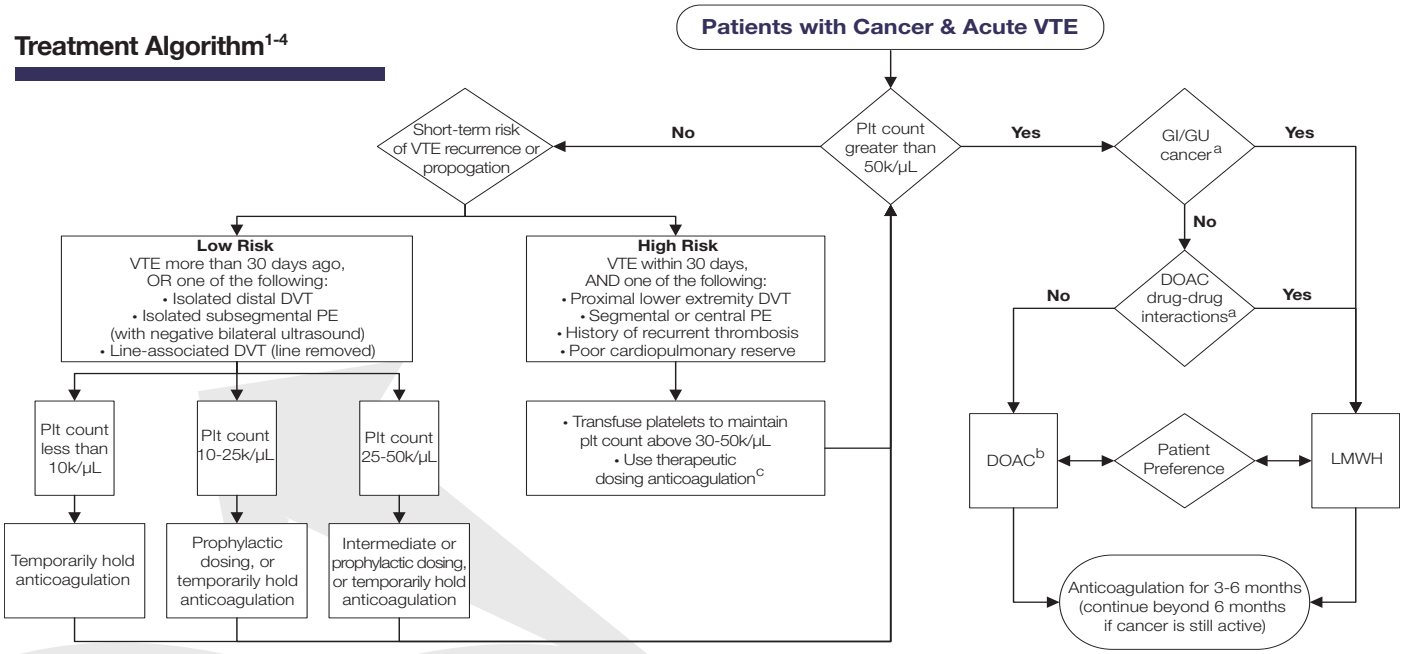
Treatment of Cancer-Associated Venous Thromboembolism (VTE)

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

Treatment Algorithm[1-4]



[a]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.

[b]Patients unable to tolerate or access DOACs or LMWH may be considered for a vitamin K antagonist.

[c]If platelet transfusion not an option, consider intermediate dosing anticoagulation if platelets remain above 25k/μL, and prophylactic dosing if platelets 10-25k/μL.

Landmark Trial Characteristics

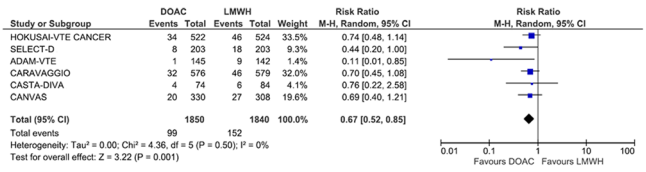
	Hokusai VTE Cancer[5]	Select-D[6]	Caravaggio[7]
DOAC	Edoxaban	Rivaroxaban	Apixaban
N	1046	406	1155
Primary outcomes	Composite of recurrent VTE or major bleeding	Recurrent VTE	Recurrent VTE (efficacy) Major bleeding (safety)
Study duration	12 months	6 months	6 months
Incidental VTE	32.5%	52.5%	20%
Cancer 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

Landmark Trial Meta-Analysis[8]

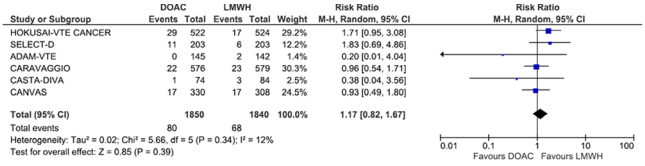
When compared to LMWH in active cancer patients with acute DVT/PE:

- DOACs decrease the risk of recurrent VTE[d]
- There was no significant difference in major bleeding between DOAC[d]
- There was no significant difference in recurrent VTE and major bleeding between DOAC and VKA
- The risk of CRNMB was non-significantly increased with DOACs

Recurrent VTE[d]



Major Bleeding[d]



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

References: **1.** Lyon AR, López-Fernández T, Couch LS, et al. Euro Heart J; 2022; 43(41) 4229–4361 **2.** Stevens SM, Woller SC, Kreuziger LB, et al. Chest 2021; 160(6):2247-2259 **3.** Streiff MB, Holmstrom B, Angelini, etal. J Natl Compr Canc Netw. 2021;19(10): 1181-1201 **4.** Lyman GH, Carrier M, Ay Cihan, et al. Blood Adv. 2021; 5(4):927-974. **5.** Raskob GE, et al. N Eng J Med. 2018;378(7):615-624. **6.**Young AM, et al. J Clin Oncol. 2018;36(20):2017-2023. **7.** Agnelli G, et al. N Engl J Med. 2020;382(17):1599-1607. **8.** Frere C, et al. J Hematol Oncol. 2022; 15(1):69. **9.** https://jhoonline.biomedcentral.com/articles/10.1186/s13045-022-01289-1/figures/1

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

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

Last updated 3/2023

Guideline Recommendations

2022 European Society of Cardiology Guidelines on Cardio-Oncology[1]

- Apixaban, edoxaban, or rivaroxaban recommended for treatment of symptomatic or incidental VTE in patients without contraindications (Class I, Level of Evidence A).
- LMWH recommend for treatment of symptomatic or incidental VTE in patients with cancer with platelet count >50,000/μL (Class I, Level of Evidence A).
- In patients with platelet counts of 25,000-50,000/μL, anticoagulation with half-dose LMWH may be considered after a multidisciplinary discussion (Class IIb, Level of Evidence C).
- Prolongation of anticoagulation therapy beyond 6 months should be considered in selected patients with active cancer, including metastatic disease (Class IIa, Level of Evidence A).

2021 CHEST Antithrombotic Therapy for VTE Disease[2]

- In patients with acute VTE in the setting of cancer (cancer-associated thrombosis) we recommend an oral Xa inhibitor (apixaban, edoxaban, rivaroxaban) over LMWH for initiation and treatment phases of therapy (strong recommendation, moderate-certainty evidence).

2021 National Comprehensive Cancer Network[3]

- Apixaban (Category 1), edoxaban after 5 days of parenteral anticoagulation (Category 1), or rivaroxaban (Category 2A) preferred over LMWHs for patients without gastric or gastroesophageal lesions.
- LMWH (dalteparin; Category 1) preferred over DOACs in patients with gastric or gastroesophageal lesions.
- Dabigatran after at least 5 days of parenteral anticoagulation when apixaban, edoxaban, rivaroxaban, or LMWH are not appropriate or unavailable (Category 2A).

2021 American Society of Hematology – Patients with Cancer & VTE[4]

- Panel suggestion (apixaban or rivaroxaban) or LMWH be used for initial treatment of VTE for patients with cancer (conditional recommendation, very low certainty in the evidence of effects).
- Recommends LMWH over UFH (strong recommendation, moderate certainty in the evidence of effects) or fondaparinux (conditional recommendation, very low certainty in the evidence of effects) for initial treatment of VTE for patients with cancer.
- For the short-term treatment of VTE (3-6 months) for patients with active cancer, panel suggests DOAC over LMWH (conditional recommendation, low certainty of evidence of effect) or VKA (conditional recommendation, very low certainty of evidence of effect). LMWH is preferred over VKA.

References: **1.** Lyon AR, López-Fernández T, Couch LS, et al. Euro Heart J; 2022; 43(41) 4229–4361 **2.** Stevens SM, Woller SC, Kreuziger LB, et al. Chest 2021; 160(6):2247-2259 **3.** Streiff MB, Holmstrom B, Angelini, etal. J Natl Compr Canc Netw. 2021;19(10): 1181-1201 **4.** Lyman GH, Carrier M, Ay Cihan, et al. Blood Adv. 2021; 5(4):927-974. **5.** Raskob GE, et al. N Eng J Med. 2018;378(7):615-624. **6.**Young AM, et al. J Clin Oncol. 2018;36(20):2017-2023. **7.** Agnelli G, et al. N Engl J Med. 2020;382(17):1599-1607. **8.** Frere C, et al. J Hematol Oncol. 2022; 15(1):69. **9.** https://jhoonline.biomedcentral.com/articles/10.1186/s13045-022-01289-1/figures/1

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

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

Last updated 3/2023