Word count (limit 350; not including titles, authors, keywords, and affiliations): 349

Real-World Impact of Atrial Fibrillation (AFib) on Cardiovascular (CV) Outcomes and Healthcare Resource Utilization (HCRU) in Patients With Chronic Lymphocytic Leukemia (CLL)

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Prior Presentation: Abstract submitted to ASCO 2026

Introduction: While the association between AFib and CLL has been reported, real-world evidence on its clinical and economic impact is limited. This study evaluated impact of AFib on CV outcomes and HCRU in patients with CLL overall, by age, and by Bruton tyrosine kinase inhibitor (BTKi) therapy.

Methods: This retrospective observational study used the US Symphony database to identify adults newly diagnosed with CLL (2014-2024). Patients were followed for 1 year post-diagnosis to assess incidence of AFib. Subsequent CV outcomes (stroke, bleeding, heart failure) and HCRU were compared in CLL patients with and without AFib. Multivariate regression analyses assessed associations between AFib and outcomes. Subgroup analyses were conducted in patients aged ≥65 years. Exploratory analyses compared outcomes among first-line (1L) BTKi (ibrutinib, acalabrutinib, or zanubrutinib).

Results: In 233,362 newly-diagnosed CLL patients, 13.1% had AFib within 1 year of diagnosis. A significantly greater proportion of CLL patients with AFib had ≥1 inpatient visit within 1 year of diagnosis vs without AFib (54.9% vs 23.2%, $P<.0001$), and higher likelihood to incur inpatient service (OR: 2.28, 95%CI [2.21, 2.35], $P<.0001$). Significantly higher proportions of CLL patients with AFib had subsequent stroke (14.3% vs 8.9%), bleeding (27.9% vs 19.1%), and heart failure (54.5% vs 18.9%) vs without AFib ($P<.0001$). Age ≥65, male, non-white, and AFib were associated with subsequent stroke, bleeding, or heart failure ($P<.01$). Results were consistent in patients aged ≥65 years. In patients initiating 1L BTKi, AFib rate within 1 year of treatment was 11% (zanubrutinib), 13% (acalabrutinib), and 16% (ibrutinib) ($P<.0001$). Compared with ibrutinib and acalabrutinib, a lower proportion of CLL patients with AFib receiving zanubrutinib had subsequent stroke (12.2% vs 9.4% vs 4.8%, respectively), bleeding (27.4% vs 21.5% vs 17.4%), and heart failure (50.9% vs 45.6% vs 39.6%) ($P<.002$). Compared with zanubrutinib, acalabrutinib (OR 1.29, 95% CI 1.12–1.50; $P=.0005$) and ibrutinib (OR 1.69, 95% CI 1.48–1.93; $P<.0001$) were associated with higher odds of inpatient service use within 1 year of initiation.

Conclusions: CLL patients with AFib experience substantial real-world CV and HCRU burden. Exploratory analyses suggested 1L zanubrutinib may offer potentially favorable outcomes over other BTKi in lessening AFib-related clinical and HCRU complications.