EUROPEAN HEMATOLOGY ASSOCIATION

EHA2021 VIRTUAL

S147

PRIMARY ANALYSIS OF THE FIXED-DURATION COHORT FROM THE PHASE 2 CAPTIVATE STUDY OF FIRST-LINE IBRUTINIB + VENETOCLAX FOR CHRONIC LYMPHOCYTIC LEUKEMIA/SMALL LYMPHOCYTIC LYMPHOMA

Topic: 06. Chronic lymphocytic leukemia and related disorders - Clinical

Keywords: BCL2 | Chronic lymphocytic leukemia | Ibrutinib | Phase II

John N. Allan[1], William G. Wierda[2], Tanya Siddiqi[3], Thomas J. Kipps[4], Ryan Jacobs[5], Stephen Opat[6], Paul M. Barr[7], Alessandra Tedeschi[8], Livio Trentin[9], Rajat Bannerji[10], Sharon Jackson[11], Bryone Kuss[12], Carol Moreno[13], Edith Szafer-Glusman[14], Kristin Russell[14], Cathy Zhou[14], Joi Ninomoto[14], James P. Dean[14], Constantine Tam[15], Paolo Ghia[16]

[1] Weill Cornell Medicine, New York, NY, United States
[2] Department of Leukemia, University of Texas MD Anderson Cancer Center, Houston, TX, United States
[3] City of Hope National Medical Center, Duarte, CA, United States
[4] UCSD Moores Cancer Center, San Diego, CA, United States
[5] Levine Cancer Institute, Charlotte, NC, United States
[6] Monash University, Clayton, VIC, Australia
[7] Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY, United States
[8] ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy
[9] Hematology and Clinical Immunology Unit, Department of Medicine, University of Padova, Padova, Italy
[10] Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, United States
[11] Middlemore Hospital, Auckland, New Zealand
[12] Flinders University and Medical Centre, Bedford Park, SA, Australia
[13] Hospital de la Santa Creu i Sant Pau, Autonomous University of Barcelona, Barcelona, Spain
[14] Pharmacyclics LLC, an AbbVie Company, Sunnyvale, CA, United States
[15] Peter MacCallum Cancer Center & St. Vincent's Hospital and the University of Melbourne, Melbourne, VIC, Australia
[16] Division of Experimental Oncology, Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milan, Italy

Background: Ibrutinib (Ibr) + venetoclax (Ven) have synergistic and complementary antitumor activity that mobilizes and clears chronic lymphocytic leukemia (CLL) cells from multiple disease compartments, providing a rationale to evaluate time-limited treatment. We previously reported results from the Minimal Residual Disease (MRD) cohort of the multicenter phase 2 CAPTIVATE study of first-line Ibr + Ven in patients with CLL/small lymphocytic lymphoma (SLL). In that cohort, undetectable MRD (uMRD) was achieved in over two-thirds of patients (pts) with 12 cycles of Ibr + Ven; 30-month progression-free survival (PFS) rates were ≥95% irrespective of subsequent randomized treatment (Wierda, ASH 2020).

Aims: Here we present results from the fixed-duration (FD) cohort, evaluating fixed-duration treatment with Ibr + Ven.

Methods: Eligible patients were aged ≤70 y with previously untreated CLL/SLL. Patients received 3 cycles of Ibr lead-in followed by 12 cycles of Ibr + Ven (Ibr 420 mg/d orally; Ven ramp-up to 400 mg/d orally). The primary endpoint was complete response (CR) rate, including CR with incomplete recovery (CRi); secondary endpoints were overall response rate (ORR), duration of response, uMRD rate ($<10^{-4}$ by 8-color flow cytometry), PFS, overall survival (OS), tumor lysis syndrome (TLS) risk reduction, and adverse events (AEs).

Results: Overall,159 patients were enrolled; median age was 60 y. High-risk features included del(17p)/*TP53* mutation (17%), del(11q) (18%), complex karyotype (19%), and unmutated IGHV (56%). 147/159 (92%) patients completed planned treatment with Ibr, and 149/159 (94%) patients completed planned treatment with Ven. Median time on study was 27.9 months (range 0.8–33.2). With fixed-duration Ibr + Ven, 55% of patients in the overall

population achieved a CR; the CR rate was consistent across high-risk subgroups. Of 88 patients who achieved CR, durable CR (duration ≥1 y from initial documentation of response) was confirmed in 78 patients (89%); an additional 9 patients (10%) were not yet evaluable with <1 y of post-CR follow-up and 1 pt died 7 months after achieving a CR. ORR was 96%. Best MRD response of uMRD was achieved in peripheral blood (PB) of 77% of patients and in bone marrow (BM) of 60% of patients. 24-month PFS and OS rates were 95% and 98%, respectively. Similar results were achieved in patients without del(17p) (n=136) (Table). In patients with del(17p)/*TP53* mutation (n=27), the CR rate was 56%, uMRD rates were 81% (PB) and 41% (BM), and the 24-month PFS rate was 84% (95% CI 63%–94%). Of 34 patients with high baseline TLS risk based on tumor burden, 32 (94%) shifted to medium or low risk after Ibr lead-in; no TLS occurred. AEs were primarily grade 1/2. The most common grade 3/4 AEs were neutropenia (33%), hypertension (6%), and decreased neutrophil count (5%). AEs led to discontinuation of Ibr in 4% of patients and to discontinuation of Ven in 2% of patients.

Image:

Table. Efficacy outcomes

	Patients without del(17p) n=136	All patients N=159
CR/CRi, n (%)	76 (56)	88 (55)
Durable CR/CRi ≥1 y, n/N (%)*	66/76 (87)	78/88 (89)
ORR, n (%)	130 (96)	153 (96)
uMRD in PB, n (%)	104 (76)	122 (77)
uMRD in BM, n (%)	84 (62)	95 (60)
24-month PFS rate, % (95% CI)	96 (91-98)	95 (90-97)
24-month OS rate, % (95% CI)	98 (93-99)	98 (94-99)

*Denominator is patients with CR/CRi.

Summary/Conclusion: First-line Ibr + Ven is an all-oral, once-daily, chemotherapy-free fixed-duration regimen that provides deep, durable responses in patients with CLL/SLL. Overall, CR, uMRD rates, PFS, and OS appear favorable, and benefit was observed regardless of genomic high-risk features. No new safety signals were identified, and the safety profile of Ibr + Ven was consistent with known safety profiles of each agent.

Abstract Book Citations: Authors, Title, HemaSphere, 2021;5:(S2):pages. Abstract Book, DOI:
http://dx.doi.org/10.1097/HS9.0000000000000566