REAL-WORLD OUTCOMES OF BTK INHIBITORS IN CHRONIC LYMPHOCYTIC LEUKEMIA/SMALL LYMPHOCYTIC LYMPHOMA PATIENTS WITH PRE-EXISTING CARDIOVASCULAR COMORBIDITIES

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Introduction

- Bruton's tyrosine kinase inhibitors (BTKi) are a highly effective therapy for Chronic Lymphocytic Leukemia / Small Lymphocytic Lymphoma (CLL/SLL) [1, 2]
- Despite their proven efficacy, concerns exist regarding potential cardiovascular (CV) toxicity associated with BTKi use [3]
- This has led to clinical hesitancy in prescribing BTKi for the significant number of CLL/SLL patients with pre-existing CV disease [3]

Aim

- To evaluate real-world outcomes of BTKi therapy in CLL/SLL patients with pre-existing cardiovascular comorbidities
- To compare those outcomes against similar cohorts of patients receiving other non-BTKi therapies

Methods

Study Design: Retrospective cohort study

Data Source: TriNetX research platform

Study Period: February 12, 2014 – April 21, 2025

Patient Population: Adult patients diagnosed with Chronic Lymphocytic Leukemia / Small Lymphocytic Lymphoma (CLL/SLL) and at least one of the following cardiovascular comorbidities:

- Heart Failure (HF)
- Atrial Fibrillation (AFib)
- Coronary Artery Disease (CAD)
- Hypertension (HTN)

Index Cohorts: Four spearate cohorts of CLL/SLL patients (one for each comorbidity above) treated with a **BTKi**

Comparator Cohorts: Four separate cohorts of CLL/SLL patients (one for each comorbidity above) treated with **non-BTKi therapies**, including:

- Fludarabine, cyclophosphamide, rituximab (FCR)
- Bendamustine, rituximab (BR)
- Venetoclax
- Obinutuzumab

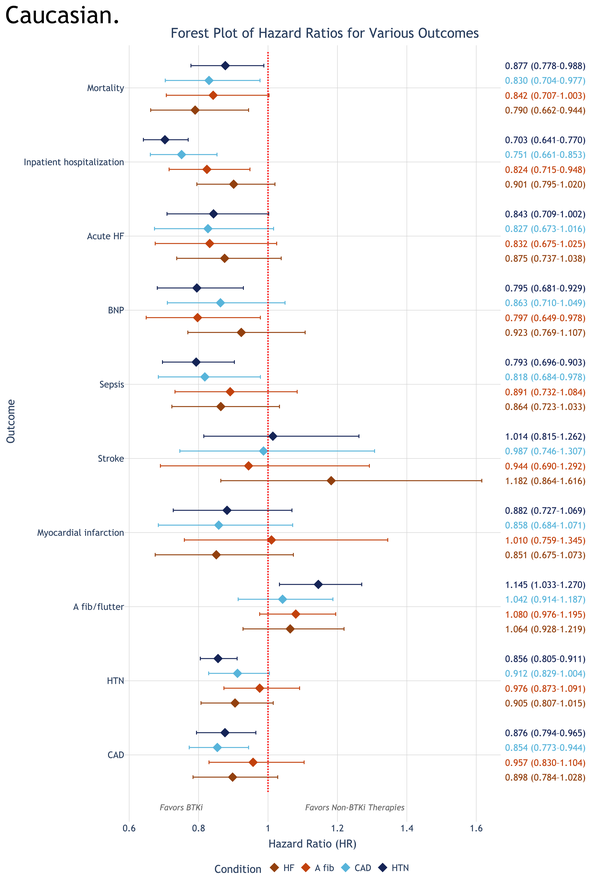
Statistical Analysis: 1:1 propensity score matching was used to balance the cohorts

Matching Variables:

- Age & Sex
- Race
- Body Mass Index (BMI)
- Nicotine Use
- Dyslipidemia
- Key CV factors (HF, AFib, CAD, HTN)

Results

After propensity score matching, sample sizes per group ranged from 831 (HF cohort) to 2600 (HTN cohort). Mean age was similar across cohorts (range 72.5-75.7 years) with 60-70% males and 80-84% Caucasian.



BTKi therapy was associated with:

- Significantly reduced mortality in HF, CAD, and HTN cohorts
- Reduced inpatient hospitalization in A fib, CAD, and HTN cohorts, with the largest hospitalization benefit in HTN patients (HR 0.703)
- HTN patients had a significantly increased risk of atrial fibrillation/flutter (HR 1.145)
- BTKi showed benefits for other cardiovascular outcomes including BNP, sepsis, and coronary artery disease in select cohorts
- Stroke and myocardial infarction risks were not significantly different between groups

Summary

BTKi therapy does not appear to worsen cardiovascular related outcomes in patients with pre-existing CV comorbidities relative to similar patients treated with non BTKi therapies. These data support BTKi use in CLL patients with underlying CV disease.

References

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