Real-world chronic lymphocytic leukemia (CLL)–specific biomarker testing patterns and frontline treatment patterns in patients with CLL/small lymphocytic lymphoma (SLL)

Authors: Timothy Reynolds,[1] William Ye,[1] Linda Chen,[1] Archana Sagar,[1] Mohammad Eskandari,[1] Xiaoliang Wang,[2] Lee Ding,[2] Gregory A. Maglinte,[2] Paul J. Godley[1]

Affiliations: [1]Baylor Scott & White Health, Temple, TX, USA; [2]BeOne Medicines Ltd, San Carlos, CA, USA

ABSTRACT

Introduction: CLL/SLL is the most common leukemia in adults in the United States, with ~21,000 cases diagnosed annually. National Comprehensive Cancer Network (NCCN) guidelines recommend testing for certain prognostic variables prior to initiation of CLL/SLL treatment (tx). For patients (pts) with higher-risk genomic aberrations (eg, del[17p], *TP53* gene mutation, unmutated immunoglobulin heavy chain variable region [IGHV]) targeted agents such as second-generation Bruton tyrosine kinase (BTK) inhibitors are preferred over chemoimmunotherapy (CIT) or ibrutinib as frontline (1L) tx options (NCCN, 2024; CLL Society, 2024). However, genomic testing patterns may differ by geographic region or institution. Baylor Scott & White Health (BSWH) is an integrated healthcare system that provides a combination of acute, primary, and/or specialty care to a widely dispersed population in Texas, USA. Examining real-world testing frequency, factors associated with genetic testing, and 1L tx patterns in pts with CLL in this setting presents a unique opportunity to highlight these differences.

Methods: This was a retrospective, observational study including pts diagnosed with CLL/SLL who initiated 1L tx at BSWH between January 1, 2020, and December 31, 2024. Pts enrolled in a clinical trial or diagnosed with Richter's transformation at 1L were excluded. In this study, biomarker tests were defined as CLL-specific fluorescence in situ hybridization (FISH), *TP53*, or IGHV tests as determined by orders in the electronic health record system, including test dates and results. Tx regimens at 1L were defined as the first CLL prescription order in the system. Descriptive statistics were used to summarize demographic, social (i.e. urban/rural residential status and Social Vulnerability Index [SVI]), clinical characteristics, and 1L tx regimens by biomarker test status. The proportions of pts who underwent testing were also summarized overall, by timing (before vs after tx) and by test type (FISH, *TP53*, IGHV). In an exploratory analysis, multivariable logistic regression was used to assess factors associated with FISH testing.

Results: A total of 327 pts were included in the analysis. Pts had a median age of 73 years, 62.4% were male, 79.5% were non-Hispanic White, and 80.1% were living in an urban area (Rural-Urban Commuting Area [RUCA] scores 1-3). Of these, 140 pts (42.8%) had documented FISH test orders, 11 (3.4%) had *TP53* test orders, and 26 (8.0%) had documented IGHV test orders. Pts with vs without FISH testing were younger (median 72 vs 74 years, respectively), less likely to be male (60.0% vs 64.2%),

more likely to live in rural areas (RUCA scores 4-10; 22.9% vs 17.6%), and more likely to have commercial insurance (26.4% vs 20.3%). In addition, pts without FISH testing were more likely to have missing SVI (18.2% vs 8.6%). Among those with SVI, pts without FISH testing were more likely to live in areas with median-high or high SVI (49.1% vs 42.2%). Among pts with test orders, most had orders prior to 1L therapy orders (FISH, 85.0%; *TP53*, 90.9%; IGHV, 84.6%).
Pts with FISH testing were more likely than those without FISH testing to receive a regimen of BTK inhibitor monotherapy (60.7% vs 48.7%, respectively) or B-cell lymphoma 2 (BCL2) inhibitor + anti-CD20 therapy (13.6% vs 5.3%) and were less likely to receive a regimen of CIT (9.3% vs 14.4%). Additionally, pts with FISH testing were more likely to receive second-generation BTK inhibitors versus those without FISH testing (44.3% vs 34.2%, respectively). In a multivariable analysis, pts with unknown SVI had 63.6% lower odds of receiving FISH testing than those with known SVI (odds ratio [OR]: 0.36; 95% CI, 0.15-0.86). Missing SVI is likely a proxy for an unreliable residential address. In contrast, pts with a test order for β-2 microglobulin were more likely to receive FISH tests (OR, 2.34; 95% CI, 1.39-3.94).

Conclusions: In this real-world study among pts treated in an integrated delivery system in Texas, frequencies of test orders for CLL-specific biomarkers, especially DNA sequencing for *TP53* and IGHV, remained low in recent years. Pts with testing were more likely to receive second-generation BTK inhibitor- or BCL2 inhibitor-based tx, while pts without testing were more likely to receive CIT. The observed differences in testing rates by tx groups and factors associated with social and practice patterns highlight opportunities to improve quality of care and optimize tx decisions.