CLL-573

CHARACTERIZATION AND OUTCOMES OF THE SPANISH PATIENTS INCLUDED IN THE GLOW AND CAPTIVATE-FD STUDIES: IBRUTINIB PLUS VENETOCLAX FOR FIRST-LINE TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

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INTRODUCTION

The combination of fixed duration (FD) ibrutinib and venetoclax (I+V) was approved for patients with previously untreated chronic lymphocytic leukemia (CLL) based on two pivotal studies. However, there is limited data on the outcomes and management of I+V in Spanish CLL patients.

AIMS

To describe the baseline characteristics, efficacy, and safety outcomes of previously untreated CLL patients who received FD I+V in GLOW or CAPTIVATE-FD studies and were recruited in Spain.

METHODS

Here, we report a post-hoc analysis of pooled data from Spanish CLL patients enrolled in the pivotal studies GLOW and CAPTIVATE-FD cohort performed to characterize and evaluate the outcomes for patients recruited in these trials in Spain. Efficacy outcomes included investigator-assessed PFS, OS, TTNT and response rates. Safety data also assessed.

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RESULTS

Phase III randomized clinical trial GLOW[1] and phase II CAPTIVATE-FD[2] cohort included 10 and 17 patients from Spain, respectively. Median age was 64 years old, 14.8% of patients had del(17p) and 70.4% of patients had unmutated IGHV, a slightly higher proportion of high-risk characteristics than in the main cohorts of the trials (Table 1).

Table 1: Baseline characteristics

Characteristic	Spanish population Glow and CAPTIVATE-FD (N=27)
Median (range)	64 (35-83)
≥65	13 (48.1%)
Sex	
Male	16 (59.3%)
ECOG performance status	
0	18 (66.7%)
≥1	9 (33.3%)
del11q	
Yes	5 (18.5%)
No	22 (81.5%)
del17p	
No	20 (74.1%)
Yes	4 (14.8%)
Missing	3 (11.1%)
TP53 mutation	
Yes	3 (11.1%)
No	24 (88.9%)
IGHV status‡	
Mutated	8 (29.6%)
Unmutated	19 (70.4%)
Bulky Disease	
Yes	7 (25.9%)
Creatinine clearance (mL/min)	
<60 mL/min	1 (3.7%)
60-<70 mL/min	5 (18.5%)
≥70	21 (77.8%)
Cytopenia⁋	
Yes	9 (33.3%)
No	18 (66.7%)
Time from initial diagnosis (months)	
Median	38
History hypertension*	
Hypertension history	10 (37%)
Cardiac history†	
Cardiac history	5 (18.5%)

CLL=chronic lymphocytic leukemia; CrCl=creatinine clearance; del11q=deletion of long (q) arm of 11th chromosome; del17p=deletion of short (p) arm of 17th chromosome; ECOG PS=Eastern Cooperative for Oncology Group performance status; IGHV=Immunoglobulin heavy-chain variable gene region; LDH=lactate dehydrogenase; med=median; TP53mut=tumor protein 53 mutation; SD=standard deviation;
‡ reclassified IGHV data[2]
⁋ Cytopenia is defined as hemoglobin ≤ 110 g/L, platelet counts ≤ 100x109/L, or absolute neutrophil count ≤ 1.5x109/L
*% of hypertension refers to patients with medical history of hypertension
† % of cardiac history refers to patients with medical history of cardiac disorders (body system classification)

With a median follow-up of 49.7 months, median PFS was not reached (95% CI: 48.8 – not estimable [NE]) and the 48-month PFS estimate was 80%. Median TTNT was not reached (95% CI: 49.9 – NE), and TTNT estimation at 48 months was 83.6%. Only one death was observed, being the OS rate at 48 months 96% (median not reached, CIs not estimable) (Figure 1). ORR was 96.3%, with 63.0% of patients achieving CR/CRi.

Figure 1: (A) Progression Free Survival, (B) Overall Survival and (C) Time to Next Treatment

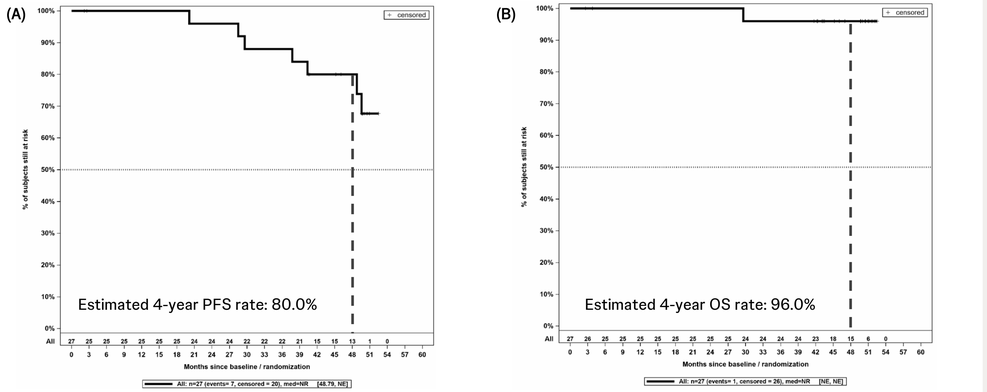
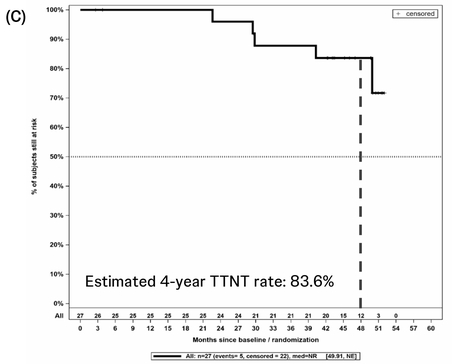


Figure 1: (C) Time to Next Treatment*



* Patients were censored at death

Table 2: Adverse Events Occurring in Pooled CAPTIVATE FD and GLOW Patients recruited in Spain §

Event	Any grade	Grade ≥ 3
TEAE any grade	26 (96.3%)	17 (63%)
Atrial fibrillation	0 (0%)	0 (0%)
Cardiac arrest	0 (0%)	0 (0%)
Cardiac failure	0 (0%)	0 (0%)
Diarrhea	11 (40.7%)	2 (7.4%)
Hypertension	7 (25.9%)	1 (3.7%)
Hyponatremia	0 (0%)	0 (0%)
Ischaemic stroke	0 (0%)	0 (0%)
Tumor lysis syndrome	0 (0%)	0 (0%)
Neutropenia	15 (55.6%)	13 (48.1%)
Sudden death	0 (0%)	0 (0%)
Thrombocytopenia	8 (29.6%)	4 (14.8%)

§ All events are treatment-emergent; Counts and % represent number of patients with at least one adverse event

The safety profile was consistent with previous findings for both Ibrutinib and venetoclax, with mostly grade 1-2 adverse events reported. Regarding TEAEs of interest, the most common any grade adverse events were neutropenia (55.6%), diarrhea (40.7%) and thrombocytopenia (29.6%) with the most common grade 3-4 events being also neutropenia (48.1%), thrombocytopenia (14.8%) and diarrhea (7.4%). Hypertension of any grade was reported in 7 patients, however, only 1 patient experienced a grade ≥3 event. No fatal adverse events occurred, and no cases of atrial fibrillation, cardiac arrest, cardiac failure, sudden death nor ischemic stroke were reported (Table 2). Only one all-cause death was reported and was probably due to Covid-19 complications.

CONCLUSIONS

Given the absence of real-world evidence of I+V, this analysis represents a relevant sample of the results for patients treated with the fixed-duration combination of I+V in Spain in the context of a clinical trial. The results of this analysis suggest that I+V was efficacious and well tolerated in this cohort of patients from Spain with previously untreated CLL, findings consistent with the main cohorts of the GLOW and CAPTIVATE clinical trials. These results may contribute to the understanding of treatment outcomes and management of the CLL population in Spain. A limitation of this analysis is the low number of enrolled patients.

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B-cell Malignancies

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