Abstract Title

Real-world treatment patterns and biomarker utilization among patients aged ≥65 years with CLL/SLL from 2020 to 2024

Authors

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Background

Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is the most common leukemia in US adults and incidence increases with age. Although the treatment (tx) landscape has evolved , it is unclear whether tx selection differs for older patients (pts), given concerns around comorbidities, toxicity, and efficacy. There is a need to better understand pt characteristics, tx patterns, and biomarker use among pts aged ≥65 yrs with CLL/SLL in the current therapeutic era.

Methods

A retrospective longitudinal study was conducted using the de-identified 100% Medicare Fee-for-Service (FFS) Research Identifiable Files. Included pts were diagnosed with CLL/SLL at age ≥65 and initiated first-line (1L) tx 1/1/2020-9/30/2024 (with ≥12 mo in database prior to 1L tx start). Index date was defined as date of 1L tx start, and pts were followed to death, end of Medicare enrollment, or study end, whichever occurred first.

1L tx was defined as any CLL pharmacologic tx within the first 90 days of index date. Tx utilization was summarized as the number and proportion of pts who received each tx at each line. Descriptive statistics were used to summarize demographic and social characteristics and baseline comorbidities, in all pts and by 1L tx. Proportion and timing of documented biomarker orders any time prior to index were summarized by test type (CLL fluorescence in situ hybridization [FISH], *TP53* DNA sequencing and immunoglobulin heavy chain variable region [IGHV] test) and by 1L tx.

Results

Of the 21,008 pts included, median age was 76.4 yrs at 1L tx, with 43% of pts aged 65-74 yrs, 43% aged 75-84 and 14% aged ≥85. The majority of pts were male (58%) and White (91%). About 8% and 9% of pts had dual eligibility status and low-income subsidy, respectively. Median Charlson Comorbidity Index (CCI) was 4 (range: 1-21), with 40% of pts having CCI ≥5.

Covalent Bruton tyrosine kinase inhibitor (cBTKi) monotherapies (mono) were most common at 1L tx (41%), including 10% zanubrutinib (zanu), 15% ibrutinib (ibr), and 16% acalabrutinib (acala). B-cell lymphoma 2 (BCL2)+anti-CD20 monoclonal antibody (mAb) was less common (11%), and chemoimmunotherapy (CIT) was used by 13% of pts, mostly BR (8%) and FCR (3%). Other less common tx included cBTKi+anti-CD20mAb (6%) or cBTKi+BCL2 therapies (1%). Among remaining pts, most received anti-CD20mAb (22%). The use of cBTKi mono increased from 41.7% in 2020 (ibr 30.6%; acala 11.1%) to 47.6% in 2024, driven by increased use of zanu (27.8%; acala 15.7%; ibr 4.2%). BCL2+anti-CD20mAb increased from 9.2% in 2020 to 12.6% in 2024.

Pts treated with cBTKi mono were older than those with BCL2+anti-CD20mAb (median age 77.2 vs 74.5), and more likely to have dual eligibility status (10% vs 4%) or low-income subsidy (11% vs 5%). More pts who received zanu mono had CCI ≥5 (39%) versus acala (36%), ibr (35%), or BCL2+anti-CD20mAb (32%). Pts with BCL2+anti-CD20mAb were less likely to have diabetes (23% vs 26%), congestive heart failure (CHF; 16% vs 19%), chronic pulmonary disease (23% vs 27%), and renal diseases (23% vs 27%). Pts with ibr were less likely to have myocardial infarction (29% vs 34%), coronary artery disease (22% vs 25%), CHF (16% vs 19%), and atrial fibrillation (12% vs 18%).

Overall, 69% of pts had FISH testing prior to 1L tx, but test orders for *TP53* (12%) or IGHV (28%) status were infrequent. Pts with ibr had the lowest rates of *TP53* tests (6%), whereas pts with CIT had the lowest rates of IGHV tests (16%). The timing of tests showed a binomial distribution where most pts received FISH, *TP53*, or IGHV tests either ≤60 days prior to 1L tx (46%, 50%, 33%), or >1 yr before 1L tx (30%, 22%, 43%).

Among pts who received ≥2 lines of therapy for CLL (n=4428; 21%), cBTKi mono was the most common in 2L (41%), including 14% zanu, 17% acala, and 10% ibr. CIT and BCL2+anti-CD20mAb were used in 12% and 9% of pts, respectively. Only 634 (3%) pts had 3L+ tx, of whom 33% received cBTKi mono, including 16% zanu, 12% acala, and 5% ibr (5%).

Conclusion

This large real-world study found that cBTKi mono was the most common 1L tx choice among pts aged ≥65 with CLL/SLL, with increased use of next-generation cBTKi. Pts with more baseline comorbidities were less likely to receive ibr or BCL2-based tx. FISH testing was not performed in nearly one-third of pts, and most pts did not have *TP53* or IGVH sequencing prior to tx. Future studies are needed to continue to evaluate evolving tx paradigms in older pts with CLL/SLL.