

# TEMPORAL TRENDS IN CARDIOVASCULAR TOXICITY WITH SECOND-GENERATION BTK INHIBITORS: ACALABRUTINIB VERSUS ZANUBRUTINIB

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## INTRODUCTION

- Second-generation BTK inhibitors (BTKi) are designed to reduce the off-target cardiotoxicity of ibrutinib.
- 2025 ACC guidance reports AF/flutter incidence of 5–9% with acalabrutinib versus 3–6% with zanubrutinib.
- FAERS pharmacovigilance data suggest divergent adverse cardiac event rates (2.4% vs 2.0%) and hypertension signals between agents.

## AIM

To compare real-world cardiovascular safety between acalabrutinib and zanubrutinib in patients with chronic lymphocytic leukemia at 1- and 3-year landmarks.

## METHOD

- **Design:** Retrospective cohort study, TriNetX Global Health Research Network
- **Cohort:** Adults ≥18 years with CLL initiating acalabrutinib (n=1,947) or zanubrutinib (n=949) through May 2026
- **Exclusions:** Pre-existing heart failure, hypertension, AF/flutter, acute MI, VF/flutter, or ischemic stroke within 1 year before BTKi initiation
- **1:1 propensity-score matching (PSM):** demographics, comorbidities, concomitant CLL therapy, anticoagulant and antiplatelet use, and baseline labs
- **Outcomes:** 1- and 3-year incidence of AF/flutter, hypertension, heart failure, and MI/ischemic stroke composite

## CONCLUSIONS

- Hypertension: Acalabrutinib < Zanubrutinib
- 3-year risk of atrial fibrillation/flutter and major adverse cardiovascular events: Acalabrutinib > Zanubrutinib (p<0.05).
- Cardiovascular profiles diverge over time and support individualized treatment selection in patients with underlying cardiac comorbidities.
- Prospective head-to-head studies are needed.

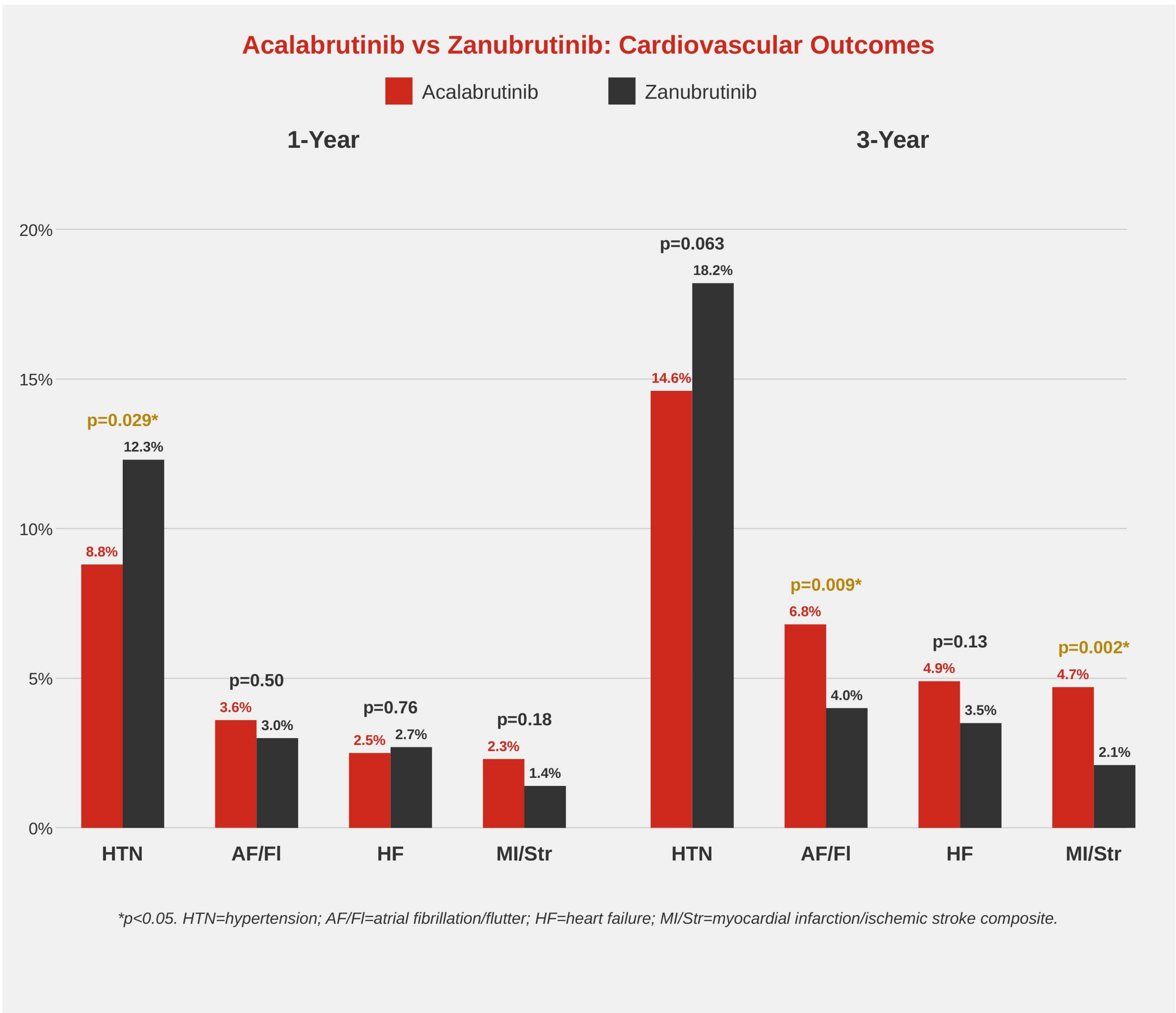
## RESULTS

### Study Population

- Acalabrutinib cohort: 1947
- Zanubrutinib: 949
- After 1:1 propensity-score matching: 939/arm with well-balanced baseline characteristics.

### Key Findings

- Hypertension was significantly **lower** with acalabrutinib at 1 year (8.8% vs 12.3%, p=0.029)
- At 3 years, AF/flutter (6.8% vs 4.0%, p=0.009) and MI/stroke composite (4.7% vs 2.1%, p=0.002) were significantly **higher** with acalabrutinib
- Heart failure did not differ significantly at either landmark
- Divergence in cardiovascular risk profiles emerged predominantly at the 3-year landmark



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## REFERENCES

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