**SEQUOIA: RESULTS OF A PHASE 3 RANDOMIZED STUDY OF ZANUBRUTINIB (ZANU) VERSUS BENDAMUSTINE + RITUXIMAB (BR) IN PATIENTS (PTS) WITH TREATMENT-NAÏVE (TN) CHRONIC LYMPHOCYTIC LEUKEMIA/SMALL LYMPHOCYTIC LYMPHOMA (CLL/SLL)**

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**Objectives**: To present interim safety and efficacy outcomes of the phase 3 SEQUOIA study (NCT03336333) of ZANU vs BR in TN pts with CLL/SLL. **Methods**: TN pts with CLL/SLL without del(17p) were randomized to receive ZANU 160 mg twice daily until progressive disease or unacceptable toxicity, or bendamustine 90 mg/m$^2$ on days 1 and 2 and rituximab 375 mg/m$^2$ in cycle 1, 500 mg/m$^2$ in cycles 2-6 for 6×28-day cycles. Eligible pts were adults with CLL/SLL per International Workshop on CLL (iwCLL) who were either ≥65 y or unsuitable for treatment with fludarabine, cyclophosphamide, and rituximab. Central verification of del(17p) status was required. Pts were stratified by age, Binet stage, immunoglobulin heavy chain gene (IGHV) mutational status, and geographic region. Primary endpoint was independent review committee (IRC)-assessed progression-free survival (PFS). Secondary endpoints were investigator-assessed (INV) PFS, overall response rate (ORR; by IRC and INV), overall survival (OS), and safety. Responses for CLL and SLL were assessed per modified iwCLL criteria and Lugano criteria, respectively. Adverse events (AEs) were recorded until disease progression. **Results**: Between Oct 31, 2017, and Jul 22, 2019, 479 pts without del(17p) were randomized (241 ZANU; 238 BR). Baseline patient characteristics were balanced (**Table**). At median follow-up (26.2 mo), PFS was significantly prolonged with ZANU vs BR (IRC: Hazard Ratio (HR) 0.42, 95% Confidence Interval (CI) 0.28-0.63, 1-sided and 2-sided $p$<0.0001; INV: HR 0.42, 95% CI 0.27-0.66, 1-sided $p$<0.0001, 2-sided $p$=0.0001). Treatment benefit for ZANU was observed across subgroups for age, Binet stage, bulky disease, del(11q) status, and for pts with unmutated IGHV (HR 0.24, 1-sided and 2-sided $p$<0.0001), but not for mutated IGHV (HR 0.67, 1-sided $p$=0.0929). Key efficacy results are shown in the **Table**. AEs of interest during the full reporting period (pooled terms, ZANU vs BR) included atrial fibrillation (any grade [gr]: 3.3% vs 2.6%), bleeding (any gr/gr≥3: 45.0%/3.8% vs 11.0%/1.8%), hypertension (any gr: 14.2% vs 10.6%), infection (any gr/gr≥3: 62.1%/16.3% vs 55.9%/18.9%), and neutropenia (any gr/gr≥3: 15.8%/11.7% vs 56.8%/51.1%). Treatment discontinuation due to AEs for ZANU vs BR occurred in 20 (8.3%) and 31 (13.7%) pts, respectively; 85.5% of pts receiving ZANU remain on treatment. AEs leading to death for ZANU vs BR occurred in 11 (4.6%) and 12 (5.3%) pts, respectively. No sudden deaths were reported. **Conclusions**: ZANU demonstrated significant improvement in PFS (IRC) and superior PFS (INV) and ORR (IRC and INV) compared to BR. ZANU was generally well tolerated, with low rates of atrial fibrillation consistent with published data. Interim results support the potential use of ZANU in the frontline management of pts with TN CLL/SLL.

**Summary of Characteristics and Efficacy Outcomes**

| | Arm A, ZANU (n = 241) | Arm B, BR (n = 238) |
|---|---|---|
| ***Baseline Demographic and Disease Characteristics*** | | |
| Median age, y | 70 | 70 |
| Unmutated IGHV, % (n) | 53.4 (125/234) | 52.4 (121/231) |
| del(11q) | 17.8 | 19.3 |
| ***Key Efficacy Outcomes in TN Pts Without del(17p)*** | | |
| Estimated 24-mo PFS (IRC), % (95% CI) | 85.5 (80.1-89.6) | 69.5 (62.4-75.5) |
| Estimated 24-mo OS, % (95% CI) | 94.3 (90.4-96.7) | 94.6 (90.6-96.9) |
| ORR (IRC), % (95% CI) | 94.6 (91.0-97.1) | 85.3 (80.1-89.5) |
| ORR (INV), % (95% CI) | 97.5 (94.7-99.1) | 88.7 (83.9-92.4) |
| Complete response rate (IRC), % | 6.6 | 15.1 |