# CAT-astrophe or Cure?

## Clinical Crossroads in Cancer Associated Thrombosis

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October 14, 2025

# Disclosure

**The planners and speakers have indicated that there are no relevant financial relationships with any ineligible companies to disclose.**

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# Objectives

01 Recall the background of pathophysiology and risk factors of thromboembolic events in oncology

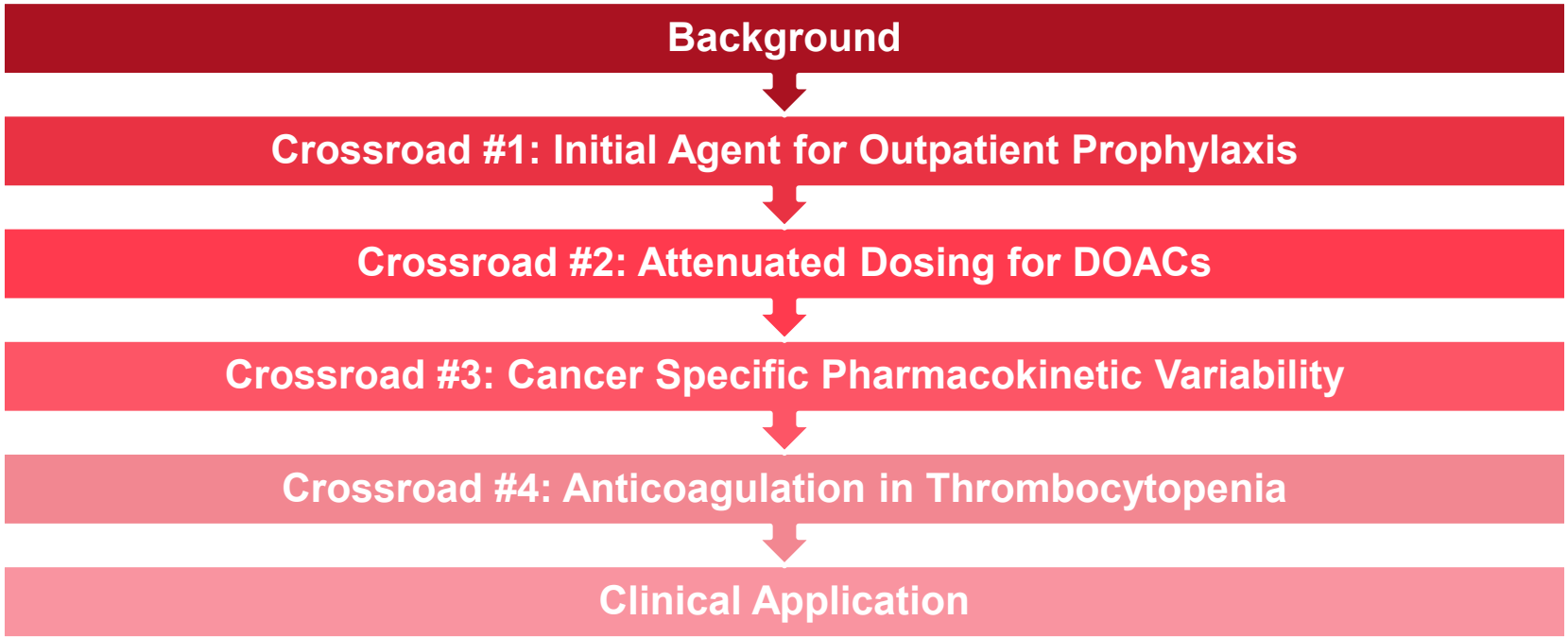
02 Outline the key literature influencing changes in practice surrounding cancer associated VTE

03 Recognize anticoagulation considerations for special populations within oncology

04 Identify strategies to safely implement the 2025 NCCN guidelines into practice

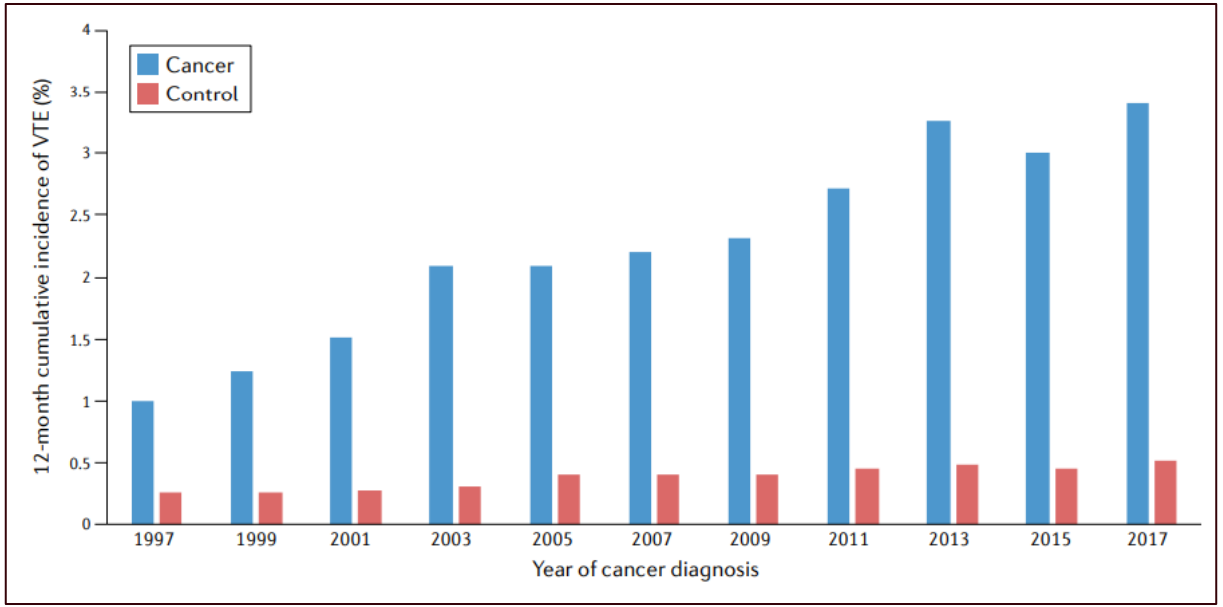
VTE: venous thromboembolism
NCCN: National Comprehensive Cancer Network

# Roadmap




DOAC: direct oral anticoagulant

# Cancer Associated Venous Thromboembolism

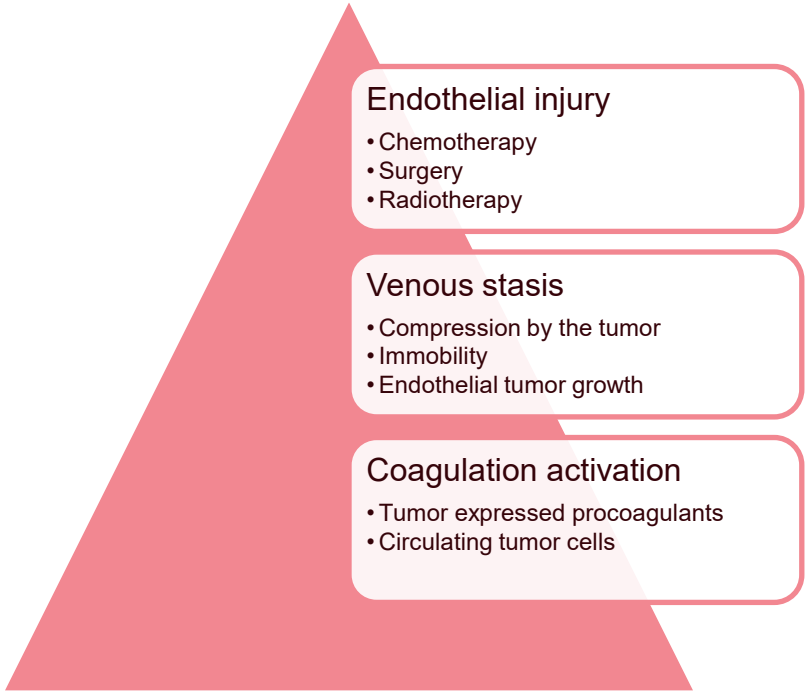



- Accounts for approximately 20% of VTE
- Mortality rate of 45.3 per 100 person-years

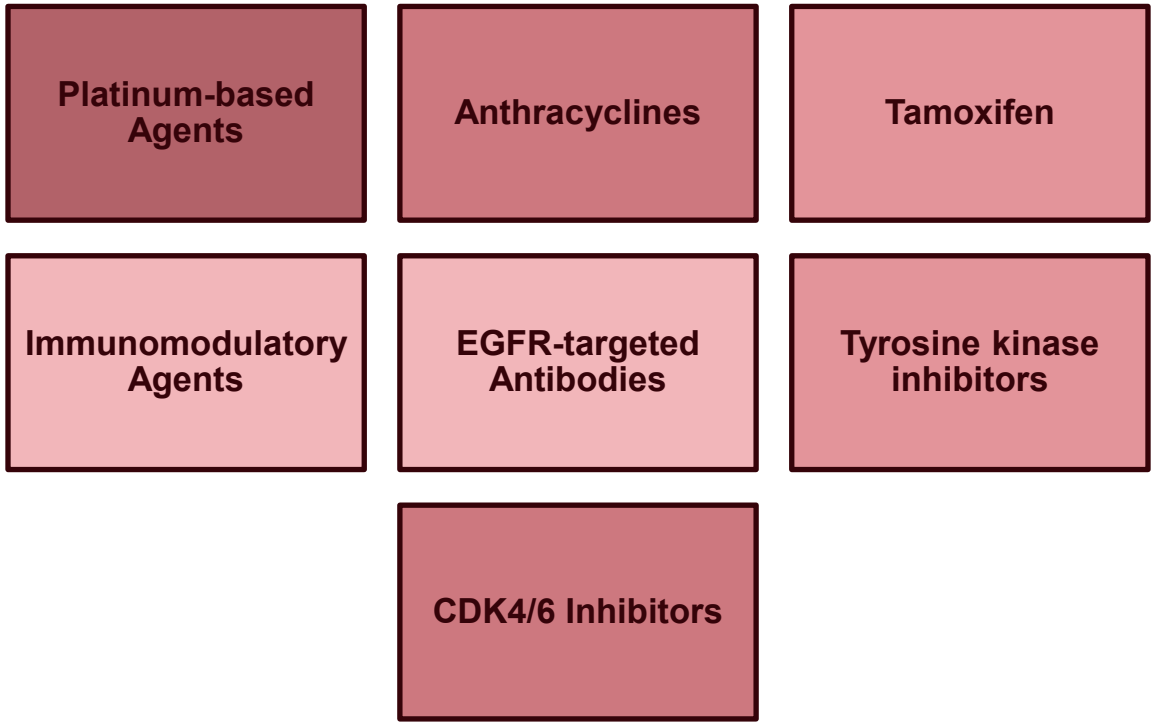
Stein PD, et al. *Am J Med*. 2006.
Khorana AA, et al. *Nat Rev Dis Primers*. 2022
Khorana, et al. Journal of thrombosis and haemostasis. 2007

VTE: venous thromboembolism

# Components of Virchow's Triad



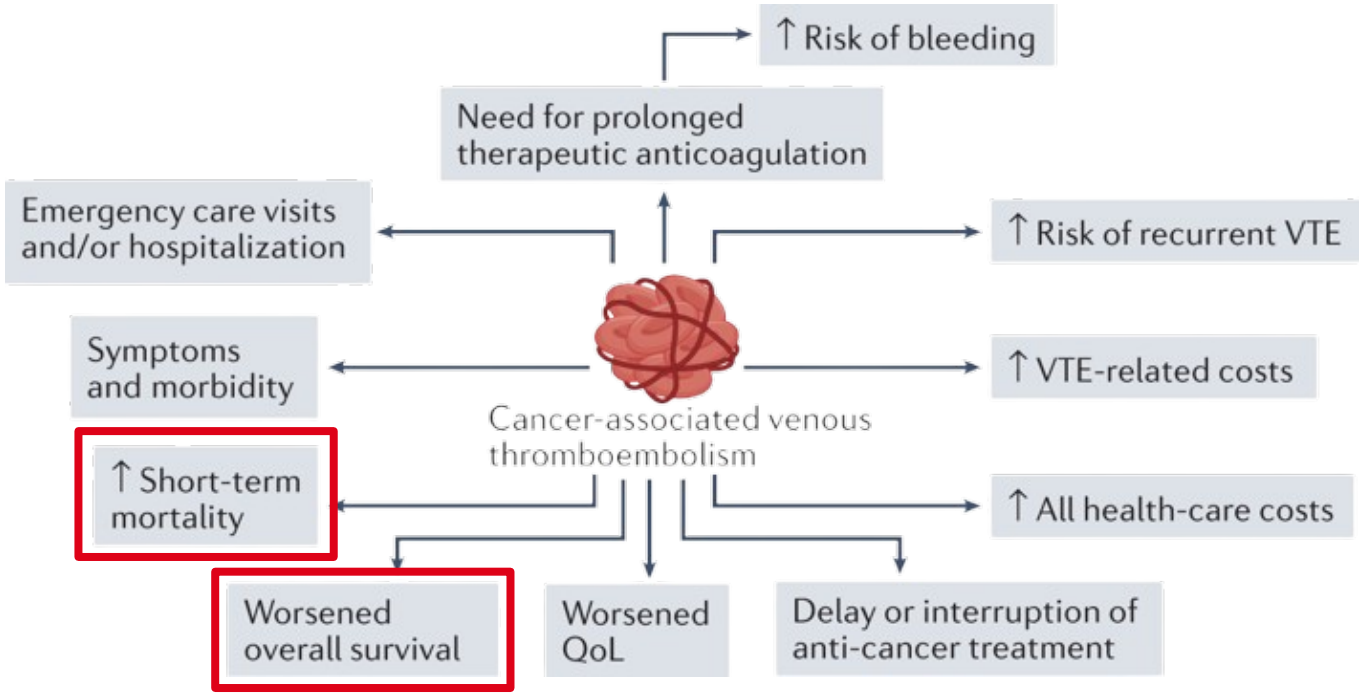
# Treatments with High -Risk for Thrombosis




Grover SP, et al. *Arterioscler Thromb Vasc Biol*. 2021

EGFR: epidermal growth factor receptor
CDK: cyclin-dependent kinase

# CAT Consequences




Khorana AA, et al. *Nat Rev Dis Primers*. 2022

CAT: cancer associated thrombosis
VTE: venous thromboembolism
QoL: quality of life

# Self-Assessment Question #1

**WM is an 80-year-old M who presented to the emergency room for shortness of breath and unilateral swelling of his leg. An ultrasound displayed an acute DVT, and he was started on a heparin drip.**

**PMH: CAD, HTN, diabetes, Stage IIIa adenocarcinoma of the lung**
**Active Chemotherapy: cisplatin + oxaliplatin**
**Medications: aspirin 81mg daily, lisinopril 10 mg daily, metformin 500 mg twice daily**

**Select all the risk factors that the patient has for developing cancer associated thrombosis.**

A. Age
B. Platinum-based chemotherapy
C. Cardiac history
D. Oncologic history

DVT: deep vein thrombosis

# NCCN 2025 Guideline Crossroads to Discuss

- Initial Agent for Outpatient Prophylaxis
- Attenuated Dosing for DOACs
- Cancer Specific Pharmacokinetic Variability
- Anticoagulation in Thrombocytopenia

NCCN: National Comprehensive Cancer Network
DOAC: direct oral anticoagulant

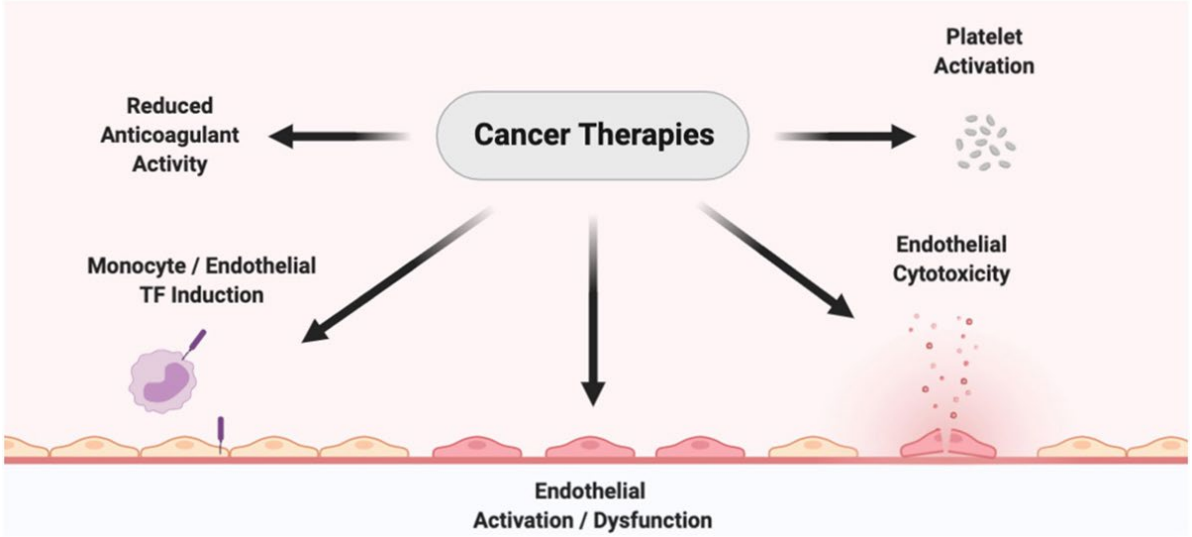
01

# Crossroad #1

*Initial Agent for Outpatient Prophylaxis*

# Thromboprophylaxis During Chemotherapy

- All hospitalized cancer patients required to start pharmacologic thromboprophylaxis
- Role of outpatient thromboprophylaxis is less certain




Grover SP, et al. *Arterioscler Thromb Vasc Biol*. 2021

# Populations at High Risk

- Adults with diagnosis of cancer hospitalized for medical or surgical care
- Received VTE prophylaxis during hospitalization
- Any outpatients at risk based on VTE risk assessment

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Cancer-Associated Venous Thromboembolic Disease, Version 5.2025

VTE: venous thromboembolism

# Other Thromboembolism Risk Scores

| IMPEDE Score | Score |
|---|---|
| Positive Factors | |
| Central venous catheter/Tunneled central line | +2 |
| Pelvic, hip, or femur fracture | +4 |
| Obesity (BMI ≥ 25) | +1 |
| Previous VTE | +5 |
| Immunomodulatory drug | +4 |
| Erythropoiesis-stimulating agent | +1 |
| Dexamethasone ≤ 160 mg/month | +2 |
| Dexamethasone > 160 mg/month | +4 |
| Doxorubicin or multiagent chemotherapy | +3 |
| Negative Factors | |
| Asian/Pacific Islander | -3 |
| Prophylactic LMWH or aspirin | -3 |
| Therapeutic LMWH or warfarin | -4 |

| SAVED Score | Score |
|---|---|
| Surgery within 90 days | +2 |
| Asian race | -3 |
| VTE history | +3 |
| Age ≥ 80 years | +1 |
| Dexamethasone (regimen dose)<br>• Standard dose (120-160 mg/cycle)<br>• High dose (> 160 mg/cycle) | <br>+1<br>+2 |

LMWH: low molecular weight heparin
VTE: venous thromboembolism

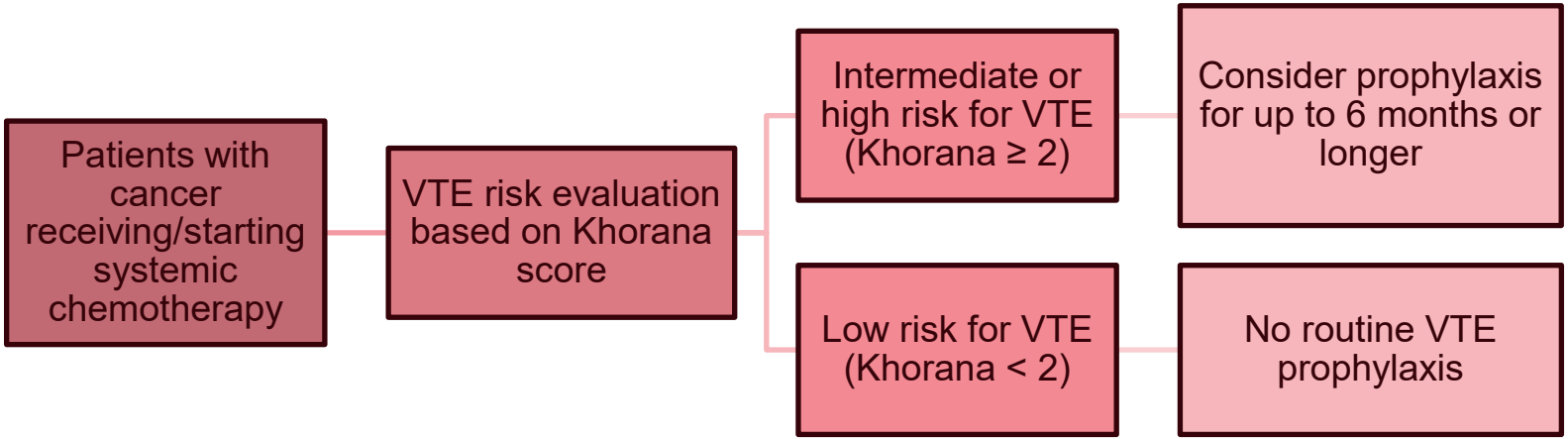
National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Cancer-Associated Venous Thromboembolic Disease, Version 5.2025

# Khorana Score

| Patient characteristic | Score | Risk Score & Incidence |
|---|---|---|
| Cancer site:<br>Stomach, pancreas<br>Lung, lymphoma, gynecologic, bladder, testicular | <br>2<br>1 | **Score 0**<br>low risk (0.3-1.5%)<br><br>**Score 1-2**<br>intermediate risk (2.0-4.8%)<br><br>**Score 3+**<br>high risk (6.7-12.9%) |
| Prechemotherapy platelet count ≥ 350/μL | 1 | |
| Hemoglobin < 10 g/dL or use of red cell growth factors | 1 | |
| Prechemotherapy leukocyte count > 11/μL | 1 | |
| BMI ≥ 35 kg/m$^2$ | 1 | |

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Cancer-Associated Venous Thromboembolic Disease, Version 5.2025

# Evaluation for VTE Prophylaxis




VTE: venous thromboembolism

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Cancer-Associated Venous Thromboembolic Disease, Version 5.2025

# Literature Review - LMWH

| Study | Tumor Type(s) | Intervention | Symptomatic VTE | Major Bleeding |
|---|---|---|---|---|
| **PROTECHT (2009)** | Lung, GI, pancreatic, breast, ovarian, or head and neck cancers | • Nadroparin for 4 months (n = 769)<br>• Placebo (n = 381) | 2% vs 3.9% (p = 0.02) | 0.7% vs 0% (p = 0.18) |
| **FRAGEM (2012)** | Advanced pancreatic cancer | • Dalteparin for 12 weeks (n = 60)<br>• No prophylaxis (n = 63) | 3.4% vs 23% (p = 0.002) | - |
| **CONKO-004 (2015)** | Advanced pancreatic cancer | • Enoxaparin 1 mg/kg daily for 3 months then 40 mg daily (n = 160)<br>• No prophylaxis (n = 152) | 1.3% vs 9.9% (p = 0.01) | 4.4% vs 3.3% (p = 1) |

Agnelli G, et al. *Lancet Oncol*. 2009
Maraveyas A, et al. *Eur J Cancer*. 2012

Pelzer U, et al. *J Clin Oncol*. 2015

LMWH: low molecular weight heparin

GI: gastrointestinal
VTE: venous thromboembolism

# Literature Review - DOACs

| Study | Tumor Type(s) | Treatment | Primary Endpoint | Major Bleeding |
|---|---|---|---|---|
| **CASSINI (2018)** | Solid tumors or lymphoma | • Rivaroxaban 10 mg daily for 6 months (n = 420)<br>• Placebo (n = 421) | Composite of symptomatic or asymptomatic DVT or PE<br>6% vs 8.8% (p = 0.1) | 2% vs 1%<br>(p = 0.26) |
| **AVERT (2018)** | All newly diagnosed cancers | • Apixaban 2.5 mg twice daily for 6 months (n = 288)<br>• Placebo (n = 275) | Documented VTE<br>4.2% vs 10.2% (p < 0.001) | 3.5% vs 1.8%<br>(p > 0.05) |

Khorana AA, et al. *N Engl J Med*. 2019
Carrier M, et al. *N Engl J Med*. 2019

DOAC: direct oral anticoagulant

VTE: venous thromboembolism
PE: pulmonary embolism

# VTE Prophylaxis Options for Ambulatory Oncology

| Agent | Standard Dosing | Renal Dose | Other Dose Modifications |
|---|---|---|---|
| Apixaban | 2.5 mg PO twice daily | Caution if CrCl < 30 mL/min | Avoid if platelet count < 50,000/μL<br>Avoid if weight < 40 kg |
| Rivaroxaban | 10 mg PO daily | Avoid if CrCl < 30 mL/min | Avoid if platelet count < 50,000/μL |
| Dalteparin | 200 units/kg subQ daily x 1 month, then 150 mg/kg subQ daily x 2 months | Avoid if CrCl < 30 mL/min | Avoid if platelet count < 50,000/μL |
| Enoxaparin | 1 mg/kg subQ daily x 3 months, then 40 mg subQ daily | Avoid if CrCl < 30 mL/min | Avoid if platelet count < 50,000/μL |

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Cancer-Associated Venous Thromboembolic Disease, Version 5.2025

# Risk Factors for Thrombosis in Surgical Oncology

- Undergoing surgery for gastrointestinal malignancies
- Previous episode of VTE
- Anesthesia time > 2 hours
- Perioperative bed rest ≥ 4 days
- Advanced-stage disease
- Age > 60 years

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Cancer-Associated Venous Thromboembolic Disease, Version 5.2025

VTE: venous thromboembolism

# VTE Prophylaxis Guidelines for Surgical Oncology

Out-of-hospital primary VTE prophylaxis postoperatively following high-risk abdominal or pelvic cancer surgery is recommended

Are the prophylactic anticoagulation options and duration the same as ambulatory medical oncology patients?

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VTE: venous thromboembolism

# Literature Review – LMWH

| Study | Surgery | Intervention | VTE | Major Bleeding |
|---|---|---|---|---|
| **Bergqvist, et al (2002)** | Curative open surgery for abdominal or pelvic cancer | • Placebo for 21 days (n = 167)<br>• Enoxaparin 40 mg daily for 21 days (n = 165) | During study period<br>12% vs 4.8%<br>(p = 0.02)<br><br>At 3 months<br>13.8% vs 5.5%<br>(p = 0.01) | During study period<br>0% vs 0.4%<br>(p > 0.99)<br><br>At 3 months<br>0.4% vs 1.2%<br>(p = 0.62) |
| **Rasmussen, et al (2006)** | Major abdominal surgery | • Dalteparin for 7 days (n = 178)<br>• Dalteparin for 28 days (n = 165) | 16.3% vs 7.3%<br>(p = 0.012) | 1.8% vs 0.5% |

Rasmussen MS, et al. *J Thromb Haemost*. 2006
Bergqvist D, et al. *N Engl J Med*. 2002

LMWH: low molecular weight heparin
VTE: venous thromboembolism

# Literature Review – DOACs

## Apixaban

| Guntupalli, et al (2020) | |
|---|---|
| **Design** | Multicenter, open-blinded, randomized clinical trial |
| **Population** | Suspected or confirmed gynecologic cancer undergoing surgery |
| **Intervention** | • Apixaban 2.5 mg twice daily x 28 days (n = 204)<br>• Enoxaparin 40 mg daily x 28 days (n = 196) |
| **Major Bleeding** | 0.5% vs 0.5% (p > 0.99) |
| **VTE Events** | 1% vs 1.5% (p = 0.68) |

## Rivaroxaban

| PROLAPS II (2022) | |
|---|---|
| **Design** | Randomized, double-blind, placebo-controlled, superiority trial |
| **Population** | Colorectal cancer undergoing surgery |
| **Intervention** | • Rivaroxaban 10 mg daily x 3 weeks (n = 287)<br>• Placebo x 3 weeks (n = 282) |
| **Major Bleeding** | 0.7% vs 0% |
| **VTE Events** | 1% vs 3.9% (p = 0.032) |

Guntupalli SR, et al. *JAMA Netw Open*. 2020
Becattini C, et al. *Blood*. 2022

DOAC: direct oral anticoagulant
VTE: venous thromboembolism

# VTE Prophylaxis Options for Surgical Oncology

Recommend for up to **4 weeks postoperative** following surgery

| Agent | Standard Dosing | Renal Dose | Other Dose Modifications |
|---|---|---|---|
| Apixaban | 2.5 mg PO twice daily x **28 days** | Caution if CrCl < 30 mL/min | Avoid if platelet count < 50,000/µL<br>Avoid if weight < 40 kg |
| Rivaroxaban | 10 mg PO daily x **21 days** | Avoid if CrCl < 30 mL/min | Avoid if platelet count < 50,000/µL |
| Dalteparin | 5000 units subQ daily x **28 days** | Avoid if CrCl < 30 mL/min | Avoid if platelet count < 50,000/µL |
| Enoxaparin | 40 mg subQ daily x **28 days** | Avoid if CrCl < 30 mL/min | Avoid if platelet count < 50,000/µL |

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# Self-Assessment Question #2

**According to NCCN guidelines, what is a difference between VTE prophylaxis regimens between medical oncology and surgical oncology patients?**

A. Anticoagulant agent
B. Dosing of DOACs
C. Duration of anticoagulation
D. No differences seen

DOAC: direct oral anticoagulant
VTE: venous thromboembolism

# Outpatient Prophylaxis Principles

| | LMWH | Apixaban | Rivaroxaban |
|---|---|---|---|
| **Medical Oncology** | ✓ | ✓ | ✓ |
| **Surgical Oncology** | ✓ | ⚠ | ⚠ |

**Duration of Anticoagulation**

| Medical Oncology | Surgical Oncology: |
|---|---|
| 6 weeks | 4 weeks |

LMWH: low molecular weight heparin

02

# Crossroad #2

*Attenuated Dosing for DOACs*

DOAC: direct oral anticoagulant

# NCCN 2024 Guidelines

## Duration

Duration should be at least 3 months or as long as active cancer or cancer therapy

## Dosing of DOACs

Apixaban 10 mg PO every 12 hours for 7 days followed by 5 mg PO every 12 hours

Edoxaban 60 mg daily after initial therapy with LMWH or UFH for at least 5 days

Rivaroxaban 15 mg PO every 12 hours for 21 days followed by 20 mg daily

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Cancer-Associated Venous Thromboembolic Disease, Version 5.2024

NCCN: National Comprehensive Cancer Network
DOAC: direct oral anticoagulant

# Prior Literature

| | Design | Population | Intervention | Recurrent VTE | Major Bleeding |
|---|---|---|---|---|---|
| **AMPLIFY-EXT (2013)** | Randomized Double-blind | Adult, symptomatic DVT or PE<br><br>Treated for 6 to 12 months with standard anticoagulant therapy | • Apixaban 2.5 mg twice daily<br>• Apixaban 5 mg twice daily<br>• Placebo | 1.7% vs 1.7% vs 8.8% (95% CI, 4.9 to 9.1; p<0.001) | 0.2% vs 0.1% vs 0.5% |
| **RENOVE (2025)** | Noninferiority Randomized Open-label | Adult with acute symptomatic thromboembolism<br><br>Received 6-24 uninterrupted months of full-dose anticoagulation | • Reduced dose (apixaban 2.5 mg twice daily or rivaroxaban 10 mg daily)<br>• Full-dose (apixaban 5 mg twice daily or rivaroxaban 20 mg daily) | 2.2% vs 1.8% (HR 1.32, 95% CI 0.67 – 2.6) | 9.9% vs 15.2% (HR 0.61, 95% CI 0.48 – 0.79) |

Agnelli G, et al. *N Engl J Med*. 2013
Couturaud F, et al. *Lancet*. 2025

DVT: deep vein thrombosis

VTE: venous thromboembolism
PE: pulmonary embolism

# Prior Literature

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|---|---|---|---|---|---|
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| **RENOVE (2025)** | Noninferiori Randomized Open-label | Received 6-24 uninterrupted months of full-dose anticoagulation | • Full-dose (apixaban 5 mg twice daily or rivaroxaban 20 mg daily) | s 1.8 % (HR 1.32, 95% CI 0.67 – 2.6) | 9.9% vs 15.2% (HR 0.61, 95% CI 0.48 – 0.79) |

Can extended reduced dosing be used in cancer patients after 6 months of full anticoagulation?

Agnelli G, et al. *N Engl J Med*. 2013
Couturaud F, et al. *Lancet*. 2025

DVT: deep vein thrombosis

VTE: venous thromboembolism
PE: pulmonary embolism

# API-CAT

| Extended Reduced-Dose Apixaban for Cancer-Associated Venous Thromboembolism | |
|---|---|
| **Design** | International, prospective, double-blind, noninferiority trial |
| **Inclusion** | • Active cancer and venous thromboembolism<br>• Completed at least 6 months of treatment with treatment doses of LMWH, DOAC, or vitamin K antagonist |
| **Exclusion** | • Documented symptomatic recurrent thromboembolism<br>• Basal-cell or squamous-cell carcinoma of the skin, primary brain tumor or intra-cerebral metastasis<br>• Indication for long-term treatment with VKA or DOAC |
| **Intervention** | • Apixaban 2.5 mg twice daily<br>• Apixaban 5 mg twice daily |
| **Primary Endpoint** | Recurrent thromboembolism |
| **Key Secondary Endpoint** | Clinically relevant bleeding |

Mahé I, et al. *N Engl J Med*. 2025

LMWH: low molecular weight heparin
DOAC: direct oral anticoagulant

# Baseline Characteristics

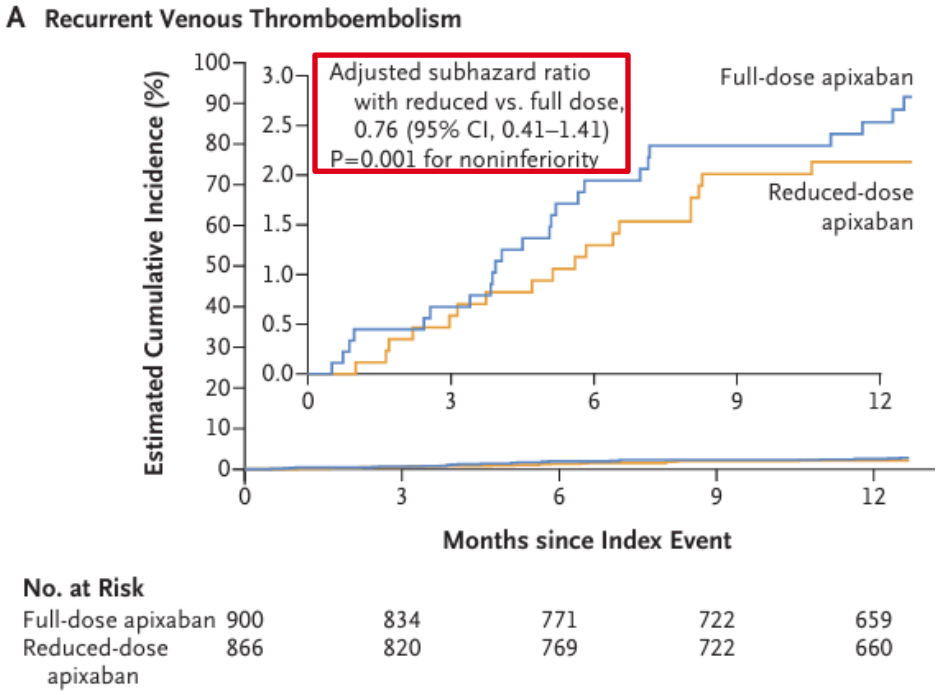
| Characteristics | Reduced-Dose Apixaban (N = 866) | Full-Dose Apixaban (N = 900) |
|---|---|---|
| Age – year | 67.2 ± 11 | 67.7 ± 11.4 |
| Male – no (%) | 375 (43.3) | 391 (43.4) |
| PE with or without lower-limb proximal DVT – no (%) | 669 (77.3) | 665 (73.9) |
| Metastatic – no (%) | 574 (66.3) | 584 (64.9) |
| Site of cancer – no (%) | | |
| Breast | 199 (23) | 202 (22.4) |
| Prostate | 77 (8.9) | 87 (9.7) |
| Colon or rectum | 123 (14.2) | 148 (16.4) |
| Lung | 99 (11.4) | 100 (11.1) |
| Other | 64 (7.4) | 83 (9.2) |

Mahé I, et al. *N Engl J Med*. 2025

DVT: deep vein thrombosis
PE: pulmonary embolism

# Primary Outcome

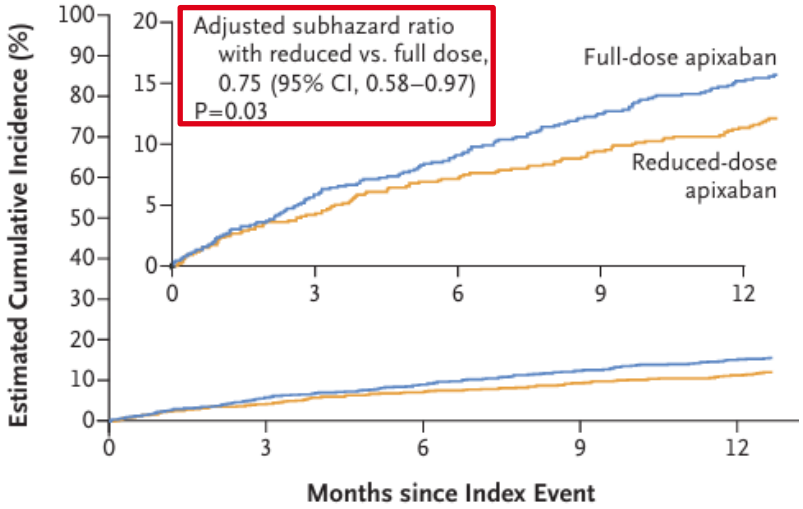
Reduced-Dose Group
18 patients (2.1%)
vs
Full-Dose Group
24 patients (2.8%)




Mahé I, et al. *N Engl J Med*. 2025

# Key Secondary Outcome

**B** Clinically Relevant Bleeding



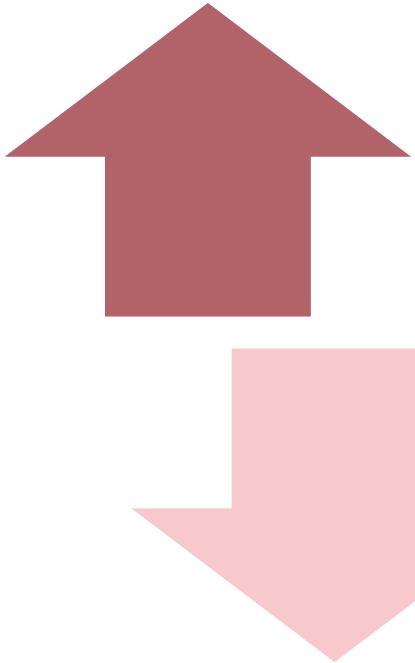

**No. at Risk**

| | | | | | |
|---|---|---|---|---|---|
| Full-dose apixaban | 900 | 796 | 725 | 682 | 593 |
| Reduced-dose apixaban | 866 | 795 | 736 | 662 | 619 |

Reduced-Dose Group
102 patients (12.1%)
vs
Full-Dose Group
136 patients (15.6%)

Mahé I, et al. *N Engl J Med*. 2025

# Assessment



## Strengths

- Study design
- Large sample size

## Limitations

- Included only European countries
- Did not include highest-risk cancers
- Duration of study
- Noninferiority margin

Mahé I, et al. *N Engl J Med*. 2025

# Key Takeaway

Using a reduced dose of apixaban for extended anticoagulant therapy is a safe option for cancer-associated thromboembolism after completion of 6 months of full-dose therapy

Mahé I, et al. *N Engl J Med*. 2025

# NCCN 2025 Guidelines

## Duration

Duration should be at least 3 months or as long as active cancer or cancer therapy

## Dosing of DOACs

Apixaban 10 mg PO every 12 hours for 7 days followed by 5 mg PO every 12 hours[a]

Edoxaban 60 mg daily after initial therapy with LMWH or UFH for at least 5 days

Rivaroxaban 15 mg PO every 12 hours for 21 days followed by 20 mg daily

[a] After 6 months of therapy, consider lower dose apixaban after assessment of patient's risk for recurrent VTE and bleeding

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Cancer-Associated Venous Thromboembolic Disease, Version 5.2025

NCCN: National Comprehensive Cancer Network
DOAC: direct oral anticoagulant

# Self-Assessment Question #3

**AP is a 65 yo F with breast cancer who presents to follow-up with her hematologist today. She has been on apixaban 5 mg twice daily for her DVT for the past 6 months. She had recently found the API-CAT and wanted to discuss it with the pharmacist in clinic to see if she was appropriate for a lower dose of apixaban.**

**Most notably, she had recently experienced a fall that did not result in bleeding, and her family is concerned of her falling and having a bleed. As the pharmacist for the clinic, would you recommend dose attenuation?**

A. No, her breast cancer makes her too high risk for thrombosis
B. No, she should stop anticoagulation due to her fall
C. No, she did not receive lovenox which is the recommended treatment for DVT
D. Yes, she completed at least 6 months of full anticoagulation

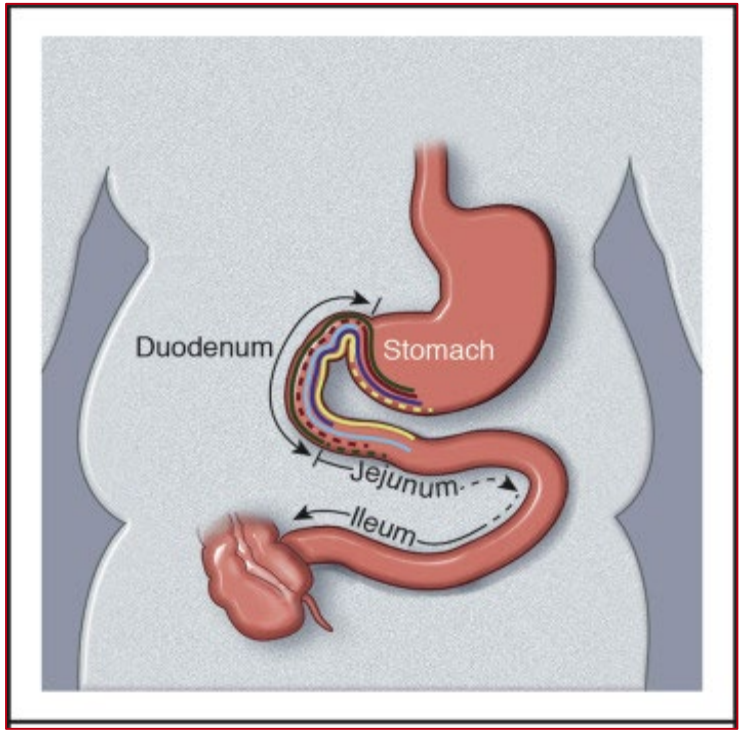
DVT: deep vein thrombosis

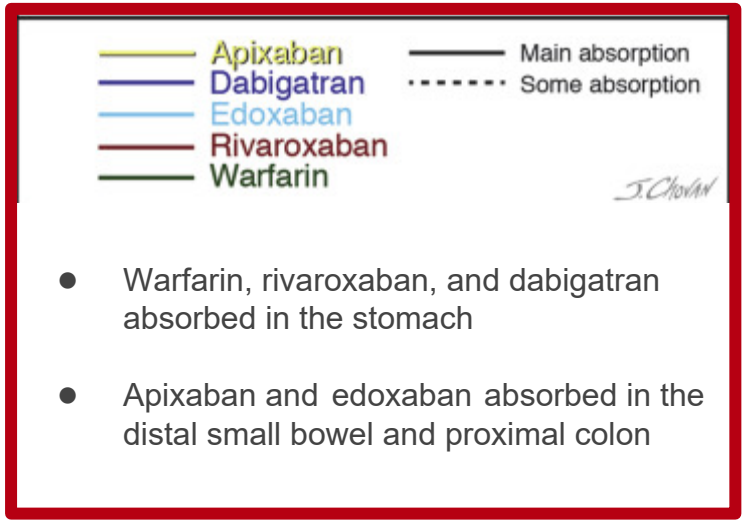
03

# Crossroad #3

*Cancer-Specific Pharmacokinetic Variability*

# DOAC Absorption




- Warfarin, rivaroxaban, and dabigatran absorbed in the stomach
- Apixaban and edoxaban absorbed in the distal small bowel and proximal colon

Martin KA, et al. *Am J Med*. 2017.

DOAC: direct oral anticoagulant

# Therapeutic DOAC Considerations in GI Surgery

DOACs are primarily absorbed in stomach and small bowel

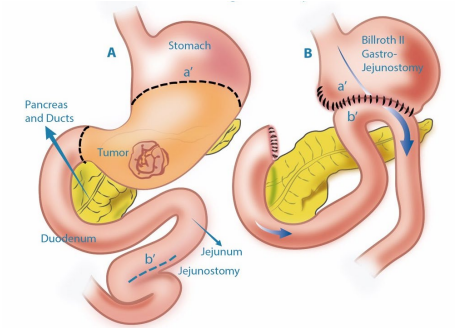
- Anatomic changes from GI surgeries can affect drug absorption and bioavailability
  - Motility and transit time of drugs can increase OR decrease
- Alternate routes of administration may also impact drug absorption, bioavailability, and stability
  - Important for patients requiring enteral feeding tubes

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Cancer-Associated Venous Thromboembolic Disease, Version 5.2025

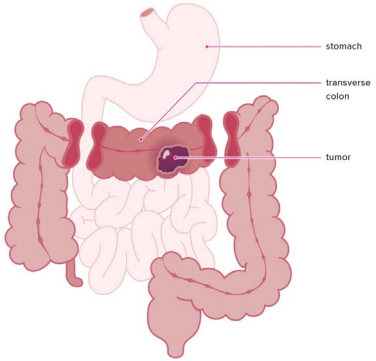
DOAC: direct oral anticoagulant
GI: gastrointestinal

# GI Oncologic Surgical Procedures

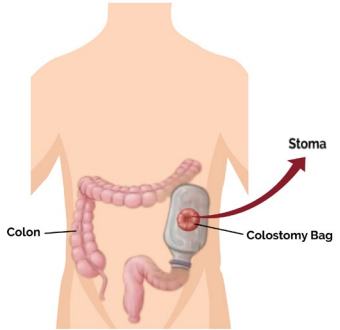
Total or partial gastrectomy




Distal resection or short bowel syndrome




Colectomy




The Surgeons Collective, 2023.
Bowel Cancer Foundation Trust. 2025.
Cincinnati Children's. Treations. 2025.

GI: gastrointestinal

# Surgical Procedures and DOAC Absorption

| Surgical Procedure | Apixaban | Rivaroxaban | Dabigatran | Edoxaban |
|---|---|---|---|---|
| **Total or partial gastrectomy** | Possibly reduced or not impacted | Possibly reduced or not impacted | Possibly reduced | Possibly reduced |
| **Distal resection or short bowel syndrome** | Possibly reduced | **Not impacted** | Possibly reduced | **Not impacted** |
| **Colectomy** | Possibly reduced | **Not impacted** | **Not impacted** | **Not impacted** |

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DOAC: direct oral anticoagulant

# DOAC Alternate Routes of Administration

| Enteral Feeding Tube Administration (NG, NJ, ND, G, J, GJ -tubes) | | | |
|---|---|---|---|
| **DOAC** | **Suspension vehicle/volume** | **Stability** | **Comments** |
| Apixaban | Water or D5W (60 mL) | 4 hrs | • Bioavailability is reduced if administered distal to stomach (ND or J -tube) |
| Rivaroxaban | Water (50 mL) | 4 hrs | • 15 mg and 20 mg tablets require enteral feeding following administration<br>• 2.5 mg and 10 mg tablets can be administered without food<br>• Absorption is reduced if administered distal to stomach (ND or J -tube) |
| Dabigatran | Do not administer through enteral feeding tube | | |
| Edoxaban | Water (2-3 oz) | Unknown | • Administer immediately |

**Nasogastric (NG), Nasojejunal (NJ), Nasoduodenal (ND), Gastrostomy (G), Jejunostomy (J), Gastrojejunostomy (GJ)**

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DOAC: direct oral anticoagulant

# DOAC Drug Level Monitoring

| DOAC | Effect on Drug Level After Surgery | Recommendations |
|---|---|---|
| Apixaban | Likely to remain in therapeutic range | Due to uncertainty and limited available information for some of these agents, it is recommended to consider obtaining drug levels post-surgery |
| Rivaroxaban | Less likely to remain in therapeutic range | |
| Dabigatran | Below therapeutic range | |
| Edoxaban | Likely to remain in therapeutic range | |

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DOAC: direct oral anticoagulant

# Self-Assessment Question #4

**Patient XY is a 56-year-old male with grade I gastric cancer. PMH includes hypertension and chronic jejunostomy tube.**

**They are D2 post-op partial gastrectomy.**

**Which anticoagulant would be appropriate for patient XY based on this information?**

A. Apixaban
B. Rivaroxaban
C. Enoxaparin
D. Fondaparinux

DOAC: direct oral anticoagulant

# Therapeutic Anticoagulant Preference in Gastric Cancer

## LMWH

- **Preferred in patients with gastric or gastroesophageal lesions**
- Use in caution with decreased renal function (CrCl < 30 mL/min)
- Difficulty with PO intake or frequent nausea/vomiting

## DOACs

- **Preferred in patients without gastric or gastroesophageal lesions (increased risk for hemorrhage)**
- Use in caution with decreased renal function (CrCl < 30mL/min)
- Use in caution with liver disease
- Consider drug interactions
- Consider drug absorption

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LMWH: low molecular weight heparin
DOAC: direct oral anticoagulant

# GI Cancer Representation in Clinical Trials

| CLOT | HOKUSAI | SELECT-D | CARVAGGIO |
|---|---|---|---|
| 2003 | 2017 | 2018 | 2020 |
| LMWH vs Warfarin | LMWH vs Edoxaban | LMWH vs Rivaroxaban | LMWH vs Apixaban |
| **None listed** | **5.2% (54/1046) Upper GI** | **2.7% (11/406) Gastric<br>7.4% (30/406) Upper GI** | **4.7% (54/1155) Upper GI** |

**Low representation of patients with gastro-intestinal (GI) cancers.**

Agnelli, et al. *N Engl J Med*. 2020.
Young, et al. *J Clin Oncol*. 2018.
Lee, et al. *N Engl J Med*. 2003.
Raskob, et al. *N Engl J Med*. 2017.

GI: gastrointestinal
LMWH: low molecular weight heparin

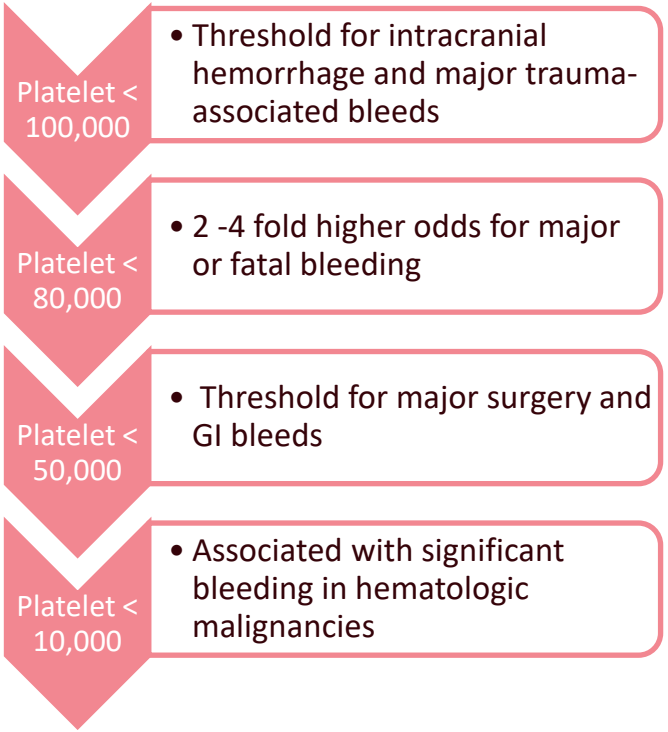
04

# Crossroad #4

*Anticoagulation in Thrombocytopenia*

# Thrombocytopenia

- Thrombocytopenia = platelet count < 150,000/μL
  - Anticoagulation is generally safe with platelet count ≥ 50,000/μL
  - Anticoagulation is generally held with platelet count < 25,000/μL
- Common complications increasing bleed risk
  - Reduced platelet counts from chemotherapy
  - Certain cancers have a higher bleed risk
    - Leukemia, brain tumors




Hsu C, et al. *Blood Adv*. 2023.
Escobar A, et al. *Support Care Cancer*. 2022.

# Management Strategies

## High risk for recurrent thromboembolism

- Continue therapeutic anticoagulation
  - Consider IVC filter placement in unable to continue therapeutic anticoagulation
- Maintain platelet count ≥ 50,000/µL (platelet transfusions)

## Low risk for recurrent thromboembolism

- Lower-dose anticoagulation with Enoxaparin with platelet count < 50,000/µL*
  - DOACs generally not recommended for < 50,000/µL
- More frequent monitoring for VTE if anticoagulation needs to be stopped

*Enoxaparin dosing strategies outlined in next slide

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VTE: venous thromboembolism
DOAC: direct oral anticoagulant

# Enoxaparin Dose Modifications

| Platelet Count | Dose Adjustment | Suggested Dose of Enoxaparin | Alternative Once-Daily Dosing Regimen |
|---|---|---|---|
| > 50,000/μL | Full-dose enoxaparin | 1 mg/kg twice daily | 1.5 mg/kg daily |
| 25,000 - 50,000/μL | Half-dose enoxaparin | 0.5 mg/kg twice daily | - |
| < 25,000/μL | Temporarily hold enoxaparin | | |

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# Enoxaparin Literature Review

| Study | Comparison | Outcomes | Conclusion |
|---|---|---|---|
| **Mantha, et al (2017)** | • Full dose enoxaparin at platelet count > 50,000/mcL<br>• Half dose enoxaparin at platelet count of 25,000–50,000/mcL<br>• Hold enoxaparin at platelet count < 25,000 | • No recurrent VTE events or major bleeding episodes when the anticoagulant dose was reduced or held. | • Validation of current guideline practices |
| **Vichaidit, et al (2025)** | • Recommended enoxaparin dose (n=169)<br>• Lower than recommended enoxaparin dose (n=60) | • 2.4% vs 5% recurrent VTE with full dose vs half dose<br>• 4.1% vs 1.7% bleeding events with full dose vs half dose | • Reduced-dose enoxaparin had a higher risk of recurrent VTE and lower bleeding risk |

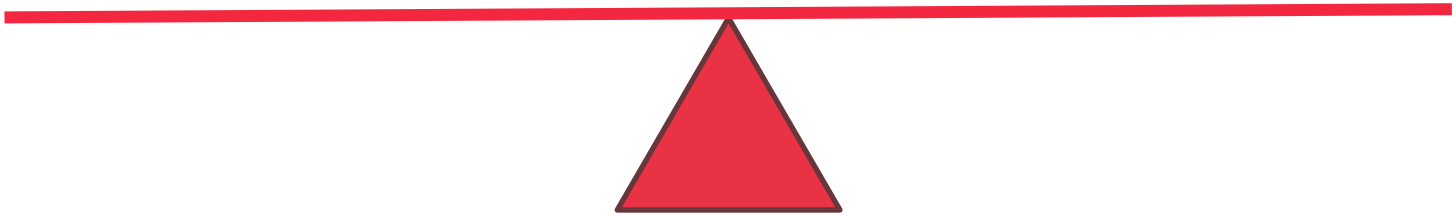
Mantha, et al. *J Thromb Thrombolysis*. 2017.
Vichaidt, et al. *Res Pract Thromb Haemost* . 2025.

VTE: venous thromboembolism

# Clinical Controversy

Full-dose anticoagulation with transfusion support to maintain platelet goal

Reduced-dose enoxaparin or temporary discontinuation of anticoagulation



# Bannow et al Systematic Review

| **Management of anticoagulation for cancer-associated thrombosis in patients with thrombocytopenia: A systematic review** | |
|---|---|
| Study design | Systematic review of the literature (N=121) |
| Population | • Included studies that reported recurrent venous thromboembolism (VTE) and major bleeding complications among patients treated with the two most common management strategies: therapeutic anticoagulation with platelet transfusion support and dose-modified anticoagulation for periods when the platelet count is <50 × 109/L. |
| Outcomes | • 27% of patients, regardless of their treatment strategy, experienced recurrent VTE<br>• 13% of anticoagulated patients (15% of all patients) experienced a major bleeding episode |
| **Key takeaway: Heightened risk of recurrent VTE in cancer-associated thrombosis (CAT) patients despite the thrombocytopenia. Neither management strategy was supported with this study.** | |

Bannow, et al. *Res Pract Thromb Haemost*. 2018.

VTE: venous thromboembolism

# TROVE

| Anticoagulation in cancer-associated thromboembolism with thrombocytopenia: a prospective, multicenter cohort study | |
|---|---|
| Study design | Prospective, multi-center, cohort study (N=121) |
| Population | • 75 (62%) patients were treated with full-dose anticoagulation and 33 (27%) patients with modified-dose anticoagulation |
| Outcomes | • The median platelet count was higher in patients who were initially started on full-dose anticoagulation, with a median of 65 000/μL compared with 37 000/μL in the modified-dose anticoagulation cohort (P < .001)<br>• In patients who initially received full-dose anticoagulation, the cumulative incidence of major hemorrhage at 60 days was 12.8% (95% CI, 4.9-20.8) compared with 6.6% (95% CI, 2.4-15.7) in the modified-dose anticoagulation group<br>• 4 recurrent VTEs occurred in patients who initially received full-dose anticoagulation and 1 occurred in a patient who did not receive anticoagulation |
| **Key takeaway: In select patients with cancer who develop VTE in the setting of thrombocytopenia, modified-dose anticoagulation was well tolerated with a low rate of recurrent VTE** | |

Carney, et al. *Blood Adv*. 2021.

VTE: venous thromboembolism

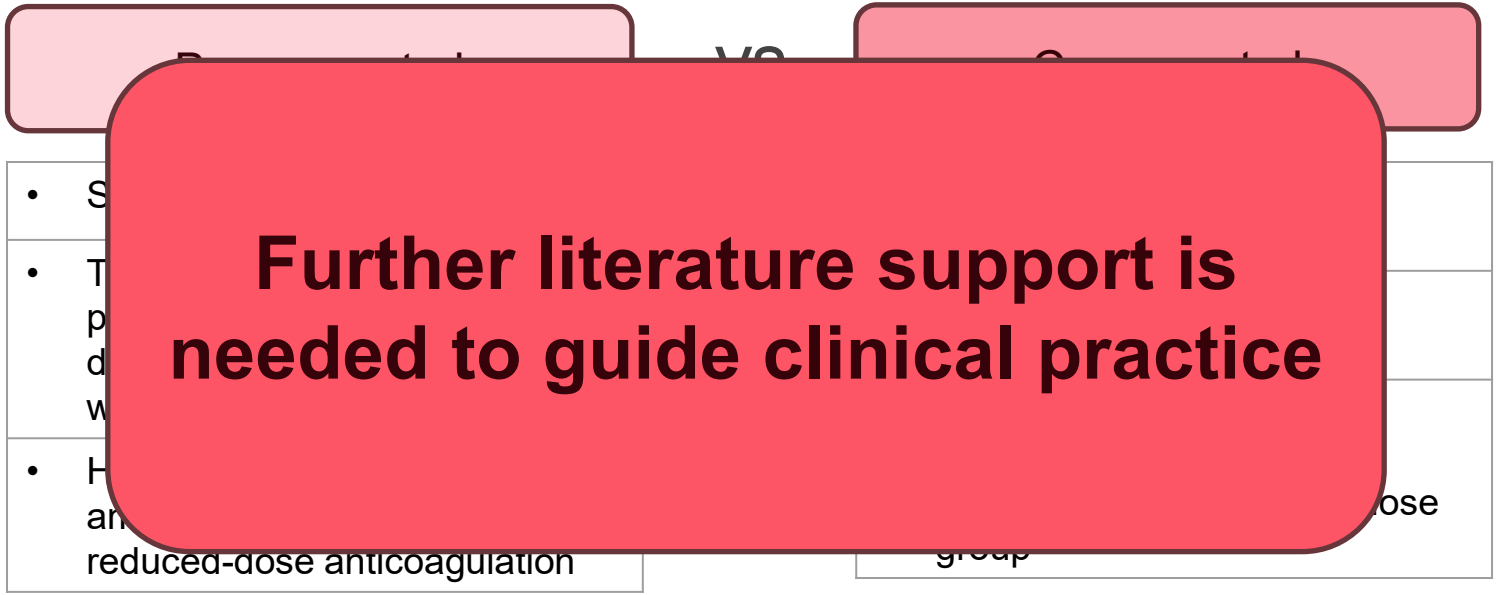
# Varying Literature Support Summary

| Bannow, et al | VS | Carney, et al |
|---|---|---|
| • Systematic review | | • Prospective, multicenter, observational study |
| • Therapeutic anticoagulation with platelet transfusion support vs dose-reduced anticoagulation when platelet count is <50,000 | | • Full dose vs reduced dose anticoagulation |
| • Higher risk of recurrent VTE among patients receiving reduced-dose anticoagulation | | • Higher rates of major hemorrhagic events and recurrent VTEs in the full-dose group |

Bannow, et al. *Res Pract Thromb Haemost*. 2018.
Carney, et al. *Blood Adv*. 2021.

VTE: venous thromboembolism

# Varying Literature Support Summary




Bannow, et al. *Res Pract Thromb Haemost*. 2018.
Carney, et al. *Blood Adv*. 2021.

# Self-Assessment Question #5

**Patient LJ is a 74-year-old female currently admitted for a severe COVID infection. She has a past medical history of advanced stage non-small cell lung cancer with metastasis to the brain and bilateral PEs (managed by long-term enoxaparin 1 mg/kg twice daily).**

**WBC = 12, Hgb = 9.8, Plt = 32**

**The team reaches out about how to manage her anticoagulation while she's thrombocytopenic. Which of the following options can be considered? (select all that apply)**

A. Stop the enoxaparin and switch to a DOAC
B. Discuss platelet goals with the team and maintain that goal with platelet transfusions while continuing her enoxaparin
C. Hold enoxaparin since platelet count is < 50,000
D. Discuss reducing enoxaparin dose to 0.5 mg/kg twice daily

05

# Implementation in Practice

# Principles for Anticoagulation

Prophylaxis

Treatment

# Key Considerations for Prophylaxis

## Malignancy

- Cancer type & site
- Active malignancy?
- Undergoing surgery
- Ongoing treatment

## Anticoagulant

- Dosing
- Duration
- Affordability

## Patient-Specific Factors

- Risk of recurrent VTE
- Bleeding risk
- Patient preference

# Key Considerations for Treatment

## Malignancy

- Cancer type & site

## Anticoagulant

- Dosing
- Duration

## Patient-Specific Factors

- Risk of recurrent VTE
- Bleeding risk
- Patient preference

# Take Home Points

01 Cancer patients are at a higher risk of developing venous thromboembolism

02 Prophylaxis is used in patients at high-risk for VTE while undergoing chemotherapy or post-operatively

03 DOAC treatment can be extended beyond 6 months at a lower dose

04 Utilizing LMWH is preferred in patients with gastric cancer

05 Consider dose reducing enoxaparin in patients with thrombocytopenia

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# Questions?

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# CAT-astrophe or Cure?

## Clinical Crossroads in Cancer Associated Thrombosis

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October 14, 2025