Evaluating Uptake of Targeted Agents by Race/Ethnicity in Patients Receiving First-line Treatment for Chronic Lymphocytic Leukemias

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CONCLUSIONS

- Inequities in patients with chronic lymphocytic leukemia (CLL) receiving preferred first-line (1L) treatment suggests disproportionate use of chemoimmunotherapy (CIT) and ibrutinib by race/ethnicity
- Use of preferred targeted therapies also differed by practice type and time period, with increased adoption after pivotal trials

INTRODUCTION

- The National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for 1L regimens in CLL have evolved over the past decade, shifting from ibrutinib and CIT to second-generation Bruton tyrosine kinase (BTK) inhibitor and venetoclax combinations[1-3]
- Previous research suggested that racial and socioeconomic disparities in CLL clinical outcomes can be reduced by providing equal access to effective CLL treatment[4,5]

Aim

- This study was conducted to evaluate real-world use of preferred 1L treatment as defined by NCCN guidelines for CLL patients in routine care since 2016 to identify differences in prescribing patterns based on race/ethnicity and practice type

METHODS

Data Source and Study Population

- This retrospective observational study utilized the US nationwide Flatiron Health electronic health record-derived de-identified database. Eligible patients had confirmed CLL and initiated 1L treatment between January 1, 2016, and July 31, 2024

Study Design

- The primary outcome was receipt of preferred 1L treatment, defined as the initiation of 1L treatment based on the contemporaneous NCCN guidelines across four time periods, by race/ethnicity (Hispanic, White, Black, Asian/other) and practice type
- **Table 1** shows the time period, NCCN guideline version and change date, and preferred 1L treatment for the four time periods in this study

Table 1. NCCN Guideline Version, Change Date and Preferred 1L Treatment Across the Four Time Periods

Time Period	NCCN Guideline Version	Change Date	Preferred 1L Treatment
2016-2018	-	-	Ibrutinib[a]
2019	v2.2019	Jan 2019	Ibrutinib
2020-Jun 2022	v4.2020	Feb 2020	Acalabrutinib, VO, ibrutinib
Jul 2022-Jul 2024	v2.2023	Aug 2022	Acalabrutini, VO, zanubrutinib

[a]NCCN guideline did not indicate preference. Preferred 1L treatment was coded as ibrutinib.
VO, venetoclax + obinutuzumab.

- The secondary outcome was the impact of NCCN guidelines updates on the likelihood of CLL patients receiving preferred 1L treatment by race/ethnicity and practice type
- Odds ratios (ORs) were estimated using logistic regression, additionally adjusting for age, sex, Eastern Cooperative Oncology Group (ECOG) performance status, immunoglobulin heavy chain variable region (IGHV), del17p/*TP53* mutation status, time period, and practice type

RESULTS

Patient Demographics and Characteristics

- A total of 7528 patients were included. Patient demographics and characteristics by race/ethnicity are shown in **Table 2**
  - Compared with White patients, Black patients were younger (median age at receiving 1L treatment: 68 vs 71 years)
  - More Black (86%) and Hispanic (87%) patients were treated at community practices versus academic centers, compared with White patients (80%)
  - Of those patients tested, more Black patients had unmutated IGHV than White (77% vs 56%). Presence of del17p/*TP53* mutation was similar across races/ethnicities (11% overall)
  - Only 19% of patients were aged ≤65 years, had an ECOG status of 0-2, and did not have del17p/*TP53* mutation
- Patient demographics and characteristics by treatment are shown in **Table 3**
  - Patients receiving VO were younger (median age at receiving 1L treatment: 69 vs 71 years overall) and fitter (ECOG 0-1: 84% vs 68% overall) than the overall population
  - This group of patients were also more likely to be without del17p/*TP53* mutation (86%)

Patients Receiving Preferred 1L Treatment

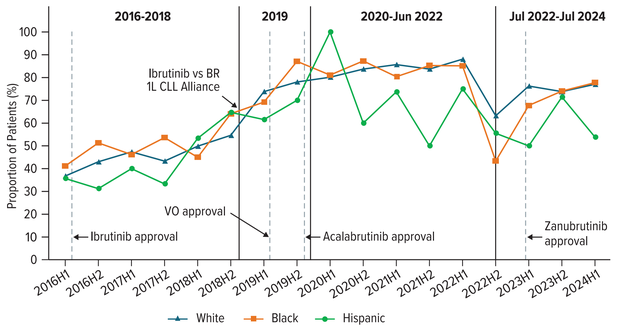
- The proportion of patients receiving preferred 1L treatment based on the NCCN guidelines significantly differed by race/ethnicity (P=.0021)
  - Hispanic patients had the lowest proportion receiving preferred 1L treatment across the four time periods, and the gap persisted, and potentially widened in more recent 6-month periods (**Figure 1**)
  - The proportion of Hispanic patients who received preferred 1L treatment over the entire time period was significantly lower than White patients (OR, 0.61; 95% confidence interval [CI]: 0.47-0.79; **Figure 2A**)
  - There was no difference in proportions of patients overall receiving preferred 1L treatment between Black and White patients (OR, 1.07; 95% CI: 0.89-1.30; **Figure 2B**)

Table 2. Patient Demographics and Characteristics by Race/Ethnicity

	White (n=5472)	Black (n=640)	Hispanic (n=290)	Asian/Other (n=598)	Unknown Race/Ethnicity (n=528)
Age at Index date[a]					
Median (range), years	71 (32, 84)	68 (30, 84)	70 (19, 84)	72 (35, 84)	71 (30, 84)
ECOG status at baseline, n (%)					
0	2186 (40.0)	262 (40.9)	113 (39.0)	210 (35.1)	198 (37.5)
1	1591 (29.1)	189 (29.5)	79 (27.2)	149 (24.9)	122 (23.1)
2-4	428 (7.8)	48 (7.5)	16 (5.5)	45 (7.5)	34 (6.4)
Unknown	1267 (23.2)	141 (22.0)	82 (28.3)	194 (32.4)	174 (33.0)
Del17p/*TP53* status, n (%)					
Del17p or *TP53*-positive	585 (10.7)	64 (10.0)	32 (11.0)	57 (9.5)	65 (12.3)
Del17p and *TP53*-negative	4164 (76.1)	474 (74.1)	223 (76.9)	446 (74.6)	387 (73.3)
Not tested	723 (13.2)	102 (15.9)	35 (12.1)	95 (15.9)	76 (14.4)
IGHV status at diagnosis, n (%)					
Mutated	534 (9.8)	31 (4.8)	34 (11.7)	63 (10.5)	48 (9.1)
Unmutated	819 (15.0)	160 (25.0)	48 (16.6)	66 (11.0)	89 (16.9)
Unsuccessful/Indeterminate/ Unknown/Not documented	121 (2.2)	18 (2.8)	12 (4.1)	16 (2.7)	16 (3.0)
Not tested	3998 (73.1)	431 (67.3)	196 (67.6)	453 (75.8)	375 (71.0)
Practice type, n (%)					
Academic	1076 (19.7)	91 (14.2)	38 (13.1)	66 (11.0)	13 (2.5)
Community	4396 (80.3)	549 (85.8)	252 (86.9)	532 (89.0)	515 (97.5)
Year of Index[a] (1L start), n (%)					
2016-2018	1972 (36.0)	232 (36.3)	98 (33.8)	220 (36.8)	99 (18.8)
2019	662 (12.1)	83 (13.0)	33 (11.4)	84 (14.1)	46 (8.7)
2020-Jun 2022	1738 (31.8)	204 (31.9)	104 (35.9)	184 (30.8)	210 (39.8)
Jul 2022-Jul 2024	1100 (20.1)	121 (18.9)	55 (19.0)	110 (18.4)	173 (32.8)

[a]Index date is defined as 1L treatment initiation.

Figure 1. Proportion of 1L Preferred Treatment by Race/Ethnicity (Time Unit: Every 6 Months)



Race/Ethnicity	2016-2018	2019	2020-Jun 2022	Jul 2022-Jul 2024
White	46%	76%	84%	72%
Black	50%	76%	84%	65%
Hispanic	43%	67%	69%	56%
Asian/Other	45%	79%	83%	72%

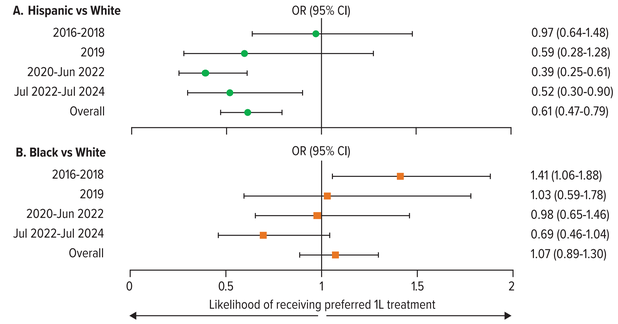
BR, bendamustine-rituximab.

Table 3. Patient Demographics and Characteristics by Treatment

	All (N=7528)	Zanubrutinib (n=261)	VO (n=580)	Acalabrutinib (n=1281)	Ibrutinib (n=3091)	CIT (n=2315)
Age at Index date[a]						
Median (range), years	71 (19, 84)	73 (34, 84)	69 (36, 84)	73 (31, 84)	72 (30, 84)	69 (19, 84)
ECOG status at baseline, n (%)						
0	2969 (39.4)	108 (41.4)	300 (51.7)	494 (38.6)	1146 (37.1)	921 (39.8)
1	2130 (28.3)	68 (26.1)	186 (32.1)	351 (27.4)	827 (26.8)	698 (30.2)
2-4	571 (7.6)	23 (8.8)	32 (5.5)	103 (8.0)	249 (8.1)	164 (7.1)
Unknown	1858 (24.7)	62 (23.8)	62 (10.7)	333 (26.0)	869 (28.1)	532 (23.0)
Del17p/*TP53* status, n (%)						
Del17p or *TP53*-positive	803 (10.7)	42 (16.1)	46 (7.9)	168 (13.1)	431 (13.9)	116 (5.0)
Del17p and *TP53*-negative	5694 (75.6)	185 (70.9)	497 (85.7)	968 (75.6)	2189 (70.8)	1855 (80.1)
Not tested	1031 (13.7)	34 (13.0)	37 (6.4)	145 (11.3)	471 (15.2)	344 (14.9)
IGHV status at diagnosis, n (%)						
Mutated	710 (9.4)	26 (10.0)	70 (12.1)	131 (10.2)	244 (7.9)	239 (10.3)
Unmutated	1182 (15.7)	57 (21.8)	137 (23.6)	227 (17.7)	442 (14.3)	319 (13.8)
Unsuccessful/Indeterminate/ Unknown/Not documented	183 (2.4)	9 (3.4)	23 (4.0)	41 (3.2)	64 (2.1)	46 (2.0)
Not tested	5453 (72.4)	169 (64.8)	350 (60.3)	882 (68.9)	2341 (75.8)	1711 (73.9)
Practice type, n (%)						
Academic	1284 (17.1)	57 (21.8)	84 (14.5)	253 (19.8)	519 (16.8)	371 (16.0)
Community	6244 (82.9)	204 (78.2)	496 (85.5)	1028 (80.3)	2572 (83.2)	1944 (84.0)
Year of Index[a] (1L start), n (%)						
2016-2018	2621 (34.8)	0	0	0	1211 (39.2)	1410 (60.9)
2019	908 (12.1)	0	0	0	685 (22.2)	223 (9.6)
2020-Jun 2022	2440 (32.4)	0	300 (51.7)	708 (55.3)	1017 (32.9)	415 (17.9)
Jul 2022-Jul 2024	1559 (20.7)	261 (100.0)	280 (48.3)	573 (44.7)	178 (5.8)	267 (11.5)

[a]Index date is defined as 1L treatment initiation.

Figure 2. Adjusted ORs for Receipt of Preferred 1L Treatment by Race/Ethnicity Across Four Time Periods



Multivariate logistic regression model adjusted for age at index, sex, race/ethnicity, ECOG Status, IGHV status, practice type, del17p/*TP53* status, and time period.

Impact of Guidelines Update on Receipt of Preferred 1L Treatment

- From 2016 to 2018, 44% of community practices and 55% of academic centers adopted targeted therapies, which include all treatment options beyond CIT; in 2019, ibrutinib use increased in both practices (77% and 67%, respectively)
- Adherence to preferred treatment, defined by NCCN guidelines, improved across practices in 2020 but decreased with the prioritization of the second-generation BTK inhibitors in 2022
- After the approval of zanubrutinib, use of targeted therapies was 71% in community practices and 74% in academic centers
- Updates to NCCN guidelines were significantly associated with patients receiving preferred 1L treatment by practice type (P=.0005)
- Compared with academic centers, the proportion of patients initiating preferred 1L treatment in community practices was lower from 2016 to 2018 (OR, 0.68; 95% CI: 0.55-0.85) but became significantly higher after the update to NCCN guidelines in 2019 (OR, 1.73; 95% CI: 1.18-2.54). In the 2020-Jun 2022 and Jul 2022-Jul 2024 time periods, the receipt of preferred 1L treatment was similar in community practices and academic centers (OR, 1.02; 95% CI: 0.75-1.39 and OR, 0.89; 95% CI: 0.66-1.20; respectively)

LIMITATIONS

- Missing data and unmeasured confounders may affect observed inequities (ie, 7% of patients had unknown race/ethnicity)
- Other social determinants of health may contribute to the observed differences and require further investigation

REFERENCES

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma V.2.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed March 17, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
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