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

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Background
The National Comprehensive Cancer Network (NCCN) guidelines for first-line (1L) regimens in chronic lymphocytic leukemia (CLL) have evolved over the past decade, shifting from ibrutinib and chemoimmunotherapy (CIT) to second-generation Bruton tyrosine kinase inhibitor and venetoclax combinations.

Aims
We evaluated real-world use of preferred 1L treatment since 2016 in CLL patients in routine care to identify differences in prescribing based on race/ethnicity and practice type.

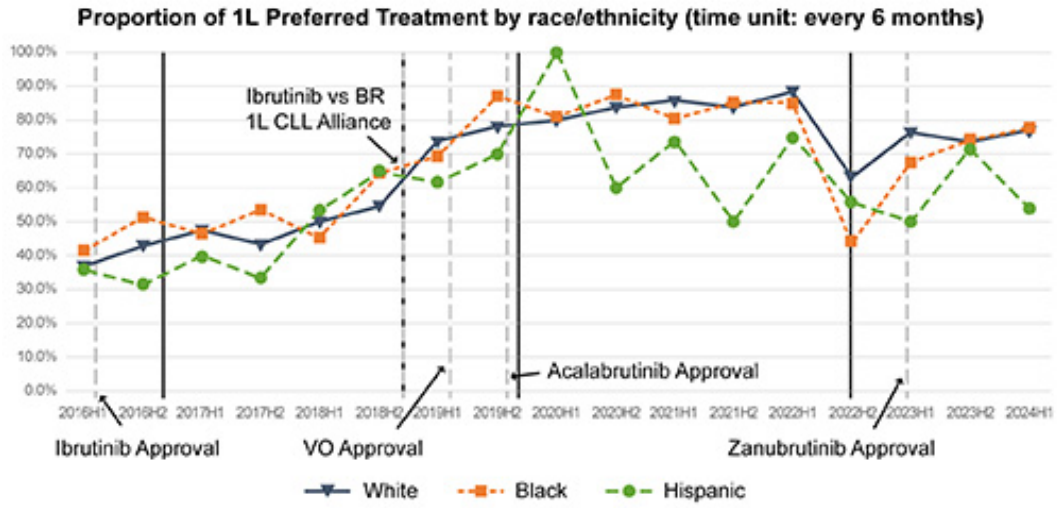
Methods
This retrospective observational study utilized the US nationwide Flatiron Health electronic health record -derived de-identified database. Eligible patients had confirmed CLL and initiated 1L treatment between January 1, 2016, and July 31, 2024. Primary outcome was receipt of preferred 1L treatment, 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). 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
A total of 7528 patients were included. Compared with White patients (n=5472), Black patients (n=640) were younger (median age in years at 1L: 68 vs 71). More Black and Hispanic (n=290) patients were treated at community practices compared with academic centers (86% vs 80% White). 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 young and fit (age $\leqslant$65 years, ECOG 0-2) and without del17p/*TP53* mutation. Patients with venetoclax and obinutuzumab (VO) combination were more likely to be younger (median age in years at 1L: 68.5 vs 71 overall) and fitter (ECOG 0-1: 84% vs 68% overall) than the overall population and without del17p/*TP53* mutation (86%). The proportion of patients receiving preferred 1L treatment based on the NCCN guidelines significantly differed by race/ethnicity (*P*=0.0021). Hispanic patients had the lowest proportion receiving preferred 1L treatment across the four time periods, and the gap widened in more recent 6-month periods (Figure). The proportion of Hispanic patients treated with preferred 1L treatment was significantly lower than White patients (OR, 0.61; 95% confidence interval [CI]: 0.47, 0.79), and there was no difference in proportions

between Black and White patients (OR, 1.07; 95% CI: 0.89, 1.30). From 2016 to 2018, 44% of community practices and 55% of academic centers adopted targeted therapies (TTs); in 2019, ibrutinib use increased in both practices (77% vs 68%, respectively). Adherence to preferred treatment, defined by NCCN guidelines, improved across practices in 2020 but decreased with the prioritization of second-generation therapies. After the approval of zanubrutinib, use of TTs 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*=0.0005).

Conclusions

Inequities in patients with CLL receiving preferred 1L treatment suggests disproportionate use of CIT and ibrutinib by race/ethnicity. Use of preferred TTs also differed by practice type and time period, with increased adoption after pivotal trials.



	Time period (NCCN guideline version: change date) [preferred treatment]			
Race/ Ethnicity	**2016–2018** [ibrutinib]	**2019** (v2.2019: Jan 2019) [ibrutinib]	**2016-Jun 2022** (v4.2020: Feb 2020) [acalabrutinib, VO, ibrutinib]	**Jul 2022-Jul 2024** (v2.2023: Aug 2022) [acalabrutinib, VO, zanubrutinib]
White	46%	76%	84%	72%
Black	50%	76%	84%	66%
Hispanic	43%	67%	69%	56%

1L, first-line; BR, bendamustine-rituximab; CLL, chronic lymphocytic leukemia; NCCN, National Comprehensive Cancer Network; VO, venetoclax + obinutuzumab