well as high overall response rate (ORR) and PFS benefit in patients with del(17p) (arm C). Additionally, the 5-year follow-up in arm A demonstrated durable PFS benefit, with estimated 54- and 60-month PFS rates of 80% and 76%, respectively.

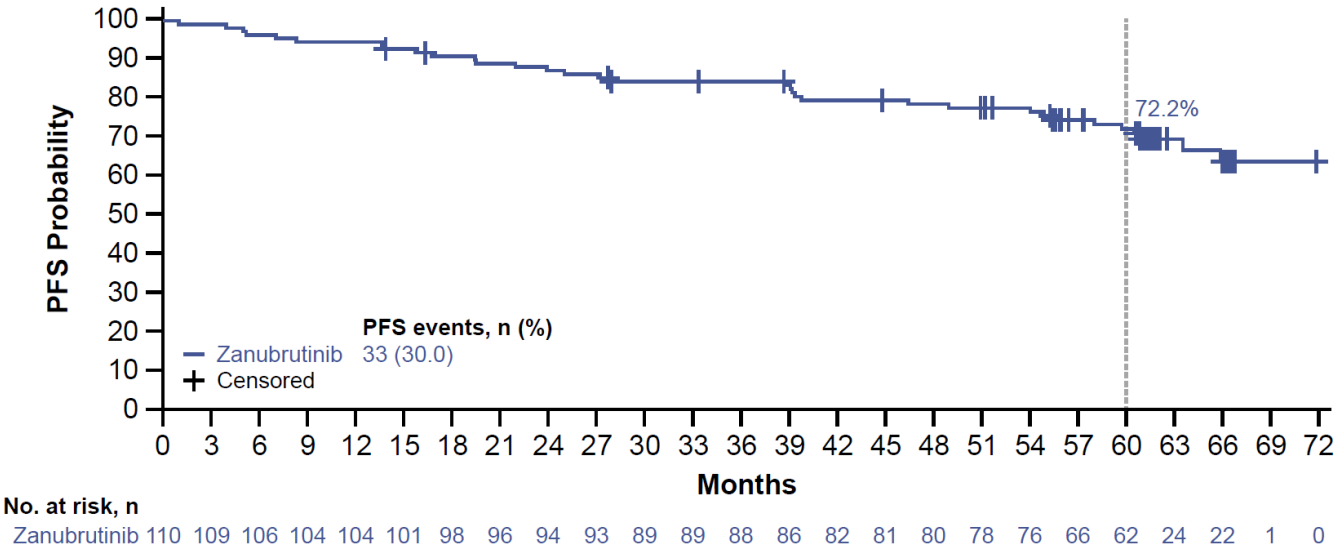
Aims: Here we report updated results in SEQUOIA arm C, in patients with del(17p), after approximately 5 years of follow-up (data cutoff: Apr 30, 2024).

Methods: Arm C is a nonrandomized cohort of SEQUOIA patients with del(17p) that received zanubrutinib monotherapy. 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 and Mar 2019, 111 treatment-naive patients with del(17p) were enrolled to receive zanubrutinib. The median age was 71 years (range, 42-87 years), 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 months), median PFS was not reached. The estimated 60-month PFS rate was 72.2% (62.4%-79.8%) (Figure), 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. The most common causes for treatment discontinuation were AEs and progressive disease (in 17.1% and 15.3%, respectively). Key AEs of interest (AEI) included any-grade infection (82%), bleeding (60%), neutropenia (19%), hypertension (18%), anemia (9%), thrombocytopenia (8%), and atrial fibrillation/flutter (7%). Grade ≥3 AEI included infection (33%), neutropenia (16%), hypertension (8%), bleeding (6%), atrial fibrillation/flutter (5%), and thrombocytopenia (2%).

Summary/Conclusion: With this 5-year follow-up in SEQUOIA, the efficacy of zanubrutinib in treatment-naive higher-risk patients with del(17p) was maintained, and patients continue to demonstrate PFS benefits consistent with the randomized cohort of patients without del(17p) (arm A). 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.

Figure: PFS[a]



No. at risk, n

Zanubrutinib	110	109	106	104	104	101	98	96	94	93	89	89	88	86	82	81	80	78	76	66	62	24	22	1	0

[a]Kaplan-Meier plot of PFS in patients with del(17p), confirmed by central laboratory (N=110).