Changes in Real-World Treatment Patterns Over Time by Patient Characteristics and Time Burden of Treatment in CLL/SLL

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CONCLUSIONS

- Treatment patterns for patients with CLL have changed drastically in recent years, with the use of next-generation cBTKi surpassing ibrutinib
- As of 2024, zanubrutinib monotherapy was the most frequently prescribed cBTKi in 1L CLL and the most common therapy in older patients and those with high-risk disease characteristics, indicating its accepted use in practice
- Use of fixed-duration venetoclax-based therapies in 2024 was common among younger patients with lower-risk disease characteristics
- Time burden was higher for patients treated with infusion-containing regimens in the first year of treatment, and was similar between treatment types in following years despite discontinuation of fixed-duration therapies

INTRODUCTION

- In recent years, the chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) treatment landscape has evolved[1]
- Treatment decisions are often based on factors associated with disease progression, including age, presence of high-risk genomic features (eg, 17p deletion [del17p], *TP53* mutation [*TP53*m] and immunoglobulin heavy chain variable region [IGHV] mutations), Eastern Cooperative Oncology Group performance status (ECOG PS), general patient fitness, and comorbidities[2,3]
- Different treatments may have different time burdens (eg, time required for clinical visits, phlebotomy, and infusions) throughout patients' journeys[4]

Aim:

- To describe first-line (1L) CLL treatment patterns over time, by patient characteristics, and treatment-related time burden in the past 5 years (2020-2024)

METHODS

Data Source and Study Population

- This retrospective, observational study utilized the US electronic health record–derived de-identified Flatiron Health Research Database
- Eligible patients included adults with CLL/SLL who started 1L treatment between January 1, 2020, and December 21, 2024
- Key subgroups included age, ECOG PS, del17p or *TP53*m status, IGHV status, and comorbidities at index date (1L start)

Study Design and Statistical Analysis

- Descriptive statistics were used to summarize baseline characteristics
- Common treatment regimens were summarized by year of 1L treatment initiation and key patient subgroups
- Time burden was defined as average number of days of clinical visits (outpatient clinic, lab, or infusion) per person-year (p-y) in Years 1-3 during 1L treatment and follow-up (initiation of next treatment, death, or end of Year 3, whichever occurred first)
- Wilcoxon rank sum test was performed for time burden across treatment groups

RESULTS

Patient Demographics and Clinical Characteristics by 1L Treatment

- A total of 4929 patients were assessed (**Table 1**)
- Most patients were aged ≥65 years at 1L (74.6%; median age 72 years), male (62.3%), White (72.8%), had ECOG PS of 0 (41.6%) or 1 (28.3%), and were treated at a community practice (80.8%)
- Del17p/*TP53*m were identified in 11.0% of patients and 29.9% had unmutated IGHV

Table 1. Patient Demographics and Clinical Characteristics by 1L Treatment

	Total (N=4929)	Zanubrutinib[a] (n=405)	Acalabrutinib[a] (n=1475)	Ibrutinib[a] (n=1291)	Venetoclax-based regimen[b] (n=855)	CIT (n=287)
Median age at index date, years (range)	72.0 (19-85)	74.0 (34-85)	73.0 (31-85)	71.0 (32-85)	69.0 (34-85)	71.0 (40-85)
Age (years) at index date, n (%)						
<65	1901 (38.6)	125 (30.9)	506 (34.3)	497 (38.5)	400 (46.8)	117 (40.8)
≥65	3028 (61.4)	280 (69.1)	969 (65.7)	794 (61.5)	455 (53.2)	170 (59.2)
Sex, n (%)						
Male	3073 (62.3)[c]	258 (63.7)	893 (60.5)	740 (57.3)	574 (67.1)[c]	180 (62.7)
Race and ethnicity, n (%)						
White	3587 (72.8)	298 (73.6)	1086 (73.6)	902 (69.9)	657 (76.8)	194 (67.6)
Black	381 (7.7)	41 (10.1)	97 (6.6)	130 (10.1)	53 (6.2)	18 (6.3)
Hispanic	192 (3.9)	≤5	47 (3.2)	54 (4.2)	31 (3.6)	23 (8.0)
Other[d]	407 (8.3)	<30	140 (9.5)	107 (8.3)	62 (7.3)	23 (8.0)
Unknown	362 (7.3)	36 (8.9)	105 (7.1)	98 (7.6)	52 (6.1)	29 (10.1)
ECOG PS at index date, n (%)						
0	2052 (41.6)	176 (43.5)	551 (37.4)	531 (41.1)	430 (50.3)	117 (40.8)
1	1396 (28.3)	103 (25.4)	399 (27.1)	343 (26.6)	264 (30.9)	85 (29.6)
2-4	370 (7.5)	35 (8.6)	120 (8.1)	102 (7.9)	46 (5.4)	20 (7.0)
Unknown	1111 (22.5)	91 (22.5)	405 (27.5)	315 (24.4)	115 (13.5)	65 (22.6)
Comorbidity, n (%)						
0	3973 (80.6)	323 (79.8)	1186 (80.4)	1077 (83.4)	686 (80.2)	225 (78.4)
1	652 (13.2)	52 (12.8)	191 (12.9)	152 (11.8)	121 (14.2)	45 (15.7)
2+	304 (6.2)	30 (7.4)	98 (6.6)	62 (4.8)	48 (5.6)	17 (5.9)
Del17p/*TP53*m status, n (%)						
Positive[e]	540 (11.0)	59 (14.6)	195 (13.2)	144 (11.2)	80 (9.4)	12 (4.2)
Negative[f]	3782 (76.7)	301 (74.3)	1110 (75.3)	938 (72.7)	715 (83.6)	217 (75.6)
Not tested	607 (12.3)	45 (11.1)	170 (11.5)	209 (16.2)	60 (7.0)	58 (20.2)
IGHV status, n (%)						
Mutated	1015 (20.6)	88 (21.7)	316 (21.4)	216 (16.7)	203 (23.7)	59 (20.6)
Unmutated	1473 (29.9)	138 (34.1)	444 (30.1)	366 (28.4)	301 (35.2)	40 (13.9)
Unknown[g]	2441 (49.5)	179 (44.2)	715 (48.5)	709 (54.9)	351 (41.1)	188 (65.5)
Practice type, n (%)						
Academic	944 (19.2)	97 (24.0)	327 (22.2)	176 (13.6)	164 (19.2)	31 (10.8)
Community	3985 (80.8)	308 (76.0)	1148 (77.8)	1115 (86.4)	691 (80.8)	256 (89.2)
SES index, n (%)						
5 (highest)	1207 (24.5)	97 (24.0)	375 (25.4)	284 (22.0)	242 (28.3)	53 (18.5)
4	1114 (22.6)	95 (23.5)	345 (23.4)	279 (21.6)	206 (24.1)	67 (23.3)
3	864 (17.5)	81 (20.0)	247 (16.7)	252 (19.5)	137 (16.0)	56 (19.5)
2	771 (15.6)	75 (18.5)	236 (16.0)	196 (15.2)	103 (12.0)	50 (17.4)
1 (lowest)	593 (12.0)	36 (8.9)	162 (11.0)	175 (13.6)	92 (10.8)	43 (15.0)
Unknown	380 (7.7)	21 (5.2)	110 (7.5)	105 (8.1)	75 (8.8)	18 (6.3)
Insurance, n (%)						
Medicare	3055 (62.0)	286 (70.6)	963 (65.3)	803 (62.2)	473 (55.3)	175 (61.0)
Commercial	946 (19.2)	66 (16.3)	272 (18.4)	255 (19.8)	183 (21.4)	55 (19.2)
Medicaid	102 (2.1)	7 (1.7)	28 (1.9)	28 (2.2)	23 (2.7)	<5
Others	333 (6.8)	15 (3.7)	73 (4.9)	70 (5.4)	74 (8.7)	24 (8.4)
Uninsured/ Unknown	493 (10.0)	31 (7.7)	139 (9.4)	135 (10.5)	102 (11.9)	29 (10.1)

[a]Monotherapy or combination. [b]VO, VR or venetoclax monotherapy. [c]One patient's sex information missing from treatment category. [d]Includes Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or a race description that falls into multiple race categories. [e]Positive for del17p or *TP53*m. [f]Negative for del17p and *TP53*m. [g]Includes Unsuccessful/Indeterminate, Unknown/Not documented, and Not tested. CIT, chemoimmunotherapy; SES, socioeconomic status; VO, venetoclax + obinutuzumab; VR, venetoclax + rituximab.

Overall Trends in Treatment Patterns Over Time

- Treatment patterns changed dramatically over the 5 years assessed (**Figure 1**)
  - In 2020, ibrutinib monotherapy was the most frequently administered 1L treatment followed by anti-CD20 monotherapy (obinutuzumab or rituximab) and acalabrutinib monotherapy
  - However, the use of ibrutinib dropped over time, and by 2024, next-generation covalent Bruton tyrosine kinase inhibitor (cBTKi) monotherapy (zanubrutinib and acalabrutininb) was the most frequent 1L treatment, followed by VO
  - While not an approved systemic therapy for CLL, the use of anti-CD20 monotherapies was observed across all years assessed

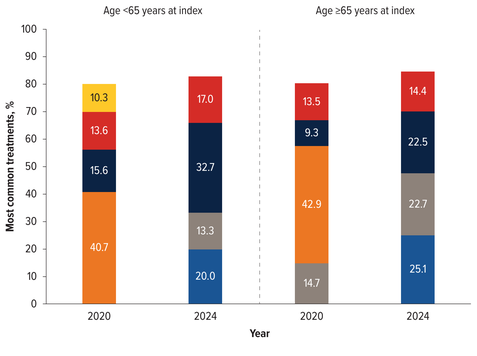
Figure 1. Trends in Four Most Common 1L Treatments Over Time[a]

[a]Treatments shown per year only include top four most common and therefore percentages may not add up to 100. [b]Obinutuzumab or rituximab.

Trends in Treatment Patterns Over Time Stratified by Patient Characteristics

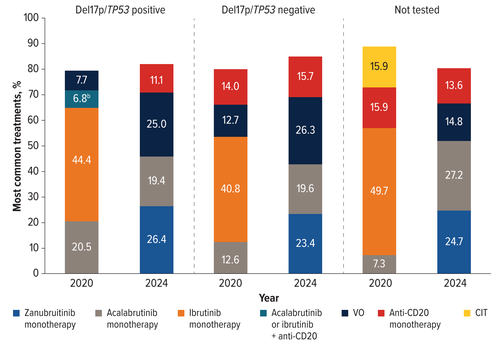
- In 2020, ibrutinib monotherapy was the most common 1L treatment in the overall patient population (**Figure 1**) regardless of patient characteristics including age (**Figure 2**) and del17p/*TP53*m status (**Figure 3**)
- By 2024, zanubrutinib monotherapy was the most common 1L treatment among patients aged ≥65 years (**Figure 2**), in those with del17p/*TP53*m (**Figure 3**), or with ≥2 comorbidities (**Figure 4**)
- In contrast, VO was most commonly used among younger patients with lower-risk disease characteristics, such as ECOG PS 0 or 1 (**Figure 5**), no del17p/*TP53*m (**Figure 3**), or 0 or 1 comorbidities (**Figure 4**) in 2024
- In 2024, VO and zanubrutinib monotherapy were the most common treatments for both mutated and unmutated IGHV (**Figure 6**), and acalabrutinib monotherapy was the most common in patients untested for del17p/*TP53*m (**Figure 3**) or IGHV (**Figure 6**)

Figure 2. Four Most Common 1L Treatments Over Time by Age at Initiation[a]



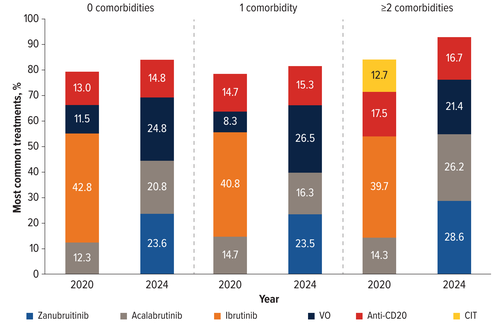
[a]Treatments shown per year only include top four most common and therefore percentages may not add up to 100.

Figure 3. Four Most Common 1L Treatments Over Time by Del17p/*TP53*m Status[a]



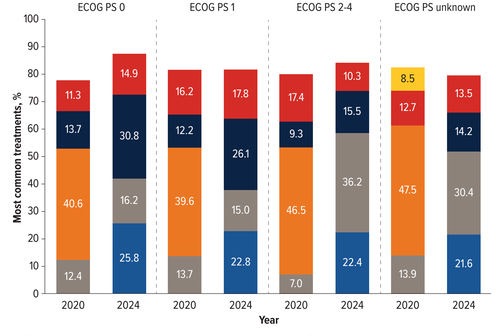
[a]Treatments shown per year only include top four most common and therefore percentages may not add up to 100. [b]Acalabrutinib + anti-CD20 and ibrutinib + anti-CD20 were tied for fourth most common.

Figure 4. Four Most Common 1L Treatments Over Time by Number of Comorbidities[a]



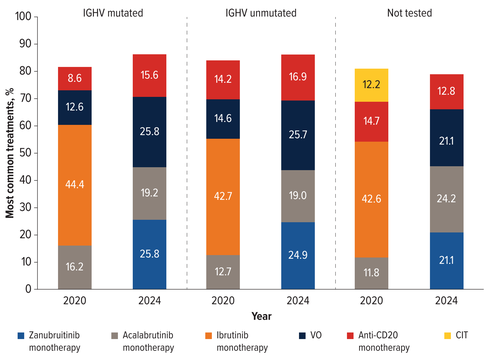
[a]Treatments shown per year only include top four most common and therefore percentages may not add up to 100.

Figure 5. Four Most Common 1L Treatments Over Time by ECOG PS Status[a]



[a]Treatments shown per year only include top four most common and therefore percentages may not add up to 100.

Figure 6. Four Most Common 1L Treatments Over Time by IGHV Status[a]

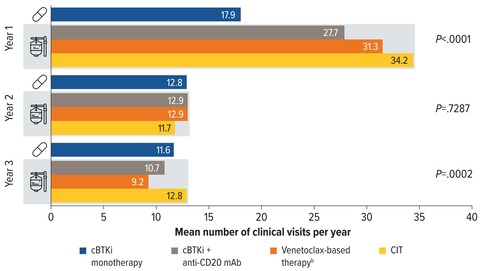


[a]Treatments shown per year only include top four most common and therefore percentages may not add up to 100.

Time Burden Associated With 1L Treatment

- In the first year of treatment, infusion-containing regimens had a higher time burden for patients than oral regimens (**Figure 7**)
  - Patients who received CIT or venetoclax-based regimens had the highest average number of clinical visit days per p-y in the first year, followed by cBTKi + anti-CD20, whereas cBTKi monotherapy was associated with almost half the clinic time (*P*<.0001)
- By the second year, the number of clinical visit days per py was similar between treatment groups (*P*=.7287)
- In the third year, venetoclax-based regimens had slightly fewer clinical visit days per p-y during follow-up (*P*=.0002)

Figure 7. Time Burden[a] Associated With 1L Treatment Type Over Years 1-3 of Treatment and Follow-Up



[a]Time burden is defined as average number of clinical visits per p-y. [b]VO or VR. mAb, monoclonal antibody.

LIMITATIONS

- The Flatiron Health database is derived from electronic health records and patient data may be incomplete or missing. Tests (p-y) ordered outside the practices may be missing if the documentation is not included in patient records
- Most patients in this study were treated at community practices and may receive different management than those in academic practices
- The generalizability of the results to patients outside of the Flatiron Health database and outside of the US may be limited

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