### Title

71 | FINAL ANALYSIS OF FIXED-DURATION IBRUTINIB + VENETOCLAX FOR CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)/SMALL LYMPHOCYTIC LYMPHOMA (SLL) IN THE PHASE 2 CAPTIVATE STUDY




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## 71 | FINAL ANALYSIS OF FIXED-DURATION IBRUTINIB + VENETOCLAX FOR CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)/SMALL LYMPHOCYTIC LYMPHOMA (SLL) IN THE PHASE 2 CAPTIVATE STUDY

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**Clinical Trial Information:** NCT02910583

**Introduction:** First-line ibrutinib (Ibr) + venetoclax (Ven) treatment for CLL/SLL was tested in the phase 2 CAPTIVATE

study, including minimal residual disease (MRD)–guided randomized discontinuation (MRD cohort) and Fixed Duration (FD) cohorts. We report final analysis results for patients (pts) treated with FD Ibr+Ven in the FD cohort and MRD cohort placebo arm.

**Methods:** Pts ≤ 70 y with previously untreated CLL/SLL received 3 cycles of Ibr, then 12 cycles of Ibr+Ven (Ibr, 420 mg/d orally; Ven, 5-wk ramp up to 400 mg/d orally), up to 13 cycles in the MRD cohort placebo arm. On-study retreatment included single-agent Ibr; FD cohort pts with progressive disease (PD) > 2 y after end of treatment (EOT) could be retreated with FD Ibr+Ven.

**Results:** 202 pts completed FD Ibr+Ven (FD cohort, $n = 159$; MRD cohort placebo arm, $n = 43$). With median follow-up of 68.9 mo (range, 0.8–83.9), 5.5-y PFS and OS rates (95% CI) were 66% (58–72) and 97% (93–99), respectively. 5.5-y PFS rates (95% CI) in pts without and with del(17p)/mutated *TP53* were 70% (62–76) and 36% (17–55), respectively. In pts with unmutated IGHV, 5.5-y PFS was 55% (45–64): 63% (49–74) in pts without, and 44% (28–60) in pts with, concomitant del (17p)/mutated *TP53*/complex karyotype. The corresponding rates for pts with mutated IGHV were 79% (68–87), 85% (71–93), and 62% (34–81). Undetectable MRD (uMRD4; $< 10^{-4}$ by flow cytometry) was achieved in peripheral blood (PB) in 54% of pts at C7 and 69% at EOT, and in bone marrow in 69% of pts at EOT. 5.5-y PFS rates (95% CI) were higher in pts with uMRD4 in PB at EOT (75% [67–82]) versus those with MRD (47% [33–59]). 64 pts had PD after completion of FD Ibr+Ven. 5.5-y freedom from next-line treatment was 73% (95% CI 66–79). Of 40 pts with available samples at PD to date, 1 had an acquired subclonal mutation in *BCL2* of unclear significance (A113G, VAF 8.3%); none had acquired resistance-associated mutations in *BTK* or *PLCG2*. 36 pts initiated retreatment with Ibr ($n = 25$) or Ibr+Ven ($n = 11$). With 28.4 mo median follow-up on Ibr retreatment (range, 3.7–59.1), ORR was 76% (best response: 1 CR; 1 nodular PR; 17 PR; 4 SD; 1 PD [Richter transformation]; 1 no assessment); 2-y PFS and OS rates from the start of retreatment were 91% and 96%, respectively. With 15.2 mo median follow-up on Ibr+Ven retreatment (range, 7.4–29.3), ORR was 82% (best response: 1 CR; 8 PR; 2 SD); 1-y PFS and OS rates from the start of retreatment were both 100%. Second malignancies occurred in 24 pts across the entire study period, including 12 initial treatment and 4 retreatment TEAEs.

**Conclusions:** Ibr+Ven is an all-oral, once-daily, chemotherapy-free FD regimen for first-line treatment of CLL/SLL that continues to provide durable PFS and OS with long-term follow-up, including in pts with high-risk genomic features. Ibr-based retreatment provided durable responses in pts needing subsequent therapy after completion of FD Ibr+Ven.

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## 72 | SEQUOIA 5-YEAR FOLLOW-UP IN ARM C: FRONTLINE ZANUBRUTINIB IN PATIENTS WITH DEL(17P) AND TREATMENT-NAIVE CHRONIC LYMPHOCYTIC LEUKEMIA/SMALL LYMPHOCYTIC LYMPHOMA (CLL/SLL)

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**Introduction:** Zanubrutinib is a next-generation Bruton tyrosine kinase inhibitor that is approved for five 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 versus 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. 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