Poster PO-311

Evaluación de los patrones de tratamiento y de seguridad en pacientes con leucemia linfocítica crónica (LLC) mediante el procesamiento del lenguaje natural (PLN): Perspectiva de un estudio observacional multicéntrico en España

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INTRODUCTION

- Chronic lymphocytic leukemia (CLL) is the most common type of leukemia in Western countries
- Targeted therapy has improved patient outcomes, but limited data are available on real-world treatment patterns and safety outcomes, especially in Spain
- Natural language processing (NLP) applied to electronic health records (EHRs) can analyze large, diverse datasets of real-world data (RWD), minimizing selection bias and improving the understanding of the management of CLL[1]
- The aim of this study was to describe treatment patterns and safety outcomes in patients diagnosed with CLL in Spain

METHODS

- This observational, multicenter, retrospective study was based on secondary use of EHR data from all adult patients with a CLL diagnosis between January 1, 2016, and December 31, 2021, at 3 Spanish hospitals: Hospital Universitari Son Espases, Mallorca; Hospital Regional Universitario Carlos Haya, Málaga; and Hospital Universitario Infanta Leonor, Madrid
  - Patients diagnosed with Richter syndrome or prolymphocytic leukemia were excluded
- EHRs were evaluated using NLP based on clinical terminology (SNOMED-CT) and machine learning (**Figure 1**)
  - Unstructured clinical information related to clinical characteristics and treatment was assessed
  - Data ownership remained with the participant sites; EHR data were anonymized before analysis, in compliance with corresponding data protection and privacy laws
  - A total of 205 clinical variables were extracted and summarized at the patient level using descriptive statistics

Figure 1. Study Schema

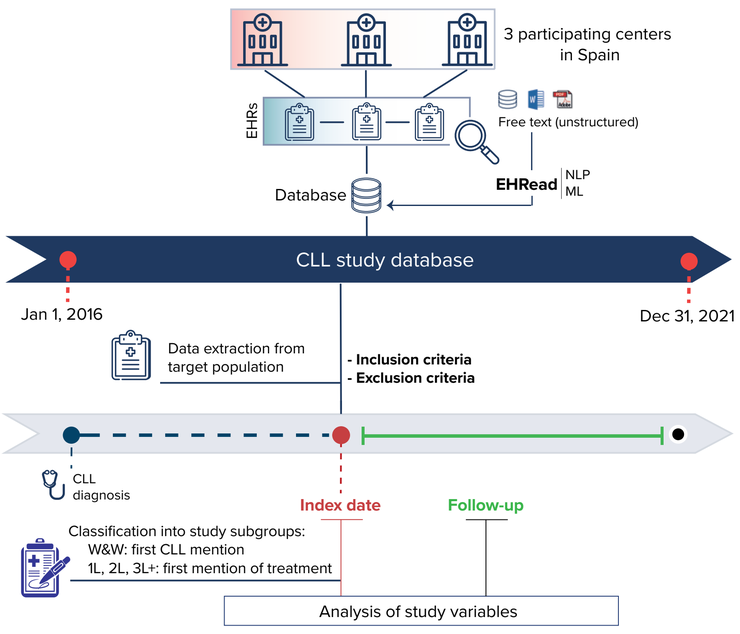

Figure adapted from Loscertales J, et al. Cancers (Basel). 2023;15(16):4047. This study used EHRead,[2] an innovative technology that applies NLP and machine learning to extract, organize, and analyze the unstructured clinical information jotted down by health professionals in patients' EHRs from the 3 participating hospitals. EHR, electronic health record; ML, machine learning; NLP, natural language processing; W&W, watch and wait.

RESULTS

- In total, 697 patients with CLL met the study inclusion criteria from among 2,069,341 patients with a total of 88,872,628 EHRs and were classified into treatment subgroups (**Table 1**); demographics and clinical characteristics of study patients are shown in **Tables 2 to 4**
- The overall age-standardized (2013 European population) incidence for the study period was 3.38 (95% CI, 2.55-4.22) cases per 100,000 person-years

Table 1. Study Subgroup According to Line of Therapy

Patients, n (%)	Total N=697
W&W	406 (58.2)
Treated patients	291 (41.8)
Treated outside SP[a]	54 (18.6)
Treated inside SP	237 (81.4)
1L	192 (81)
2L	79 (33.3)
3L+	26 (11.0)
3L[b]	23 (9.7)
4L[b]	8 (3.4)
5L[b]	2 (0.8)
6L[b]	1 (0.4)

[a] Outside SP refers to the time before the SP; [b] Percentages calculated based on the total number of patients treated within the SP (n=237). L, line; SP, study period; W&W, watch and wait.

Table 2. Demographics and Clinical Characteristics at Index Date

	W&W[a]		Treated[b]		
	Incident n=201	Prevalent n=205	Incident n=39	Prevalent n=252	Total N=697
Age at index, years[c]					
Mean (SD)[d]	72.2 (13)	75.1 (11.4)	67.3 (12.8)	70.3 (12.6)	72.1 (12.6)
Median (Q1, Q3)	74 (65, 83)	77 (68, 83)	67 (60.5, 78.5)	72 (63, 79)	73 (65, 82)
Sex, n (%)[c]					
Male	109 (54.2)	101 (49.3)	30 (76.9)	158 (62.7)	398 (57.1)
Female	92 (45.8)	104 (50.7)	9 (23.1)	94 (37.3)	299 (42.9)
Family history of CLL, n (%)[e]	3 (1.5)	4 (2)	1 (2.6)	11 (4.4)	19 (2.7)
Family history of other hematological malignancies, n (%)[e]	2 (1.0)	0 (0)	0 (0)	6 (2.4)	8 (1.1)
Follow-up, months[c]					
Mean (SD)[d]	34 (203)	40.7 (24.2)	21.6 (17)	34 (24)	35.3 (23.1)
Median (Q1, Q3)	34.3 (14.1, 49.8)	39.7 (18.7, 66.5)	19.1 (7.7, 34.6)	32 (12.8, 56.1)	33.4 (13.8, 56.7)

[a] For W&W, *incident* and *prevalent* refer to disease diagnosis (incident=during SP; prevalent=before SP); [b] In the treated cohort, *incident* refers to patients who initiated 1L during the SP; *prevalent* refers to those patients who initiated ≥1L before the start of the SP; [c] Age at index, sex, and follow-up were analyzed without a window; [d] Median (Q1, Q3) is preferred over mean (SD) for interpretation as the feature is nonnormal; [e] Family history variables were analyzed at first report and end of follow-up. Q, quartile; SP, study period; W&W, watch and wait.

Table 3. Clinical Comorbidities at Index Date

	W&W		Treated		
Comorbidity, n (%)	Incident n=201	Prevalent n=205	Incident n=39	Prevalent n=252	Total N=697
Respiratory					
COPD	41 (20.4)	52 (25.4)	4 (10.3)	61 (24.2)	158 (22.7)
Asthma	13 (6.5)	19 (9.3)	2 (5.1)	16 (6.3)	50 (7.2)
Bronchitis	21 (10.4)	25 (12.2)	2 (5.1)	28 (11.1)	76 (10.9)
Emphysema	6 (3.0)	9 (4.4)	1 (2.6)	8 (3.2)	24 (3.4)
Cardiovascular					
Ischemic heart disease	38 (18.9)	36 (17.6)	4 (10.3)	38 (15.1)	116 (16.6)
Congestive heart failure	25 (12.4)	40 (19.5)	4 (10.3)	22 (8.7)	91 (13.1)
Arterial hypertension	140 (69.7)	139 (67.8)	23 (59)	148 (58.7)	450 (64.6)
Cerebrovascular disease	21 (10.4)	24 (11.7)	5 (12.8)	11 (4.4)	61 (8.8)
Transient ischemic stroke	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Peripheral vascular disease	1 (0.5)	1 (0.5)	0 (0)	1 (0.4)	3 (0.4)
Pulmonary embolism	3 (1.5)	5 (2.4)	0 (0)	2 (0.8)	10 (1.4)
Deep vein thrombosis	9 (4.5)	12 (5.9)	4 (10.3)	14 (5.6)	39 (5.6)
Metabolic					
Obesity/overweight	55 (27.4)	41 (20.0)	4 (10.3)	46 (18.3)	146 (20.9)
Diabetes	67 (33.3)	75 (36.6)	9 (23.1)	79 (31.3)	230 (33.0)
Hypercholesterolemia	43 (21.4)	42 (20.5)	6 (15.4)	35 (13.9)	126 (18.1)
Cancer					
Solid tumors	12 (6.0)	19 (9.3)	2 (5.1)	16 (6.3)	49 (7.0)

The presence of each feature was analyzed at first report and index date + 1 month.
COPD, chronic obstructive pulmonary disease; W&W, watch and wait.

Table 4. Symptoms and Clinical Observations at Index Date

	W&W		Treated		
Parameter, n (%)	Incident n=201	Prevalent n=205	Incident n=39	Prevalent n=252	Total N=697
Binet stage	16 (8.0)	17 (8.3)	7 (17.9)	47 (18.7)	87 (12.5)
Stage A	11 (68.8)	13 (76.5)	2 (28.6)	14 (29.8)	40 (46.0)
Stage B	5 (31.2)	3 (17.6)	3 (42.9)	19 (40.4)	30 (34.5)
Stage C	0 (0)	1 (5.9)	2 (28.6)	14 (29.8)	17 (19.5)
Rai stage	23 (11.4)	33 (16.1)	9 (23.1)	41 (16.3)	106 (15.2)
Stage 0	15 (65.2)	26 (78.8)	0 (0)	5 (12.2)	46 (43.4)
Stage I	7 (30.4)	5 (15.2)	3 (33.3)	11 (26.8)	26 (24.5)
Stage II	0 (0)	2 (6.1)	2 (22.2)	10 (24.4)	14 (13.2)
Stage III	0 (0)	0 (0)	2 (22.2)	10 (24.4)	12 (11.3)
Stage IV	1 (4.3)	0 (0)	2 (22.2)	5 (12.2)	8 (7.5)
Any cytogenetic alterations detected[a]	32 (15.9)	43 (21.0)	20 (51.3)	97 (38.5)	192 (27.5)

[a] Cytogenetic alterations: p53, IGHV, del13, del11, del17, NOTCH, complex karyotype. W&W, watch and wait.

- In this study population, chemoimmunotherapy, anti-CD20 monotherapy, or chemotherapy alone was reported as first-line (1L) treatment for 193 patients (66.3%) (**Table 5**)
- Bruton tyrosine kinase (BTK) inhibitors were the targeted therapy most often prescribed in 1L and second-line (2L)
- BCL2 inhibitors were the preferred targeted therapy for patients with relapsed/refractory (R/R) disease in the third-line (3L) and later

Table 5. Treatment Groups Among Patients With CLL

Patients, n (%)	1L n=291	2L n=98	3L+ n=28
Chemoimmunotherapy/ anti-CD20 monotherapy/ chemotherapy alone	193 (66.3)	40 (40.8)	7 (25.0)
BTKi (ibrutinib in >95% of cases)	89 (30.6)	40 (40.8)	8 (28.6)
Venetoclax	6 (2.1)	11 (11.2)	10 (35.7)
Idelalisib	3 (1.0)	7 (7.1)	2 (7.1)
Anti-CD52	0 (0)	0 (0)	1 (3.6)

1L, first-line; 2L, second-line, 3L+, third line and later; BTKi, Bruton tyrosine kinase inhibitor.

- Treatment discontinuation occurred in 67 patients (23%) in 1L, 37 (37.8%) in 2L, and 13 (46.4%) in 3L
- As shown in **Table 6**, potential reasons for discontinuation were detected in up to 40% of cases
  - In 1L, toxicity was the most frequent reason for discontinuation of a BTKi (66.7%), chemotherapy (25%), and anti-CD20 monotherapy (20.7%)
- The most common adverse events in 1L are shown in **Table 7**

CONCLUSIONS

- About 50% of patients received 1L treatment, and up to 10% of patients received 3L treatment
- Chemoimmunotherapy was the preferred treatment for 1L patients, and the leading targeted therapy in 1L was BTKi; BTKi remained the preferred option for 2L, while BCL2i was preferred for 3L and later lines
- Treatment discontinuation rates were notable across all treatment categories, and toxicity rates were high around the time of treatment discontinuation, highlighting the need for newer, less toxic therapies as potential alternatives
- Study limitations: Only data extracted from free-text narratives written by healthcare professionals were analyzed; no structured information (eg, laboratory, pharmacy) was available, potentially decreasing the sensitivity of information capture from these sources; and a small number of artifactual findings could be expected regarding treatment combination and sequences, as well as laboratory results or cytogenic findings
- Overall, these study findings corroborate the clinical characteristics reported in the existing literature and reinforce the credibility of artificial intelligence and NLP as reliable methodologies for obtaining a comprehensive understanding of real-world disease landscapes

Table 6. Reasons for Treatment Switch or Discontinuation in 1L (Incident Cases)

Patients, n (%)	BTKi n=83	Chemo-immunotherapy n=53	Anti-CD20 monotherapy n=29	Chemotherapy n=20
Treatment switch	17 (20.5)	12 (22.6)	4 (13.8)	7 (35.0)
Treatment discontinuation	16 (19.3)	15 (28.3)	12 (41.4)	5 (25.0)
Reasons for switch or discontinuation				
Toxicity	18 (21.7)	7 (13.2)	6 (20.7)	5 (25.0)
Hospital death	1 (1.2)	1 (1.9)	2 (6.9)	1 (5.0)
Clinical progression	9 (10.8)	14 (26.4)	5 (17.2)	3 (15.0)
Not detected	55 (66.3)	31 (58.5)	16 (55.2)	11 (55.0)

1L, first-line; BTKi, Bruton tyrosine kinase inhibitor.

Table 7. Most Common Adverse Events in 1L

Patients, n (%)	BTKi n=83	Chemo-immunotherapy n=53	Anti-CD20 monotherapy n=29	Chemotherapy n=20	1L n=192
Cardiovascular					
Cardiac arrhythmia	1 (1.2)	2 (3.8)	0 (0)	1 (5.0)	4 (2.1)
Atrial fibrillation[a]	9 (10.8)	7 (13.2)	4 (13.8)	0 (0)	20 (10.4)
Hypertension[a]	6 (7.2)	7 (13.2)	3 (10.3)	2 (10.0)	19 (9.9)
Infectious diseases					
Pneumonia	12 (14.5)	11 (20.8)	4 (13.8)	2 (10.0)	30 (15.6)
Cytomegalovirus infection	5 (6.0)	6 (11.3)	4 (13.8)	2 (10.0)	20 (10.4)
SARS-CoV2 infection	13 (15.7)	8 (15.1)	2 (6.9)	0 (0)	23 (12.0)
Nervous system					
Headache	14 (16.9)	11 (20.8)	5 (17.2)	3 (15.0)	34 (17.7)
Stroke	6 (7.2)	1 (1.9)	1 (3.4)	0 (0)	8 (4.2)
TIA	1 (1.2)	0 (0)	0 (0)	1 (5.0)	2 (1.0)
Immune, blood, and lymphatic system					
Anemia	32 (38.6)	29 (54.7)	16 (55.2)	10 (50)	89 (46.4)
Thrombocytopenia	25 (30.1)	24 (45.3)	9 (31.0)	5 (25.0)	65 (33.9)
Lymphocytosis	48 (57.8)	37 (69.8)	13 (44.8)	5 (25.0)	107 (55.7)
Gastrointestinal and hepatobiliary					
Vomiting	16 (19.3)	10 (18.9)	7 (24.1)	3 (15.0)	36 (18.8)
Nausea	18 (21.7)	17 (32.1)	10 (34.5)	7 (35.0)	53 (27.6)
Diarrhea	25 (30.1)	13 (24.5)	8 (27.6)	4 (20.0)	51 (26.6)
Skin and subcutaneous tissue					
Alopecia	0 (0)	3 (5.7)	0 (0)	0 (0)	3 (1.6)
Rash	12 (14.5)	6 (11.3)	3 (10.3)	2 (10.0)	24 (12.5)
Hives	12 (14.5)	6 (11.3)	3 (10.3)	2 (10.0)	24 (12.5)
Musculoskeletal and connective tissue					
Arthralgia	11 (13.3)	4 (7.5)	1 (3.4)	0 (0)	17 (8.9)
Myalgia	1 (1.2)	2 (3.8)	0 (0)	1 (5)	4 (2.1)
Contusion	10 (12)	2 (3.8)	4 (13.8)	2 (10)	18 (9.4)
Respiratory					
Pneumonitis	1 (1.2)	3 (5.7)	0 (0)	0 (0)	4 (2.1)
General					
Toxicity	8 (9.6)	16 (30.2)	6 (20.7)	3 (15.0)	36 (18.8)
Asthenia	43 (51.8)	28 (52.8)	13 (44.8)	5 (25.0)	90 (46.9)
Fever	31 (37.3)	30 (56.6)	13 (44.8)	7 (35.0)	84 (43.8)
Bleeding	23 (27.7)	17 (32.1)	9 (31.0)	3 (15.0)	53 (27.6)
Major bleeding	4 (4.8)	2 (3.8)	3 (10.3)	2 (10.0)	11 (5.7)
Nonmajor bleeding or minor bleeding	22 (26.5)	17 (32.1)	9 (31.0)	3 (15.0)	52 (27.1)
Second primary neoplasms[a]	4 (4.8)	2 (3.8)	4 (13.8)	1 (5.0)	12 (6.2)

The presence of each feature is analyzed from 1L start to 1L end. [a] Chronic events. Only new events during treatment administration were considered. 1L, first-line; BTKi, Bruton tyrosine kinase inhibitor; TIA, transient ischemic attack.

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DISCLOSURES

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