Abstract Title

Mediators of racial and ethnic inequities in access to front-line therapies for chronic lymphocytic leukemia in the United States: A real-world evidence study

Authors

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Background

The treatment (tx) landscape for chronic lymphocytic leukemia (CLL) has evolved, with National Comprehensive Cancer Network (NCCN) guideline-preferred novel therapies (NTs), such as acalabrutinib, zanubrutinib, and venetoclax-based regimens, now preferred over ibrutinib and chemoimmunotherapy (CIT) in front-line (1L) settings. We previously showed that patients (pts) from different racial/ethnic groups may not have equitable access to NTs. Here, we examined racial/ethnic inequities in 1L NT utilization among US pts with CLL and potential social determinants of health (SDOH) drivers of these inequities.

Methods

This retrospective cohort study utilized the US-based, electronic health record-derived de-identified Flatiron Health Research Database, linked to neighborhood (US Census track or block group) data from American Community Survey and Agency for Healthcare Research and Quality datasets. Eligible pts included adults with CLL who started 1L tx 01/01/2019-07/31/2024. The primary outcome was receipt of 1L therapy (CIT vs preferred NTs, ibrutinib vs preferred NTs), with NCCN guideline-preferred NTs (v2.2023-v3.2025) as a reference. Associations between race/ethnicity (White, Black, Hispanic) and 1L tx types were assessed using logistic regressions, adjusting for age, sex, year of 1L start, immunoglobulin heavy chain variable region status, and del17p/*TP53* status. To better understand which SDOH factors contribute to racial and ethnic inequities in tx utilization, we performed mediation analysis using Multiple Mediation Analysis implemented through nonlinear multiple additive regression tree models. Individual-level (Eastern Cooperative Oncology Group status, practice type, insurance) and 20 area-level SDOH factors measuring social deprivation (defined as limited access to economic, social, neighborhood, physical, or healthcare resources) were assessed as potential mediators.

Results

Of the 4452 pts included in the study, 3717 were White (83%), 371 were Black (8%), 209 were Hispanic (5%), and 155 were Other race (4%). Black and Hispanic pts were more likely to live in neighborhoods with higher social deprivation, such as residential segregation (predominant race/ethnicity in the area: White, Black, Hispanic, Diverse), with no internet access, no vehicle ownership, and no health insurance coverage. Overall, 37% of pts received a preferred NT, highest among White (38%) pts, followed by Black (35%) and Hispanic (26%) pts. Compared with White pts, Hispanic pts were more likely to receive CIT than preferred NTs (adjusted odds ratio [aOR] 2.12; 95% confidence interval [CI] 1.46-3.09); Black (aOR 1.44; 95% CI 1.05-1.97) and Hispanic pts (aOR 1.83; 95% CI 1.17-2.85) were more likely to receive ibrutinib than preferred NTs. Pts living in areas with the highest social deprivation were less likely than their counterparts in lowest social deprivation neighborhoods to receive preferred NTs. Specifically, residence in predominantly Black or Hispanic neighborhoods (26% or 27% vs 39% predominantly White), areas with lowest socioeconomic status (32% vs 40%), and neighborhoods with the lowest levels of internet access (32% vs 39%), vehicle ownership (32% vs 39%), and health insurance coverage (34% vs 41%) were associated with lowest receipt of preferred NTs.

In the mediation analysis, individual- and area-level SDOH factors explained 94.4% (95% CI 2.9-185.9) of the observed Black-White inequity in receipt of ibrutinib versus preferred NTs; residential segregation appeared to be the most important mediator (59.7%; 95% CI −3.5 to 123.0). Similarly, the Hispanic-White inequity in receipt of preferred NTs was driven by the combined effect of area-level SDOH and individual-level variables (88.5%; 95% CI 45.6-131.3), with residential segregation as the main driver (48.3%; 95% CI 10.7-85.9), followed by practice setting (9.8%; 95% CI −3.5 to 23.1). In contrast, measured SDOH factors did not explain the inequity in receipt of CIT versus preferred NTs between Hispanic and White pts (21.5%; 95% CI −8.3 to 51.4), suggesting that other factors may contribute to the observed inequities.

Conclusion

Black and Hispanic pts with CLL were less likely than White pts to receive preferred NTs. A significant proportion of these disparities was explained by area-level SDOH, particularly residential segregation. These findings underscore the need to address structural barriers to ensure equitable access to emerging, guideline-recommended treatments.