Bruton Tyrosine Kinase Inhibitors Versus Venetoclax and Obinutuzumab in Anticoagulated Patients With Chronic Lymphocytic Leukemia: A Propensity Score–Matched Analysis of Bleeding Outcomes

Vedant Shah, MD[1] , **Ansy Patel, MD**[2], **Canan Dirican, MD**[1], **Sri Harsha Narayana, MD**[1], **Leonardo B. D'Silva**[3], **Bolivia Crocete Aloysia Fernandes, MD**[1], **Joel Alcid, MD**[1]

1. New York Medical College Graduate Medical Education Program, St Mary's General Hospital and Saint Clare's Health, Passaic and Denville, NJ, USA
2. SUNY Upstate Medical University, Syracuse, NY, USA , 3. Northeastern University, Boston, MA, USA

NEW YORK MEDICAL COLLEGE
A MEMBER OF TOURO UNIVERSITY

1 Background

- DOACs are frequently co-prescribed in CLL due to high rates of atrial fibrillation and thromboembolism, making drug selection in this population clinically important.
- Expert consensus suggests V/O may be preferable in anticoagulated CLL patients, but no real-world comparative bleeding data exist to support this.

2 Objective

- Compare 1-year bleeding outcomes in DOAC-exposed CLL patients treated with BTKi versus V/O, and between BTKi agents.

BTKi **Functional platelet defect**
Tec and GPVI inhibition impairs collagen-induced aggregation.

V/O **Quantitative platelet deficit**
Obinutuzumab and venetoclax-related thrombocytopenia

3 Methods

- Study Design
  - Retrospective cohort, TriNetX, 173 centers
- Cohorts
  - A: BTKi + DOAC
  - B: V/O + DOAC
- Matching
  - 1:1 propensity score; demographics, comorbidities, antiplatelet use, blood counts
- Outcomes at 1 year
  - Any bleeding, GI bleeding, major bleeding

6 Conclusions

- BTKi was associated with numerically higher bleeding than V/O across all outcomes, though no comparison reached statistical significance.
- Within the BTKi class, ibrutinib showed consistently higher bleeding than acalabrutinib, suggesting the overall class signal may be largely ibrutinib-driven.
- These findings are hypothesis-generating and warrant prospective evaluation in adequately powered studies.

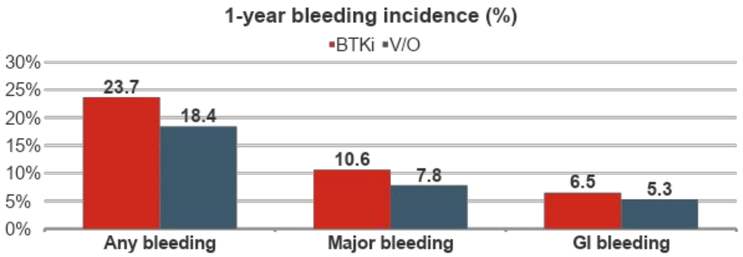
4 Results

Before matching
1749 BTKi + DOAC
328 V/O + DOAC

Matching
1:1 propensity score
nearest neighbor, caliper 0.1

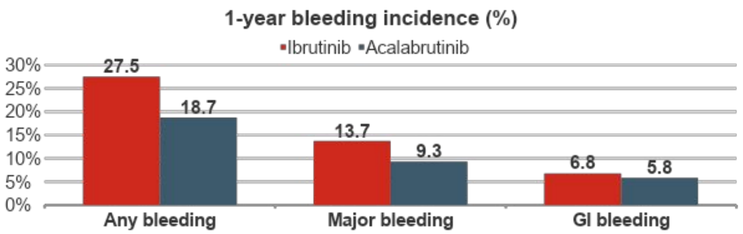
Analytic cohort
321 **BTKi** vs **321** **V/O**
matched pairs · 1-year follow-up · all std. differences <0.10

Primary analysis BTKi vs venetoclax and obinutuzumab, 321 matched pairs



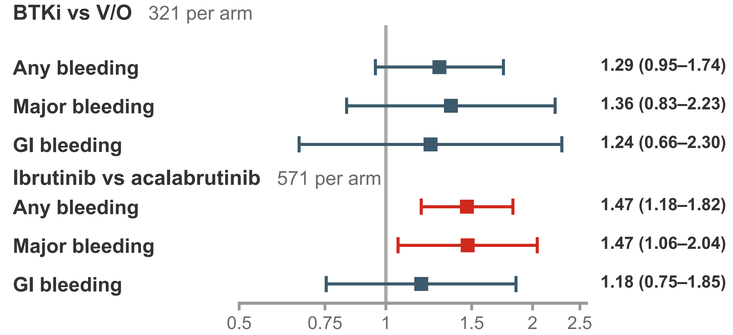
Outcome at 1 year	BTKi n=321	V/O n=321	RR (95% CI)	P
Any bleeding	76 (23.7%)	59 (18.4%)	1.29 (0.95–1.74)	.10
Major bleeding	34 (10.6%)	25 (7.8%)	1.36 (0.83–2.23)	.22
GI bleeding	21 (6.5%)	17 (5.3%)	1.24 (0.66–2.30)	.50

Secondary analysis Ibrutinib vs acalabrutinib, 571 matched pairs



Outcome at 1 year	Ibrutinib n=571	Acalabrutinib n=571	RR (95% CI)	P
Any bleeding	157 (27.5%)	107 (18.7%)	1.47 (1.18–1.82)	<.001
Major bleeding	78 (13.7%)	53 (9.3%)	1.47 (1.06–2.05)	.02
GI bleeding	39 (6.8%)	33 (5.8%)	1.18 (0.75–1.85)	.47

5 Risk ratios



7 Limitations

- Retrospective design, limited sample size, residual confounding, DOAC dose and adherence unknown, bleeding misclassification, no causal inference

Contact

Vedant Shah, MD · drvedantshah1299@gmail.com
New York Medical College Graduate Medical Education Program, St Mary's General Hospital and Saint Clare's Health, Passaic and Denville, NJ, USA