MORTALITY AND BLEEDING TRADEOFFS ASSOCIATED WITH ORAL ANTICOAGULATION IN BTK INHIBITOR-TREATED CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS WITH ATRIAL FIBRILLATION/FLUTTER: A PROPENSITY-MATCHED TRINETX ANALYSIS

Nnamdi Omenuko[1], Deydie Suarez Salazar[1], Jeffrey Afrifa-Yamoah[2], Alexander Mays[1], Emma Self[1], Janamejey Gaur[1], Alina Bhat[1]

1. East Tennessee State University, Johnson City, TN, USA
2. Trinity Health, Ann Arbor, MI, USA

INTRODUCTION

Bruton tyrosine kinase inhibitors (BTKi) have improved outcomes in chronic lymphocytic leukemia (CLL) but are associated with an increased risk of atrial fibrillation/flutter (AF) and bleeding. Anticoagulation for AF in BTKi-treated patients is a clinical dilemma, requiring a balance between stroke prevention and hemorrhagic complications.

AIM

To compare thromboembolic and hemorrhagic outcomes among patients with **CLL receiving BTK inhibitors who develop atrial fibrillation/flutter** and are **treated with versus without anticoagulation**.

METHODS

- Retrospective cohort study using TriNetX network (86 healthcare organizations today)
- Adults (18+) with CLL receiving BTKi therapy who developed atrial fibrillation
- Compared patients receiving anticoagulation (DOAC or warfarin) with those not receiving anticoagulation
- Outcomes: all-cause mortality, stroke, bleeding, MI, VTE, ICU admission, and hospitalization
- Propensity score matching (PSM) performed using demographics, comorbidities, medications, procedures, and laboratory variables
- Relative risks, hazard ratios, and 95% confidence intervals calculated

CONCLUSION

Anticoagulation was linked to lower mortality but a significantly increased bleeding risk, without a statistically significant reduction in stroke. These findings underscore the complex clinical trade-offs involved and highlight the need for further studies that assess anticoagulant class, CHA_2DS_2-VASc and HAS-BLED risk scores, and antiplatelet exposure.

RESULTS

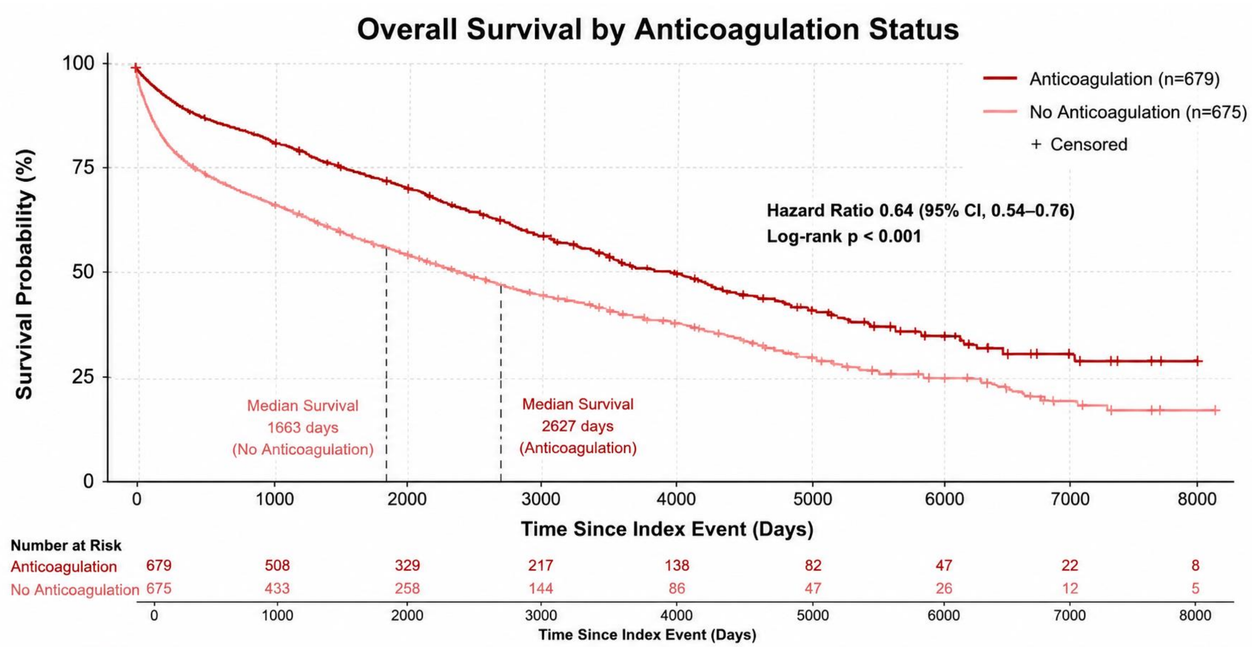

Figure 1. Overall Survival by Anticoagulation Status. *Kaplan-Meier analysis demonstrated improved survival in the AC cohort with a median survival of 2627 versus 1663 days (HR 0.64, 95% CI 0.54–0.76; p<0.001).*

Clinical Outcome	AC	No AC	Risk Ratio (95% CI)	p-value
Mortality	**35.3%**	**43.9%**	**0.81 (0.71–0.92)**	**0.001**
Bleeding	**24.7%**	**13.2%**	**1.87 (1.43–2.44)**	**<0.001**
Stroke	6.7%	4.6%	1.47 (0.93–2.35)	0.100
MI	10.2%	8.1%	1.26 (0.87–1.82)	0.215
VTE	8.2%	5.4%	1.51 (0.98–2.32)	0.058
ICU admission	22.9%	22.2%	1.03 (0.83–1.29)	0.772
Hospitalization	3.0%	4.7%	0.65 (0.37–1.15)	0.140

Table 1. Clinical Outcomes from Propensity Score Matching. *Anticoagulation was associated with significantly lower all-cause mortality compared with no anticoagulation (35.3% vs 43.9%; RR 0.81, 95% CI 0.71–0.92; p=0.001). Bleeding events were significantly higher among anticoagulated patients (24.7% vs 13.2%; RR 1.87, 95% CI 1.43–2.44; p<0.001).*

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