Oral Anticoagulation for Primary VTE Prevention in Ambulatory Patients with Active Cancer

BOTTOM LINE

DO	DON'T	CONSIDER	CAUTION
• Do assess VTE risk factors, including calculating a Khorana VTE risk score • Do assess bleeding risk factors • Do provide education regarding VTE signs and symptoms and use shared-decision making to make a treatment plan	• Do not use warfarin for primary VTE prevention • Do not use primary VTE prevention in patients with Khorana score <2*	• Consider apixaban or rivaroxaban for patients at intermediate-risk or high-risk for VTE (Khorana score ≥ 2)* • Consider factors that influence patient preference like dose frequency and affordability	• DOACs should be used with caution in patients with high risk of bleeding, such as those with unresected GI/GU luminal tumors • Anticoagulants should be used with caution in patients whose platelet count is less than less than 50,000/μL • Check for clinically important drug-drug interactions

*See table of Khorana score for score calculation

Khorana Score[4] for Prediction of VTE in Ambulatory Cancer Patients

Patient Characteristics	Risk Score[a]
Site of cancer	
Very high risk (stomach, pancreas, brain[b])	2
High risk (lung, lymphoma, gynecologic, bladder, testicular, renal[b], myeloma[b])	1
Prechemotherapy platelet count ≥ 350,000/mm^3	1
Hemoglobin < 10 g/dL or use of red cell growth factors	1
Prechemotherapy leukocyte count > 11,000/mm^3	1
Body mass index ≥ 35 kg/m^2	1

[a]High risk ≥ 3; intermediate risk = 1-2; low risk = 0
[b]These cancer types are not included in original Khorana score. Brain cancer (very high risk) and myeloma (high risk) were included as VTE risk factors in the AVERT trial. Renal cancer was a high-risk factor in both the AVERT and CASSINI trials.[7, 8]

Guideline Recommendations for VTE Prevention in Ambulatory Cancer Patients

2020 NCCN[1]	2020 ASCO[2]	2018 ISTH[3]

In summation, all three documents recommend rivaroxaban, apixaban or LMWH for Khorana score ≥2

Cumulative Risk of VTE According to Khorana Score[5]

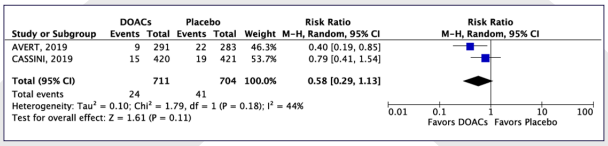
Khorana score	6 month cumulative risk of VTE
≥3	17.7%
2	9.6%
1	3.8%
0	1.5%

Meta-Analysis of Randomized Controlled Trials[6] of low-dose DOAC vs. Placebo for primary VTE prevention

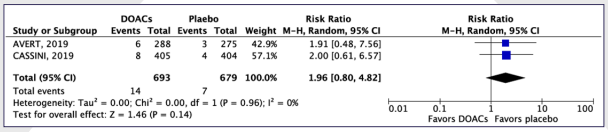
For ambulatory patients with active cancer and intermediate to high risk of VTE, the use of low-dose DOACs:

- There was a significant decrease in the risk for overall VTE
- There was a nonsignificant decrease in the risk for symptomatic VTE
- There was a nonsignificant increase in the risk of major bleeding
- There was a nonsignificant increase in the risk of clinically relevant non-major bleeding
- The largest absolute risk reduction of VTE occurred in patients at high risk (Khorana score ≥ 3)

Symptomatic VTE



Major Bleeding



Landmark Trial Characteristics

Trial	AVERT[7]	CASSINI[8]
Inclusion	New or recurrent cancer starting a new regimen of chemotherapy	Solid tumor or lymphoma starting a new systemic regimen
DOAC	Apixaban 2.5 mg twice daily	Rivaroxaban 10 mg daily
N	574	841
Khorana score	≥2	≥2
Planned duration	6 months	6 months
Early discontinuation	38%	47%
Screening ultrasound	No	Yes
Pancreatic cancer	13.6%	32.6%
Hematological malignancy	28.4%	7.0%
Myeloma	Yes (n=15)	Excluded
Brain tumor	Yes (n=24)	Excluded
Primary outcomes	Proximal upper or lower extremity DVT/PE (symptomatic or asymptomatic), VTE-related death	Proximal DVT/PE (symptomatic or asymptomatic), symptomatic distal lower extremity DVT, or upper extremity DVT, VTE-related death
NNT VTE on treatment	16	26
NNH on treatment	100	101

NNT=number needed to treat to prevent one VTE; NNH=number needed to harm to cause one excess bleeding event

For every 100 ambulatory patients with active cancer and a Khorana score ≥2 who take a low-dose DOAC for 6 months, an estimated 4 to 6 VTE events would be avoided at the expense of one additional bleeding event.

References: **1.** NCCN. Cancer-Associated Venous Thromboembolic Disease (Version 1.2020); Plymouth Meeting, PA: NCCN; 2020. **2.** Key NS, et al. J Clin Oncol. 2020;38(5):496-520. **3.** Wang TF, et al. J Thromb Haemost. 2019;17(10): 1772-1778. **4.** Khorana, et al. Blood. 2008;111(10):4902-4907. **5.** Ay, et al. Blood. 2010;116 (24): 5377–5382. **6.** Li, et al. J Thromb Haemost. 2019;17(12):2141-51. **7.** Carrier M, et al. NEJM. 2019;380(8):711-19. **8.** Khorana AA, et al. NEJM. 2019;380(8):720-28.

Faculty: Ryan Fleming, PharmD; David Garcia, MD; Nathan Clark, PharmD; Tzu-Fei Wang, MD; Marc Carrier, MD

This content was developed independently by the Anticoagulation Forum. Support for this project provided by BMS-Pfizer Alliance.

Last updated 1/2023