

ZANUBRUTINIB (ZANU) VS BENDAMUSTINE + RITUXIMAB (BR) IN PATIENTS (PTS) WITH TREATMENT-NAIVE (TN) CHRONIC LYMPHOCYTIC LEUKEMIA/SMALL LYMPHOCYTIC LYMPHOMA (CLL/SLL): EXTENDED FOLLOW-UP OF THE SEQUOIA STUDY

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Introduction: Zanu is a next-generation BTKi designed to limit off-target binding and side effects. Results from SEQUOIA (NCT03336333) showed superior PFS with zanu vs BR in pts with TN CLL/SLL without (w/o) del(17p); pts with del(17p) treated with zanu in a separate cohort had similar outcomes.

Aim: To report updated results from SEQUOIA (further 18 mo of follow-up).

Material or patients and method: Pts w/o del(17p) were randomized to receive zanu or BR. Pts with del(17p) received zanu monotherapy. PFS, OS, ORR, and safety were evaluated. AEs were recorded until progression or start of next-line therapy.

Results: As of 31 Oct 2022, 479 pts w/o del(17p) were randomized to receive zanu (n=241) or BR (n=238) (median follow-up, 43.7 mo; range, 0-60 mo). Median PFS was not reached with zanu and was 42.2 mo with BR (HR, 0.30; 95% CI, 0.21-0.43) (Figure); 42-mo PFS was 82.4% with zanu. PFS was improved with zanu vs BR in pts with mutated IGHV (HR, 0.35; 95% CI, 0.19-0.64) and was sustained in pts with unmutated IGHV (HR, 0.23; 95% CI, 0.14-0.37). CR/CRi rates in pts w/o del(17p) were 17.4% with zanu and 21.8% with BR. Median OS was not reached in either arm (zanu vs BR: HR, 0.87; 95% CI, 0.50-1.48); OS at 42 mo was 89.4% with zanu and 88.3% with BR. In 110 pts with del(17p) (zanu monotherapy), median follow-up was 47.9 mo; 42-mo PFS and OS rates were 79.4% and 89.5%, respectively, and the CR/CRi rate was 14.5%. Treatment (tx) continued in 74.7% of pts w/o del(17p) and 70.3% with del(17p). The most common causes of tx discontinuation were AEs and progressive disease in those w/o (14.9% and 5.8%, respectively) and with del(17p) (13.5% each). Any-grade AEs of interest (AEI) included atrial fibrillation/flutter (zanu, BR: 5.0%, 2.6%), hypertension (17.5%, 13.7%), bleeding (48.8%, 12.3%), infection (72.9%, 62.6%), anemia (7.1%, 20.7%), thrombocytopenia (6.3%, 18.1%), and neutropenia (16.7%, 56.8%); grade ≥ 3 AEI 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%).

Conclusions: Extended follow-up in SEQUOIA showed that efficacy and safety of zanu were maintained in pts w/o del(17p). Longer follow-up showed benefit in pts with mutated IGHV, and pts with del(17p) continue to show PFS benefit consistent with that in the randomized cohort. Atrial fibrillation rates remain low with no new safety signals. Zanu remains well tolerated with low rates of tx discontinuation and is a valuable frontline option for CLL/SLL.

Figure: Progression-Free Survival by Investigator Assessment

