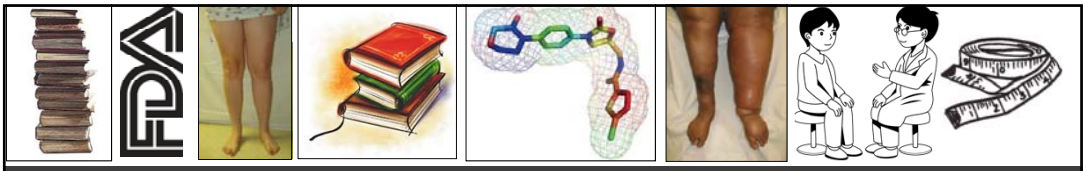


Cancer and Venous Thromboembolism

Stephan Moll, MD
University of North Carolina
Chapel Hill, NC

GASCO, Atlanta
Sept 8th, 2017

Disclosures

Consultant: Janssen, *Boehringer-Ingelheim, Portola*

Speaker bureau: *none*

Off label use drug discussion: *none*

Topics

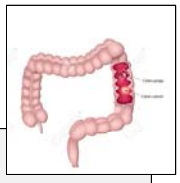
- **A DVT and PE Management**
  - 1 "Usual" DVT/PE
    - DOACs?
    - Failure of anticoagulation
    - Thrombocytopenia
  - 2 Catheter-associated thrombosis
  - 3 Incidental/asymptomatic DVT/PE
- **B Unprovoked VTE – Should One Screen for Cancer?**
- **C VTE Prophylaxis**
- **D Major Bleeding**

1 2 3 4

DVT and PE Management

1 Usual DVT/PE

DOACs in Cancer and VTE



For VTE in cancer patients, I use predominantely…

A. LMWH

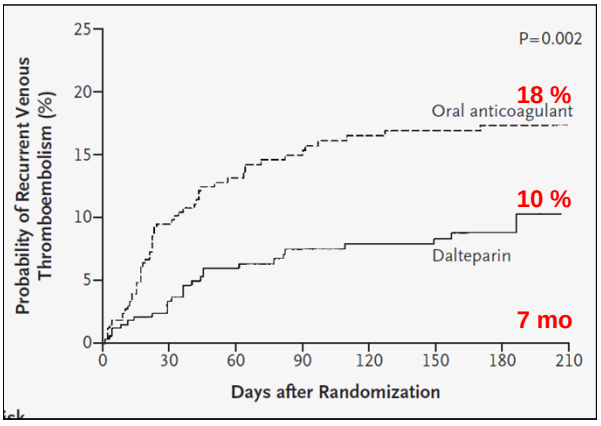
B. Warfarin

C. DOAC (Apixaban, Dabigatran, Edoxaban, Rivaroxaban)

D. Rituximab

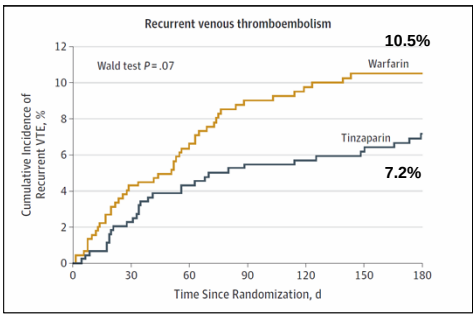
CLOT Trial

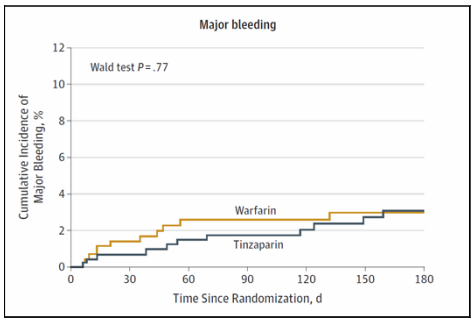
- Cancer and VTE: 772 patients; Dalteparin vs warfarin
- Heme malignancies: 70 patients (9 %)



[Lee AYY et al . NEJM 2003:349:146-153]

CATCH Trial





- 900 patients; 10.4 % heme malignancies
- Recurrent VTE at 6-month: HR 0.65 [95%CI, 0.41-1.03]; ***P* = .07**)
- No differences in major bleeding or overall mortality
- Clinically relevant non-major bleeding T vs W; HR 0.58 [95%CI, 0.40-0.84]; ***P* = .004**

[Lee AYY et al . JAMA 2015;314:677-86]

LMWH Trials in Cancer VTE

	Number of patients	LMWH	Dosage and duration
Patients with cancer			
CLOT; Lee et al (2003)[25]	672	Dalteparin	200 IU/kg once per day for 1 month, 150 IU/kg per day for 5 months
CATCH; Lee et al (2015)[26]	900	Tinzaparin	175 IU/kg once per day for 6 months
LITE; Hull et al (2006)[42]	200	Tinzaparin	175 IU/kg once per day for 3 months
CANTHANOX; Meyer et al (2002)[43]	146	Enoxaparin	1·5 mg/kg once per day for 3 months
ONCENOX; Deitcher et al (2006)[44]	122	Enoxaparin	1 mg/kg twice per day for 5 days, 1·0 mg/kg or 1·5 mg/kg once per day for 6 months
Unselected patients			
Lopez-Beret et al (2001)[45]	158	Nadroparin	0·1 mL/10 kg twice per day for 3 to 6 months
Romera et al (2009)[46]	241	Tinzaparin	175 IU/kg once per day for 6 months

Early maintenance was 10 days to 3 months. Long-term treatment was more than 3 months. LMWH=low-molecular-weight heparin.

Table 1: **Trials comparing LMWH with LMWH plus vitamin K antagonists in early maintenance and long-term treatment of venous thromboembolism**

[Farge D et al. LancetOncol 2016;17:e452-466]

LMWH Trials in Cancer VTE

Take home point

- LMWH gold standard.

DOACs in Cancer and VTE

Guidelines

1. ASCO 2015:
   - "LMHW recommended. DOACs not currently recommended"

[Lyman GH et al. J Clin Oncol 2015 Feb 20;33(6):654-6]

2. ACCP 2016:
   - "Suggest LMWH over DOAC or warfarin"

[Kearon C, et al. *Chest.* Feb;149(2):315-52]

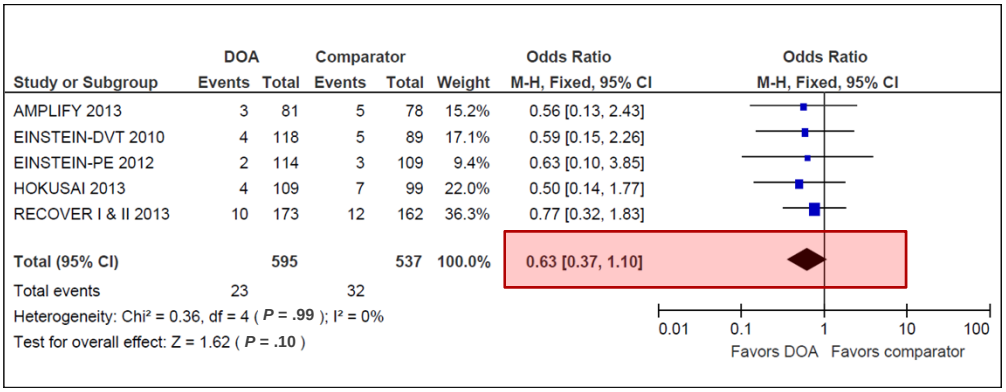
3. ACF 2016:
   - "Suggest LMWH"

[Khorana A et al. J Thrombo Thrombolys, Jan 2016]

DOAC and VTE in Patients With Cancer

Systematic review and meta-analysis

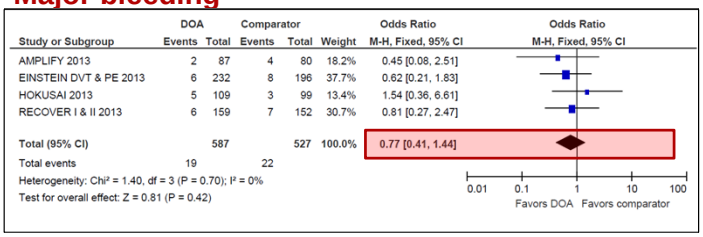
A. VTE Recurrence



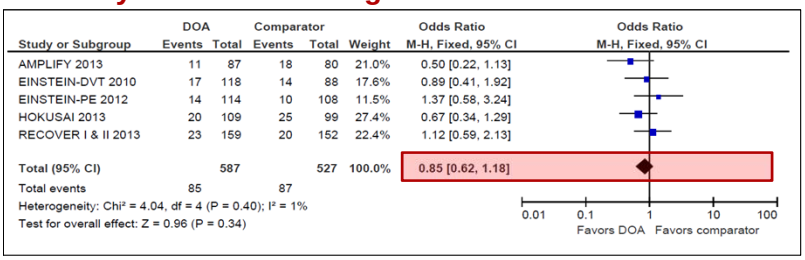
[Vedovati MC, et al. *Chest.* 2015;147(2):475-83]

DOAC and VTE in Patients With Cancer

B. Major bleeding



C. Clinically relevant bleeding



[Vedovati MC, et al. *Chest.* 2015;147(2):475-83]

DOACs in Cancer and VTE

Ongoing Trials

1. • *Edoxaban* vs dalteparin
   • Randomized, open label
   • Goal n = 1000 (*n = 1,028 completed 12/16/2016; now: f/u for 6 months)*

[ClinicalTrials.gov. identifier: NCT02073682]

2. • *Rivaroxaban* vs dalteparin (England)
   • "Select-d" trial
   • Goal n = 530 (*n=406; 12/19/2016; enrollment complete; now f/u: 6 mo*)

[PI: Young A. www2.warwick.ac.uk/fac/med/research/hscience/ctu/trials/cancer/select-d]

3. • *Apixaban* vs dalteparin
   • Randomized, open label
   • Goal n = 325 (n ="*about ½ done; Jan 4th, 2017*)

[ClinicalTrials.gov identifier: NCT02585713]

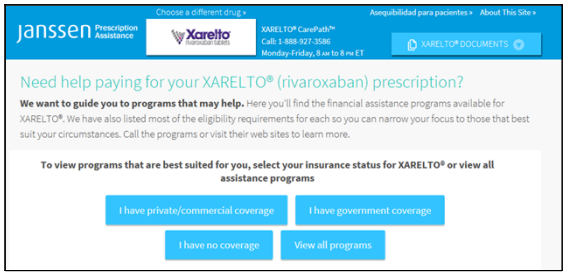
DOACs in Cancer and VTE

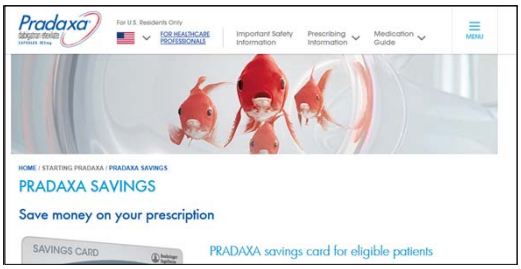
	CYP 3A4*	P-gp†
Inducers (may **reduce** DOAC plasma levels)	• **Chemotherapy:** **paclitaxel** • **Targeted therapies:** **vemurafenib** • **Hormonal therapies:** **enzalutamide** • **Immune modulators:** **dexamethasone, prednisone**	• **Chemotherapy:** vinblastine, doxorubicin • **Immunomodulators:** dexamethasone
Inhibitors (may **increase** DOAC plasma effect)	• **Chemotherapies:** Several antimitotic agents, etoposide, doxorubicin, idarubicin, cyclophosphamide, ifosphamide, lomustine • **Targeted therapies:** **imatinib, crizotinib** and other tyrosine kinase inhibitors • **Hormonal therapies:** tamoxifen, anastrozole, **bicalutamide, abiraterone** • **Immunomodulators:** **cyclosporine**, sirolimus, temsirolimus & tacrolimus • **Supportive care:** **aprepitant, fosaprepitant,** fentanyl, methadone, acetaminophen	• **Targeted therapies:** imatinib, nilotinib, lapatinib, sunitinib, crizotinib, vandetanib • **Hormonal therapies:** tamoxifen, enzalutamide, abiraterone • **Immunomodulators:** cyclosporine, temsirolimus, tacrolimus

*Moderate or strong interaction is indicated by red text. †Interaction with P-gp has been documented

Source: adapted from: Short NJ, et al. *Oncologist.* 2014;19(1):82-93. Lee AY, et al. *Blood* 2013;122(14):2310-2317. Slide courtesy of Dr. Agnes Lee - modified

DOAC and Cost





DOACs in Cancer and VTE

Take home point

- LMWH gold standard as of now.
- If LMWH not possible, then DOACs are an option.

Thrombocytopenia and Anticoagulation

Thrombosis Research 141 (2016) 104–105

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Variability in management of hematologic malignancy patients with venous thromboembolism and chemotherapy-induced thrombocytopenia

[Samuelson BT et al. Thromb Res 2016;141:104-105]

Thrombocytopenia and Anticoagulation

Methods

- 30 Ds surveyed
  - 10 heme-malignancy specialized
  - 10 non-malignant heme
  - 10 transfusion medicine
- In 19 academic centers (US, Canada)
- "At which platelet count do you feel comfortable having a patient receive prophy or full-dose anticoagulation?"
- 3 case scenarios
- 24/30 responded (80 %)

[Samuelson BT et al. Thromb Res 2016;141:104-105]

Case #2a

Case 2a: *62 year old man day + 4 after allogeneic hematopoietic cell transplant for myelofibrosis, found to have a segmental PE on CT performed for new onset dyspnea and mild tachycardia without hypoxia. His platelet count is 10,000. Lower extremity compression ultrasonography reveals a proximal DVT of the right leg. Which of the following would best describe your approach to managing this patient's thrombosis:*

	Responses
A Start therapeutic anticoagulation, transfuse to maintain platelet count >50,000/uL	52.9%
B Start therapeutic anticoagulation, transfuse to maintain a platelet count >20,000/uL	17.7%
C Place an IVC filter and postpone anticoagulation until platelet count spontaneously recovers to >50,000/uL	29.4%

[Samuelson BT et al. Thromb Res 2016;141:104-105]

Thrombocytopenia and Anticoagulation

ISTH Guidance

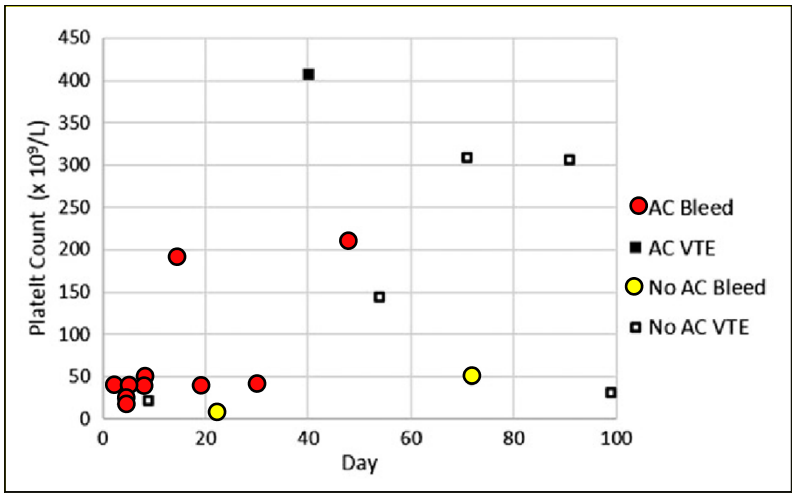
1. Platelets **> 50k**: full-dose anticoagulation

2. **Acute VTE** and platelets **< 50k**:
   - Plt transfusion to keep plts > 50k + full-dose anticoagulation
   - If plt transfusion not possible: IVC filter; once plts recovered: remove filter and anticoagulate

3. **Sub-acute or chronic VTE** and platelets **< 50k**:
   - Plts 25-50k: 50 % dose-reduction of LMWH
   - Plts < 25k: d/c anticoagulation

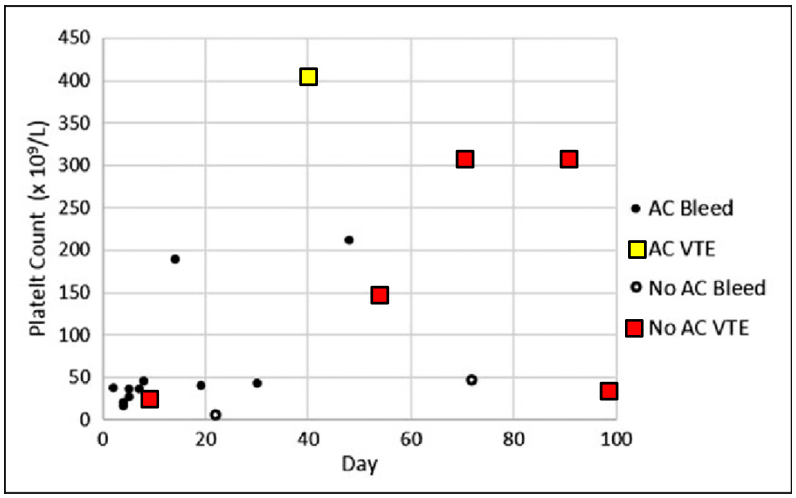
[Carrier M et al. J Thromb Haemost 2013;11:1760-1765]

Thrombocytopenia and Anticoagulation



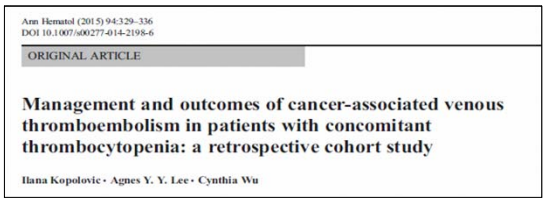
[Houghton D et al. Leukemia & Lymphoma 2017;58:2573–25]

Thrombocytopenia and Anticoagulation



[Houghton D et al. Leukemia & Lymphoma 2017;58:2573–25]

Thrombocytopenia + Anticoagulation



Ann Hematol (2015) 94:329–336
DOI 10.1007/s00277-014-2198-6

ORIGINAL ARTICLE

Management and outcomes of cancer-associated venous thromboembolism in patients with concomitant thrombocytopenia: a retrospective cohort study

Ilana Kopolovic · Agnes Y. Y. Lee · Cynthia Wu

[Kopolovic I, et al. *Ann Hematol.* 2015;94(2):329-336]

- 74 pts at 1 institution (Edmonton, Alberta, Canada)
- Prolonged plts <100k, for >4 wks
- *Conclusion*:
  - Heterogenous management
  - High-rate recurrent VTE and bleeding
  - More research needed

[Herishanu Y, et al. *Leuk Lymphoma.* 2004;45(7):1407–1411]
[Babilonia KM, et al. *Clin Appl Throm Hemost.* 2014;20(8):799-806]

Thrombocytopenia and Anticoagulation

Finding:

- Bleeds occur with low platelets on anticoagulation
- Recurrent clots occur late, when plts have normalized

[Houghton D et al. Leukemia & Lymphoma 2017;58:2573–25]

Consequence:

- No anticoagulation when platelets are low, but don't forget to start once platelets are higher.

Anticoagulate?

Conglomerate decision of:

1. Risk of recurrent VTE or progression
(a)…., (b)…., (c) …..

2. Risk for Bleeding
(a)…., (b)…., (c) …..

3. Patient preference

Recurrent VTE on Anticoagulation

Predictors of Recurrent VTE in Cancer Patients on Anticoagulation

CATCH Trial

- Metastatic disease
- Hepato-biliary cancer
- Active treatment with chemotherapy
- Hospitalization within previous 3 months
- ECOG performance status of 2
- Venous compression from bulky tumor or adenopathy

[Lee AYY et al . JAMA 2015;314:677-86]
[Khorana AA et al. ASCO 2015]

Recurrent VTE on Anticoagulation

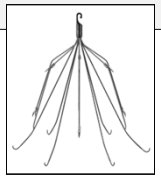
Options

- Increase LMWH by 20-25 %

[Carrier M et al J Thromb Haemost 2009;7:760-5]
[Farge D et al. LancetOncol 2016;17:e452-466]

- Switch from qd to bid LMWH
- Switch to a different anticoagulant (fondaparinux, warfarin, DOAC)
- Add Aspirin

- IVC filter



Recurrent VTE: ISTH Guidance

RECOMMENDATIONS AND GUIDELINES

Management of challenging cases of patients with cancer-associated thrombosis including recurrent thrombosis and bleeding: guidance from the SSC of the ISTH

M. CARRIER,* A. A. KHORANA,† J. I. ZWICKER,‡ S. NOBLE,§ A. Y. Y. LEE¶ and ON BEHALF OF THE SUBCOMMITTEE ON HAEMOSTASIS AND MALIGNANCY FOR THE SSC OF THE ISTH

Recommendation:

- "Increase LMWH 25 %"
- "Against IVC filters if anticoagulation can be given"

[Carrier M et al. J Thromb Haemost 2013;11:1760-1765]

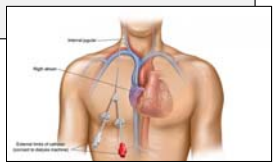
1 2 3 4

DVT and PE Management

2 Catheter-Associated DVT/PE

Case #1

54 year old woman with AML, moderate arm swelling; Doppler: catheter-associated subclavian and axillary DVT. Platelets 125k.



How do YOU treat?

A. Remove catheter, NO anticoagulation
B. Remove catheter, full-dose anticoagulation; observe platelets closely
C. Leave catheter in, NO anticoagulation
D. Leave catheter in, full-dose anticoagulate; observe platelets closely

Catheter-Associated VTE: Guideline

International Clinical Practice Guideline

1. Symptomatic CRT in cancer patients: we recommend anticoagulation for at least 3 months.
2. Leave catheter in, if functional + good symptom resolution; observe platelets closely.
3. Whether catheter is left in place or not: best length of anticoagulation not known – no standard approach established.

[Farge D et al. LancetOncol 2016;17:e452-466]

1 2 3 4

DVT and PE Management

3 Incidental/asymptomatic DVT/PE

Incidental VTE

- Up to 50 % of VTE in cancer patients are incidentally discovered
- Best treatment is poorly studied
- “Incidental”: Carefully review symptoms
- Sub-segmental PE: Review CT with good radiologist

[Di Nisio M et al. J Thromb Haemost 2015; 13: 880–3]

Incidental VTE

Journal of Thrombosis and Haemostasis, **13**: 880–883 DOI: 10.1111/jth.12883

RECOMMENDATIONS AND GUIDELINES

Diagnosis and treatment of incidental venous thromboembolism in cancer patients: guidance from the SSC of the ISTH

M. DI NISIO,*† A. Y. Y. LEE,‡ M. CARRIER,§ H. A. LIEBMAN¶ and A. A. KHORANA,** FOR THE SUBCOMMITTEE ON HAEMOSTASIS AND MALIGNANCY

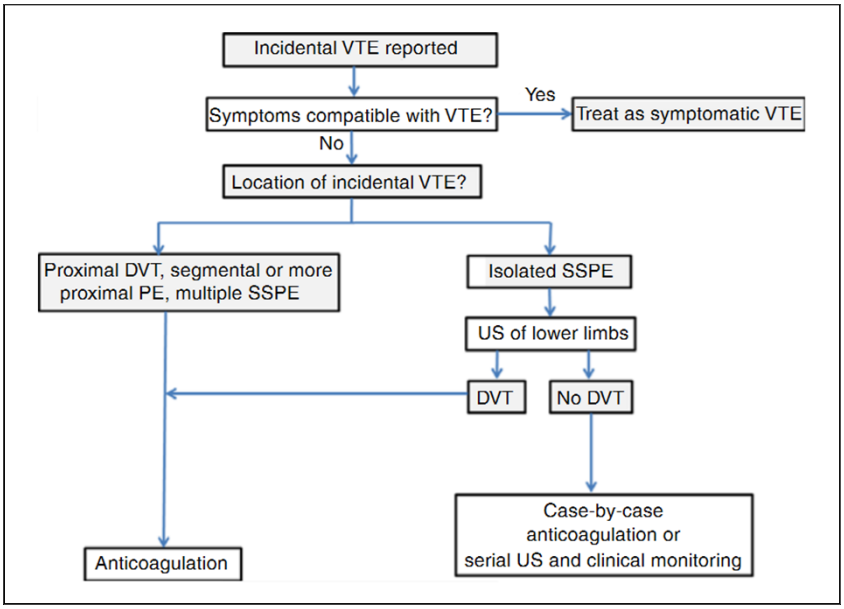
[Di Nisio M, et al. *J Thromb Haemost.* 2015;13(5):880-883]

Incidental VTE

Anticoagulation	Case-by-case	No anticoagulation
1. Symptomatic VTE 2. Prox DVT, or bigger PE (main, lobar, segmental, multiple subsegmental) 3. Isolated SSPE + prox DVT 4. Splanchnic vein thrombosis if acute	Isolated SSPE with distal DVT or without DVT. If no anticoagulation, then repeat B Doppler US after 1 wk in pts with distal DVT.	Splanchnic vein thrombosis, chronic or acute with very high risk of bleeding.

[O'Connell C, et al. *Hematology Am Soc Hematol Educ Program.* 2015;2015(1):197-201]
[Di Nisio M, et al. *J Thromb Haemost.* 2015;13(5):880-883]

Incidental VTE: ISTH Guideline



[Di Nisio M et al. J Thromb Haemost 2015; 13: 880–3]

Incidental VTE: ISTH Guideline

Conclusion

Incidental VTE:

- Treat as a symptomatic VTE, except a sub-segmental PE (case-by-case)

1 2 3 4

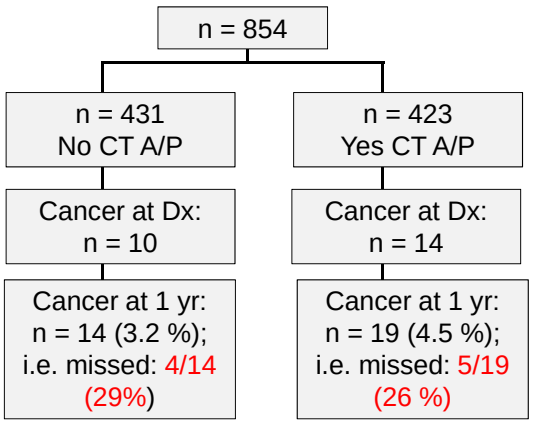
Unprovoked VTE

Should We Screen for Cancer?

Unprovoked VTE: w/u for Cancer?

[Delluc A et al. *J Thromb Haemost* 2017;15:1-4]

Unprovoked VTE: Screen for Cancer?



Tumors missed

- 2 leukemia
- 2 gyn
- 2 colorectal
- 1 melanoma
- 1 prostate
- 1 pancreatic

#3

Conclusion

No benefit from more extensive screening

[Carrier M, et al. *N Engl J Med.* 2015;373(8):697-704]

VTE: When to Screen for Cancer

Journal of Thrombosis and Haemostasis, **15**: 1–4 DOI: 10.1

RECOMMENDATIONS AND GUIDELINES

Occult cancer screening in patients with venous thromboembolism: guidance from the SSC of the ISTH

A. DELLUC,* D. ANTIC,† R. LECUMBERRI,‡ C. AY,§ G. MEYER¶ and M. CARRIER**

1 2 **3** 4

VTE Prophylaxis

VTE Prevention

ASCO 2014

Recommendation:

- Inpatients: Most patients
- Outpatients: selected high-risk patients
- MM: anti-angiogenesis agents with chemo and/or dex should receive prophylaxis: LMWH or ASA
- Major surgery:
  - Prophy before and for at least 7-10 days afterwards
  - Extension up to 4 weeks after major abdo/pelvic surgery with high-risk features.

[Lyman GH et a. JCO 2014;33:654-656]

Guideline – ASCO 2015

THE BOTTOM LINE

Key Recommendations

- Most hospitalized patients with active cancer require thromboprophylaxis throughout hospitalization. Data are inadequate to support routine thromboprophylaxis in patients admitted for minor procedures or short chemotherapy infusion.
- Routine thromboprophylaxis is not recommended for ambulatory patients with cancer. It may be considered for highly select high-risk patients.
- Patients with multiple myeloma receiving antiangiogenesis agents with chemotherapy and/or dexamethasone should receive prophylaxis with either low–molecular weight heparin (LMWH) or low-dose aspirin to prevent venous thromboembolism (VTE).
- Patients undergoing major cancer surgery should receive prophylaxis starting before surgery and continuing for at least 7 to 10 days.
- Extending postoperative prophylaxis up to 4 weeks should be considered in those undergoing major abdominal or pelvic surgery with high-risk features.
- LMWH is recommended for the initial 5 to 10 days of treatment of established deep vein thrombosis and pulmonary embolism as well as for long-term secondary prophylaxis for at least 6 months.
- Use of novel oral anticoagulants is not currently recommended for patients with malignancy and VTE.
- Anticoagulation should not be used to extend survival of patients with cancer in the absence of other indications.
- Patients with cancer should be periodically assessed for VTE risk.
- Oncology professionals should educate patients about the signs and symptoms of VTE.

[Lyman GH, et al. J Clin Oncol. 2015;33 (6):654-656]

1 2 3 4

Major Bleeding

Predictors of Bleeding in Cancer Patients

- Thrombocytopenia
- Coagulopathy
- Surgery, interventions
- Renal dysfunction
- Previous bleeding

- Type of tumor (bladder > gastric >
- Ulcerated tumor
- Performance status

[Menapace LA et al Thromb Res 140S1(2016);S93-S98]

1. Risk of recurrent VTE or progression
(a)…., (b)…., (c) …..

2. Risk for Bleeding
(a)…., (b)…., (c) …..

DOACs and Major Bleeding: Management

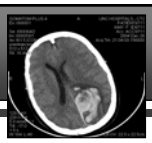
1
- Time (t ½)
- Lab tests (TT, ECT, anti-Xa, mass spec)
- Local measures, pressure
- Charcoal (2-3 hrs)
- HD (Dabigatran)

2
- *Anti-fibrinolytics*
  - Tranexamic acid
  - Aminocaproic acid

3
- *FFP*
- *Cryo*
- PCC
- *aPCC*
- *rVIIa*

4
- *Specific reversal agents*

DOAC Reversal Agents



1 **Dabigatran** — Idarucizumab

[Schiele F, et al. *Blood* 2013;121(18):3554-3562]
[Glund S, et al. *Blood.* 2014;124: Abstract 344]
[Pollack CV et al. NEJM 2015;373(6):511-20]

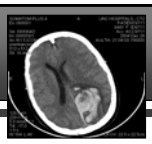
2 **Anti-Xa** — Andexanet

[Lu G, et al. *Nat Med.* 2013;19(4):446-453]
[Siegal DM, et al. *N Engl J Med.* 2015;373(25):2413-2424]

3 **Anti Xa + Anti-IIa** — PER-977 (aripazine, ciraparantag)

Ansell JE, et al. *N Engl J Med.* 2014;371(22):2141-2142]
[Ansell J. Am J Cardiovasc Drugs 2016 Feb 12. [Epub ahead of print]

TS8



Warfarin Major Bleeding

2013

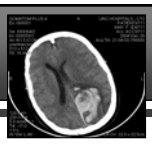
FDA Approval:
4-Factor Prothrombin Complex Concentrate (PCC)

1. ***Major Bleeding*** on warfarin

[Sarode R, et al. *Circulation.* 2013;128(11):1234-1243]

2. ***Urgent Surgery*** on warfarin

[Goldstein JN et al. Lancet. 2015;23;385(9982):2077-87]



Bleeding on Anticoagulants

UNC HEALTH CARE GUIDELINE
Emergent Anticoagulation Reversal

UNC HEALTH CARE

March 2016

Warfarin

TABLE 1: MANAGEMENT OF WARFARIN RELATED BLEEDING EVENTS

INR	Bleeding	Risk Factors for Bleeding	Intervention	Monitoring
Supratherapeutic, but < 4.5	No	Yes/Yes	Lower or omit next VKA dose (s), reduce subsequent dose (s)	Recheck INR the next day
4.5-10.0	No	Yes/Yes	Omit next VKA dose (s), reduce subsequent dose(s)	Recheck INR the next day
> 10	No	Yes/Yes	Vitamin K 1.25-2.5 mg PO* Omit next VKA dose (s), reduce subsequent dose(s)	Recheck INR the next day
Non-life threatening major bleed or surgery/procedure requiring emergent warfarin reversal			Vitamin K 5 - 10 mg IV + KCentra (4-factor PCC) (stocked in Pharmacy) INR 2.0-3.9: KCentra 25 units/kg x 1 (Max 2500 units) INR 4.0-6.0 KCentra 35 units/kg x 1 (Max 3500 units) INR > 6.0 KCentra 50 units/kg x 1 (Max 5000 units)	Recheck INR 10-30 minutes after 4-factor PCC administration. Due to short half-life of PCC, check INR q6hrs for 24 hours
Serious, life threatening bleed at ANY INR in the ED	Yes		Vitamin K 10 mg IV + KCentra (4-factor PCC) (stocked in Pharmacy) INR 1.4-2.0 or unknown: KCentra 35 units/kg x 1 (Max 3500 units) INR > 6.0: KCentra 50 units/kg x 1 (Max 5000 units) *SEE KCENTRA DOSING GUIDELINES AVAILABLE IN APPENDIX .8*	Recheck INR 10-30 minutes after 4-factor PCC administration. Due to short half-life of PCC, check INR q6hrs for 24 hours

American Society of Hematology Self-Assessment Program, 2011
KCentra Package Insert, CSL Behring, 2013
Witt, J Thromb Thrombolysis (2016) 41:187–205

* If patient is unable to tolerate PO, Vitamin K via IV route may be substituted for PO above

Dabigatran

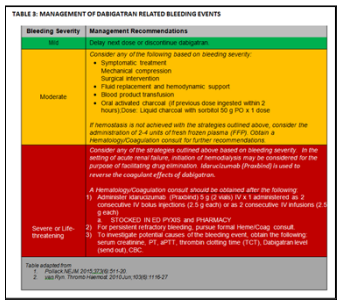


TABLE 3: MANAGEMENT OF DABIGATRAN RELATED BLEEDING EVENTS

Bleeding Severity	Management Recommendations
Mild	Delay next dose or discontinue dabigatran
Moderate	*Consider any of the following based on bleeding severity:* • Symptomatic treatment Mechanical compression Surgical intervention • Fluid replacement and hemodynamic support • Blood product transfusion • Oral activated charcoal (if previous dose ingested within 2 hours) Dose: Liquid charcoal with sorbitol 50 g PO x 1 dose *If hemostasis is not achieved with the strategies outlined above, consider the administration of 2-4 units of fresh frozen plasma (FFP). Obtain a Hematology/Coagulation consult for further recommendations.*
Severe or Life-threatening	*Consider any of the strategies outlined above based on bleeding severity. In the setting of acute renal failure, initiation of hemodialysis may be considered for the purpose of facilitating drug elimination. Idarucizumab (Praxbind) is used to reverse the coagulant effects of dabigatran.* *A Hematology/Coagulation consult should be obtained after the following:* 1) Administer idarucizumab (Praxbind) 5 g (2 vials) IV x 1 administered as 2 consecutive IV bolus injections (2.5 g each) or as 2 consecutive IV infusions (2.5 g each) a. STOCKED IN ED PYXIS and PHARMACY 2) For persistent refractory bleeding, pursue formal Heme/Coag consult. 3) To investigate potential causes of the bleeding event, obtain the following: serum creatinine, PT, aPTT, thrombin clotting time (TCT), Dabigatran level (send out), CBC.

Table adapted from
1. Pollack NEJM 2015;373(6):511-20.
2. Lippi Ann Thromb Haemost 2010 Jun;103(6):11 16-27

Anti-Xa Agents

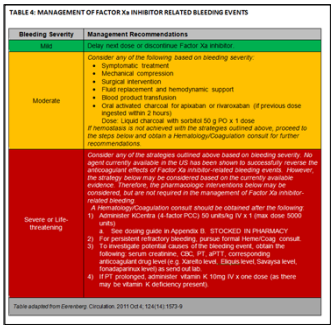


TABLE 4: MANAGEMENT OF FACTOR Xa INHIBITOR RELATED BLEEDING EVENTS

Bleeding Severity	Management Recommendations
Mild	Delay next dose or discontinue Factor Xa inhibitor
Moderate	*Consider any of the following based on bleeding severity:* • Symptomatic treatment • Mechanical compression • Surgical intervention • Fluid replacement and hemodynamic support • Blood product transfusion • Oral activated charcoal for apixaban or rivaroxaban (if previous dose ingested within 2 hours) Dose: Liquid charcoal with sorbitol 50 g PO x 1 dose *If hemostasis is not achieved with the strategies outlined above, proceed to the steps below and obtain a Hematology/Coagulation consult for further recommendations.*
Severe or Life-threatening	*Consider any of the strategies outlined above based on bleeding severity. No agent currently available in the US has been shown to successfully reverse the anticoagulant effects of Factor Xa inhibitor-related bleeding events. However, the strategy below may be considered based on the currently available evidence. Therefore, the pharmacologic interventions below may be considered, but are not required in the management of Factor Xa inhibitor-related bleeding.* *A Hematology/Coagulation consult should be obtained after the following:* 1) Administer KCentra (4-factor PCC) 50 units/kg IV x 1 (max dose 5000 units) a. See dosing guide in Appendix B. STOCKED IN PHARMACY 2) For persistent refractory bleeding, pursue formal Heme/Coag consult. 3) To investigate potential causes of the bleeding event, obtain the following: serum creatinine, CBC, PT, aPTT, corresponding anticoagulant drug level (e.g. Xarelto level, Eliquis level, Savaysa level, fonadaparinux level) as send out lab. 4) If PT prolonged, administer vitamin K 10mg IV x one dose (as there may be vitamin K deficiency present).

Table adapted from Eerenberg. Circulation. 2011 Oct 4; 124(14):1573-9.

Slide 49

TS8 Since this is a CME activity, we have to remove the brand names.
Trudy Stoddert, ELS, 1/21/2015

Questions?

Comments?

Coast Redwood (Sequoia sempivirens)

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