

REAL-WORLD COMPARISON OF BLEEDING OUTCOMES BETWEEN ACALABRUTINIB AND ZANUBRUTINIB IN ANTICOAGULATED CLL PATIENTS: A 6-MONTH AND 1-YEAR PROPENSITY-MATCHED ANALYSIS USING THE TRINETX GLOBAL NETWORK

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INTRODUCTION

- Bleeding remains a significant class-effect concern with Bruton tyrosine kinase inhibitors (BTKi).
- Second-generation agents are more selective than ibrutinib, yet indirect comparisons of their bleeding profiles have yielded conflicting results.
- Clinical trials may not reflect routine practice in anticoagulated population.

AIM

To compare the incidence and severity of bleeding events between acalabrutinib and zanubrutinib in CLL patients on concurrent direct oral anticoagulants (DOACs), using real-world data from the TriNetX Global Collaborative Network.

METHOD

- TriNetX Global Collaborative Network**
- Adults with CLL initiating 1st-line acalabrutinib (n=599) or zanubrutinib (n=305) with concurrent DOAC use (apixaban, rivaroxaban, or edoxaban)
- Prior exposure to the comparator BTKi was excluded
- 1:1 propensity score matching (nearest neighbor, caliper 0.1) balanced demographics, comorbidities, antiplatelet use, DOAC type, and baseline hemoglobin and platelet counts.
- Outcomes: any bleeding, GI bleeding, and major bleeding (ICH, retroperitoneal hematoma, or transfusion) at 6-month and 1-year landmarks

CONCLUSIONS

- 6 months and 1 year bleeding rates: acalabrutinib ~ zanubrutinib.
- Neither agent showed a consistent bleeding advantage, suggesting similar real-world hemorrhagic risk when combined with anticoagulation.
- Prospective trials are needed to definitively guide BTKi selection in this high-risk population.

RESULTS

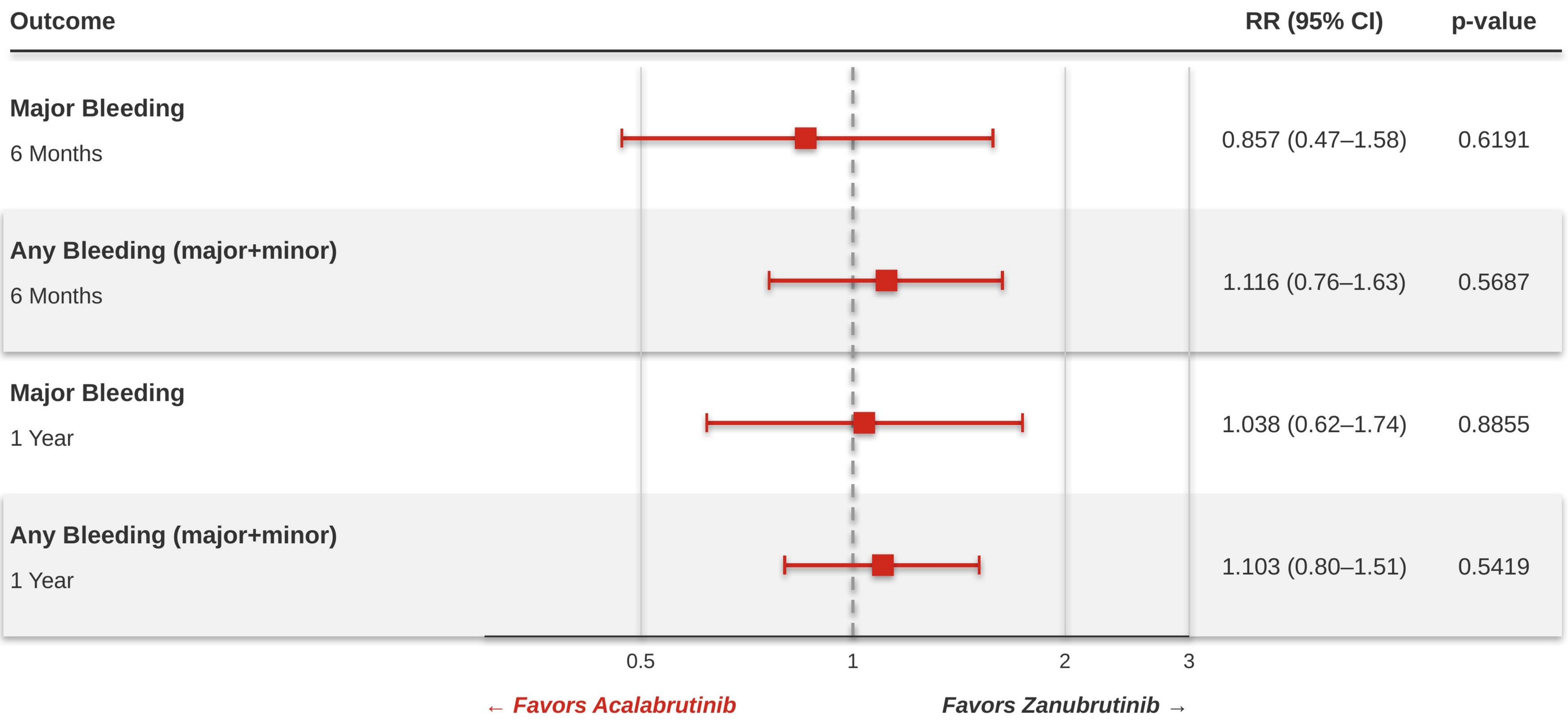
- After 1:1 propensity matching (n=295/arm), baseline characteristics were well-balanced between arms.

- Acalabrutinib vs. Zanubrutinib at 6 months,
 - Major bleeding: 6.10% vs. 7.12% (RR 0.857, 95% CI 0.47–1.58; p=0.6191)
 - Combined major + minor bleeding: 16.27% vs. 14.58% (RR 1.116, 95% CI 0.76–1.63; p=0.5687)
- Acalabrutinib vs. Zanubrutinib at 1 year,
 - Major bleeding: 9.15% vs. 8.81% (RR 1.038, 95% CI 0.62–1.74; p=0.8855)
 - Combined major + minor bleeding was 21.70% vs. 19.66% (RR 1.103, 95% CI 0.80–1.51; p=0.5419)

No statistically significant differences in bleeding risk were observed between agents at either landmark.

Acalabrutinib vs Zanubrutinib: Bleeding Outcomes

Forest Plot of Relative Risk (95% CI), n=295 per arm



No statistically significant differences in bleeding risk were observed between agents at either landmark (all 95% CIs cross RR=1.0). Abbreviations: RR, relative risk; CI, confidence interval.

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REFERENCES

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