

Clinical Outcomes Among Anticoagulated Patients with CLL and Atrial Fibrillation/Flutter Treated With First- Versus Second-Generation BTK Inhibitors



Nnamdi Omenuko MD, MPH¹, Janamejey Gaur MD¹, Sakshi Singal MD¹
1. East Tennessee State University, Johnson City, TN, USA

INTRODUCTION

• Bruton tyrosine kinase inhibitors (BTKi) play a key role in treating chronic lymphocytic leukemia (CLL) but are linked to increased risks of atrial fibrillation/flutter (AF) and bleeding, especially in patients who require oral anticoagulation.

AIM

- To evaluate outcomes between anticoagulated CLL patients treated with first-generation and second-generation BTKi.

METHODS

- This retrospective cohort study leveraged data from the TriNetX Research Network.
- We identified adults with CLL who had a diagnosis of AF/flutter, were exposed to oral anticoagulants, and received BTKi therapy.
- Cohort 1 comprised patients who received the first-generation BTKi ibrutinib, while Cohort 2 included those treated with second-generation BTKis (acalabrutinib or zanubrutinib).
- Eligible oral anticoagulants were apixaban, rivaroxaban, dabigatran, edoxaban, or warfarin.
- Propensity score matching (1:1) was performed using demographic, clinical, procedural, medication, and laboratory data.
- Outcomes were assessed from one day after the index event through follow-up.
- Patients with a prior history of each endpoint were excluded from the corresponding incident outcome analysis.

RESULTS

- Propensity score matching resulted in 972 patients per cohort.
- The risk of major bleeding was comparable between groups (ibrutinib 29.2% vs. second-generation BTKi 29.9%; RR 0.98, 95% CI 0.83 - 1.15).
- Rates of ischemic stroke (5.9% vs. 7.3%; RR 0.82, 95% CI 0.57 - 1.16), TIA (3.0% vs. 4.5%; RR 0.67, 95% CI 0.42 - 1.08), and systemic embolism (1.4% vs. 1.6%; RR 0.87, 95% CI 0.42 - 1.82) were also similar.
- Hospitalizations, ICU admissions, and ED visits showed no significant differences between groups.
- However, all-cause mortality was higher in the ibrutinib group (34.8% vs. 29.1%; RR 1.20, 95% CI 1.05 - 1.36).
- Kaplan-Meier analysis indicated worse survival with ibrutinib (HR 1.46, 95% CI 1.24 - 1.71).

Outcome	RR	95% CI	Interpretation	
Major Bleeding	0.98	0.83-1.15	=	
Ischemic Stroke	0.82	0.57-1.16	↓	
TIA	0.67	0.42-1.08	↓	
Embolism	0.87	0.42-1.82	↓	
All-cause Mortality	1.20	1.05-1.36	^	

CONCLUSIONS

- In this real-world, propensity-matched analysis of anticoagulated CLL patients with AF/flutter, risks of major bleeding, thromboembolic events, and acute-care utilization were similar between first- and second-generation BTKi groups.
- However, ibrutinib was linked to higher all-cause mortality compared to acalabrutinib or zanubrutinib.
- Further studies are needed to understand these differences and inform clinical practice.