CLL-1557

Cardiovascular Toxicity of Ibrutinib versus Acalabrutinib in Chronic Lymphocytic Leukemia: A Propensity Score-Matched TriNetX Database Analysis

Wei Ju Lin, DO[1]; **Juhi Ardeshna-Chovatiya, MD**[1]; **Zin Thandar Win**[1]

[1]University of California, Riverside School of Medicine, Riverside, CA, US

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INTRODUCTION

- BTK inhibitor cardiovascular toxicity is a key clinical challenge in CLL.
- ELEVATE-RR established lower atrial fibrillation (AF) rates with acalabrutinib, but real-world data characterizing hypertension as a distinct toxicity — and AF risk stratified by cardiovascular disease (CVD) status — are lacking.
- We compared new antihypertensive initiation and incident AF between ibrutinib and acalabrutinib in a propensity score–matched real-world CLL cohort.

METHODS

- **Design:** Retrospective cohort study using the TriNetX US Collaborative Network (66 HCOs, ~94 million patients).
- **Population:** Adult CLL patients (ICD-10 C91.10–C91.12) initiating ibrutinib or acalabrutinib as first BTK inhibitor.
- **Exclusions:** AF/flutter within 12 months pre-index or prior antihypertensive medication use, excluded from their respective endpoints.
- **Matching:** Propensity-score matching to balance baseline characteristics.
- **Endpoints:** Primary – New antihypertensive initiation (ACEi, ARB, CCB, thiazide). Secondary – Incident AF/flutter (I48.x).

Wei Ju Lin, DO
University of California, Riverside School of Medicine
Email: **weijul@medsch.ucr.edu**

COHORT

Adult CLL patients initiating ibrutinib or acalabrutinib as first BTK inhibitor

↓

1:1 Propensity-Score Matching
(age, sex, HTN, diabetes, HF, CAD, stroke/TIA, PVD)

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3,784 matched pairs per cohort (7,568 total)
Median follow-up: 1,337 days (ibrutinib) vs. 613 days (acalabrutinib)

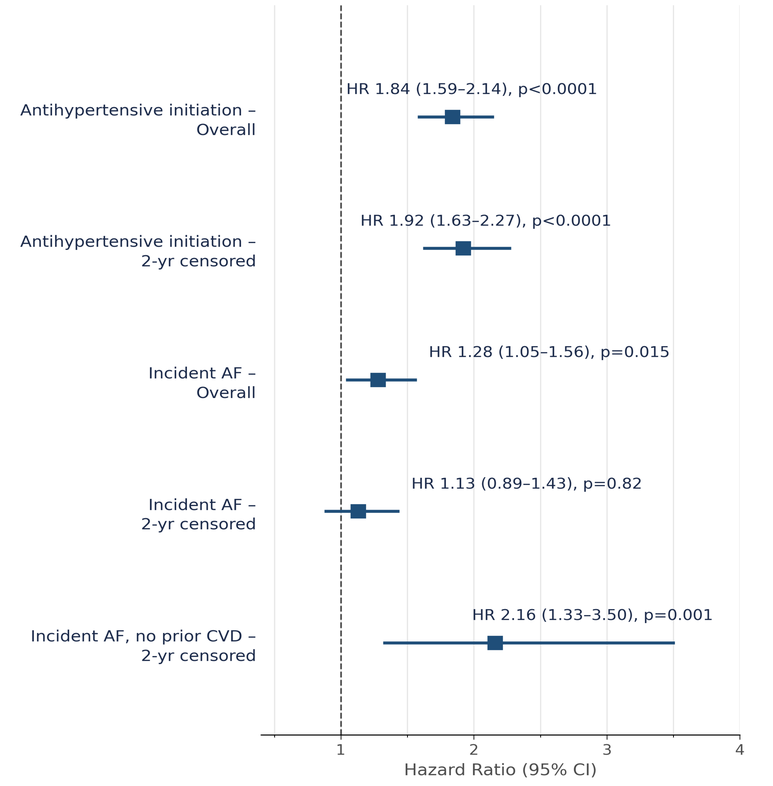
RESULTS

Outcome	Ibrutinib (%)	Acalabrutinib (%)	HR	P value
New antihypertensive initiation	32.0	12.2	1.84	<0.0001
Incident AF	9.2	4.3	1.28	0.015

Subgroup analysis	HR	P value
Antihypertensive initiation – Prior CVD	1.78	<0.0001
Antihypertensive initiation – No prior CVD	2.15	<0.0001
Incident AF – Prior CVD, overall	1.21	0.073
Incident AF – Prior CVD, 2-year censored	1.20	0.34
Incident AF – No prior CVD, overall	1.68	0.007

AF = atrial fibrillation; HR = hazard ratio

Hazard Ratios: Ibrutinib vs. Acalabrutinib



CONCLUSIONS

- Ibrutinib was associated with markedly higher antihypertensive initiation, robust across risk strata and follow-up durations.
- The overall AF signal was largely driven by differential observation time and was absent in patients with prior CVD.
- Among cardiovascularly naive patients, ibrutinib carried a genuine, follow-up-independent AF risk — supporting acalabrutinib as the preferred BTK inhibitor in this population.