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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Background: While the association between AFib and CLL has been reported, real-world evidence on its clinical and economic impact is limited.

Aims: This study evaluated impact of AFib on CV outcomes (stroke, bleeding, heart failure) 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 after CLL diagnosis to assess incidence of AFib. Subsequent CV outcomes (stroke, bleeding, heart failure) and HCRU (inpatient, outpatient, other services) were compared in CLL patients with and without AFib. Multivariate regression analyses assessed associations between AFib and outcomes. Subgroup analyses were conducted in elderly patients aged ≥65 years. Exploratory analyses compared first-line (1L) BTKi use (ibrutinib, acalabrutinib, or zanubrutinib).

Results: In 233,362 newly diagnosed CLL patients, 13.1% had AFib within 1 year of CLL diagnosis. A significantly greater proportion of CLL patients with AFib had ≥1 inpatient visit within 1 year of CLL diagnosis than those without AFib (54.9% vs 23.2%, *P*<.0001), as well as a 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%) than those 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 for 1L zanubrutinib vs acalabrutinib vs ibrutinib was 11% vs 13% vs 16%, respectively; *P*<.0001. Compared to 1L ibrutinib and 1L acalabrutinib, a lower proportion of CLL patients with AFib treated with 1L 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). CLL patients with AFib treated with 1L zanubrutinib had less inpatient services than 1L ibrutinib and 1L acalabrutinib within 1 year of BTKi treatment (46.4% vs 51.5% vs 60.4%; *P*<.0001). In multivariate regression, 1L acalabrutinib patients had 29% higher odds than 1L zanubrutinib patients (OR: 1.29, 95% CI [1.12, 1.50], *P*=.0005); 1L ibrutinib patients had 69% higher odds than 1L zanubrutinib patients (OR: 1.69, 95% CI [1.48, 1.93], *P*<.0001) to incur inpatient service within 1 year after initiating BTKi treatment.

Conclusions: Findings highlight significant real-world CV and HCRU burden incurred by CLL patients with AFib. Exploratory analyses suggested 1L zanubrutinib may offer potentially favorable outcomes over other BTKi in lessening AFib and related clinical and HCRU complications. Future studies with longer follow-up are warranted to confirm these findings.