Recent Patterns of Care With BTK Inhibitors and Distribution of Social Determinants of Health Among Patients With Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma in the US Community Setting

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INTRODUCTION

- Bruton tyrosine kinase (BTK) inhibitors, including ibrutinib, acalabrutinib, and zanubrutinib have been the mainstay treatments for patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)[1,2]
- In 2 recent randomized clinical trials, acalabrutinib and zanubrutinib demonstrated significantly longer progression-free survival compared with ibrutinib among patients with relapsed or refractory CLL/SLL[3,4]
- The aim of this study was to examine the characteristics, treatment patterns, and social determinants of health (SDOH) among patients with CLL/SLL who received BTK inhibitors in a large network of community oncology practices

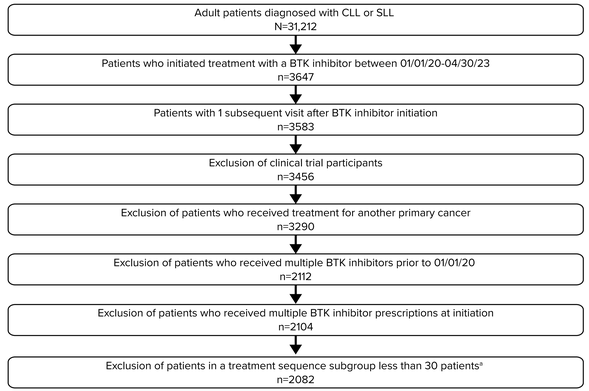
METHODS

- **Study Design:** A retrospective, observational cohort study
- **Data Source:** Study data were sourced from structured fields of The US Oncology Network's electronic healthcare record (EHR)–iKnowMed (iKM)–and the associated claims database, the Financial Data Warehouse (FDW). EHR and FDW data were linked to the following external databases for evaluation of SDOH measures:
  - The Neighborhood Atlas® for Area Deprivation Index (ADI) scores, which were determined by mapping patients' home addresses to census block groups (CBGs), are based on the following socioeconomic factors: income, education, employment, and housing quality of residents within CBGs. Low socioeconomic status (SES) was defined as the top 20% of ADI scores on a national and state level (cut-off based on literature review)
  - The US Department of Agriculture's rural/urban commuting area code database (these codes are based on population data from the 2020 census, the latest urban area delineations from the Census Bureau, and updated community data from the American Community Survey)
  - Insurance coverage was reported as documented in the FDW, with Medicaid as an indicator of low SES
- **Study Population:** Adult patients with CLL/SLL whose first documented prescription for a BTK inhibitor occurred between January 1, 2020 and April 30, 2023. Patients without a subsequent visit after BTK inhibitor initiation, those with inaccessible EHR data, those who received multiple BTK inhibitors on their treatment initiation date, clinical trial participants, and those who received treatment for another primary cancer following treatment initiation were excluded. Patients were followed until the last date of the study (April 30, 2023) or their last visit date, whichever occurred first
- **Statistical Analysis:** Patients were stratified into mutually exclusive treatment sequence subgroups based on their immediate subsequent treatment following index. Patient characteristics and SDOH measures were assessed descriptively, with Chi-squared *P* values reported for select SDOH measures. Data are presented for treatment subgroups with at least 30 eligible patients

RESULTS

- In total, 2082 patients were identified across 6 treatment sequence subgroups, each having at least 30 patients (**Figure 1**)
- Demographic and clinical characteristics across the treatment sequences were similar, including sex, race, and ethnicity distributions, along with Rai stage and Eastern Cooperative Oncology Group performance status scores at baseline (**Table 1**)
- The highest proportion of patients received acalabrutinib, ibrutinib, or zanubrutinib, without an observed subsequent BTK inhibitor (n=1159 [55.7%], n=628 [30.2%], and n=113 [5.4%], respectively) (**Figure 1**)
- Temporal trends were observed in BTK inhibitor use over time across the 6 included subgroups (**Figure 2**)

Figure 1. Study Attrition and Treatment Sequence Subgroups



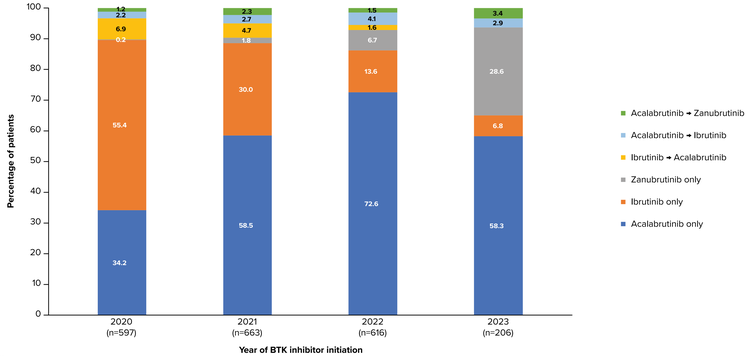
[a] Per protocol, the analyses were limited to subgroups with at least 30 patients for 2 reasons: 1) results with <30 patients may result in small cell sizes, which is associated with a risk of re-identification, and 2) subgroups of <30 patients would have been insufficient for statistical analyses.
BTK, Bruton tyrosine kinase; CLL, chronic lymphocytic leukemia; SLL, small lymphocytic lymphoma.

Table 1. Demographics and Clinical Characteristics

	Overall (N=2082)	Acalabrutinib → no subsequent BTK inhibitor (n=1159)	Ibrutinib → no subsequent BTK inhibitor (n=628)	Zanubrutinib → no subsequent BTK inhibitor (n=113)	Switched from ibrutinib → acalabrutinib (n=82)	Switched from acalabrutinib → ibrutinib (n=62)	Switched from acalabrutinib → zanubrutinib (n=38)
Median age at index, y (range)	73 (21-90+)	73 (21-90+)	74 (28-90+)	74 (51-90+)	73 (40-89)	70.5 (40-89)	76.5 (44-90+)
Sex, n (%)							
Male	1288 (61.9)	716 (61.8)	387 (61.6)	78 (69.0)	50 (61.0)	35 (56.5)	22 (57.9)
Female	794 (38.1)	443 (38.2)	241 (38.4)	35 (31.0)	32 (39.0)	27 (43.5)	16 (42.1)
Race, n (%)							
Asian	17 (0.8)	7 (0.6)	7 (1.1)	0	1 (1.2)	2 (3.2)	0
Black	178 (8.5)	93 (8.0)	64 (10.2)	9 (8.0)	5 (6.1)	3 (4.8)	4 (10.5)
White	1530 (73.5)	860 (74.2)	454 (72.3)	81 (71.7)	59 (72.0)	47 (75.8)	29 (76.3)
Other	82 (3.9)	49 (4.2)	23 (3.7)	3 (2.7)	4 (4.9)	3 (4.8)	0
No information	275 (13.2)	150 (12.9)	80 (12.7)	20 (17.7)	13 (15.9)	7 (11.3)	5 (13.2)
Ethnicity, n (%)							
Hispanic or Latino	51 (2.4)	31 (2.7)	16 (2.5)	1 (0.9)	1 (1.2)	1 (1.6)	1 (2.6)
Not Hispanic or Latino	1692 (81.3)	954 (82.3)	500 (79.6)	91 (80.5)	69 (84.1)	46 (74.2)	32 (84.2)
No information	339 (16.3)	174 (15.0)	112 (17.8)	21 (18.6)	12 (14.6)	15 (24.2)	5 (13.2)
Rai stage, n (%)							
Stage 0	405 (19.5)	225 (19.4)	120 (19.1)	23 (20.4)	22 (26.8)	10 (16.1)	5 (13.2)
Stages I and II	551 (26.5)	315 (27.2)	146 (23.2)	32 (28.3)	24 (29.3)	22 (35.5)	12 (31.6)
Stages III and IV	565 (27.1)	339 (29.2)	146 (23.2)	30 (26.5)	21 (25.6)	18 (29.0)	11 (28.9)
No information	561 (26.9)	280 (24.2)	216 (34.4)	28 (24.8)	15 (18.3)	12 (19.4)	10 (26.3)
ECOG performance status at baseline, n (%)							
0	334 (16.0)	180 (15.5)	102 (16.2)	18 (15.9)	17 (20.7)	13 (21.0)	4 (10.5)
1	582 (28.0)	343 (29.6)	160 (25.5)	27 (23.9)	21 (25.6)	15 (24.2)	16 (42.1)
2+	123 (5.9)	72 (6.2)	37 (5.9)	8 (7.1)	5 (6.1)	1 (1.6)	0
No information	1043 (50.1)	564 (48.7)	329 (52.4)	60 (53.1)	39 (47.6)	33 (53.2)	18 (47.4)
Index treatment year, n (%)							
2020	597 (28.7)	204 (17.6)	331 (52.7)	1 (0.9)	41 (50.0)	13 (21.0)	7 (18.4)
2021	663 (31.8)	388 (33.5)	199 (31.7)	12 (10.6)	31 (37.8)	18 (29.0)	15 (39.5)
2022	616 (29.6)	447 (38.6)	84 (13.4)	41 (36.3)	10 (12.2)	25 (40.3)	9 (23.7)
2023	206 (9.9)	120 (10.4)	14 (2.2)	59 (52.2)	0	6 (9.7)	7 (18.4)
Median follow-up duration (range), mo[a]	14.1 (0-41)	12.7 (0-40.7)	19.9 (0-41.0)	3.7 (0-31.8)	22.6 (0.5-41.0)	12.9 (0.5-40.0)	18.5 (1.4-38.6)

[a] Follow-up was assessed from the first prescription for a BTK inhibitor during the study identification period until the end of the study observation period, date of last visit, or date of death, whichever occurred first.
BTK, Bruton tyrosine kinase; CLL, chronic lymphocytic leukemia; ECOG, Eastern Cooperative Oncology Group; mo, month; SLL, small lymphocytic lymphoma; y, year.

Figure 2. Changes in BTK Inhibitor Use Between 2020 and 2023



BTK, Bruton tyrosine kinase.

CONCLUSIONS

- The results of this study indicate that the treatment landscape of BTK inhibitor use among patients with CLL/SLL is shifting, with increased adoption of acalabrutinib and zanubrutinib over time
- Similarities in SDOH measures across the treatment sequence subgroups suggest that patients' SES and Medicaid utilization do not influence prescribing patterns
- Differences across treatment subgroups regarding rural/urban status warrant further consideration
- Further real-world investigations and longitudinal follow-up are needed to examine the impacts of SDOH on treatment choice, treatment switching, reasons for switching, and outcomes among users of BTK inhibitors

- Overall, 137 patients (6.6%; 95% CI, 5.6-7.7) were classified as living in rural locations, and having low SES status based on state and national indicators was observed among 361 patients (17.3%; 95% CI, 15.7-19.0) and 125 (6.0%; 95% CI, 5.0-7.1), respectively
- The highest proportion of patients had Medicare insurance coverage (42.1%; n=877; 95% CI, 40-44.3), followed by managed Medicare (24.4%; n=508; 95% CI, 22.6-26.3)
- A statistical difference was found in treatment regimen groups classified by rural/urban status ($P<.01$), but not for state ADI ($P=.52$), national ADI ($P=.36$), or Medicaid insurance coverage vs all other coverage ($P=.18$) (**Table 2**)

Table 2. SDOH by Treatment Sequence Subgroup

	Overall (N=2082)	Acalabrutinib → no subsequent BTK inhibitor (n=1159)	Ibrutinib → no subsequent BTK inhibitor (n=628)	Zanubrutinib → no subsequent BTK inhibitor (n=113)	Switched from ibrutinib → acalabrutinib (n=82)	Switched from acalabrutinib → ibrutinib (n=62)	Switched from acalabrutinib → zanubrutinib (n=38)	*P* value
Rural/urban status category, n (%, LL-UL)								
Urban	1749 (84.0, 82.4-85.6)	961 (82.9, 80.6-85.0)	546 (86.9, 84.1-89.5)	94 (83.2, 75.0-89.6)	72 (87.8, 78.7-94.0)	49 (79.0, 66.8-88.3)	27 (71.1, 54.1-84.6)	.0015
Rural	137 (6.6, 5.6-7.7)	83 (7.2, 5.7-8.8)	25 (4.0, 2.6-5.8)	13 (11.5, 6.3-18.9)	4 (4.9, 1.3-12.0)	6 (9.7, 3.6-19.9)	6 (15.8, 6.0-31.3)	
No information	196 (9.4, 8.2-10.8)	115 (9.9, 8.3-11.8)	57 (9.1, 7.0-11.6)	6 (5.3, 2.0-11.2)	6 (7.3, 2.7-15.3)	7 (11.3, 4.7-21.9)	5 (13.2, 4.4-28.1)	–
Low SES[a] (state), n (%, LL-UL)	361 (17.3, 15.7-19.0)	195 (16.8, 14.7-19.1)	109 (17.4, 14.5-20.6)	22 (19.5, 12.6-28.0)	12 (14.6, 7.8-24.2)	13 (21.0, 11.7-33.2)	10 (26.3, 13.4-43.1)	.5195
Low SES[a] (national), n (%, LL-UL)	125 (6.0, 5.0-7.1)	69 (6.0, 4.7-7.5)	40 (6.4, 4.6-8.6)	10 (8.8, 4.3-15.7)	1 (1.2, 0-6.6)	3 (4.8, 1.0-13.5)	2 (5.3, 0.6-17.8)	.3603
Payor distribution, n (%, LL-UL)								
Medicaid	73 (3.5, 2.8-4.4)	38 (3.3, 2.3-4.5)	22 (3.5, 2.2-5.3)	3 (2.7, 0.6-7.6)	3 (3.7, 0.8-10.3)	5 (8.1, 2.7-17.8)	2 (5.3, 0.6-17.8)	.182
Medicare	877 (42.1, 40.0-44.3)	481 (41.5, 38.7-44.4)	265 (42.2, 38.3-46.2)	52 (46.0, 36.6-55.7)	40 (48.8, 37.6-60.1)	24 (38.7, 26.6-51.9)	15 (39.5, 24.0-56.6)	
Managed Medicare[b]	508 (24.4, 22.6-26.3)	275 (23.7, 21.3-26.3)	158 (25.2, 21.8-28.7)	30 (26.5, 18.7-35.7)	17 (20.7, 12.6-31.1)	10 (16.1, 8.0-27.7)	18 (47.4, 31.0-64.2)	
Commercial	226 (10.9, 9.6-12.3)	115 (9.9, 8.3-11.8)	80 (12.7, 10.2-15.6)	12 (10.6, 5.6-17.8)	8 (9.8, 4.3-18.3)	10 (16.1, 8.0-27.7)	1 (2.6, 0.1-13.8)	
No information	398 (19.1, 17.5-20.9)	250 (21.6, 19.2-24.1)	103 (16.4, 13.6-19.5)	16 (14.2, 8.3-22.0)	14 (17.1, 9.7-27.0)	13 (21.0, 11.7-33.2)	2 (5.3, 0.6-17.8)	–

[a] Patients' ADI rank based on a scale of 1-10 (deciles) was based on their census block group; the top 20% of overall national and state scores was classified as being low SES. [b]Managed Medicare insurance coverage is provided by commercial insurance plans that work with Medicare.
ADI, Area Deprivation Index; BTK, Bruton tyrosine kinase; LL, lower limit; UL, upper limit; SDOH, Social Determinants of Health; SES, socioeconomic status.

Strengths of the Study

- The study leveraged real-world clinical data from patients treated in The US Oncology Network practices, which represents a sizable proportion of patients with cancer in the US
- The iKM EHR has been deployed across all of The US Oncology Network practices, facilitating a homogenized dataset for research

Limitations

- As data for this study were originally recorded for clinical practice purposes, errors of omission and commission may be present in the dataset
- The study design did not have a minimum follow-up time; therefore, there is a potential of differential follow-up time for patients who initiated BTK inhibitors earlier in the study compared with those who initiated them later
- This study utilized an intent-to-treat approach, which assumed that all prescribed oral therapies were taken, although this could not be verified with structured data alone
- Results are most generalizable for community oncology practices that utilize the iKM EHR and decision–support technology

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DISCLOSURES

IZ: Consultancy: Epizyme, Morphosys. **DA:** Consultancy: AbbVie, AstraZeneca. **TW, KA, CW:** Employment: McKesson; Consultancy: BeiGene. **YF:** nothing to disclose. **SG, KY, EKS, MB, GAM:** Employment: BeiGene.

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