Abstract: P617

Title: FIXED-DURATION (FD) IBRUTINIB + VENETOCLAX FOR FIRST-LINE TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)/SMALL LYMPHOCYTIC LYMPHOMA (SLL): 4-Y FOLLOW-UP FROM FD COHORT OF PHASE 2 CAPTIVATE STUDY

Abstract Type: Poster Presentation

Session Title: Chronic lymphocytic leukemia and related disorders - Clinical

Background:

CAPTIVATE (PCYC-1142) is a multicenter phase 2 study of first-line ibrutinib (Ibr) + venetoclax (Ven) in CLL/SLL. Follow-up results from the fixed duration (FD) cohort showed a 3-year progression-free survival (PFS) rate of 88% overall and rates ≥80% in patients with high-risk features (Wierda, ASCO 2022).

Aims:

Here we present updated results from the FD cohort with 4-year follow-up.

Methods:

Patients aged ≤70 years with previously untreated CLL/SLL received 3 cycles of ibrutinib then 12 cycles of Ibr + Ven (Ibr 420 mg/day orally; Ven ramp-up to 400 mg/day orally). Responses were investigator assessed per iwCLL 2008 criteria. Undetectable minimal residual disease (uMRD; $<10^{-4}$) was assessed by 8-color flow cytometry.

Results:

159 patients were enrolled, including patients with high-risk features of unmutated IGHV (uIGHV) (56%) or del(17p) and/or *TP53* mutation (17%). Median time on study was 50 months (range 1–53). At 4 years of follow-up, the best complete response (CR) rate was 58% and the overall response rate was unchanged at 96%. At 4 years, the PFS rate was 79% (95% CI 71–84) and the overall survival (OS) rate was 98% (95% CI 94–99). 4-year PFS rates were numerically lower in patients with uIGHV (73%) or del(17p) and/or *TP53* mutation (63%), while OS rates remained consistently high (Table). 4-year PFS rates by MRD status 3 months after stopping treatment (EOT+3) were significantly higher overall in patients with uMRD vs detectable MRD (dMRD) in peripheral blood (PB) (90% vs. 66%, Table); this difference was minimal at 24 months (100% vs 91%). Median time to next treatment was not reached overall (range 1–53 months); the 4-year rate of freedom from next treatment was 84% (95% CI 77–89). Second malignancies continue to be collected off treatment; 1 adverse event (AE) of prostate cancer occurred during this year of follow-up.

To date, 19 patients with progressive disease (PD) after completing fixed duration Ibr + Ven in either the FD cohort or MRD cohort placebo arm initiated retreatment with ibrutinib. Responses in 17 patients with available data were 1 CR, 13 partial responses (PR), and 1 each PR with lymphocytosis, stable disease, and PD. Median time on retreatment was 11 months (range 0–39). The most common AEs (≥10%) with retreatment were diarrhea (n=3), COVID-19 (n=3), and anemia (n=2). In addition, 4 patients have started Ibr + Ven retreatment to date.

Summary/Conclusion:

Results of the CAPTIVATE study support Ibr + Ven an all-oral, once-daily, chemotherapy-free fixed-duration regimen for previously untreated patients with CLL/SLL. With 4-year follow-up, fixed-duration Ibr + Ven continues to provide deep, durable remissions with clinically meaningful PFS and time off treatment, including in patients with high-risk disease features. New safety findings off-treatment were negligible, highlighting the benefits of a fixed-duration regimen. Promising responses were observed upon retreatment with ibrutinib in progressing patients.

Clinical trial information: NCT02910583

	4-year PFS, % (95% CI)	4-year OS, % (95% CI)
FD Cohort (N=159)	79 (71–84)	98 (94–99)
del(17p) and/or *TP53* (n=27)	63 (41–79)	96 (76–99)
uIGHV (n=89)	73 (62–81)	97 (90–99)
uMRD at EOT+3, PB (n=90)	90 (81–95)	100
dMRD at EOT+3, PB (n=57)	66 (52–77)	100

Keywords: Chronic lymphocytic leukemia, Clinical trial, ibrutinib