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Fixed-duration ibrutinib plus venetoclax in frontline CLL/SLL: updated real-world outcomes from the Spanish LI+VE study

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Conclusions

- The LI+VE study reinforces that I+V FDT is an effective 1L treatment option for patients with CLL/SLL. The data are strong (N=93; ORR 98.7%, CR 71.8%; 18–24m PFS 94.5% and OS 97.4%). These outcomes are achieved in routine practice with substantial comorbidity/CV-risk burden (65.2% with comorbidities; 70.3% with CV risk factors; 58.2% medium/high CV risk).
- The safety profile compares favourably with clinical trial data, despite the high burden of comorbidities and CV risk factors. Most AEs were grade 1–2, serious events were infrequent and cardiac events were rare. The three-cycle ibrutinib lead-in serves as an effective TLS prophylactic strategy, resulting in zero TLS events.
- AEs leading to dose modifications or temporary treatment interruptions were manageable and frequently resolved or improved. This highlights the effective use of dose flexibility with I+V FDT, allowing most patients to remain on treatment and optimizes treatment delivery to enable treatment- free intervals. Treatment discontinuation rates remained low.
- With THRIVE,[6] REALITY-2/WW,[7] and IVANDA[8], cumulative real-world experience provides clinically relevant evidence to guide clinical management and inform decision-making. I+V remains the only all-oral fixed-duration treatment with comprehensive clinical trial and real-world data across all patient profiles.
- RWE I+V FDT demonstrates high efficacy with a favorable safety profile, supporting its potential as an optimized treatment approach

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Poster

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Background

- Ibrutinib plus venetoclax (I+V) is the only all-oral once-daily fixed-duration therapy (FDT) regimen approved by the European Medicines Agency (EMA; August 2022) for the treatment of previously untreated patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).[1]
- Preference for FDT is increasing for most patients. I+V FDT enables high efficacy while improving tolerability through reduced treatment exposure.[2]
- The phase 2 CAPTIVATE (fit patients),[3,4] phase 3 GLOW (unfit),[5] and CLL17 (intermediate fitness)[2] trials demonstrated high undetectable minimal residual disease (uMRD) rates, durable PFS, and prolonged treatment-free remissions with first-line I+V FDT across fitness levels. CAPTIVATE achieved 77% of best MRD,[1] GLOW showed superior overall survival (OS) vs chemoimmunotherapy,[5] and CLL17 study confirmed efficacy and safety in a population more representative of real-world clinical practice.
- While randomized clinical trials have established the clinical value of I+V, real-world evidence (RWE) has remained limited. The LI+VE study, together with complementary initiatives such as THRIVE[6], REALITY[7] and IVANDA[8], is contributing to a growing and increasingly robust RWE base supporting the effectiveness and tolerability of I+V FDT in routine clinical practice.

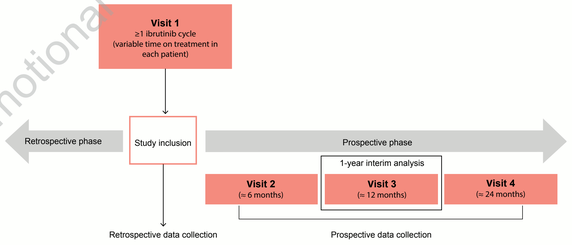
Objective

- To evaluate the effectiveness, safety and clinical management of first-line (1L) I+V FD treatment for patients with CLL/SLL, based on updated prospective data from the 1-year interim analysis of the LI+VE study, in routine clinical practice in Spain.

Methods

- LI+VE is a multicenter, ambispective, observational study conducted in 40 centers in Spain, evaluating 1L I+V FDT in patients with CLL/SLL. The study includes retrospective baseline data collection and prospective follow-up of participants for up to 2 years, with CRO-supported data management (**Figure 1**).
- The primary objective of the study is to describe PFS. Key secondary objectives include characterization of patient profiles, assessment of treatment response, OS, duration of treatment, time to next treatment, and safety.

Figure 1. Study design



Results

Patient characteristics

- At cut-off (22 Oct 2025), 93 patients were included in the LI+VE study (CLL: 88.0%; SLL: 12.0%). The median age was 63 years (range: 41–84), with 29.0% ≥70 years (**Table 1**).
- Cardiovascular (CV) risk factors were present in 70.3%, and among these, hypertension was the most common (60.9%). Overall, 58.2% were at medium/high CV risk. Comorbidities were reported in 65.2% (≥2 in 51.7%) and del(17p)/*TP53* mutations were observed in 5.5% (**Table 1**).

Table 1. Demographics and baseline characteristics of the patients

Characteristic	Value (N=93)
Age (years), median (range) [93]	63.0 (41–84)
≥70 years	27 (29.0)
Male, n (%) [93]	63 (67.7)
Histology, n (%) [92]	
Chronic lymphocytic leukemia	81 (87.1)
Small lymphocytic lymphoma	11 (11.8)
RAI stage 0-II, n (%) [82]	66 (71.7)
ECOG 0-1 n (%) [67]	65 (97.0)
Bulky disease ≥5 cm, n (%) [87]	28 (32.2)
High-risk genomic features, n (%)	
Unmutated *IGHV* [82]	49 (59.8%)
del(11q) [78]	10 (16.7%)
del(17p) and/or mutated *TP53* [91]	5 (5.5%)
Unmutated *IGHV*/del(17p)/*TP53* mutation/del(11q) [91]	55 (60.4%)
Cardiovascular risk, n (%) [91]	
High	10 (11.0)
Medium	43 (47.2)
Low	38 (41.8)
Cardiovascular risk factors (>15%), n (%) [91]	64 (70.3)
Hypertension	39 (60.9)
Dyslipidemia	35 (54.7)
Obesity	14 (21.9)
Active Smoking	13 (20.3)
Diabetes Mellitus	12 (18.8)
Patients with comorbidities, n (%) [92]	60 (65.2)
≥2 comorbidities	31 (51.7)
Concomitant medications, n (%) [93]	71 (76.3)
≥3 medications	43 (60.6)

The number of patients with available data is shown in square brackets. CV risk according to Online calculator 'Fundación Española del Corazón'.

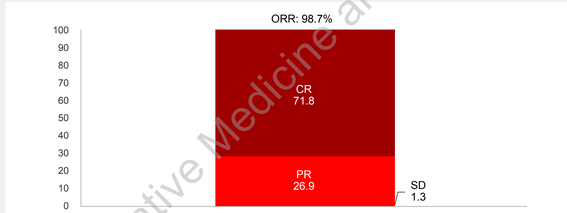
Patient status at Visit 3

- At analysis, 69.9% (65/93) had completed Visit 3 and 66.7% (62/93) had completed I+V FDT, with a median treatment duration of 14.4 months. Three patients initiated second-line therapy (2 due to Richter's transformation).
- Venetoclax ramp-up was completed in 95.4% (83/87); 10 patients required hospitalization for tumor lysis syndrome (TLS) prophylaxis, with no TLS events reported.

Effectiveness

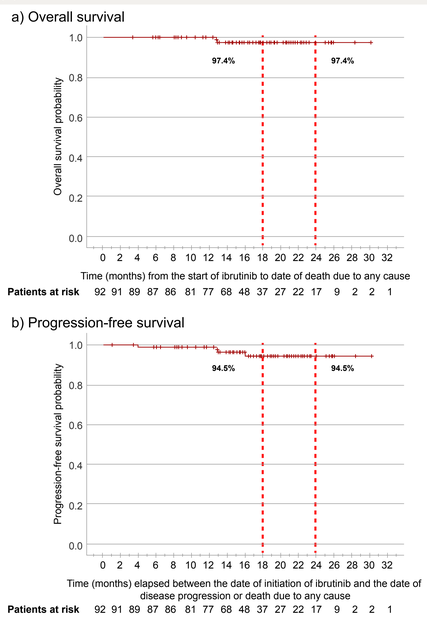
- After a median follow-up of 21.2 months from ibrutinib initiation, response data were available for 78/93 patients. According to iwCLL 2018 criteria and routine clinical practice, 56 patients (71.8%) achieved a complete response, 21 (26.9%) a partial response, 1 (1.3%) had stable disease (**Figure 2**). One patient progressed after permanently discontinuing treatment due to an AE unrelated to treatment.
- The OS and PFS rates at 18 months were 97.4% and 94.5%, respectively, and remained unchanged at 24 months (**Figure 3**).

Figure 2. Best overall response (N = 78)



CR (CR+CRnt+CRi); PR (PR+PR-L); ORR (CR+PR).
CR, complete response; CRnt, not confirmed by MRI or CT scan; CRi, CR with incomplete bone marrow recovery; ORR, overall response rate; PR, partial response; PR-L, partial response with lymphocytosis; SD, stable disease.

Figure 3. Kaplan–Meier curve of overall survival (a) and progression-free survival (b)



Safety

- Most AEs were grade 1–2 in severity (86.0%), while the most common grade ≥3 AEs were neutropenia (16.1%) and diarrhea (3.2%) (**Table 2**). G-CSF was used in 28.9% of patients.
- Cardiac events were infrequent. Atrial fibrillation occurred in 3 patients (3.2%), all grade 1–2 (**Table 2**).
- Two treatment-unrelated deaths were reported, one due to intestinal sepsis and another due to traumatic brain injury.

Table 2. Adverse events in patients treated with ibrutinib + venetoclax (N=93)

AEs	Any grade	Grade ≥3
Patients with any AE n (%)	85 (91.4)	35 (37.6)
Most common AEs (≥ 5%)		
Diarrhea	32 (34.4)	3 (3.2)
Neutropenia	28 (30.1)	15 (16.1)
Upper respiratory tract infection	18 (19.4)	2 (2.2)
Arthralgia	13 (14.0)	0 (0.0)
Bleeding (including contusion)	12 (12.9)	1 (1.1)
Thrombocytopenia	12 (12.9)	2 (2.2)
Nausea	9 (9.7)	0 (0.0)
Asthenia	7 (7.5)	0 (0.0)
Fatigue	7 (7.5)	1 (1.1)
Headache	6 (6.5)	0 (0.0)
Hypertension	6 (6.5)	1 (1.1)
Lymphocytosis	5 (5.4)	2 (2.2)
Rash	5 (5.4)	1 (1.1)
Aphthous ulcer	5 (5.4)	0 (0.0)
Constipation	5 (5.4)	0 (0.0)
Urinary tract infection	6 (6.5)	1 (1.1)
Skin infection	5 (5.4)	0 (0.0)
Other AEs of clinical interest		
Second primary malignancy	6 (6.5)	2 (2.2)
Atrial fibrillation	3 (3.2)	0 (0.0)
Arrhythmia	1 (1.1)	1 (1.1)
Palpitations	1 (1.1)	0 (0.0)
TLS	0 (0.0)	0 (0.0)
SAEs	23 (24.7)	19 (20.4)

AE, adverse event; TLS, tumor lysis syndrome; SAE, severe adverse event.

- AEs led to dose reductions of ibrutinib in 3/93 patients (3.2%), and of venetoclax in 13/93 patients (14.0%), most commonly due to gastrointestinal events and cytopenias (**Table 3**). AEs leading to dose modification resolved or improved in all cases with ibrutinib and in 85.7% of those with venetoclax.
- Temporary treatment interruptions occurred in 39/93 patients (41.9%). Notably, nearly half of the interruptions (46.2%) were not related to toxicity (**Table 3**). Among AEs leading to treatment interruption, 78.6% were resolved and 17.9% partially resolved.
- Permanent discontinuation of I+V combination was infrequent, occurred in 7/93 patients (7.5%). The underlying reasons are detailed in the **Table 3**. Notably, only one discontinuation was attributed to CV toxicity, specifically grade 1 palpitations.

Table 3. Summary of adverse events leading to treatment modifications

AEs	All treated patients (N=93)
AEs leading to ibrutinib dose reduction	3 (3.2)
Thrombocytopenia	1
Neutropenia	1
Atrial fibrillation	1
AEs leading to venetoclax dose reduction	13 (14.0)
Diarrhea	6
Neutropenia	2
Thrombocytopenia	2
Abdominal pain	1
Food poisoning	1
Fatigue	1
Nephrotoxicity	1
Temporary treatment interruptions*	39 (41.9)
AEs leading to temporary interruption†	28 (30.1)
Neutropenia	9
Thrombocytopenia	2
Lymphocytosis	1
Leukopenia and neutropenia	1
Infection	5
Diarrhea	4
Bleeding	1
Fatigue	1
Rash	1
Other arrhytmias	1
Other	8
AEs leading to I+V combination discontinuation	7 (7.5)
Richter's transformation	1
Glioblastoma	1
Intestinal perforation	1
Pyoderma gangrenosum	1
Hypertransaminasemia	1
Death	1
Lymphocytosis and palpitations‡	1

*27 patients interrupted ibrutinib only, 14 patients interrupted venetoclax only and 14 patients interrupted both ibrutinib and venetoclax (non-mutually exclusive). †18 patients interrupted treatment for reasons not related to treatment toxicity (non-mutually exclusive). ‡Patient with a sequential ibrutinib→venetoclax discontinuation

References

1. Tam CS. et al. Blood 2022 Jun;139(22):3278–3289.
2. Al-Sawaf O, et al. N Engl J Med. 2026 Mar 12;394(11):1084-1096.
3. Wierda W, et al. Presented at: European Hematology Association (EHA) Hybrid Congress. Milan, Italy; 2025 Jun 12–15. Poster S156.
4. Niemann CU, et al. Presented at: American Society of Hematology Annual Meeting and Exposition; San Diego, (CA), USA; 2024 Dec 7–10. Poster 1871.
5. Kater AP et al. NEJM Evid. 2022 Jul;1(7):EVIDoa2200006.
6. Visentin A, et al. Blood 2025; 146 (Supplement 1): 6287.
7. Thieblemont C, et al. Blood 2025; 146, (Supplement 1): 3903.
8. Fernández de la Mata M, et al. Presented at: LXVII Congreso SEHH y XLI Congreso SETH 2025.