Abstract: P639

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

Abstract Type: Poster Presentation

Session Title: Chronic lymphocytic leukemia and related disorders - Clinical

Background:

ZANU is a next-generation Bruton tyrosine kinase inhibitor (BTKi) designed to minimize off-target binding and limit associated side effects that is approved in the US and EU for CLL/SLL. Results from the SEQUOIA study (NCT03336333), at a median follow-up of 26.2 mo, demonstrated superior progression-free survival (PFS) by independent review for ZANU vs BR in pts with treatment-naïve (TN) CLL/SLL without (w/o) del(17p); pts with del(17p) treated with ZANU in a separate cohort had similar outcomes to pts w/o del(17p).

Aims:

To report updated efficacy and safety results from the SEQUOIA study after approximately 18 mo of additional follow-up (data cutoff 31 Oct 2022).

Methods:

Patients w/o del(17p) were randomized to receive ZANU or BR. Pts with del(17p) were assigned to ZANU monotherapy. Investigator-assessed (INV) PFS, overall survival (OS), overall response rate (ORR) and safety/tolerability were evaluated. Adverse events (AEs) were collected until disease progression or start of next-line therapy.

Results:

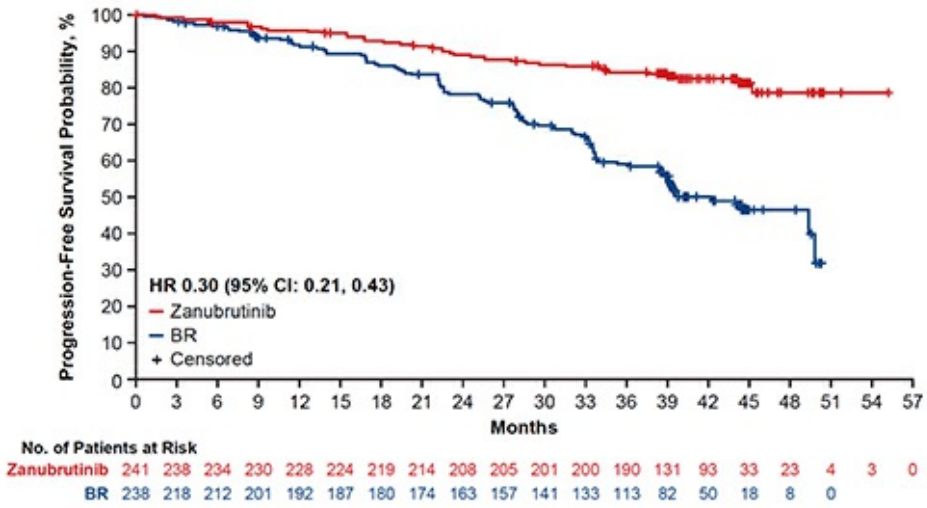
A total of 479 pts w/o del(17p) were randomized to receive ZANU (n=241) or BR (n=238). At a median follow-up of 43.7 mo (range: 0–60 mo), median PFS was not reached for ZANU; however, for BR median PFS was 42.2 mo (HR 0.30; 95% CI: 0.21, 0.43; **Figure**). At 42 mo, estimated PFS rates were 82.4% for ZANU. With additional follow-up, PFS for ZANU vs BR was now improved for pts with mutated IGHV (HR 0.35; 95% CI: 0.19, 0.64); benefit was also sustained for pts with unmutated IGHV (HR 0.23; 95% CI: 0.14, 0.37) or del(11q) (HR 0.26; 95% CI: 0.13, 0.51). Complete response/complete response with incomplete hematological recovery (CR/CRi) rates in pts w/o del(17p) were 17.4% and 21.8% with ZANU and BR, respectively. While median OS was not reached in either arm, HR for OS was 0.87 (95% CI: 0.50, 1.48) for ZANU vs BR, and estimated 42-month rates were 89.4% and 88.3%, respectively. For 110 pts with del(17p) assigned to ZANU monotherapy, after a median follow-up of 47.9 mo, the estimated 42-month PFS and OS rates were 79.4% and 89.5%, respectively. In this population, the CR/CRi rate was 14.5%.

As of 31 Oct 2022, ZANU treatment was ongoing in 74.7% pts w/o del(17p) and 70.3% pts with del(17p). The most common causes for treatment discontinuation were AEs and progressive disease for both those w/o del(17p) (14.9%, 5.8%) and with del(17p) (13.5%, 13.5%, respectively). AEs of interest (AEI), using pooled terms, were as expected for the class in the pts w/o del(17p) (ZANU vs BR). AEI included any grade (gr) atrial fibrillation/flutter (5.0% vs 2.6%), hypertension (17.5% vs 13.7%), bleeding (48.8% vs 12.3%), infection (72.9% vs 62.6%), anemia (7.1% vs 20.7%), thrombocytopenia (6.3% vs 18.1%), and neutropenia (16.7% vs 56.8%). Additionally, Gr≥3 AEI included bleeding (5.8% vs 1.8%), infection (23.8% vs 22.0%), anemia (0.4% vs 2.2%), thrombocytopenia (2.1% vs 7.9%), and neutropenia (12.5% vs 51.1%).

Summary/Conclusion:

With extended follow-up in the SEQUOIA study, the efficacy of ZANU was maintained in pts w/o del(17p) with a safety profile aligned with long term follow-up for the BTKi class. In addition to the previously reported benefit in pts with unmutated IGHV, longer follow-up now shows benefit in those with mutated IGHV as well, and pts with del(17p) continue to demonstrate PFS benefits consistent with the randomized cohort. Rates of atrial fibrillation remain low and no new safety signals were identified. ZANU continues to be well tolerated over time with low rates of treatment discontinuation and remains a valuable frontline treatment option for CLL/SLL.

Figure: Progression-Free Survival by Investigator Assessment



Keywords: Chronic lymphocytic leukemia, Bruton's tyrosine kinase inhibitor (BTKi)