Real-World Treatment Patterns and Biomarker Utilization Among Patients Aged ≥65 Years With CLL/SLL From 2020 to 2024

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CONCLUSIONS

- This longitudinal, real-world study found that cBTKi monotherapies were the most common 1L treatment in patients aged ≥65 years with CLL/SLL between 2020 and 2024
  - cBTKi monotherapies had the greatest increase in usage (42% to 48% of all treatments), with zanubrutinib use comprising 28% of all treatments in 2024
  - Within this cohort of older adults, patients treated with cBTKi monotherapies had a higher median age and were more likely to have a severe CCI than those treated with ven + anti-CD20 mAb
  - In this exploratory analysis, patients treated with zanubrutinib were less likely to discontinue treatment than patients treated with acalabrutinib or ibrutinib
- Despite the treatment advances of novel therapies available, a sizeable subgroup still received CIT or anti-CD20 mAb alone and informative biomarker testing remained under-utilized

INTRODUCTION

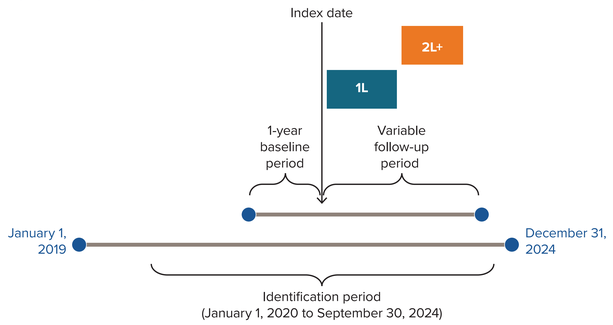
- Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is the most common leukemia in US adults and incidence increases with age, with 67% of patients being >65 years at diagnosis[1-3]
- The introduction of novel therapies, such as zanubrutinib, acalabrutinib, and venetoclax (ven), has transformed the CLL/SLL treatment landscape, with these therapies now recommended for first-line (1L) use in National Comprehensive Cancer Network® (NCCN) guidelines[4]
- However, there are concerns around comorbidities, toxicity, and efficacy of CLL/SLL therapies in older patients[5,6]
- Given the evolving treatment landscape, there is a need to better understand treatment patterns and considerations in the clinical management of older patients

METHODS

Data Source and Study Population

- This retrospective, longitudinal study used de-identified 100% Medicare Fee-for-Service Research Identifiable Files
- Eligible patients included US adults with CLL/SLL diagnosis at age ≥65 who initiated 1L treatment between January 1, 2020, and September 30, 2024, and had ≥12 months' enrollment prior to 1L treatment initiation (**Figure 1**)
- The index date was defined as the date of 1L treatment initiation
- Patients were followed to death, end of Medicare enrollment, or study end, whichever occurred first

Figure 1. Study Design



Index date: start date of patient's 1L treatment. 2L+, second line or later.

Statistical Analyses

- 1L treatment was defined as any CLL pharmacologic treatment within the first 90 days of the index date; the number and proportion of patients who received each treatment were summarized
- Descriptive statistics summarized demographic and baseline characteristics of patients, both in the overall population and by 1L treatment
- The proportion and timings of documented biomarker testing orders any time prior to index date, including CLL fluorescence in situ hybridization (FISH), *TP53* DNA sequencing and immunoglobulin heavy chain variable region (IGHV) mutation status testing, were summarized overall and by 1L treatment
- Exploratory analysis assessing time to treatment discontinuation (TTD) among patients with covalent Bruton tyrosine kinase inhibitor (cBTKi) monotherapy (mono) was performed using Kaplan-Meier methods and Cox proportional hazard model adjusting for demographics and Charlson Comorbidity Index (CCI)

RESULTS

Baseline Demographics and Characteristics

- A total of 21,008 patients were included in the study; baseline characteristics and demographics are shown in **Tables 1 and 2**
- Patients starting cBTKi mono were older than patients starting ven + anti-CD20 monoclonal antibody (mAb) therapies (median age: 77.2 vs 73.7 years)
- More patients who received zanubrutinib mono had CCI ≥5 (39.0%) versus acalabrutinib (36.0%), ibrutinib (34.9%), or ven + anti-CD20 mAb (31.6%)
- Comorbidities differed by treatment; patients with ven + anti-CD20 mAb were less likely to have diabetes (23% vs 26%), congestive heart failure (CHF; 16% vs 19%), chronic pulmonary disease (23% vs 27%), and renal diseases (23% vs 27%).
  - Patients with ibrutinib were less likely to have myocardial infarction (29% vs 34%), coronary artery disease (22% vs 25%), CHF (16% vs 19%), and atrial fibrillation (12% vs 18%)

Table 1. Baseline Characteristics and Demographics Overall and by 1L Treatment

	Overall N=21,008	cBKTi n=8661	Anti-CD20 mAb n=4664	CIT n=2767	Ven + anti-CD20 mAb n=2363
Age at 1L treatment (years), median (min-max)	76.4 (65.2-102.4)	77.2 (65.3-102.4)	77.4 (65.2-100.7)	75.1 (65.2-97.0)	73.7 (66.0-97.0)
Age range (years) at 1L treatment, n (%)					
65-74	9061 (43.1)	3425 (39.5)	1781 (38.2)	1365 (49.3)	1377 (58.3)
75-84	8959 (42.6)	3730 (43.1)	2075 (44.5)	1193 (43.1)	860 (36.4)
≥85	2988 (14.2)	1506 (17.4)	808 (17.3)	209 (7.6)	126 (5.3)
Gender, n (%)					
Male	12,097 (57.6)	5072 (58.6)	2437 (52.3)	1547 (55.9)	1518 (64.2)
Race,[a] n (%)					
White	19,144 (91.1)	7863 (90.8)	4263 (91.4)	2535 (91.6)	2152 (91.1)
CCI,[b] n (%)					
Mild (CCI=1-2)	4989 (23.7)	2246 (25.9)	943 (20.2)	558 (20.2)	641 (27.1)
Moderate (CCI=3-4)	5598 (26.6)	2221 (25.6)	1311 (28.1)	785 (28.4)	616 (26.1)
Severe (CCI=≥5)	8424 (40.1)	3151 (36.4)	2144 (46.0)	1326 (47.9)	747 (31.6)

[a]Based on CMS Beneficiary Race Code; [b]Excluding CLL and SLL diagnosis codes.
CIT, chemoimmunotherapy; CMS, Centers for Medicare & Medicaid Services.

Table 2. Baseline Characteristics and Demographics in cBTKi Subgroups

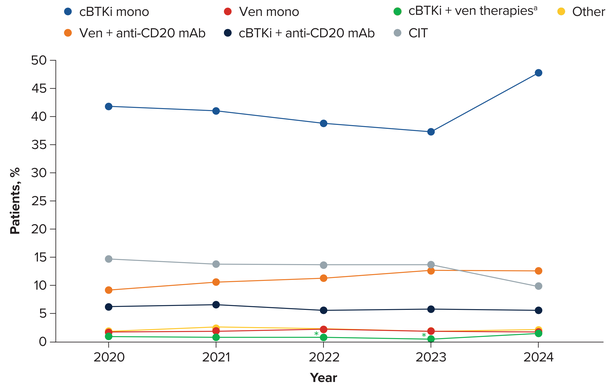
	Zanubrutinib mono n=2123	Acalabrutinib mono n=3446	Ibrutinib mono n=3092
Age at 1L (years), median (min-max)	77.1 (65.3-102.1)	77.7 (66.0-102.4)	76.8 (65.3-100.8)
Age range at 1L (years), n (%)			
65-74	833 (39.2)	1313 (38.1)	1279 (41.4)
75-84	929 (43.8)	1473 (42.7)	1328 (42.9)
≥85	361 (17.0)	660 (19.2)	485 (15.7)
Gender, n (%)			
Male	1257 (59.2)	2050 (59.5)	1765 (57.1)
Race,[a] n (%)			
White	1939 (91.3)	3122 (90.6)	2802 (90.6)
CCI,[b] n (%)			
Mild (CCI=1-2)	497 (23.4)	886 (25.7)	863 (27.9)
Moderate (CCI=3-4)	579 (27.3)	917 (26.6)	725 (23.4)
Severe (CCI=≥5)	829 (39.0)	1242 (36.0)	1080 (34.9)
Year of index (1L treatment start), n (%)			
2020	*	468 (13.6)	1291 (41.8)
2021	>10[d]	898 (26.1)	882 (28.5)
2022	180 (8.5)	881 (25.6)	555 (17.9)
2023	818 (38.5)	586 (17.0)	200 (6.5)
2024[c]	1086 (51.2)	613 (17.8)	164 (5.3)

[a]Based on CMS Beneficiary Race Code. [b]Excluding CLL and SLL diagnosis codes. [c]Through September 2024. [d]Due to low cell counts. *Data in this cell are blinded due to use agreement with CMS.

Treatment Patterns

- The most common 1L treatments were cBTKi mono (41.2%), including zanubrutinib (10.1%), ibrutinib (14.7%), and acalabrutinib (16.4%)
- CIT was used by 13.2% of patients, mostly bendamustine + rituximab (8.2%) and fludarabine + cyclophosphamide + rituximab (3.4%)
- Less common 1L treatment included cBTKi + anti-CD20 mAb therapy (6.0%) or cBTKi + ven therapies (0.8%)
- From 2020 to 2024, cBTKi mono had the largest increase in use (~5%), mainly driven by increased uptake of zanubrutinib (27.8%), while use of ven + anti-CD20 mAb therapy increased by 3.4% (**Figure 2**)

Figure 2. Changes in 1L Treatment Patterns Among Older Patients With CLL/SLL Over Time

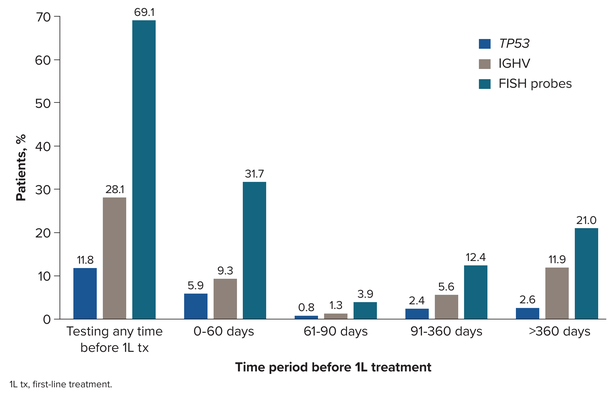


[a]Treatment group included patients who received cBTKi + ven ± anti-CD20 mAb. *Data were censored due to agreement with CMS. Values within these groups are approximate rather than exact.

Biomarker Testing Utilization

- Overall, 72.6% of patients received a biomarker test for CLL/SLL, with an average of 1.8 tests per patient
- Prior to 1L treatment, 69.1% of patients had a FISH test, but IGHV status (28.1%) and *TP53* (11.8%) testing were infrequent (**Figure 3**)
- The timing of tests showed a binomial distribution among patients who had tests, where most patients received FISH, *TP53*, or IGHV tests either within 60 days prior to 1L treatment (45.9%, 50.4%, 32.9%, respectively), or >1 year before 1L treatment (30.4%, 22.4%, 42.5%, respectively)
- Patients treated with ibrutinib had the lowest rates of *TP53* tests (6.0%), whereas patients with CIT had the lowest rates of IGHV tests (15.9%)

Figure 3. Biomarker Testing Utilization and Timing Before 1L Treatment in All Older Patients With CLL/SLL



1L tx, first-line treatment.

2L+ Treatment

- Among patients who received ≥2 lines of therapy (n=4428; 21.1%), cBTKi mono was the most common in 2L (40.6%), including 13.9% zanubrutinib, 16.7% acalabrutinib, and 10.0% ibrutinib
- CIT and ven + anti-CD20 mAb were used in 12% and 9% of patients as 2L therapy, respectively
- Only 634 (3.0%) patients had third-line or later treatment, of whom 32.8% received cBTKi mono, including 15.8% zanubrutinib, 12.3% acalabrutinib, and 4.7% ibrutinib

TTD Among 1L cBTKi

- Median TTD was not reached (NR) for zanubrutinib (95% confidence interval [CI]: 36-NR), 19 months for acalabrutinib (95% CI: 17-20), and 13 months for ibrutinib (95% CI: 12-14)
- Patients with zanubrutinib were 24% (hazard ratio [HR]=0.76; 95% CI: 0.69-0.84; *P*<.0001) and 50% (HR=0.50; 95% CI: 0.45-0.55; *P*<.0001) less likely to discontinue treatment at 12 months, compared with acalabrutinib and ibrutinib, respectively
- At 12 months from 1L start, 70% (95% CI: 67-72%) of patients with zanubrutinib remained on treatment, compared with 58% (95% CI: 57-60%) and 51% (95% CI: 49-53%) of patients for acalabrutinib and ibrutinib, respectively

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