

# Thrombosis and Cancer

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# Disclosure

Consulting: Stago Diagnostica

# Topics

1. **Basics**
2. **Specifics** regarding cancer and VTE



Take-home points

# Defining the Clot

“Curbside”:

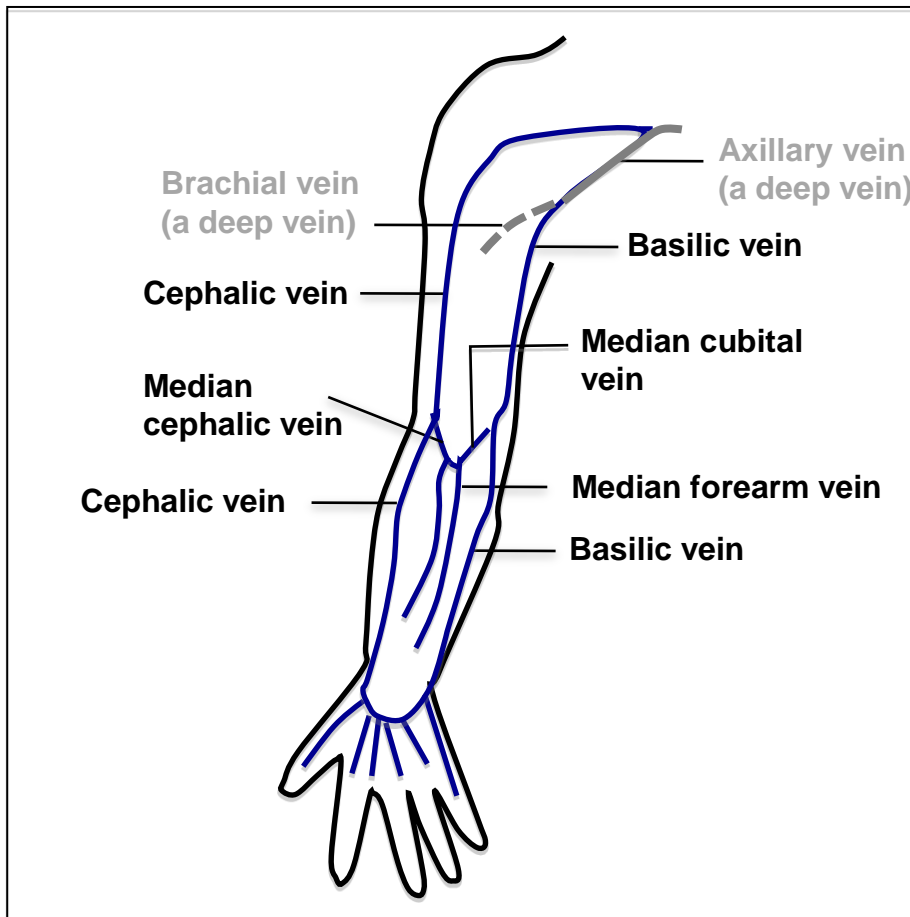
*“Quick question: Superficial clot in the right leg superficial femoral vein; not very symptomatic. My plan was to observe.”*

**Caveat!**

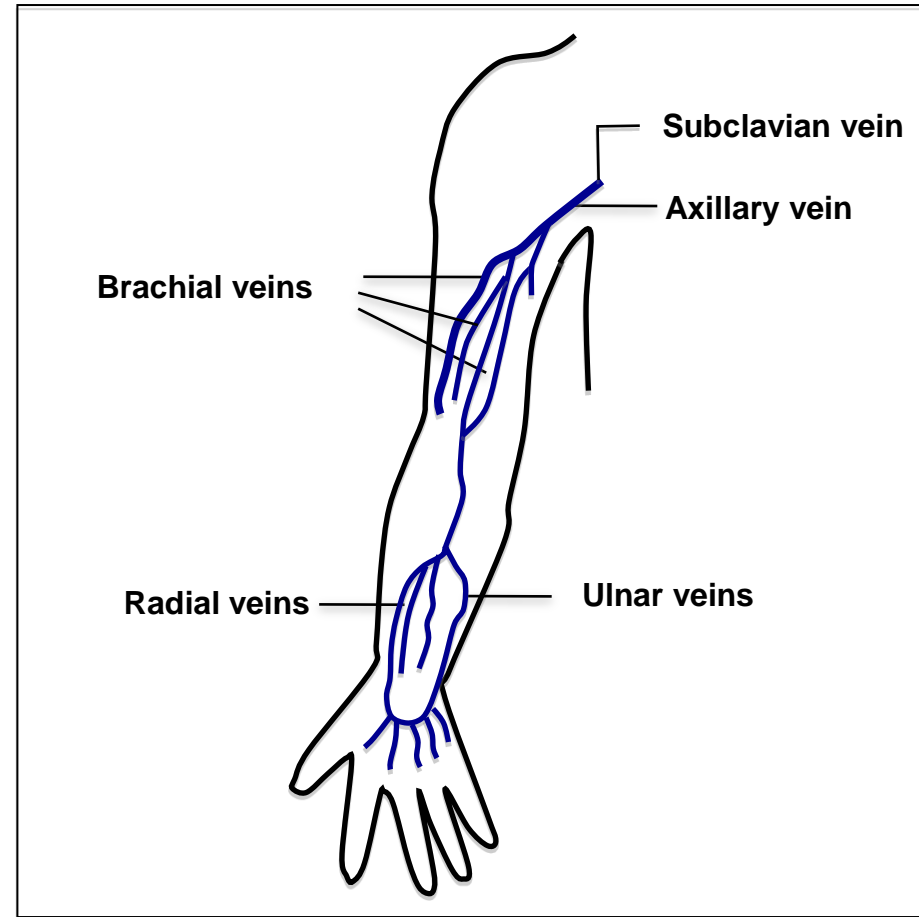
- “Superficial femoral vein” is NOT a superficial vein.
- This patient has a proximal leg DVT.

# Defining the Clot

## Superficial Veins



## Deep Veins



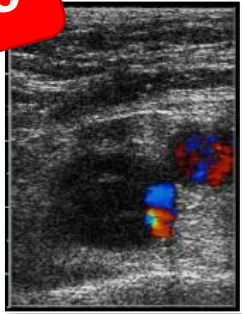
# Defining the Clot

## IMPRESSION:

1. Noncompressible popliteal vein, suspicious for possibility of nonocclusive deep venous thrombus. No definitive visible thrombus is noted, however.

## Imaging characteristics:

Example



Acute? Chronic?

### Acute" (= days to up to 3 months)

1. Dilated vein
2. "Spongy"
3. Hypo-echoic

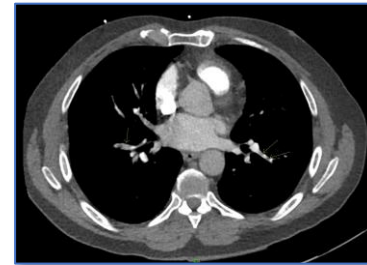
### "Chronic"

1. Retracted vein
2. Firm clot
3. Hyper-echoic

# Defining the Clot

## Sub-segmental PE

- 43 patients with diagnosis of **sub-segmental** PE
- 93 % received anticoagulation



Another radiologist reviewed the studies:

- 13/43 **(30%) of studies were negative**



[Batayneh O et al. ASH 2023, abstract # 4030]

# Defining the Clot



## Teaching points

Know limitations of Doppler ultrasound and CTA.

Question radiology reports.

Review imaging with Doppler technician / radiologist.



# VTE Risk Factors



## Weak risk factors (OR < 2)

Bed rest >3 days  
Diabetes mellitus  
Arterial hypertension  
Immobility due to sitting (e.g. prolonged car or air travel)  
Increasing age  
Laparoscopic surgery (e.g. cholecystectomy)  
Obesity  
Pregnancy  
Varicose veins

## Moderate risk factors (OR 2–9)

Arthroscopic knee surgery  
Autoimmune diseases  
Blood transfusion  
Central venous lines  
Intravenous catheters and leads  
Chemotherapy  
Congestive heart failure or respiratory failure  
Erythropoiesis-stimulating agents  
Hormone replacement therapy (depends on formulation)  
*In vitro* fertilization  
Oral contraceptive therapy  
Post-partum period  
Infection (specifically pneumonia, urinary tract infection, and HIV)  
Inflammatory bowel disease  
Cancer (highest risk in metastatic disease)  
Paralytic stroke  
Superficial vein thrombosis  
Thrombophilia

## Strong risk factors (OR > 10)

Fracture of lower limb  
Hospitalization for heart failure or atrial fibrillation/flutter (within previous 3 months)  
Hip or knee replacement  
Major trauma  
Myocardial infarction (within previous 3 months)  
Previous VTE  
Spinal cord injury



## Take-home point

VTE is typically multifactorial:

A....., B....., C.....

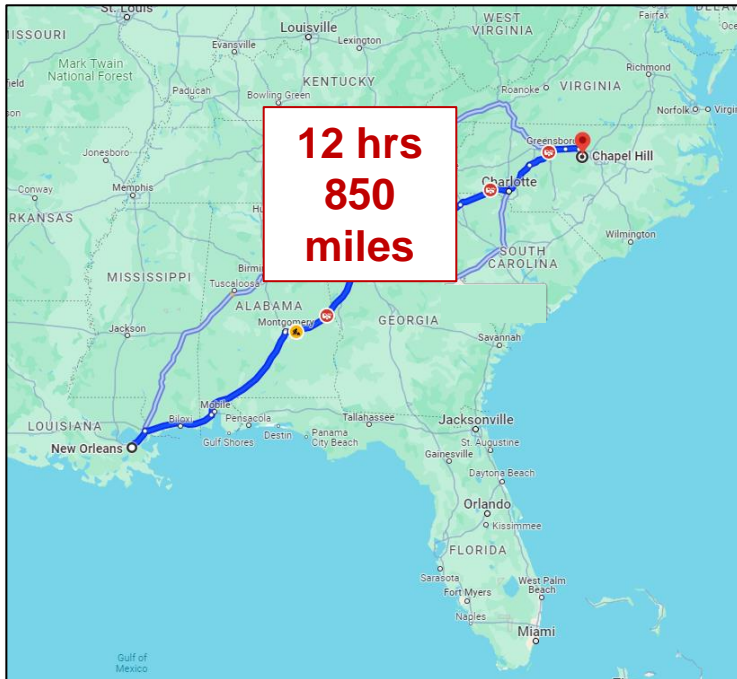
# Case

How long to anticoagulate?

- 79 year old healthy man
- Nov 2019:
  - Neck pain; PSA↑.
  - Newly diagnosed **metastatic prostate cancer**
- Jan 2020: L leg popliteal acute **DVT**. Rivaroxaban started.

# Case

How long to anticoagulate?



VTE risk factors: **A. Metastatic cancer,**  
**B. long-distance travel**

2023: PSA undetectable with Apalutamide.



**Take-home point**

VTE is typically multifactorial:  
A....., B....., C.....

# How Long to Anticoagulate?

**Conglomerate decision of:**

**1. Risk of Recurrent VTE**

A. ..., B. ..., C. ...



**2. Risk for Bleeding**

A. ..., B. ..., C. ...

**3. Patient Preference**





# How Long to Anticoagulate?

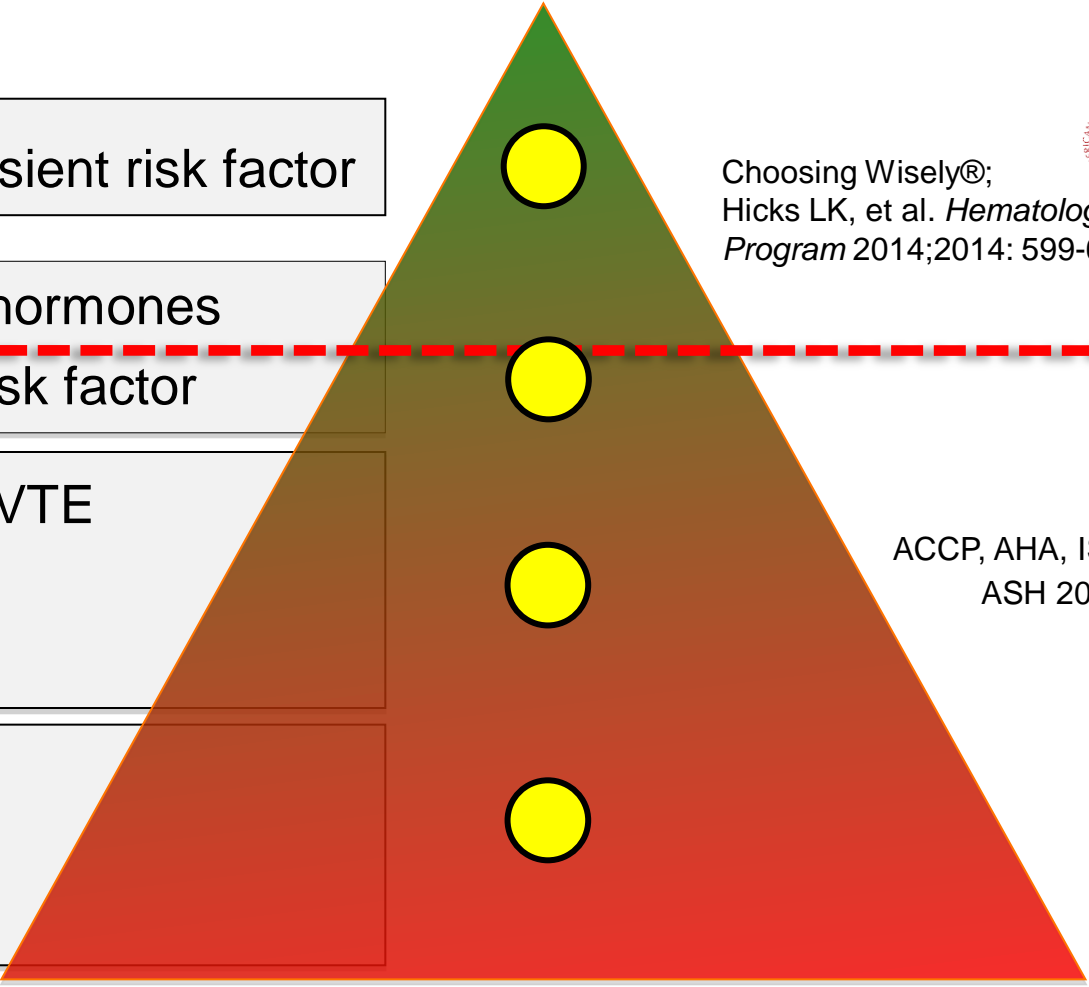


**3 months**

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**Long-term**

VTE due to major transient risk factor
Woman with VTE on hormones Non-major transient risk factor
Woman, unprovoked VTE <ul style="list-style-type: none"> <li>• DVT</li> <li>• PE</li> </ul>
Man, unprovoked VTE <ul style="list-style-type: none"> <li>• DVT</li> <li>• PE</li> </ul>



Choosing Wisely®;  
 Hicks LK, et al. *Hematology ASH Education Program* 2014;2014: 599-603



ACCP, AHA, ISTH, BJH  
 ASH 2020

Abbreviations: DVT = deep vein thrombosis; PE = pulmonary embolism



# DOAC Patient Assistance Programs



Get Help Paying For Your Medicine

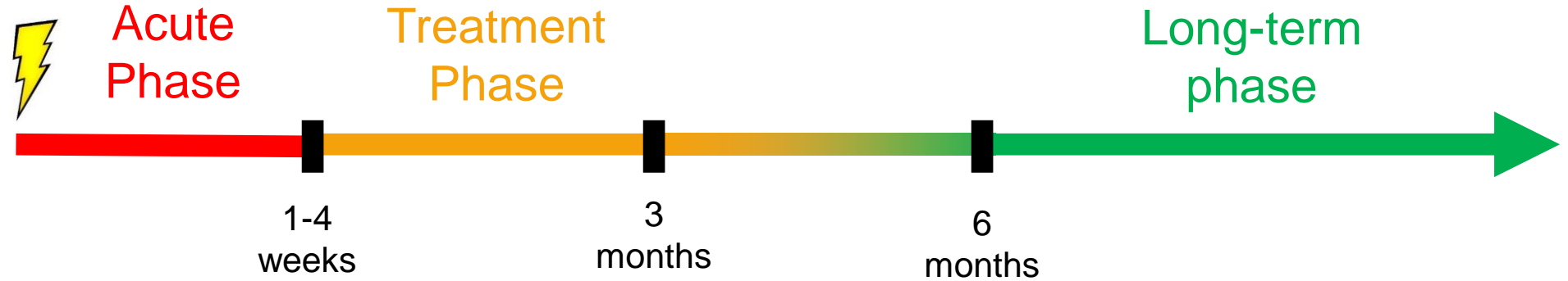
**Company XYZ** is committed to helping patients with access to our medicines.

Sign Up for **Drug XYZ** Savings Card

Home ▶ Savings & Support ▶ Savings Card & Support

Get Savings and Support for **Drug XYZ**

# DOAC Dosing



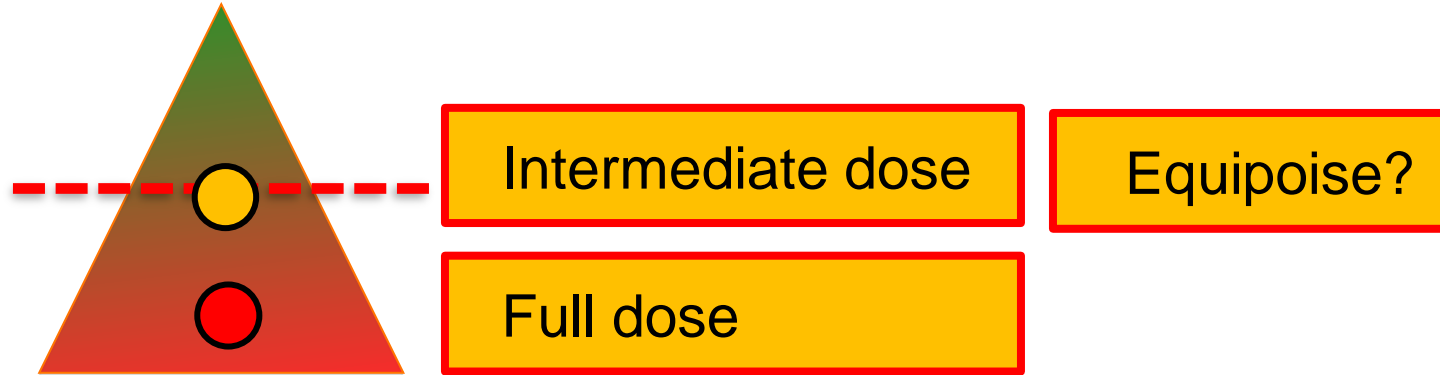
Apixaban	7 days 10 mg bid x 7 d	5 mg bid maintenance	2.5 mg bid
Rivaroxaban	3 weeks 15 mg bid x 3 weeks	20 mg qd maintenance	10 mg qd
Dabigatran	All the time 150 mg bid all the time		

# DOAC Dosing in Non-Cancer Patients

“Lower DOAC dose after 6 months?”



My Practice



Or:

- Elderly
- Lower body weight
- Higher risk bleeding



# B. Specifics

# DOAC Use in Cancer Patients

## Completed prospective randomized trials

	New Drug	Comparator	n	
1. HOKUSAI	Edoxaban	Dalteparin	1046	Rascob GE et al. NEJM 2018 Feb 15;378(7):615-624
2. SELECT-D	Rivaroxaban	Dalteparin	406	Young AM et al. J Clin Oncol 2018 Jul 10;36(20):2017-23
3. ADAM	Apixaban	Dalteparin	300	McBane RD et al. JTH 2020 Feb;18:411-421
4. CARAVAGGIO	Apixaban	Dalteparin	1155	Agnelli G et al. NEJM; 2020:1599-1607



“LMWH, edoxaban, rivaroxaban, or apixaban **preferred** over warfarin”

[Key NS, et al. *J Clin Oncol.* 2023; Jun 1;41(16):3063-3071]

# DOAC Use in Cancer Patients



ASCO

## **DOACs:**

*”Caution using DOACs in GI and GU cancers –  
and other settings of high risk for mucosal bleeding.”*

[Key NS, et al. *J Clin Oncol.* 2023; Jun 1;41(16):3063-3071]



**Caveat:** Check DOAC drug interactions!

# DOAC Dosing in Cancer Patients

“Can we lower DOAC dose after 6 months?”

Trial name	Treatment after 6 months	Size	Publication
Norwegian study	Apix 2.5 mg bid; single arm	N = 298	Published Larsen TL et al. J Thromb Haemost <b>2022</b> ;20:116-1181
EVE trial	Apixaban 2.5 bid vs. Apixaban 5 mg bid	N = 370	Published [McBane RD et al. J Thromb Haemost <b>2024</b> ;22:1704-1714]
API-CAT  ClinicalTrials.gov Identifier: NCT03692065	Apixaban 2.5 bid vs. Apixaban 5 mg bid	Goal: N = 1,722	Ongoing* [design: Mahe I et al. Thromb Haemost; <b>2022</b> ;122:646-656]



Take Home Point

- **Best dosing after 6 months unclear.**
- Wait for API-CAT study

\* Last patient f/u: Sept 2024; maybe ASH 2024 LBA?

# Guidelines

1

ASCO®

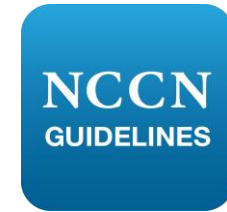
## Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: ASCO Clinical Practice Guideline Update

Key NS et al. *J Clin Oncol* 2020;38:496-520.

## Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: ASCO Guideline Update

Key NS, et al. *J Clin Oncol*. 2023; Jun 1;41(16):3063-3071.

2



Guidelines for Supportive Care

 Cancer-Associated Venous Thromboembolic Disease Version 2.2024

July 22, 2024

3

Isth  
International Society on  
Thrombosis and Haemostasis

[https://www.isth.org/page/Published\\_Guidance](https://www.isth.org/page/Published_Guidance)

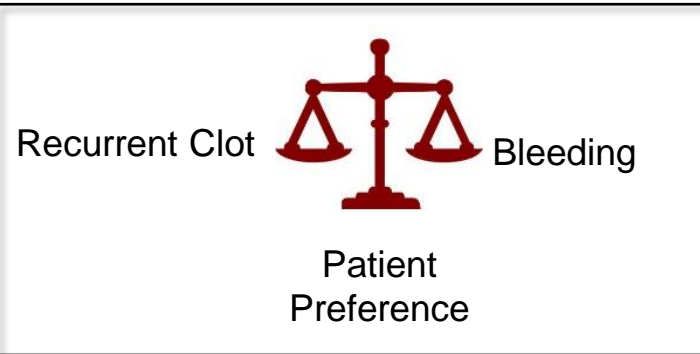
Last topic: 2019



# Incidental VTE



Key NS, et al. *J Clin Oncol.* 2020;38:496-520.



1. “Incidental PE and DVT should be treated in the same manner as symptomatic VTE”.

➔ Evidence quality: low; Strength of recommendation: moderate

2. “Incidental isolated sub-segmental PE: Case by case decision”.

➔ Evidence quality: insufficient; Strength of recommendation: moderate

3. “Incidental splanchnic vein thrombosis: Case by case decision”

➔ Evidence quality: insufficient; Strength of recommendation: moderate

# Thrombocytopenia in Cancer and VTE

1. **How recent** was the VTE?
2. **Bleeding risk factors?**
  - A. Thrombocytopenia, B....., C....., D.....

# Thrombocytopenia in Cancer and VTE

NCCN  
GUIDELINES

• Platelets > 50k  
full-dose

• Platelets 25-50k  
reduced dose

• Platelets < 25k  
no anticoagulation

[Streiff M et al. NCCN  
Guidelines Version 2.2024]

ASCO

• Platelets > 50k  
full-dose

• Platelets 20-50k<sup>1</sup>  
reduced dose

• Platelets < 20k<sup>2</sup>  
no anticoagulation

<sup>1</sup> relative contraindication

<sup>2</sup> absolute contraindication

[Key NS, et al. *J Clin Oncol.*  
2020;38:496-520]

ASCO

Vena cava filter?

- Role is uncertain, controversial
- No randomized studies exist
- Potential for harm

[Key NS, et al. *J Clin Oncol.* 2020;38:496-520]



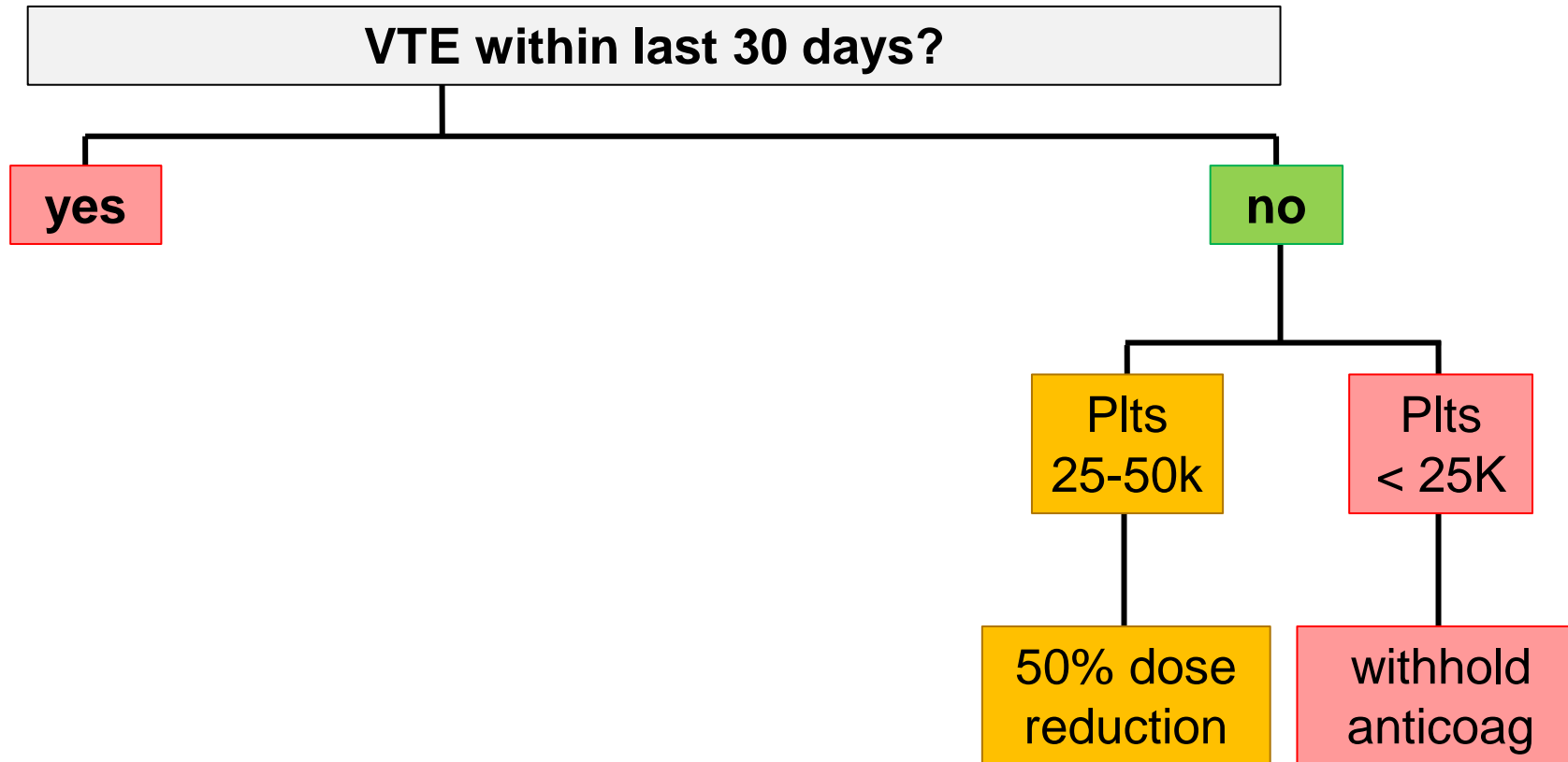


# Thrombocytopenia in Cancer and VTE

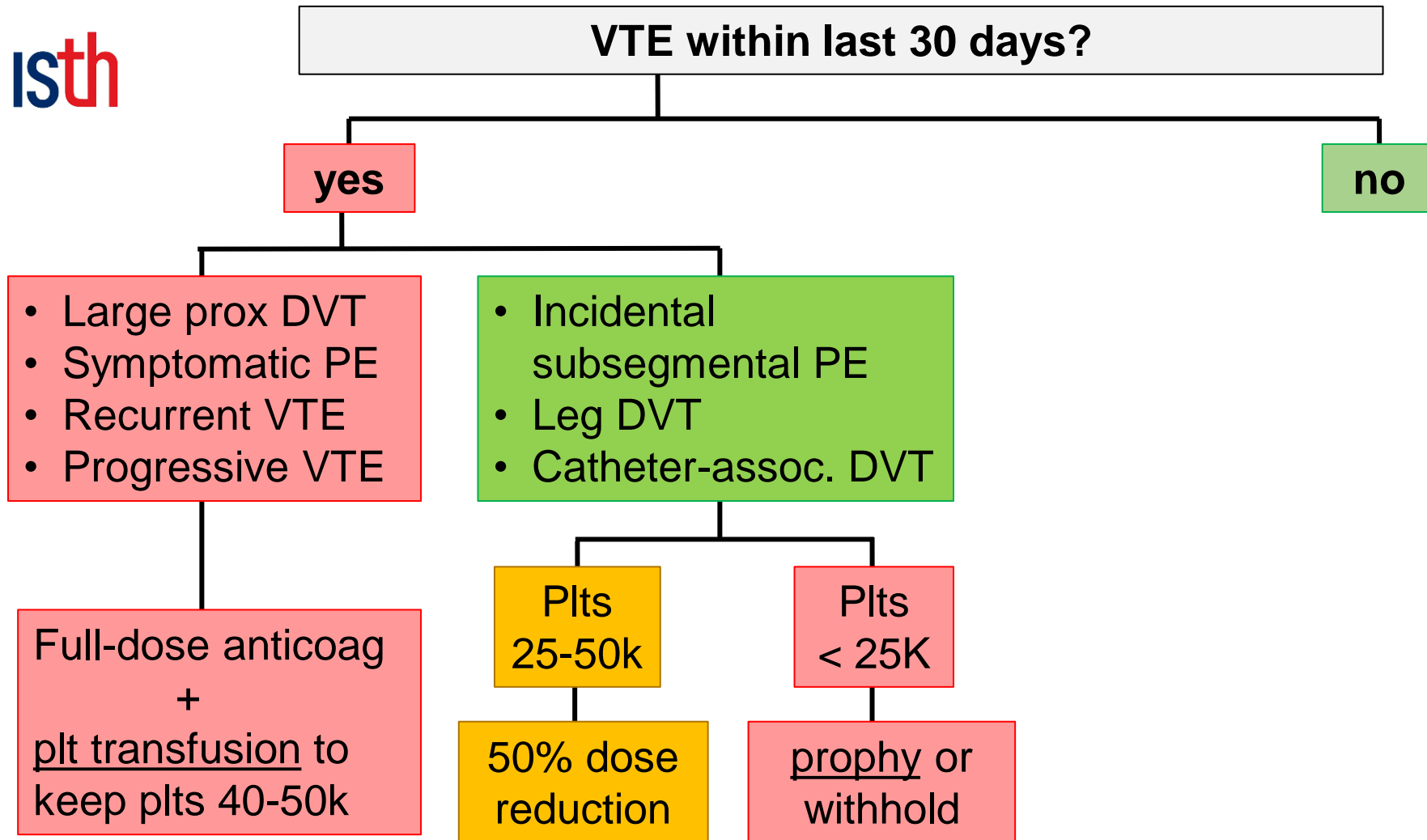
Platelet Count	Dose Adjustment	Suggested Dose of Enoxaparin
>50,000/ $\mu$ L	Full-dose enoxaparin	1 mg/kg twice daily
25,000–50,000/ $\mu$ L	Half-dose enoxaparin	0.5 mg/kg twice daily
<25,000/ $\mu$ L	Temporarily hold enoxaparin	

NCCN currently (7-2024) does NOT recommend use of DOACs with platelets <50k.

# Thrombocytopenia in Cancer and VTE



# Thrombocytopenia in Cancer and VTE



# Anticoagulation Failure

## Assessment

- Medication adherence?
- HIT?
- Mechanical vein compression from tumor?



Key NS, et al. *J Clin Oncol.* 2020;38:496-520.

## Management

- LMWH: use 2x/day; increase by 25%
- Consider switch to a different anticoagulant
- Consider adding aspirin

# C. Other

# Other

1. Severe Obesity + DOACs
2. Bariatric Surgery + DOACs



Isth  
International Society on  
Thrombosis and Haemostasis



[Martin K et al J Thromb Haemost. 2021 Aug;19(8):1874-1882]

3. Renal failure



[Parker K et al. J Nephrol 2022; Nov;35(8):2015-2033]

4. DOAC interruption for procedures

**PAUSE trial**

Douketis JD et al. 2019;179(11):1469-1478. doi:10.1001/jamainternmed.2019.2431]



5. Antiphospholipid syndrome 



**2023 ACR/EULAR antiphospholipid syndrome classification criteria**

Criteria

[Barbhaiya M et al. Ann Rheum Dis. 2023 Oct;82(10):1258-1270]

Thank you  
for your attention



*Desert Ironwood*