Impact of Type 2 Diabetes on Cardiovascular Toxicity, Infectious Complications, and Survival Among Patients With Chronic Lymphocytic Leukemia Treated With Bruton Tyrosine Kinase Inhibitors

A Propensity Score–Matched TriNetX Analysis • CLL-580

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INTRODUCTION

- BTK inhibitors have transformed CLL/SLL treatment but are associated with cardiovascular and infectious toxicities.
- T2DM independently increases cardiovascular risk and contributes to immune dysfunction.
- Its effect on BTKi-associated toxicity and survival in CLL/SLL remains poorly characterized.

AIM

Evaluate whether T2DM is associated with worse survival and increased cardiovascular and infectious complications among adults with CLL/SLL treated with ibrutinib, acalabrutinib, or zanubrutinib.

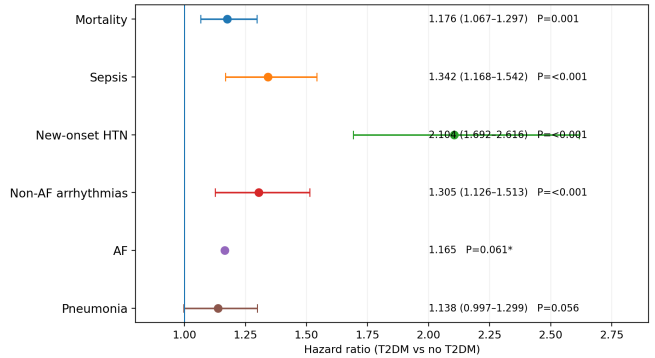
METHODOLOGY

- Retrospective propensity score–matched cohort study.
- TriNetX US Collaborative Network: 67 health care organizations.
- Adults with CLL/SLL receiving ibrutinib, acalabrutinib, or zanubrutinib.
- Exposure groups: T2DM vs no T2DM.
- Matching on 22 demographic and clinical variables.
- Five-year outcomes: mortality, sepsis, pneumonia, new-onset hypertension, AF, and other cardiac arrhythmias.
- Kaplan–Meier survival analysis and Cox proportional hazards models.

Final cohort: 3,127 matched pairs

RESULTS

3,127 PROPENSITY-MATCHED PAIRS



MORTALITY

39.9% vs 35.2%

HR 1.176
95% CI 1.067–1.297
P<0.001

SEPSIS

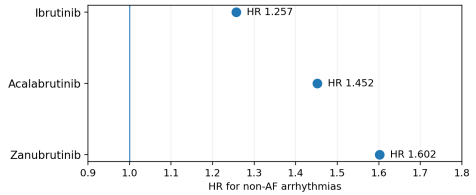
26.4% vs 20.3%

HR 1.342
95% CI 1.168–1.542
P<0.001

NEW-ONSET HTN

58.0% vs 31.6%

HR 2.104
95% CI 1.692–2.616
P<0.001



Non-AF arrhythmias were the only outcome significantly increased across all three BTK inhibitors (all P<0.05).

AF: borderline association (risk-analysis P=0.061) • Pneumonia: nonsignificant trend (P=0.056)

CONCLUSION

T2DM identifies a higher-risk phenotype in CLL/SLL patients receiving BTKi therapy.

- Significantly worse overall survival.
- Significantly higher risk of sepsis.
- New-onset hypertension demonstrated the strongest association.
- Non-AF arrhythmias were increased and showed the most consistent cardiovascular signal across agents.
- Enhanced cardiovascular and infection surveillance may be warranted in patients with diabetes receiving BTKi therapy.

KEY TAKE-HOME

T2DM + BTKi = HIGHER-RISK CLINICAL PHENOTYPE

These data support closer blood-pressure monitoring, cardiovascular risk assessment, arrhythmia surveillance, and vigilance for infection during BTKi therapy.

REFERENCES

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2. Brown JR, Eichhorst B, Hillmen P, et al. Zanubrutinib or Ibrutinib in Relapsed or Refractory Chronic Lymphocytic Leukemia. *N Engl J Med*. 2023;388:319-332. doi:10.1056/NEJMoa2211582
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Abbreviations: AF, atrial fibrillation; BTKi, Bruton tyrosine kinase inhibitor; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; HR, hazard ratio; PSM, propensity score matching; T2DM, type 2 diabetes mellitus.