Outcomes, Inequities, and Access to Front-Line Preferred Therapies for Chronic Lymphocytic Leukemia in the United States: A Real-World Evidence Study

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CONCLUSIONS

- In this real-world study, receipt of front-line (1L) National Comprehensive Cancer Network® (NCCN) guideline-preferred novel therapies was associated with improved real-world overall survival (rwOS) and greater treatment durability than with ibrutinib and chemoimmunotherapy (CIT) in patients with chronic lymphocytic leukemia (CLL)
- We observed lower use of preferred novel therapies among Black and Hispanic patients, and among patients residing in neighborhoods with higher social deprivation

INTRODUCTION

- The treatment landscape for CLL has evolved over the past decade, shifting from CIT and first-generation Bruton tyrosine kinase (BTK) inhibitors (eg, ibrutinib) to novel therapies, including next-generation BTK (eg, acalabrutinib and zanubrutinib) and B-cell lymphoma 2 (BCL2) inhibitors[1-3]
- While these novel therapies are now NCCN guideline-preferred,[2,3] evidence supporting their real-world effectiveness and equitable use remains limited
- Prior research suggests that socioeconomic and racial/ethnic disparities may impact cancer treatment access and outcomes[4,5]

Aim

- This study evaluated real-world clinical outcomes and inequities with 1L novel therapy utilization among patients with CLL in the US

METHODS

Data Source and Study Population

- This retrospective cohort study utilized the US-based, electronic health record-derived deidentified Flatiron Health Research Database,[6] linked to neighborhood (US Census track or block group) data from the American Community Survey and the Agency for Healthcare Research and Quality
- Eligible patients included adults with CLL who started 1L treatment between January 1, 2019 and July 31, 2024

Study Design and Statistical Analysis

- Outcomes included rwOS and time-to-next treatment or death (rwTTNT), assessed using Kaplan-Meier (KM) estimates
- Patients were grouped by 1L therapy: CIT, ibrutinib, or NCCN guideline-preferred novel therapies (acalabrutinib, zanubrutinib, and BCL2-based regimens)[2,3]
- Trends in treatment utilization by race/ethnicity, insurance coverage, practice type, and 19 area-level social determinants of health (SDOH) factors were assessed
- The association between race/ethnicity and 1L treatment was assessed using multinomial logistic regression, adjusting for age, sex, year of 1L initiation, immunoglobulin heavy chain variable region (IGHV) status, and 17p deletion (del17p)/*TP53* status

RESULTS

Patient Characteristics

- A total of 4452 patients were included in the study (**Table 1**)

Table 1. Patient Demographic and Clinical Characteristics

	N=4452
Age[a], years, n (%)	
<65	1823 (40.9)
65-74	1572 (35.3)
≥75	1057 (23.7)
Gender, n (%)	
Female	1731 (38.9)
Male	2721 (61.1)
Race and ethnicity, n (%)	
White	3717 (83.5)
Black	371 (8.3)
Hispanic	209 (4.7)
Asian	39 (0.9)
Other[b]	116 (2.6)
ECOG PS at 1L, n (%)	
0-1	3110 (69.9)
2-4	354 (8.0)
Unknown	988 (22.2)
TP53 status, n (%)	
Not tested/Unknown or not documented	3279 (73.7)
Tested	1173 (26.3)
Ever *TP53*-positive[c]	167 (14.2)
TP53-negative/Unknown or not documented[d]	1006 (85.8)
FISH testing status, n (%)	
Not tested/Unknown or not documented	775 (17.4)
Tested	3677 (82.6)
Del17p-positive[e]	379 (11.2)
Del17p-negative[e]	3008 (88.8)
IGHV status, n (%)	
Not tested/Not documented	1916 (43.0)
Tested	2536 (57.0)
Mutated	977 (38.5)
Unmutated	1328 (52.4)
Unsuccessful/Indeterminate	231 (9.1)
Insurance type, n (%)	
Commercial	1856 (41.7)
Medicare	1764 (39.6)
Medicaid	68 (1.5)
Other	224 (5.0)
Unknown/Not documented	540 (12.1)
Practice type, n (%)	
Academic	942 (21.2)
Community	3331 (74.8)
Both	179 (4.0)

Due to decimal rounding, percentages may not add up to 100. [a]Age categories are inclusive of the upper bound. [b]Includes American Indian/Alaskan Native, Native Hawaiian/Other Pacific Islander, and people reporting multiple races. [c]At 1L. [d]Negative/Unknown results for *TP53* test results are inclusive of results that are negative, equivocal, results pending, Unsuccessful/indeterminate test, or Unknown. [e]Percentages calculated among patients with FISH testing for del17p.
ECOG PS, Eastern Cooperative Oncology Group performance status; FISH, fluorescence in situ hybridization.

Treatment Patterns

- Overall, 37.2% of patients received an NCCN guideline-preferred novel therapy (**Table 2**). Among preferred novel therapies, BTK inhibitor monotherapy was the most common (59.9%)

Table 2. Overall Treatment Patterns at 1L

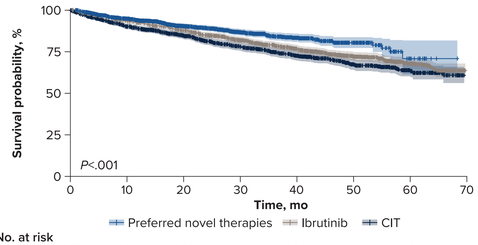
1L Therapy, n (%)	N=4452
CIT[a]	1272 (28.6)
Ibrutinib[b]	1372 (30.8)
Preferred novel therapies	1657 (37.2)
Other therapies[c]	151 (3.4)

[a]Includes rituximab monotherapy; regimens containing rituximab (or a biosimilar) in combination with cytarabine, carboplatin, cisplatin, oxaliplatin, cyclophosphamide, vincristine, doxorubicin, bendamustine, gemcitabine, fludarabine, chlorambucil); chemotherapy-only regimens, and other anti-cancer therapies. [b]Includes ibrutinib monotherapy and ibrutinib in combination with an anti-CD20 monoclonal antibody (rituximab or other biosimilars). [c]Includes: ibrutinib + venetoclax, lenalidomide-based therapies, CAR-T, bortezomib based therapies, clinical trial drugs, stem cell transplant (autologous, allogenic).
CAR-T, chimeric antigen receptor T-cell therapy.

Treatment Outcomes

- With a median follow-up of 28.5 months, median rwOS was not reached (NR; **Figure 1**)
  - Survival probabilities tended to be highest with NCCN guideline-preferred novel therapies at 6, 12, and 18 months (97%, 94%, and 91%, respectively), followed by ibrutinib (96%, 92%, and 89%) and CIT (94%, 89%, and 86%)
- Overall median (95% confidence interval [CI]) rwTTNT was 38 (36-41) months (**Figure 2**)
  - Time to next treatment tended to be longest with NCCN guideline-preferred novel therapies at 6, 12, and 18 months (89%, 83%, and 78%, respectively), followed by ibrutinib (87%, 78%, and 71%) and CIT (61%, 51%, and 45%)

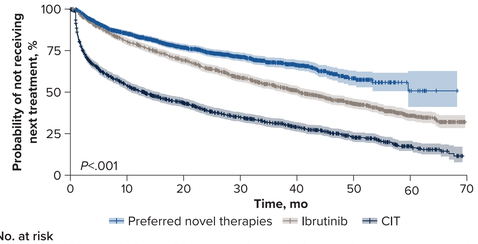
Figure 1. rwOS by 1L Therapy



No. at risk

Preferred novel therapies	1657	1336	879	547	280	99	13	0
Ibrutinib	1372	1223	1101	904	684	459	210	0
CIT	1272	1030	809	615	449	284	127	0

Figure 2. rwTTNT by 1L Therapy



No. at risk

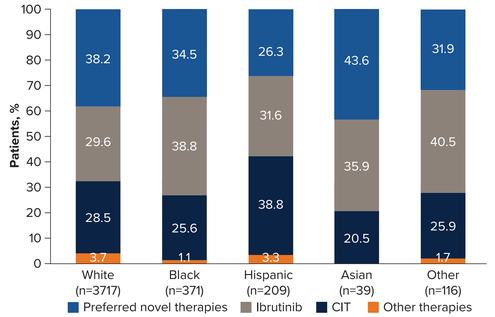
Preferred novel therapies	1657	1203	754	460	233	71	9	0
Ibrutinib	1372	1060	870	664	471	290	115	0
CIT	1272	629	432	292	195	113	41	0

Patients with other therapies were mostly patients participating in clinical trials and are excluded from the KM curves.

Treatment Access by Race/Ethnicity

- Rates of the receipt of preferred novel therapies differed by race/ethnicity (**Figure 3**)
- Compared with White patients, Hispanic patients were more likely to receive CIT (adjusted odds ratio [aOR] 2.04; 95% CI: 1.98-2.09) and ibrutinib (aOR 1.69; 95% CI: 1.65-1.73) than preferred novel therapies
- Black patients were also more likely to receive ibrutinib than preferred novel therapies (aOR 1.38; 95% CI: 1.20-1.59) compared with White patients

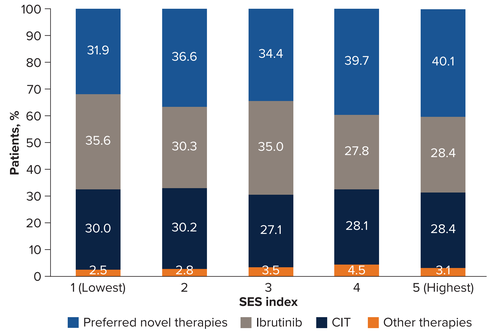
Figure 3. Treatment Patterns by Race/Ethnicity



Treatment Access by Area-Level SDOH Factors

- More patients receiving preferred novel therapies were treated at academic centers (22.9% vs 14.9% ibrutinib), while more patients receiving ibrutinib were treated at community practices (81.4% vs 73.3% of those receiving preferred novel therapies)
- In general, compared with patients living in census tracts with the lowest social deprivation, those residing in areas with the highest social deprivation appeared less likely to receive preferred novel therapies (**Figure 4**)

Figure 4. Treatment Access by Socioeconomic Status (SES) Index



- In total, 25.8% and 26.7% of patients residing in predominantly Black or Hispanic neighborhoods, respectively, received a preferred novel therapy versus 38.6% of patients residing in predominantly White neighborhoods
  - Higher preferred novel therapy use was associated with residence in areas with the highest levels of internet access (39.3% vs 31.9% in areas with lowest levels of internet access), vehicle ownership (39.2% vs 32.5% in areas with lowest vehicle ownership), and health insurance coverage (40.7% vs 34.1% in areas with least health insurance coverage)
  - This trend was consistently observed across nearly all SDOH factors (**Supplemental Table 1. Treatment access by SDOH**; please scan QR code to the right to access)

DISCUSSION

- The results of this study revealed differences in clinical outcomes for patients with CLL based on race/ethnicity and SES
- These patterns highlight potential inequities in the adoption of guideline-recommended treatments, underscoring the need for research to better understand barriers leading to these inequities and tailored interventions to promote equitable treatment access

STUDY LIMITATIONS

- Generalizability of the results to patients outside of the Flatiron Health database and outside of the US may be limited
- Because the Flatiron Health database is derived from electronic health records, patient data may be incomplete or missing

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