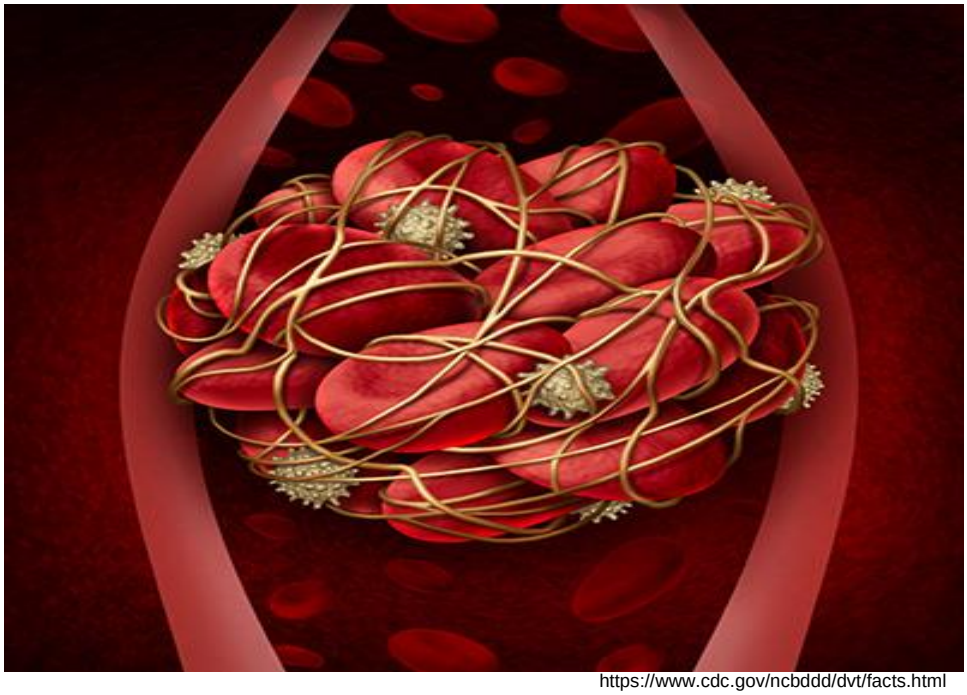
Use or Use Not:
DOACs for Treatment of Cancer-Associated Venous Thromboembolism



https://www.cdc.gov/ncbddd/dvt/facts.html

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LEARNING OBJECTIVES:

Pharmacists:

1. Describe the pathophysiology and risks to developing venous thromboembolism (VTE) in patients with cancer.
2. Evaluate clinical evidence of using direct oral anticoagulants (DOACs) for the treatment of cancer-associated VTE.
3. Discuss the DOACs' place in therapy for the treatment of cancer-associated VTE.

Pharmacy Technicians:

1. Identify risk factors to developing venous thromboembolism (VTE) in patients with cancer.
2. Compare the direct oral anticoagulants (DOACs) for the treatment of cancer-associated VTE.

3. Discuss the DOACs' place in therapy for the treatment of cancer-associated VTE.

Epidemiology[1-3]

- Second-leading cause of death in patients with cancer
- Up to 7-fold increase in risk of developing VTE compared to those without cancer
- Up to 6-fold increase in bleeding complications compared to those without cancer
- 15-20% of all VTE diagnoses are in patients with cancer

Pathophysiology[4-7]

- First described by French physicians Jean-Baptiste Bouillaud and Armand Trousseau in the early- to mid-1800s

Direct and Indirect VTE Mechanisms in Cancer
Overproduction of Procoagulants Tissue Factor (TF), Plasminogen Activator Inhibitor-1 (PAI-1), Cancer Procoagulant (CP)
Decrease in Anticoagulants Antithrombin III, Heparin Cofactor II, Proteins C and S, and Thrombomodulin
Increased Cytokine Release Tumour Necrosis Factor Alpha (TNF-α), Interleukin-1β (IL-1β)
Deficits in Coagulation Genes Factor V Leiden, Prothrombin
Damage-Associated Molecular Patterns (DAMPs)
Hypoxia
Chemotherapy e.g. platinum-based therapy, gemcitabine

Risk Factors for Cancer-Associated VTE[4,8-12]

- **Age >70**
- **Female**
- **Immobility**
- **Previous History of VTE**
- **Comorbidities**
  - Infection
  - Heart Failure
  - Heart Disease
  - Respiratory Disease

Khorana Risk Score[13]

Patient Characteristic	Risk Score
Very High Risk Cancer Site (Stomach, Pancreas)	+2
High Risk Cancer Site (Lung, Lymphoma, Gynecologic, Bladder, Testicular)	+1
Pre-chemotherapy platelet count ≥ 350 × 109/L	+1
Hemoglobin < 100 g/L or use of red cell growth factors	+1
Pre-chemotherapy leukocyte count > 11 × 10^9/L	+1

BMI ≥ 35 kg/m^2	+1

Khorana Risk Score Interpretation		
Risk Group	Total Risk Score	2.5-Month Rate of VTE
Low	0	0.3 - 0.8%
Intermediate	1-2	1.8 - 2.0%
High	≥3	6.7 - 7.1%

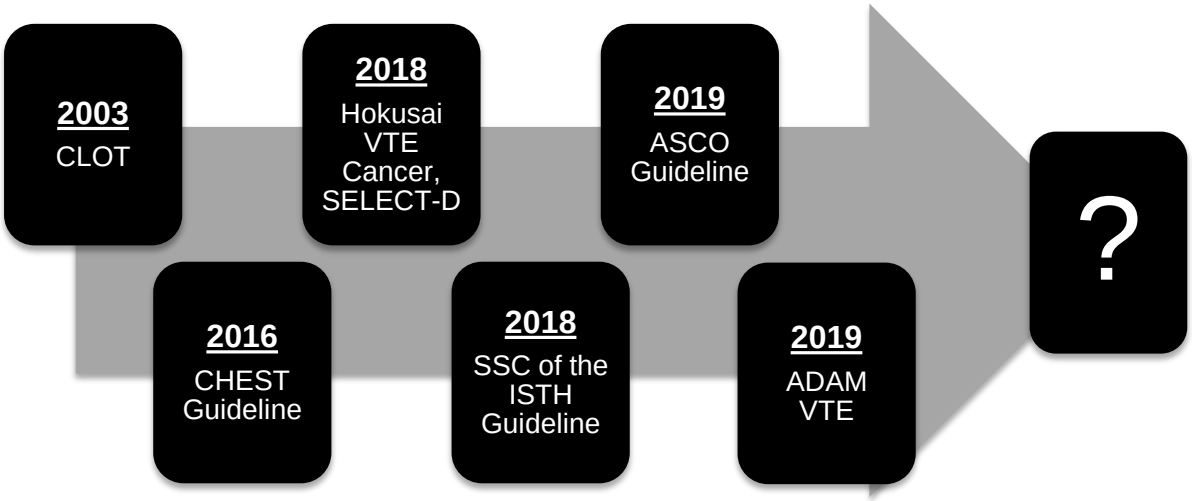
2016 CHEST Guideline Recommendation[15]:

- "For VTE and cancer, we suggest LMWH over VKA therapy, dabigatran, rivaroxaban, apixaban, or edoxaban."

CLOT Trial[14]

Population	Study Drugs	Duration	Outcomes
Active Cancer and Symptomatic VTE	**Dalteparin (n=336)** 200 IU/kg daily x 1 month, then 150 IU/kg daily **Warfarin (n=336)** Dose-adjusted to an INR of 2-3	6 Months	**Dalteparin vs. Warfarin:** Recurrent VTE: 27 vs. 53 (P=0.002) Major Bleeding: 6% vs. 4% (P=0.27) Any Bleeding: 14% vs. 19% (P=0.09)

Cancer-Associated VTE Treatment History[14-20]



Why DOACs over LMWH?

- No laboratory monitoring

- Ease of administration

Clinical Controversy: Is it safe and efficacious to use DOACs for treating cancer-associated venous thromboembolism?

DOACs in Cancer-Associated Venous Thromboembolism: A Literature Review

Raskob GE, van Es N, Verhamme P, et al. Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism (Hokusai VTE Cancer). *N Engl J Med.* 2018;378(7):615-624.	
Objective	To compare edoxaban to dalteparin for the treatment of cancer-associated venous thromboembolism (VTE).
Methods	
Study design	▪ Randomized, open-label, noninferiority trial performed at 114 centers in 13 countries (including the U.S.). ▪ Funding: by Daiichi Sankyo ▪ Study interventions: Edoxaban or dalteparin in 1:1 ratio o Edoxaban arm: LMWH for 5 days, then edoxaban 60 mg daily or 30mg daily o Dalteparin arm: 200 IU/kg once daily (maximum 18,000 IU/day) for 30 days, then 150 IU/kg once daily thereafter ▪ Follow-up: at 1 month, 3 months, 6 months, 9 months, and 12 months
Inclusion criteria	▪ 18 years or older ▪ Symptomatic or unsuspected DVT or PE ▪ Cancer (either active or diagnosed within 2 years prior to randomization) ▪ Intention for long-term treatment (≥ 6 months) with LWMH.
Exclusion criteria	▪ Thrombectomy, caval filter, use of a fibrinolytic agent ▪ >72 hours of treatment with an anticoagulant to treat the current episode ▪ Active bleed ▪ CrCl<30 mL/min ▪ History of HIT ▪ Life expectancy <3 months ▪ Platelet <50,000/mL ▪ Uncontrolled HTN ▪ Use of NSAIDS or DAPT during the study
Outcomes	▪ Primary: Composite of recurrent venous thromboembolism and major bleeding ▪ Secondary Outcomes: Recurrent VTE; major bleeding; clinically-relevant non-major bleeding (CRNMB)
Statistical Analysis	▪ 1000 patients would be required to observe 191 primary-outcome events and to give the trial 80% power ▪ Cox proportional-hazards regression model: used for analyzing the intention-to-treat population for the primary composite outcome to test for the non-inferiority of edoxaban to dalteparin. ▪ Non-inferiority confirmed by an upper limit of the hazard ratio confidence interval (CI) of less than 1.5 with a two-sided alpha level of 0.05
Results	

Baseline Characteristics

Total patients: 1046

Characteristic	Edoxaban (n=522)	Dalteparin (n=524)
Male – no.(%)	53.1%	50.2%
Age (yrs) – median (range)	64.3 ± 11	63.7 ± 11.7
BMI (kg/m^2) – median (range)	26.6 (15.1 - 50.4)	26.7 (14.9 - 46.2)
Qualifying VTE – no. (%)		
PE ± DVT	62.8%	62.8%
DVT Only	37.2%	37.2%
Incidental VTE	32%	33%
Metastatic Disease	52.5%	53.4%
Primary Tumor Type (%)		
Colorectal	15.9%	15.1%
Lung	14.8%	14.3%
Genitourinary	12.5%	13.5%
Breast	12.3%	11.5%
Pancreatic	9.4%	7.6%
Upper GI	6.3%	4%

Baseline Characteristics (Cont'd)

Outcomes

Outcome	Edoxaban (n=522)	Dalteparin (n=524)	HR (95% CI)	p value
Recurrent VTE or major bleeding (%)	12.8%	13.5%	0.97 (0.70-1.36)	Non-inferiority, P=0.006; Superiority, P=0.87
Recurrent VTE	7.9%	11.3%	0.71 (0.48-.06)	0.09
Major Bleeding	6.9%	4.0%	1.77 (1.03-3.04)	0.04 (NNH=34)
CRNMB	14.6%	11.1%	1.38 (0.98-1.94)	---
Death from Any Cause	39.5%	36.6%	1.12 (0.92-1.37)	---

Major Bleeding			
Gastrointestinal Cancer – Y/N	**Edoxaban**	**Dalteparin**	**p value**
No	18/386 (4.7%)	18/399 (4.5%)	---
Yes	18/136 (13.2%)	3/125 (2.4%)	0.0169 (NNH=9)

Edoxaban vs. dalteparin

- Discontinuation due to dosing inconvenience: 4% vs. 14.9%
- 6+ months of therapy: 58% vs. 54.4%
- Therapy for 12 months or until end of trial: 38.3% vs. 29.4%

Author's Conclusion

"Edoxaban was non-inferior to dalteparin with respect to the composite outcome of recurrent venous thromboembolism or major bleeding. The rate of recurrent venous thromboembolism was lower but the rate of major bleeding was higher with edoxaban than with dalteparin."

Critique

- STRENGHTS:
  - Randomized design
  - Use of modified intention-to-treat for analysis
  - Use of independent review committee
  - Assessment of adherence
  - Stratification by bleeding risk factors
  - Objectively-confirmed cancer diagnoses
- LIMITATIONS
  - Open-label design
  - Role of Daiichi Sankyo in collection and maintenance of the data, and statistical analysis

	○ Lower than expected primary endpoint ○ Difference in treatment duration between groups ○ Inclusion of only proximal DVTs
Take Home Points	Compared to dalteparin, edoxaban showed similar rates of recurrent VTE and CRNMB, but had significantly more major bleeding. Edoxaban should be avoided in patients with gastrointestinal cancers.

Young AM, et al. Comparison of an Oral Factor Xa Inhibitor With Low Molecular Weight Heparin in Patients With Cancer With Venous Thromboembolism: Results of a Randomized Trial (SELECT-D). *J Clin Oncol*. 2018 Jul 10;36(20):2017-2023.	
Objective	To assess venous thromboembolism (VTE) recurrence rates in patients with active cancer treated with either rivaroxaban or dalteparin.
Methods	
Study design	• Randomized, open-label, multicenter pilot trial, conducted at 58 sites across the United Kingdom, with patients recruited to the trial from 2013 to 2016. • Study Interventions: dalteparin or rivaroxaban in 1:1 ratio ○ Dalteparin dosing: 200 IU/kg SQ once daily x 30 d, then 150 IU/kg was administered subcutaneously once daily for 5 months ○ Rivaroxaban dosing: 15mg PO BID x 21 days, then 20mg daily for a total of 6 months • Follow-Up: Every 3-months for 1 year, and then every 6 months during year 2
Inclusion criteria	• Active cancer (excluding basal-cell and squamous cell skin carcinoma) ○ Definition: diagnosis of cancer in the previous 6 months; any treatment for cancer within the previous 6 months; recurrent or metastatic cancer; cancer not in complete remission • Primary objectively confirmed VTE, either symptomatic lower-extremity proximal DVT, symptomatic PE, or incidental PE • ≥ 18 years of age • Weight ≥ 40 kg • Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 2 • Adequate hematologic, hepatic, and renal function
Exclusion criteria	• Any previous treatment dose of anticoagulant or > 75 mg aspirin per day • History of VTE • Clinically significant liver disease • Bacterial endocarditis • Active bleeding or high risk of bleeding • Uncontrolled hypertension • Inadequate contraceptive measures if of childbearing potential • Concomitant use of strong CYP450 3A4 inhibitors or inducers, or P-glycoprotein inhibitors or inducers
Outcomes	Primary outcome: VTE recurrence Secondary outcomes: Major bleeding and clinically relevant non-major bleeding (CRNMB)
Statistical Analysis	• Cumulative incidence curves for the time to VTE recurrence and bleeding and survival were estimated using Kaplan-Meier estimates • Kaplan-Meier estimates were also obtained for bleeding and survival • Cox model was used to obtain hazard ratios (HRs) and associated 95% CIs • 400 patients (200 patients on each arm) would allow estimates of the primary outcome to be within a width of the 95% CI of 9%, assuming a 10% 6-month VTE recurrence rate
Results	
Patient Characteristics	

Characteristic	**Dalteparin (n=203)**	**Rivaroxaban (n=203)**
Male – no.(%)	98 (48%)	116 (57%)
Age (yrs) – median (range)	67 (34 - 87)	67 (22 - 87)
BMI (kg/m^2) – median (range)	26.6 (15.1 - 50.4)	26.7 (14.9 - 46.2)

Qualifying VTE – no. (%)			
Symptomatic VTE	98 (48%)	95 (47%)
PE	38 (18%)	40 (19%)
DVT	57 (28%)	53 (25%)
Incidental PE	105 (52%)	108 (53%)
Currently receiving cancer treatment – no. (%)	142 (70%)	140 (69%)
Chemotherapy	120 (85%)	113 (81%)
Radiotherapy	10 (7%)	6 (4%)
Targeted therapy	22 (15%)	21 (15%)
Endocrine therapy	15 (11%)	15 (11%)
Primary Tumor Type– no. (%)		
Colorectal	47 (23%)	55 (27%)
Lung	25 (12%)	22 (11%)
Breast	20 (10%)	20 (10%)
Pancreatic	11 (5%)	19 (9%)
Gastric	7 (3%)	4 (2%)

Enrollment and outcomes (Dalteparin vs. rivaroxaban – no.)

- Discontinued intervention: 90 vs. 86
  - Death: 33 vs. 28
  - Participant decision: 10 vs. 7
  - Withdrew consent: 11 vs. 5
  - Clinical decision: 8 vs. 7
  - Adverse event (VTE recurrence, bleeding, or other): 22 vs. 35
- Withdrawal: 20 vs. 16
  - Patient choice: 19 vs. 11
  - Clinical decision: 1 vs. 3

Outcomes

Dalteparin vs. Rivaroxaban:

- 6-month cumulative VTE recurrence rate: 11% vs. 4% (HR 0.43; 95% CI 0.19 - 0.99) (NNT=14)
- 6-month major bleeding rate: 4% vs. 6% (HR 1.83; 95% CI 0.68 - 4.96)
- CRNMB: 4% vs.13% (HR 3.76; 95% CI 1.63 - 8.69) (NNH=11)
- 6-month survival: 70% vs. 75%

Outcome	Dalteparin (n=203)	Rivaroxaban (n=203)
VTE Recurrence – no. (%)	18 (9%)	8 (4%)
DVT – no.	7	3
PE – no.	9	4
Other	2	2
Bleeding		
Major bleeding – no (%)	6 (3%)	11 (5%)
CRNMB – no. (%)	7 (3%)	25 (12%)

Author's Conclusions

- "Rivaroxaban was associated with relatively low VTE recurrence but higher CRNMB compared with dalteparin."

Critique

- STRENGHTS:
  - Randomized, multi-center design
  - High percentage of patients with VTE high-risk tumor type
  - Use of an independent data and safety monitoring committee
  - Adjudication of outcomes
- LIMITATIONS:
  - Open label, pilot trial
  - Small number of included patients and primary events
  - Slow rate of recruitment; could not investigate second random assignment of rivaroxaban vs. placebo for 5 months in patients with residual DVT or presentation of PE while on rivaroxaban
  - High numbers of withdrawal and discontinuation of therapy
  - No noted adherence measures
  - High mortality rates

	• OTHER:
	  ○ Difficult to extrapolate data to therapy beyond 6 months
	  ○ No analysis of chemotherapy agents in each group

Take Home Points	Compared to dalteparin, rivaroxaban was shown to have a lower rate of VTE recurrence, but a higher rate of clinically relevant non-major bleeding.

McBane RD 2nd, et al. Apixaban and dalteparin in active malignancy-associated venous thromboembolism: The ADAM VTE trial. *J Thromb Haemost.* 2019 Oct 20.	
Objective	To test the hypothesis that apixaban is associated with a significantly lower rate of major bleeding, compared to dalteparin, in the treatment of patients with active cancer and confirmed acute VTE
Methods	

Study design	• Multicenter, randomized, open-label, superiority trial, conducted at 28 sites in the United States, with patients recruited from 2015 to 2017
	• Study interventions: apixaban or dalteparin in a 1:1 ratio
	  ○ Apixaban dosing: 10 mg PO twice daily for 7 days followed by 5 mg PO twice daily
	  ○ Dalteparin dosing: 200 IU/kg subQ daily for the first month, then 150 IU/kg subQ daily for months 2 through 6
	• Follow-up: monthly for 6 months

Inclusion criteria	• 18 years or older • Confirmed active cancer ○ Evidence of cancer on cross-sectional or PET imaging, metastatic disease, and/or cancer-related surgery, chemotherapy or radiation therapy within 6 months • Life expectancy > 60 days • ECOG performance score ≤ 2 • Platelet ≥ 50,000/mcL • ALT/AST < 3 times upper limit of normal • INR ≤ 1.6 • Negative serum or urine pregnancy test for women of childbearing potential
Exclusion criteria	• Received anticoagulant therapy for > 7 days prior to randomization • Active bleeding • Child-Pugh Class B or C • Calculated CrCl < 30 mL/min • Known anticoagulant failure • Prior heparin-induced thrombocytopenia
Outcomes	Primary outcome: major bleeding Secondary outcomes: any thromboembolic recurrence including DVT, PE, fatal PE, or arterial thromboembolism
Statistical Analysis	• Log-rank tests used for the primary and secondary safety and efficacy endpoints • Secondary analysis of the primary safety endpoint performed in the intention-to-treat population • Categorical data assessed using chi-squared test • 80% power met by the inclusion of 300 patients, with an assumed 6-month cumulative incidence of 6% in the dalteparin arm and 1.4% in the apixaban arm • One-sided p value = 0.05
Results	

Baseline Characteristics

Characteristic	Apixaban (n=150)	Dalteparin (n=150)
Female – no. (%)	78 (52.0%)	77 (51.3%)
Age (yrs)	64.4	64.0
Body weight (kg) – mean (SD)	84.8 (23.2)	86.8 (20.5)
Qualifying VTE – no. (%)		
Any PE	81 (55.1%)	75 (50.7%)
Any DVT	71 (48.3%)	70 (47.3%)
Upper Extremity DVT	25 (17.0%)	21 (14.2%)
Lower Extremity DVT	46 (31.3%)	50 (33.8%)
Splanchnic VT	12 (8.2%)	27 (18.2%)
Concurrent Systemic Cancer Therapy	108 (73.5%)	110 (74.3%)
Primary Tumor Type– no. (%)		
Colorectal	18 (12.2%)	29 (19.6%)
Lung	32 (21.8%)	19 (12.8%)
Breast	7 (3%)	4 (2%)
Pancreatic/Hepatobiliary	23 (15.6%)	24 (16.2%)
Upper GI	7 (4.8%)	4 (2.7%)
Hematologic Malignancy – no. (%)	13 (8.7%)	15 (10%)
Previous VTE	8 (5.4%)	12 (8.1%)

Outcomes

Outcome	Apixaban (n=150)	Dalteparin (n=150)	HR (95% CI)	p value
Major Bleeding – no. (%)	0 (0%)	2 (1.4%)	0.0 (0.0)	0.138
CRNMB – no. (%)	9 (6.2%)	7 (4.2%)	---	---
Major Bleeding + CRNMB – no. (%)	9 (6.2%)	9 (6.3%)	---	0.8816
VTE Recurrence – no. (%)	1 (0.7%)	9 (6.3%)	0.099 (0.013-0.78)	0.0281 (NNT=17)
PE	0 (0.0)	1 (0.7%)	---	---
Lower Extremity DVT	0 (0.0)	4 (2.8%)	---	---
Upper Extremity DVT	0 (0.0)	2 (1.4%)	---	---
Mortality	23 (16%)	15 (11%)	---	0.3078

Quality of Life Survey Summary:

- Favors apixaban: excessive bruising, added stress, worry, difficulty of administration, irritation, frustration, impacted quality of life, drug satisfaction, burden
- Favors dalteparin: confidence in protection from clots
- Neutral: fear of bleeding, diet limitations

Apixaban vs. dalteparin: Refused further treatment: 6 vs. 22 (P=0.0012)

Author's Conclusions

"Apixaban was associated with low major bleeding and VTE recurrence in cancer patients."

Critique

STRENGHTS:

- Randomized, multi-center design
- Performed medication reconciliations and monitored drug compliance at follow-up
- Allowed for temporary interruption/adjustment of anticoagulant for invasive procedures
- Adjudication of outcomes
- Assessed quality of life

LIMITATIONS:

- Open label design
- Small sample size
- Lower number of upper GI cancers compared to other trials
- Included patients on another anticoagulant prior to the study period
- Small number of VTE recurrences, major bleeding, CRNMB, and mortality
- Primary investigator responsible for trial design and oversight, data collection/interpretation, and statistical analysis

OTHER:

	• No analysis of chemotherapy agents in each arm • Cannot extrapolate to treatments > 6 months • High proportion of patients with upper extremity and splanchnic VT • Did not provide data on incidental VTE • Included patients with history of VTE • Funded by a grant from the Bristol Myer Squibb Pfizer Alliance
Take Home Points	Compared to dalteparin, apixaban had a lower rate of recurrent VTE and similar rate of bleeding. This trial's small number of VTE recurrences and bleeding events relative to other studies limits its applicability.

Summary of Additional Literature[21-25]

Study	Design	Duration	Study Drug(s)	Outcomes	Leading Cancer Types
Oh et al. 2019 (n=123)	Retrospective	Median: 95 days (IQR 2-406)	Rivaroxaban	-Major bleeding: 4.9% -Minor bleeding: 9.8% -Recurrent VTE: 0.9%	Colorectal (13%), Lung (13%), Stomach (8.9%)
Sato et al. 2019 (non-cancer, n=95; active cancer, n=92)	Retrospective	Median: 77 days (IQR 23-189)	Edoxaban, Rivaroxaban, Apixaban	**Non-Cancer vs. cancer patients:** **Clinically Relevant Bleeding:** 3.2% vs. 9.8% (P=0.078) **Recurrent VTE:** 1.1 % vs. 2.2% (P=0.328)	Gynecological (28.3%), GI (19.6%)
Niklaus et al. 2018 (n=90)	Retrospective	Mean: 169 days vs. 110 days	Rivaroxaban vs. Enoxaparin	**Rivaroxaban vs. Enoxaparin:** **Recurrent VTE:** 9% vs. 13% (p=0.74)	Did Not Assess
Raskob et al. 2016 (n=771)	post hoc of Hokusai VTE	Median: 213 days (IQR 176–358)	Edoxaban (n=378) vs. Warfarin	**Edoxaban vs. Warfarin:** **Recurrent VTE:** 4% vs. 7% (P=0.0007) **Clinically relevant bleeding:** 12% vs. 19% (P=0.017)	Breast (18%), Prostate (14%), Colorectal (10%); Gastric (1%)
Agnelli et al. 2015 (n=159 with active cancer)*	post hoc of AMPLIFY	6 months	Apixaban vs. Warfarin	**Apixaban vs. Warfarin:** **Recurrent VTE:** 3.7% vs. 6.4% (95% CI 0.13–2.37) **Major bleeding:** 2.3% vs. 5.0% (95% CI 0.08–2.46)	Prostate (15.9%), Breast (14.8%), Colon (12.5%)

Rivaroxaban dosing: 15mg PO BID for 21 days, then 20mg daily
Edoxaban dosing: Parental anticoagulant for 5 days, then 30mg or 60mg daily
Apixaban dosing: 10mg BID for 7 days, then 5mg BID

*Study population included patients who had active cancer and a history of cancer

Work in Progress[26,27]

Apixaban for the Treatment of Venous Thromboembolism in Patients With Cancer: A Prospective Randomized Open Blinded End-Point (Probe) Study [CARAVAGGIO]	
Intervention:	Apixaban vs. Dalteparin
Primary Outcome:	Recurrent VTE (symptomatic or incidental)
Included Patients:	1168
Estimated Completion Date:	December 2019

Summary of Primary Literature

Hokusai VTE Cancer (edoxaban)

VTE: Similar Risk

Major Bleeding: Increased Risk

CRNMB: Similar Risk

SELECT-D (rivaroxaban)

VTE: Decreased Risk

Major Bleeding: Similar Risk

CRNMB: Increased Risk

ADAM VTE (apixaban)

VTE: Decreased Risk

Major Bleeding: Similar Risk

CRNMB: Similar Risk

Comparison of Recommendations[15-17]

	CHEST	SSC of the ISTH	ASCO
DOACs of Choice	**N/A**	**Edoxaban, Rivaroxaban**	**Edoxaban, Rivaroxaban**
When DOACs are preferred	**---**	**Low Risk of Bleeding** **No DDIs**	**---**
When LMWH is preferred	**All patients**	**High Risk of Bleeding** **GI Abnormalities** **Risk of Bleeding in High-Risk Sites**	**High Risk of Bleeding** **>40 kg/m^2 or >120kg** **Anticipated Nausea/Vomiting** **DDIs**

Recommendations Based on Primary Literature

DOACs of Choice

- Recommend apixaban and rivaroxaban over edoxaban
- Recommend against the use of dabigatran
- Rivaroxaban 15mg PO BID x 21 days, then 20 mg daily
- Apixaban 10mg PO BID x 1 week, then 5mg BID
- Parenteral anticoagulant x 5d, then Edoxaban 60mg PO daily
- Duration of therapy: 6 months

When DOACs are Preferred

- Patient preference
- Concern with adherence
- No drug-drug interactions
- Low bleeding risk

When LMWH is Preferred

- Cancers with high risk of bleeding (e.g. GI cancer)
- Chemotherapy with high risk of bleeding
- Unable to tolerate PO meds
- Drug-drug interactions

Conclusion

- I agree with suggestions from the SSC of the ISTH and ASCO guidelines regarding patient populations in which the use of LMWH and DOACs are appropriate.
- I recommend the use of apixaban and rivaroxaban over the use of edoxaban for treatment of cancer-associated venous thromboembolism.

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