Rivaroxaban versus Apixaban for Treatment of Cancer-Associated Venous Thromboembolism in Patients at Lower Risk of Bleeding

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Background

- Patients with active cancer are at as high as 12-fold more likely to develop a venous thromboembolism (VTE) than those without.
- When VTE occurs, patients with cancer carry up to a threefold higher rate of thrombosis recurrence and approximately twice the risk of bleeding during anticoagulation.
- Current guidelines recommend LMWH, edoxaban, rivaroxaban, or apixaban for at least 6 months for VTE treatment in patient with cancer. Caution with direct factor Xa inhibitors is warranted in GI and genitourinary malignancies and other settings with high risk for mucosal bleeding.
- To date, no head-to-head RCT of rivaroxaban versus apixaban in the treatment of cancer associated VTE is available.

AIM of the study

- To evaluate the effectiveness and safety of rivaroxaban versus apixaban for VTE treatment in a retrospective cohort of patients with active cancer considered at low risk of bleeding.

Methods

- Retrospective trial
- Electronic health record (EHR) data were used
- Adult patients with active cancer (excluding esophageal, gastric, unresected colorectal, bladder, noncerebral central nervous system cancers, and leukemia), with diagnosis of acute deep vein thrombosis (DVT) and/or pulmonary embolism (PE) and treated with therapeutic VTE doses of rivaroxaban or apixaban on day 7 after the qualifying event, were included.
- Primary endpoint: a composite of recurrent VTE or any bleed resulting in hospitalization at 3 months.
- Secondary endpoint: a composite of recurrent VTE or any critical organ bleed, recurrent VTE, any bleed resulting in hospitalization, and any critical organ bleed at 3 and at 6 months.

Results (I)

- 2437 patients: 1093 treated with rivaroxaban and 1344 treated with apixaban.
- Characteristics of patients receiving rivaroxaban and apixaban were similar.
- Of included patients, 29.0% were ≥75 years of age, 56.9% were female, 20.6% had a body mass index (BMI) 35kg/m2, and 18.7% had an estimated glomerular filtration rate (eGFR) <60mL/minute at baseline.
- The index VTE event was a PE ± DVT in 45.6% of patients, 37.7% had metastatic disease.
- The most common cancer types included breast (23.5%), lung (20.1%), prostate (14.6%), and hepatobiliary (12.1%).

Results (II)

- At 3 months, rivaroxaban and apixaban were found to be associated with a similar hazard of developing the composite of recurrent VTE or any bleed resulting in hospitalization (5.3 vs. 6.0% for rivaroxaban and apixaban [referent], respectively; HR: 0.87, 95% CI: 0.60–1.27).
- No significant differences were observed between anticoagulation cohorts for this outcome at 6 months (HR: 1.00, 95% CI: 0.71–1.40) or for any other outcome at 3 or 6 months.

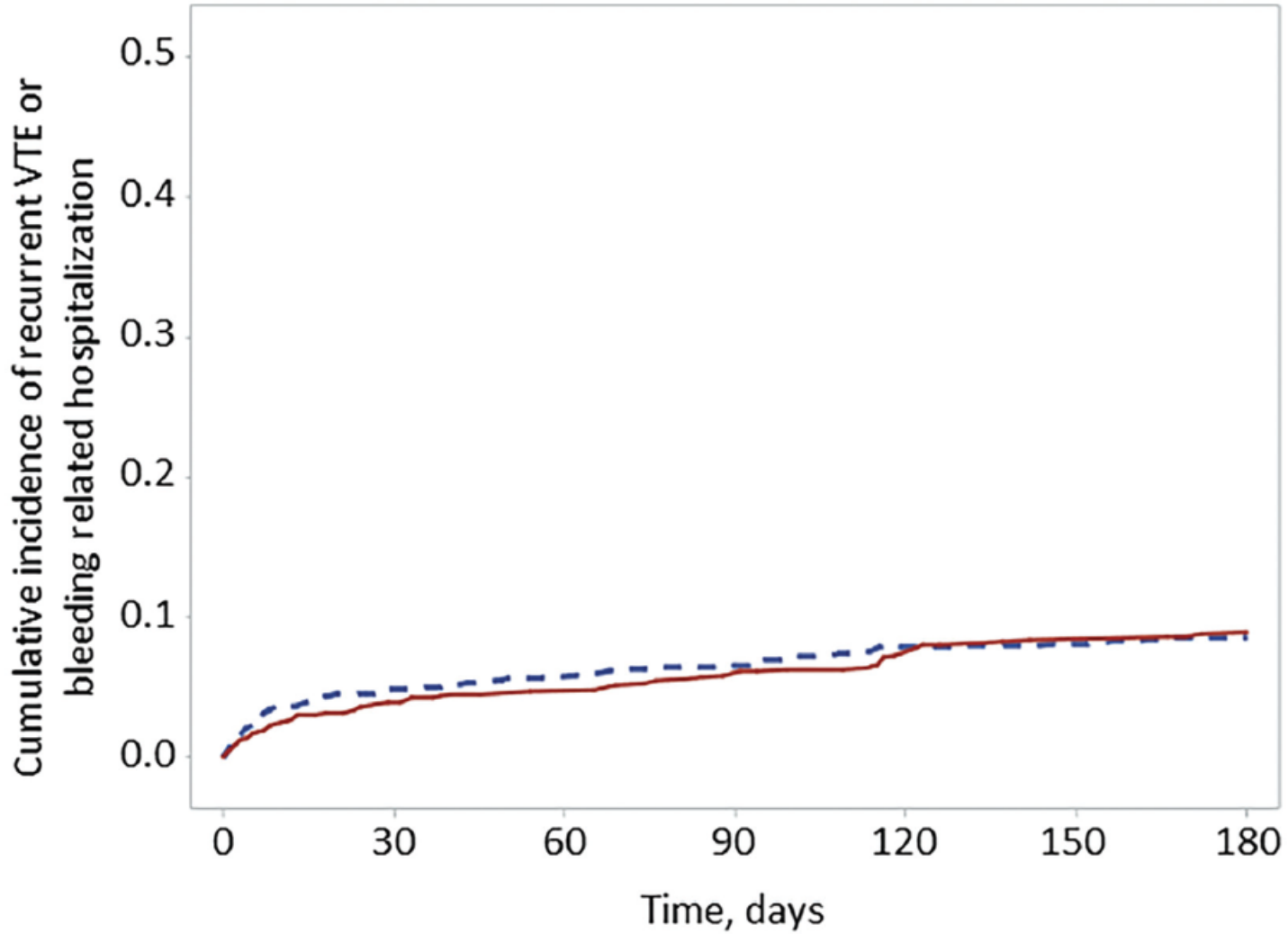


Fig. 2 Time to recurrent VTE or bleeding-related hospitalization in rivaroxaban and apixaban patients. Kaplan–Meier curve for the composite of recurrent VTE or bleeding-related hospitalization (rivaroxaban = solid line, apixaban = dashed line). VTE, venous thromboembolism.

Table 2 Outcomes of stabilized IPTW-weighted rivaroxaban and apixaban cohorts at 3 and 6 months

Outcome	Rivaroxaban, $n = 1{,}093$, %	Apixaban $n = 1{,}344$, %	sIPTW,[a] HR (95% CI)
3 months			
Recurrent VTE or bleeding-related hospitalization	5.3	6.0	0.87 (0.60–1.27)
Recurrent VTE	3.8	4.2	0.92 (0.59–1.42)
Bleeding-related hospitalization	2.4	2.3	1.05 (0.59–1.88)
Critical organ bleed	0.2	0.4	0.49 (0.09–2.59)
Recurrent VTE or critical organ bleed	3.8	4.5	0.85 (0.56–1.31)
6 months			
Recurrent VTE or bleeding-related hospitalization	7.5	7.5	1.00 (0.71–1.40)
Recurrent VTE	5.1	4.9	1.05 (0.71–1.57)
Bleeding-related hospitalization	3.5	3.3	1.06 (0.63–1.79)
Critical organ bleed	0.3	0.7	0.44 (0.13–1.51)
Recurrent VTE or critical organ bleed	5.2	5.3	0.98 (0.66–1.44)

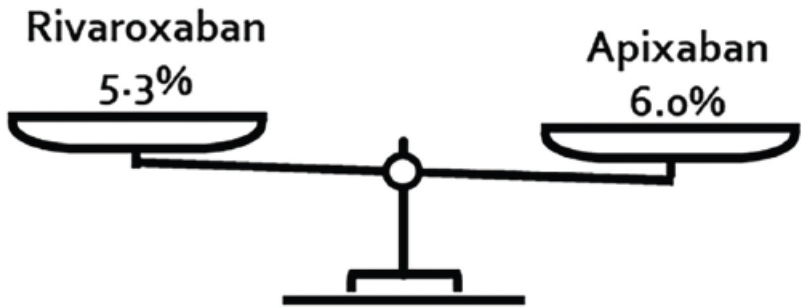
Abbreviations: IPTW, inverse probability of treatment weighting; sIPTW, stabilized inverse probability of treatment weighting; VTE, venous thromboembolism.

Rivaroxaban Versus Apixaban for Treatment of Cancer-Associated Venous Thromboembolism (OSCAR-US-H2H)

Recurrent VTE or Bleeding Related Hospitalization†

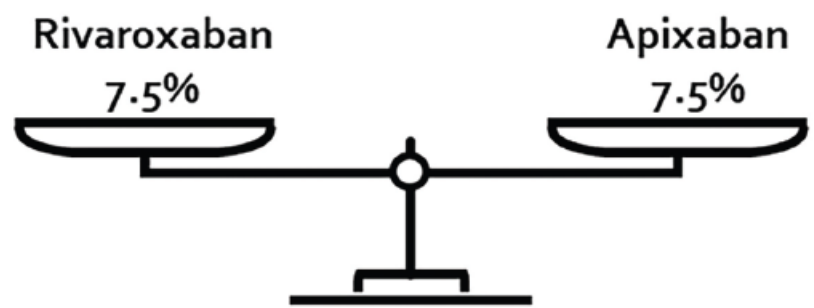
Rivaroxaban N=1093 / Apixaban N=1344

3-Months



HR* 0.87, 95%CI 0.60 to 1.27

6-Months



HR* 1.00, 95%CI 0.71 to 1.40

CI=confidence interval; HR=hazard ratio; VTE=venous thromboembolism
*Stabilized inverse probability of treatment weighted Cox regression
†The primary study outcome was the incidence of the composite of recurrent VTE or any bleeding related hospitalization at 3-months

- No significant differences in recurrent VTE, bleeding related hospitalization, or critical organ bleeding alone were observed between rivaroxaban and apixaban at 3- or 6-months

Visual summary.

Conclusions (I)

- Among adult patients with active cancers, excluding esophageal, gastric, unresected colorectal, bladder, noncerebral central nervous system cancers, and leukemia, and experiencing an acute VTE, rivaroxaban appeared to be at least as effective and safe as apixaban at 3 months.
- No statistically significant differences were observed in any outcome between the anticoagulant cohorts at 3 or 6 months.
- The study was unable to assess edoxaban's effectiveness and safety in comparison to rivaroxaban or apixaban due to edoxaban's low usage in the United States. Future real-world studies comparing edoxaban to apixaban and/or rivaroxaban should be performed in countries where edoxaban has sufficient utilization in the treatment of cancer associated VTE.

Conclusions (II)

- This is the first head-to-head comparative study of rivaroxaban and apixaban for the treatment of cancer associated VTE.
- Given the similar effectiveness and safety of rivaroxaban and apixaban in cancer associated VTE treatment, prescribers should consider patient preference, adherence, and other patient-specific factors when choosing the optimal anticoagulant.