Impact of Real-World Treatment Sequencing Patterns on Time to Next Treatment Among Patients With Chronic Lymphocytic Leukemia in the United States

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INTRODUCTION

- The treatment landscape for chronic lymphocytic leukemia (CLL) is evolving at a rapid pace; selection of therapies is impacted by factors including patient age, comorbid conditions, and patient preference, among others[1,2]
- There is a need to better understand the performance of the wide array of currently available treatment options for CLL in the real-world setting
- The objective of this study was to assess recent real-world treatment sequencing patterns and associated clinical outcomes in patients with CLL in the United States (US)

METHODS

Study Design

- Retrospective observational study

Data Source

- ConcertAI RWD360 dataset, a real-world, de-identified dataset of >7 million patients from across the US derived from electronic health record systems and integrated with a large administrative open-claims dataset

Study Population

- Patients with ≥1 International Classification of Diseases (ICD) code for CLL (ICD-9-CM: 204.1x; ICD-10-CM: C91.1x) who received ≥1 treatment after initial diagnosis
- Patients ≥18 years of age diagnosed between January 1, 2018, and January 1, 2023
- Patients who enrolled in a clinical trial or had primary malignancies other than CLL, nonmelanoma skin cancer, and/or cervical carcinoma in situ at or after initial diagnosis were excluded from the study

Treatment Groups

- Patients were classified into 4 treatment groups based on the following hierarchy:
  - Bruton tyrosine kinase (BTK) inhibitor-based therapy (acalabrutinib, ibrutinib, zanubrutinib)
  - Venetoclax-based therapy
  - Anti-CD20–based therapy
  - Chemotherapy (including bendamustine-based chemotherapy)
- For inclusion in the groups for this study, these agents were required to have been received during the first 2 lines of therapy

Statistical Analysis

- Descriptive statistics were used to evaluate demographic and clinical characteristics at the start of the therapy for each subgroup and to describe the sequence of treatments received, along with treatment switch patterns from first line (1L) to second line (2L), 2L to third line (3L), and 3L to fourth line (4L)
- Real-world outcomes evaluated in this study include time to next treatment (TTNT) and all-cause healthcare resource utilization (HCRU)
- Time-to-event analyses for the real-world outcomes were conducted using the Kaplan-Meier method; Cox regression model was used to estimate TTNT, while adjusting for baseline characteristics

RESULTS

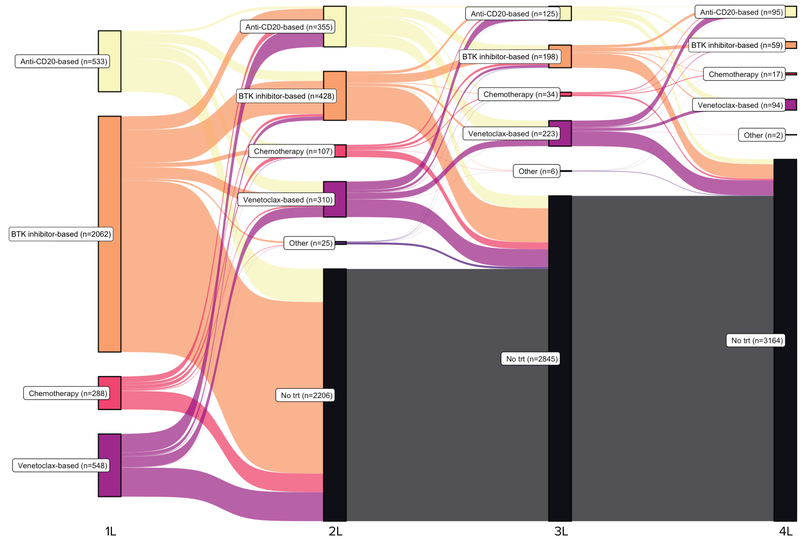
Demographic and Clinical Characteristics

- The study included 3431 patients with CLL (median age, 69 years; male, 63.8%)
- Patients were primarily treated in community rather than academic settings (76.4% vs 21.3%)
- The most common comorbid conditions were diabetes without chronic complications (17.5%), chronic obstructive pulmonary disease (13.0%), and renal disease (10.7%)

Real-World Treatment Patterns (Figure 1)

- In 1L, patients were most commonly treated with BTK inhibitor-based (60.1%), venetoclax-based (16.0%), and anti-CD20–based (15.4%) therapies
- Among patients with CLL, 1225 (35.0%) received 2L treatment, most commonly BTK inhibitor-based (35.7%), followed by anti-CD20–based (29.6%) and venetoclax-based (25.8%) therapies
- From 1L to 2L therapy, the prevailing sequencing pattern was a switch from either one BTK inhibitor to another (23.5%), venetoclax to anti-CD20 (13.2%), or a BTK inhibitor to an anti-CD20–based therapy (9.7%)
- From 2L to 3L therapy, patients most frequently switched from anti-CD20–based therapy to venetoclax (24.6%), anti-CD20–based therapy to a BTK inhibitor (13.3%), or one BTK inhibitor to another (12.6%)
- From 3L to 4L therapy, the predominant sequencing pattern was a switch from venetoclax to anti-CD20–based therapy (21.3%), anti-CD20–based therapy back to venetoclax (20.6%), or one BTK inhibitor to another (11.6%)

Figure 1. Sankey Diagram for Treatment Sequence by Treatment Class



1L, first line; 2L, second line; 3L, third line; 4L, fourth line; BTK, Bruton tyrosine kinase; trt, treatment..

Time to Next Treatment

- Median TTNT was significantly longer for patients receiving BTK inhibitors (53.9 months) in the 1L setting (*P*<.0001) (**Figure 2**)
- Median TTNT in 2L was not reached among patients using BTK inhibitors, while it was significantly shorter for those receiving anti-CD20–based treatment (1.5 months; *P*<.0001) (**Figure 3**)
- Cox regression analysis, when adjusted for age, sex, region, practice setting, and race, also confirmed these results observed in the 1L and 2L settings

Healthcare Resource Utilization

- Overall in 1L, 25% of patients had ≥1 claim for an inpatient visit, 22% of patients had ≥1 claim for an emergency department (ED) visit, and the average number of outpatient visits per patient per month (PPPM) was 2.76
- The median number of PPPM ED visits and outpatient visits were lower for those who received BTK inhibitor-based therapy compared with the overall medians (0.19 and 1.11 vs 0.23 and 1.40, respectively)

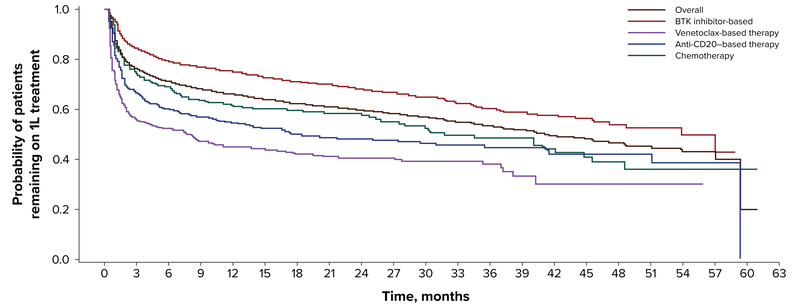
DISCUSSION

- This study demonstrated unique treatment sequencing patterns among patients with CLL in the real-world setting
- Future studies with extended follow-up are needed to allow for assessment of newer treatments and enable evaluation of long-term clinical outcomes
- This study included a broadly representative sample of US patients with CLL, but it is important to acknowledge that the findings may not be generalizable to the entire population
- Although real-world data has gained acceptance as a reliable source for understanding actual practice patterns, it may present inherent data limitations related to the completeness of the data source

CONCLUSIONS

- As the most commonly used regimen, BTK inhibitor therapy was shown to have significantly improved TTNT compared with other treatment regimens in first line
- Our findings are consistent with other real-world data on CLL regarding clinical outcomes, including longer time to next treatment and lower all-cause HCRU for patients on BTK inhibitor therapy

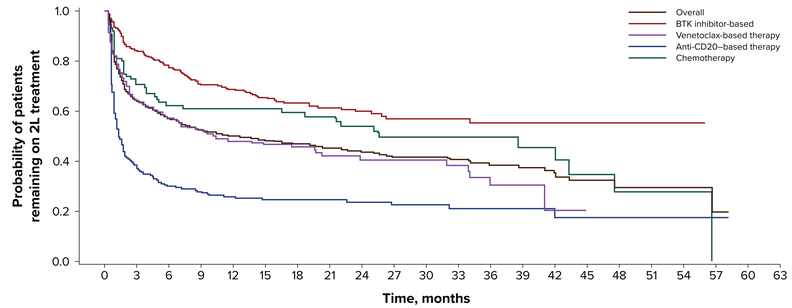
Figure 2. Kaplan-Meier Analysis of TTNT for 1L, Overall and by Treatment Category



	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63
Overall	3431	2273	1854	1589	1348	1136	953	798	679	565	460	369	300	215	167	127	87	50	30	16	1	0
BTK inhibitor-based	2062	1500	1226	1068	899	755	630	530	441	362	291	232	180	129	99	79	49	29	18	9	0	
Venetoclax-based	548	269	222	178	147	119	100	81	73	59	45	33	32	14	5	4	3	1	1	0		
Anti-CD20–based	533	307	243	208	178	150	122	103	90	81	67	57	47	38	32	22	19	12	5	3	0	
Chemotherapy	288	197	163	135	124	112	101	84	75	63	57	47	41	34	31	22	16	8	6	4	0	0

1L, first line; BTK, Bruton tyrosine kinase; TTNT, time to next treatment.

Figure 3. Kaplan-Meier Analysis of TTNT for 2L, Overall and by Treatment Category



	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63
Overall	1200	660	518	412	342	286	217	178	146	119	99	79	54	40	28	15	11	6	4	2	0	
BTK inhibitor-based	428	302	249	191	162	129	100	86	70	56	45	34	21	15	12	7	4	2	1	0		
Venetoclax-based	310	177	141	110	86	74	48	34	26	23	21	17	10	7	2	0						
Anti-CD20–based	355	117	78	64	48	42	34	27	23	20	16	13	10	8	5	3	3	3	2	2	0	
Chemotherapy	107	64	50	47	46	41	35	31	27	20	17	15	13	10	9	5	4	1	1	0		

2L, second line; BTK, Bruton tyrosine kinase; TTNT, time to next treatment.

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