





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

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

Khorana Score <sup>4</sup> for Prediction of VTE in Ambulatory Cancer Patients					
Patient Characteristics	Risk Score <sup>a</sup>				
Site of cancer					
Very high risk (stomach, pancreas, brain <sup>b</sup> )	2				
High risk (lung, lymphoma, gynecologic, bladder, testicular, renal <sup>b</sup> , myeloma <sup>b</sup> )	1				
Prechemotherapy platelet count ≥ 350,000/mm <sup>3</sup>	1				
Hemoglobin < 10 g/dL or use of red cell growth factors	1				
Prechemotherapy leukocyte count > 11,000/mm <sup>3</sup>	1				
Body mass index ≥ 35 kg/m <sup>2</sup>	1				

<sup>a</sup>High risk ≥ 3; intermediate risk = 1-2; low risk = 0

bThese 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.<sup>7, 8</sup>

## Guideline Recommendations for VTE Prevention in Ambulatory Cancer Patients

2020 NCCN1	2020 ASCO <sup>2</sup>	2018 ISTH3

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

Cumulative Risk of VTE According to Khorana Score <sup>5</sup>					
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<sup>6</sup> 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

	DOA	Cs	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
AVERT, 2019	9	291	22	283	46.3%	0.40 [0.19, 0.85]	-
CASSINI, 2019	15	420	19	421	53.7%	0.79 [0.41, 1.54]	
Total (95% CI)		711		704	100.0%	0.58 [0.29, 1.13]	•
Total events	24		41				-
Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 1.79, df = 1 (P = 0.18); I <sup>2</sup> = 44%						0.01 0.1 1 10 10	
Test for overall effect: Z = 1.61 (P = 0.11)							Favors DOACs Favors Placebo

#### **Major Bleeding**

	DOA	Cs	Plael	bo		Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random, 95% CI	
AVERT, 2019	6	288	3	275	42.9%	1.91 [0.48, 7.56]		<del></del>	
CASSINI, 2019	8	405	4	404	57.1%	2.00 [0.61, 6.57]		+-	
Total (95% CI)		693		679	100.0%	1.96 [0.80, 4.82]		-	
Total events	14		7					'	
Heterogeneity: Tau2 = 0.00; Chi2 = 0.00, df = 1 (P = 0.96); I2 = 0%				= 0%	0.01	1 10	10		
Test for overall effect	Z = 1.40	6 (P = 0	).14)					vors DOACs Favors placebo	14

Landmark Trial Characteristics							
Trial	AVERT <sup>7</sup>	CASSINI <sup>8</sup>					
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 Khorona 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.

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