Rapid Resource

Anticoagulation FORUM | ANTICOAGULATION Centers of Excellence

Treatment of Cancer-Associated Venous Thromboembolism (VTE)

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BOTTOM LINE

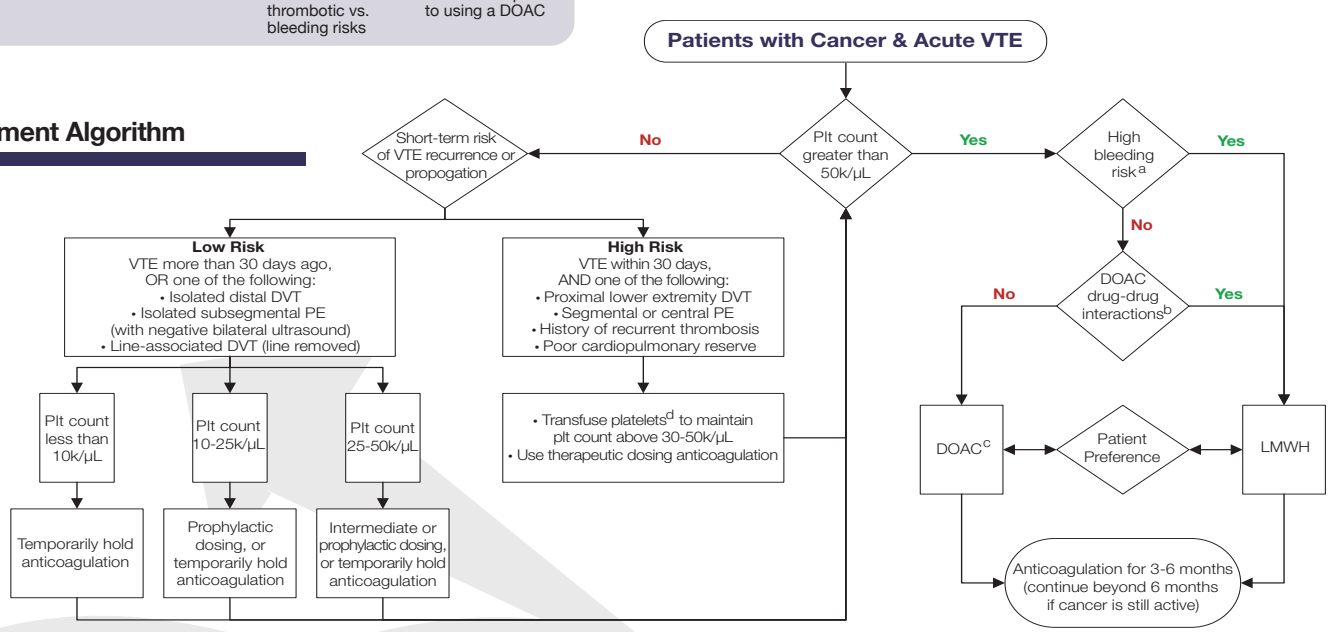
DO	DON'T	CONSIDER	CAUTION
• Do use a DOAC (apixaban, edoxaban, or rivaroxaban) or LMWH for cancer-associated VTE • Do use shared decision-making to aid patient preference	• Don't use warfarin unless patient cannot tolerate or afford DOAC or LMWH	• Consider factors that influence patient preference like route of administration, dose frequency, and affordability • Consider clinical factors like renal and hepatic functions, and overall thrombotic vs. bleeding risks	• DOACs should be used with extra caution in patients with high risk of bleeding, such as those with GI/GU cancers or lesions • Check for clinically important drug-drug interactions prior to using a DOAC

Guideline Recommendations

	2020 NCCN[1]	2020 ASCO[2,*]	2018 ISTH[3,*]
Acute VTE Treatment	DOAC (edoxaban, apixaban, and rivaroxaban) preferred for patients without gastric or gastroesophageal lesions	Initial anticoagulation (first 5–10 days): LMWH or rivaroxaban preferred Long-term (at least 6 months): LMWH, edoxaban or rivaroxaban preferred	DOACs (edoxaban and rivaroxaban) suggested for low risk of bleeding and no drug-drug interaction, LMWH suggested otherwise
GI/GU Cancer	LMWH preferred for patients with gastric or gastroesophageal lesions	There is an increase in major bleeding risk with DOACs, particularly observed in GI and potentially GU malignancies	LMWH suggested in patients with luminal GI cancers with an intact primary, patients at risk of bleeding from the GU tract, bladder, or nephrostomy tubes, or patients with active GI mucosal abnormalities

*The recommendations from ASCO and ISTH were made before apixaban was compared to LMWH

Treatment Algorithm



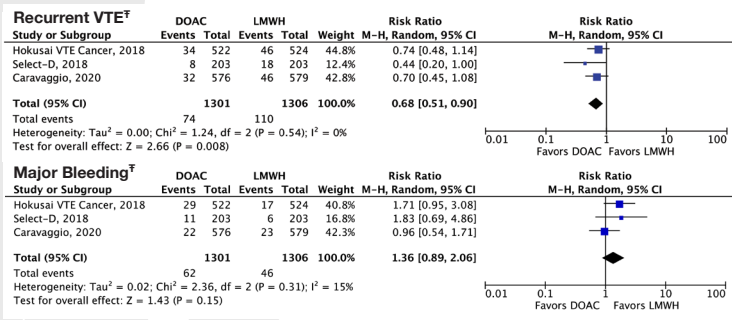
Landmark Trial Characteristics

	Hokusai VTE Cancer[4]	Select-D[5]	Caravaggio[6]
DOAC	Edoxaban	Rivaroxaban	Apixaban
N	1046	406	1155
Primary outcomes	Composite of recurrent VTE or major bleeding	Recurrent VTE	Recurrent VTE (efficacy) Major bleeding (safety)
Study duration	12 months	6 months	6 months
Incidental VTE	32.5%	52.5%	20%
Cancer diagnosis prior to enrollment	2 years	6 months	2 years
Active cancer	98%	100%	97%
Cancer treatment on enrollment	72%	69%	62%
Solid tumor	89%	92%	93%
Metastatic cancer	53%	59%	68%
GI cancer	29%	44%	33%
Upper GI cancer	5%	10%	5%
Platelet count cut-off (k/μL) for exclusion	50	100	75
CrCl cut-off for exclusion	<30 ml/min	<30 ml/min	<30 ml/min

[a]Patients with gastrointestinal (GI) cancer or GI lesions such as gastric/duodenal ulcers, gastritis, etc, or genitourinary lesions/intervention (e.g. nephrostomy tubes). Excess GI/GU bleeding has been observed with some DOACs (compared to LMWH) in some, but not all, clinical trials. Fatal or potentially life-threatening bleeding has occurred infrequently in randomized trials; no differences in the rates of fatal or potentially life-threatening bleeding have been documented.
[b]The impact and clinical significance of P-gp modifiers and CYP3A4 modifiers affecting DOACs varies widely. Consider using Lexicomp® interactions as the preferred drug-drug interaction guidance resource, as well as the AC Forum Rapid Resource on DOAC DDI Guidance.
[c]Patients unable to tolerate or access DOACs or LMWH may be considered for a vitamin K antagonist.
[d]If platelet transfusion not an option, consider intermediate dosing anticoagulation if plts remain above 25k/μL, and prophylactic dosing if plts 10-25k/μL.

Landmark Trial Meta-Analysis

When compared to LMWH in active cancer patients with acute DVT/PE:
- DOACs decrease the risk of recurrent VTE[Ŧ]
- DOACs nonsignificantly increase the risk of major bleeding[Ŧ]
- DOACs nonsignificantly decrease the composite risk of recurrent VTE and major bleeding[7]
- DOACs nonsignificantly increase the risk of CRNMB[7]



Ŧ The Forest Plots for recurrent VTE and major bleeding were derived from the 3 landmark trials using the Mantel-Haenszel random effects model. The event rates cited are 6-month event rates.

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.** Khorana AA, et al. J Thromb Haemost. 2018;16(9):1891-1894. **4.** Raskob GE, et al. N Eng J Med. 2018;378(7):615-624. **5.** Young AM, et al. J Clin Oncol. 2018;36(20):2017-2023. **6.** Agnelli G, et al. N Engl J Med. 2020;382(17):1599-1607. **7.** Mulder FI, et al. Blood. 2020;136(12):1433-1441.

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