



Prevention and treatment of VTE in patients with cancer

An Educational Slide Set

American Society of Hematology 2020 Guidelines
for Management of Venous Thromboembolism

Slide set author:

Siraj Mithoowani MD, MHPE (McMaster University)



Clinical Guidelines

American Society of Hematology 2020 Guidelines for Management of Venous Thromboembolism: Prevention and Treatment in Patients with Cancer

Gary H. Lyman, Marc Carrier, Cihan Ay, Marcello Di Nisio, Lisa K. Hicks, Alok A. Khorana, Andrew Leavitt, Agnes Y Y Lee, Fergus Macbeth, Rebecca L. Morgan, Simon Noble, Elizabeth Sexton, David Stenehjem, Wojtek Wiercioch, Lara A. Kahale, Pablo Alonso-Coello

CLINICAL GUIDELINES

 blood advances

American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer

Gary H. Lyman,^{1,2*} Marc Carrier,^{3*} Cihan Ay,⁴ Marcello Di Nisio,⁵ Lisa K. Hicks,⁶ Alok A. Khorana,⁷ Andrew D. Leavitt,^{8,9} Agnes Y. Y. Lee,^{10,11} Fergus Macbeth,¹² Rebecca L. Morgan,¹³ Simon Noble,¹⁴ Elizabeth A. Sexton,¹⁵ David Stenehjem,¹⁶ Wojtek Wiercioch,¹³ Lara A. Kahale,^{17,†} and Pablo Alonso-Coello^{18,†}

¹Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA; ²Department of Medicine, University of Washington School of Medicine, Seattle, WA; ³Department of Medicine, Ottawa Hospital Research Institute at the University of Ottawa, Ottawa, ON, Canada; ⁴Clinical Division of Haematology and Haemostaseology, Department of Medicine I, Comprehensive Cancer Center Vienna, Medical University of Vienna, Vienna, Austria; ⁵Department of Medicine and Aging Sciences, University G. D'Annunzio, Chieti, Italy; ⁶Division of Hematology/Oncology, Department of Medicine, St. Michael's Hospital, University of Toronto, Toronto, ON, Canada; ⁷Cleveland Clinic and Case Comprehensive Cancer Center, Cleveland, OH; ⁸Department of Laboratory Medicine and ⁹Division of Hematology/Oncology, Department of Medicine, University of California San Francisco, San Francisco, CA; ¹⁰Division of Hematology, Department of Medicine, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada; ¹¹Division of Medical Oncology, BC Cancer, Vancouver site, Provincial Health Services Authority, Vancouver, BC, Canada; ¹²Bristol, United Kingdom; ¹³Department of Health Research, Evidence, and Impact, McMaster University, Hamilton, ON, Canada; ¹⁴Division of Population Medicine, Cardiff University School of Medicine, Cardiff, United Kingdom; ¹⁵Salt Lake City, UT; ¹⁶College of Pharmacy, University of Minnesota, Duluth, MN; ¹⁷American University of Beirut (AUB) Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Center, American University of Beirut, Beirut, Lebanon; and ¹⁸Cochrane Iberoamérica, Biomedical Research Institute Sant Pau-CIBERESP, Barcelona, Spain

Background: Venous thromboembolism (VTE) is a common complication among patients with cancer. Patients with cancer and VTE are at a markedly increased risk for morbidity and mortality.

Objective: These evidence-based guidelines of the American Society of Hematology (ASH) are intended to support patients, clinicians, and other health care professionals in their decisions about the prevention and treatment of VTE in patients with cancer.

Methods: ASH formed a multidisciplinary guideline panel balanced to minimize potential bias from conflicts of interest. The guideline development process was supported by updated or new systematic evidence reviews. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to assess evidence and make recommendations.

Results: Recommendations address mechanical and pharmacological prophylaxis in hospitalized medical patients with cancer, those undergoing a surgical procedure, and ambulatory patients receiving cancer chemotherapy. The recommendations also address the use of anticoagulation for the initial, short-term, and long-term treatment of VTE in patients with cancer.

Conclusions: Strong recommendations include not using thromboprophylaxis in ambulatory patients receiving cancer chemotherapy at low risk of VTE and to use low-molecular-weight heparin (LMWH) for initial treatment of VTE in patients with cancer. Conditional recommendations include using thromboprophylaxis in hospitalized medical patients with cancer, LMWH or fondaparinux for surgical patients with cancer, LMWH or direct oral anticoagulants (DOAC) in ambulatory patients with cancer receiving systemic therapy at high risk of VTE and LMWH or DOAC for initial treatment of VTE, DOAC for the short-term treatment of VTE, and LMWH or DOAC for the long-term treatment of VTE in patients with cancer.

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*G.H.L. and M.C. are joint first authors.
†L.A.K. and P.A.-C. are joint last authors.

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ASH Clinical Practice Guidelines on VTE

1. Prevention of VTE in Surgical Hospitalized Patients
2. Prevention of VTE in Medical Hospitalized Patients
3. Treatment of Acute VTE (DVT and PE)
4. Optimal Management of Anticoagulation Therapy
- 5. Prevention and Treatment of VTE in Patients with Cancer**
6. Heparin-Induced Thrombocytopenia (HIT)
7. Thrombophilia
8. Pediatric VTE
9. VTE in the Context of Pregnancy
10. Diagnosis of VTE
11. VTE in Latin America
12. Anticoagulation in Patients with COVID-19

How were these ASH guidelines developed?

PANEL FORMATION

Each guideline panel was formed following these key criteria:

- Balance of expertise (including disciplines beyond hematology, and patients)
- Close attention to minimization and management of COI

CLINICAL QUESTIONS

10 to 20 **clinically-relevant questions** generated in **PICO format** (population, intervention, comparison, outcome)

Example: PICO question

“Should pre-operative thromboprophylaxis vs. post-operative thromboprophylaxis be used in patients with cancer undergoing a surgical procedure?”

EVIDENCE SYNTHESIS

Evidence summary generated for each PICO question via systematic review of health effects plus:

- Resource use
- Feasibility
- Acceptability
- Equity
- Patient values and preferences

MAKING RECOMMENDATIONS

Recommendations **made** by guideline panel members based on evidence for all factors.

ASH guidelines are reviewed annually by expert work groups convened by ASH. Resources, such as this slide set, derived from guidelines that require updating are removed from the ASH website.



How patients and clinicians should use these recommendations

	STRONG Recommendation ("The panel recommends...")	CONDITIONAL Recommendation ("The panel suggests...")
For patients	Most individuals would want the intervention.	A majority would want the intervention, but many would not.
For clinicians	Most individuals should receive the intervention.	Different choices will be appropriate for different patients, depending on their values and preferences. Use shared decision making .



Objectives

By the end of this session, you should be able to

1. Describe recommendations for primary prophylaxis in patients with cancer undergoing surgery
2. Describe recommendations for primary prophylaxis in ambulatory patients with cancer receiving systemic therapy
3. Select appropriate anticoagulant therapy for VTE in patients with cancer
4. Describe recommendations for treatment of incidental PE in patients with cancer

What is this chapter about?

Patients with cancer are at greater risk for VTE than the general population resulting in considerable morbidity, mortality and costs

Treatment decisions should be individualized taking into account consequences of VTE and/or bleeding events

This chapter provides evidence-based recommendations on **prevention and treatment of VTE in patients with cancer**



Case 1: Primary prophylaxis in patients with cancer undergoing surgery

67 year old female with newly diagnosed **stage IIIa colorectal cancer (T1N2aM0)**

Past Medical History: Hypertension, dyslipidemia

Medications: Amlodipine, rosuvastatin

Admitted to hospital:

Planned laparoscopic hemicolectomy

No symptoms of VTE or bleeding

Weight 80 kg



You judge that your patient is at moderate to high risk of perioperative VTE and low risk of surgical bleeding.

What strategy do you recommend for thromboprophylaxis?

- A. Mechanical thromboprophylaxis only
- B. Dalteparin 5,000 units SC daily post-operatively
- C. Dalteparin 5,000 units SC daily starting 12 hours pre-operatively
- D. Unfractionated heparin 5,000 units SC BID post-operatively



Recommendation

In **patients with cancer undergoing a surgical procedure**, the ASH guideline panel suggests using either LMWH or fondaparinux for thromboprophylaxis rather than UFH (*conditional recommendation based on low certainty in the evidence about effects*).

LMWH versus UFH for thromboprophylaxis

Outcomes (Quality of Evidence)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with UFH	Risk difference with LMWH
● Mortality	RR 0.82 (0.63 to 1.07)	109 out of 2155 (5.1%)	9 fewer deaths per 1,000 (19 fewer to 4 more)
● PE	RR 0.52 (0.20 to 1.34)	19 out of 3138 (0.6%)	3 fewer PEs per 1,000 (5 fewer to 2 more)
● Symptomatic DVT	RR 0.67 (0.27 to 1.69)	11 out of 1144 (1.0%)	3 fewer DVTs per 1,000 (7 fewer to 7 more)
● Major bleeding	RR 1.01 (0.69 to 1.48)	Not reported (5.6%)	1 more bleed per 1,000 (17 fewer to 27 more)
● Reoperation for bleeding	RR 1.01 (0.69 to 1.48)	32 out of 627 (5.1%)	4 fewer re-operations per 1,000 (22 fewer to 26 more)

Recommendation

In **patients with cancer undergoing a surgical procedure**, the ASH guideline panel suggests using either LMWH or fondaparinux for thromboprophylaxis rather than UFH (*conditional recommendation based on low certainty in the evidence about effects*).

Fondaparinux versus LMWH for thromboprophylaxis

Outcomes (Quality of Evidence)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with LMWH	Risk difference with Fondaparinux
Mortality		Not reported	
● PE	RR 0.40 (0.14 to 1.12)	72 per 1,000	43 fewer PEs per 1,000 (62 fewer to 9 more)
● Symptomatic DVT	RR 0.40 (0.14 to 1.12)	72 per 1,000	43 fewer DVTs per 1,000 (62 fewer to 9 more)
● Major bleeding	RR 1.34 (0.81 to 2.22)	22 per 1,000	7 more bleeds per 1,000 (4 fewer to 27 more)

Remarks

- UFH is generally preferred over LMWH for patients with cancer with severe renal impairment (defined as a creatinine clearance < 30 mL/min)
- If planning for extended thromboprophylaxis (continuing pharmacological thromboprophylaxis at home), the guideline panel suggests the use of LMWH



Recommendation

In **patients with cancer undergoing a surgical procedure**, the ASH guideline panel suggests using post-operative thromboprophylaxis over pre-operative thromboprophylaxis (*conditional recommendation based on low certainty in the evidence about effects*).

Outcomes (Quality of Evidence)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with immediate post-op prophylaxis	Risk difference with pre-operative prophylaxis
● Mortality	RR 0.74 (0.50 to 1.09)	27 per 1,000	7 fewer deaths per 1,000 (13 fewer to 2 more)
● PE	RR 0.20 (0.01 to 4.16)	1 per 1,000	1 fewer PE per 1,000 (1 fewer to 3 more)
● Symptomatic DVT	RR 0.86 (0.62 to 1.19)	51 per 1,000	7 fewer DVTs per 1,000 (19 fewer to 10 more)
● Major bleeding	RR 1.55 (1.14 to 2.12)	29 per 1,000	16 more bleeds per 1,000 (4 more to 32 more)

Case 1, continued

- You prescribe dalteparin 5,000 IU subcut daily post-operatively
- Your patient's post-operative course is uneventful and discharge is planned on post-operative day 3

What duration of pharmacological thromboprophylaxis do you recommend?

- A. Discontinue pharmacological thromboprophylaxis at discharge
- B. Discontinue pharmacological thromboprophylaxis once your patient is ambulatory
- C. Continue pharmacological thromboprophylaxis at home for 7 days
- D. Continue pharmacological thromboprophylaxis at home for 4 weeks



Recommendation

In **patients with cancer who had undergone a major abdominal/pelvic surgical procedure**, the ASH guideline panel suggests continuing pharmacological thromboprophylaxis post discharge rather than discontinuing at the time of hospital discharge (*conditional recommendation based on very low certainty in the evidence about effects*).

Outcomes (Quality of Evidence)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with limited prophylaxis	Risk difference with extended prophylaxis
● Mortality	RR 1.14 (0.73 to 1.78)	Not stated	6 more deaths per 1,000 (12 fewer to 35 more)
● PE	RR 0.18 (0.02 to 1.46)	17 per 1,000	14 fewer PEs per 1,000 (17 fewer to 8 more)
● Symptomatic DVT	RR 0.67 (0.11 to 4.06)	29 per 1,000	10 fewer DVTs per 1,000 (26 fewer to 89 more)
● Major bleeding	RR 0.83 (0.29 to 2.35)	Not stated	2 fewer bleeds per 1,000 (7 fewer to 14 more)

Remarks

- We only identified evidence to assess the benefits and harms of extended thromboprophylaxis in patients undergoing **major abdominal/pelvic surgery**.
- This recommendation should not be extended to other surgical procedures.
- Patients should be provided comprehensive anticoagulation education including self-injection technique during hospitalization to facilitate continuation of thromboprophylaxis after discharge.

Case 1, Continued:

- Four weeks later, your patient is seen in the Oncology clinic
- Adjuvant chemotherapy (oxaliplatin, leucovorin, fluorouracil) is planned

Physical examination:

Weight 80 kg, BMI 25 kg/m²
Well healed surgical incisions
No evidence of DVT or PE

Laboratory Investigations (pre-chemotherapy)

Hemoglobin 115 g/L
Leukocyte count 13 x 10⁹/L
Platelet count 405 x 10⁹/L
Creatinine 55 µmol/L



You judge that your patient is at moderate to high risk of VTE and low risk of bleeding.

What strategy do you recommend for thromboprophylaxis?

- A. No thromboprophylaxis
- B. Mechanical thromboprophylaxis only
- C. Apixaban 2.5 mg twice daily
- D. Dalteparin 5,000 IU SC daily

Khorana risk score

	Score
<i>Site of primary tumor</i>	
Very high risk (stomach, pancreas)	2
High risk (lung, lymphoma, gyne, bladder, testicular)	1
All others	0
<i>Platelet count</i> > 350 x 10⁹/L	1
<i>Hemoglobin</i> < 100 g/L or use of ESAs	1
<i>WBC</i> > 11 x 10⁹/L	1
<i>BMI</i> > 35 kg/m²	1

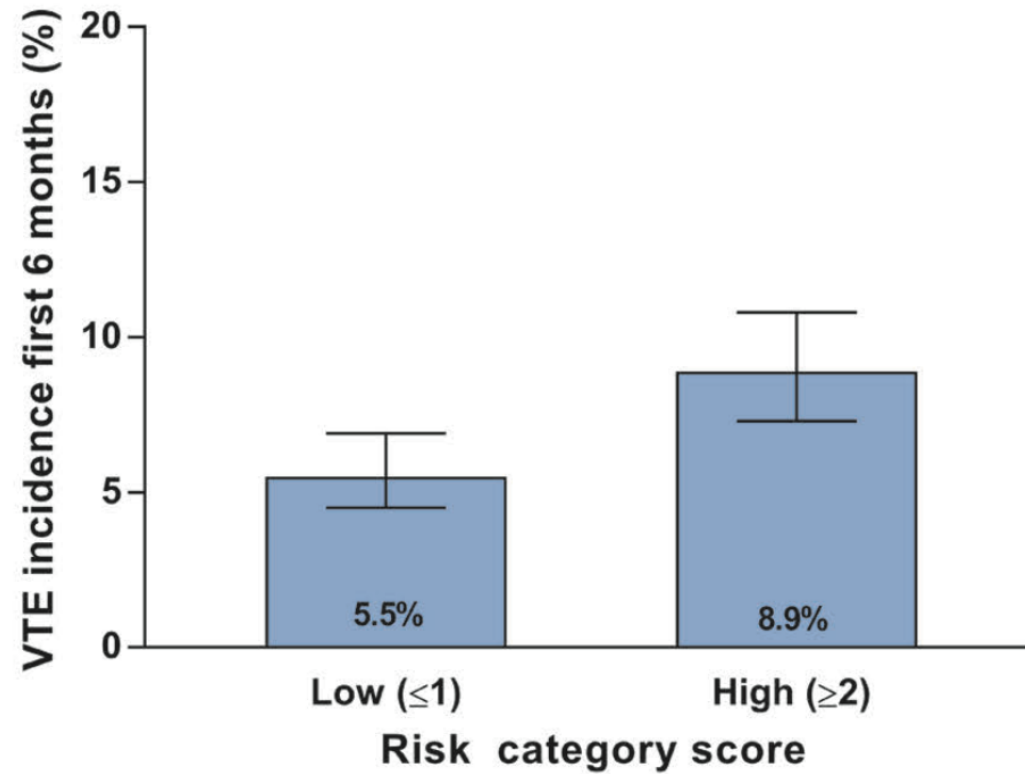


Khorana risk score

	Score	Our patient
<i>Site of primary tumor</i>		
Very high risk (stomach, pancreas)	2	Colorectal cancer
High risk (lung, lymphoma, gyne, bladder, testicular)	1	
All others	0	
<u>Platelet count > 350 x 10⁹/L</u>	<u>1</u>	<u>405 x 10⁹/L</u>
<i>Hemoglobin</i> < 100 g/L or use of ESAs	1	115 g/L
<u>WBC > 11 x 10⁹/L</u>	<u>1</u>	<u>13 x 10⁹/L</u>
<i>BMI</i> > 35 kg/m²	1	25 kg/m ²

Khorana risk score

What is this patient's risk of VTE?





Recommendations

In **ambulatory patients with cancer at low risk of thrombosis** receiving systemic therapy, the ASH guideline panel suggests no thromboprophylaxis over oral thromboprophylaxis with a DOAC (apixaban or rivaroxaban) (*conditional recommendation based on moderate certainty in the evidence about effects*).

In **ambulatory patients with cancer at intermediate risk of thrombosis** receiving systemic therapy, the ASH guideline panel suggests either thromboprophylaxis with a DOAC (apixaban or rivaroxaban) or no thromboprophylaxis (*conditional recommendation based on moderate certainty in the evidence about effects*).

In **ambulatory patients with cancer at high risk of thrombosis** receiving systemic therapy, the ASH guideline panel suggests thromboprophylaxis with a DOAC (apixaban or rivaroxaban) over no thromboprophylaxis (*conditional recommendation based on moderate certainty in the evidence about effects*).

Recommendation

In **ambulatory patients with cancer at high risk of thrombosis** receiving systemic therapy, the ASH guideline panel suggests thromboprophylaxis with a DOAC (apixaban or rivaroxaban) over no thromboprophylaxis (*conditional recommendation based on moderate certainty in the evidence about effects*).

Outcomes (Quality of Evidence)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with no thromboprophylaxis	Risk difference with DOAC thromboprophylaxis
● Mortality	RR 0.94 (0.64 to 1.38)	185 per 1,000	11 fewer deaths per 1,000 (67 fewer to 70 more)
● PE	RR 0.24 (0.12 to 0.47)	60 per 1,000	46 fewer PEs per 1,000 (53 fewer to 32 fewer)
● Symptomatic DVT	RR 0.61 (0.31 to 1.21)	95 per 1,000	37 fewer DVTs per 1,000 (66 fewer to 20 more)
● Major bleeding	RR 1.65 (0.72 to 3.80)	14 per 1,000	9 more bleeds per 1,000 (4 fewer to 40 more)

Other considerations

- Classification of patients as low, moderate or high-risk for VTE should be based on a validated score (i.e. Khorana score) complemented by **clinical judgment and experience**.
- In patients at high risk for thrombosis, thromboprophylaxis should be used with caution in those with a high risk of bleeding.

Case 2: Treatment of cancer associated VTE

A 44 year old female presents to the ED with a 3-day history of right leg swelling and pain

A doppler ultrasound of the right leg reveals an occlusive DVT in the right superficial femoral, popliteal and trifurcation veins

Past Medical History: Locally advanced breast cancer, grade 3 invasive ductal carcinoma, ER/PR negative, HER2 negative, grade 3 invasive ductal carcinoma

Medications: Neo-adjuvant dose dense AC/T (doxorubicin, cyclophosphamide, paclitaxel)

Laboratory investigations in the ED:

Hemoglobin 109 g/L
Leukocyte count $11 \times 10^9/L$
Platelet count $334 \times 10^9/L$
Creatinine 60 $\mu\text{mol/L}$

Case 2

What initial treatment do you recommend?

- A. IVC filter insertion
- B. Tinzaparin 175 IU/kg once daily
- C. Edoxaban 60mg once daily
- D. Unfractionated heparin infusion

Definitions

The ASH guideline panel divided the treatment course of VTE in cancer patients into three phases:

1. Initial treatment (within the first week of diagnosis)
2. Short-term treatment (3 to 6 months from diagnosis)
3. Long-term treatment (> 6 months from diagnosis)

Recommendation

In **patients with cancer and VTE**, the ASH guideline panel suggests either DOAC (apixaban or rivaroxaban) or LMWH be used for initial treatment of VTE in patients with cancer (*conditional recommendation based on very low certainty in the evidence about effects*).

If a DOAC is not used, we recommend LMWH over UFH for initial treatment of VTE in patients with cancer (*strong recommendation based on moderate certainty in the evidence about effects*).

Outcomes (Quality of Evidence)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)*	
		Risk with LMWH	Risk difference with DOAC
● Mortality	RR 3.00 (0.12 to 73.21)	0 per 1,000	0 fewer deaths per 1,000 (0 fewer to 0 fewer)
● Recurrent VTE	RR 0.20 (0.01 to 4.04)	14 per 1,000	11 fewer recurrent events per 1,000 (14 fewer to 43 more)
● Major bleeding	RR 0.33 (0.01 to 8.13)	3 per 1,000	2 fewer bleeds per 1,000 (3 fewer to 21 more)

* Based on results of the SELECT-D and ADAM-VTE trials only

Quality of Evidence (GRADE): Low ● Moderate ● Strong ●

Remarks

- Only two DOACs (**apixaban** and **rivaroxaban**) have been approved for the initial treatment period.
- DOACs should be used carefully in patients with gastrointestinal cancers because of a higher risk of GI bleeding.
- UFH might be preferred over LMWH for the patient with cancer with severe renal impairment (defined as creatinine clearance < 30 mL/min).
- The use of fondaparinux might be considered in patients with cancer and VTE and a prior history of heparin induced thrombocytopenia.

Case 2, continued

Four weeks later, your patient undergoes an uncomplicated right modified radical mastectomy.

She is seen in your outpatient clinic one week post-operatively.

Her right leg swelling and pain has improved and she has no bleeding.

What is your recommendation?

- A. Continue tinzaparin 175 IU/kg once daily
- B. Switch to VKA (warfarin) with target INR 2.5
- C. Switch to rivaroxaban 20mg once daily
- D. Discontinue anticoagulation



Recommendation

For the **short-term treatment of VTE (first 3-6 months)** in patients with active cancer, the ASH guideline panel suggests DOAC (apixaban, edoxaban or rivaroxaban) over LMWH (*conditional recommendation based on low certainty in the evidence about effects*).

DOAC is also suggested over VKA (*conditional recommendation based on very low certainty in the evidence about effects*).

If a DOAC is not used, the ASH guideline panel suggests LMWH over VKA (*conditional recommendation based on moderate certainty in the evidence about effects*).

Recommendation

For the **short-term treatment of VTE (first 3-6 months)** in patients with active cancer, the ASH guideline panel suggests DOAC (apixaban, edoxaban or rivaroxaban) over LMWH (*conditional recommendation based on low certainty in the evidence about effects*).

Outcomes* (Quality of Evidence)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)*	
		Risk with LMWH	Risk difference with DOAC
● Mortality	RR 0.99 (0.83 to 1.18)	245 per 1,000	2 fewer deaths per 1,000 (42 fewer to 44 more)
● Recurrent VTE	RR 0.62 (0.43 to 0.90)	83 per 1,000	32 fewer recurrent events per 1,000 (47 fewer to 8 fewer)
● Major bleeding	RR 1.31 (0.83 to 2.06)	34 per 1,000	10 more bleeds per 1,000 (6 fewer to 36 more)

* Follow-up: 12 months

Case 2, continued

Three months later, your patient has a surveillance CT scan showing metastatic deposits in the liver and bone

An MRI brain is negative for intracranial metastases

Palliative chemotherapy is planned

Laboratory investigations:

Hemoglobin 99 g/L

Leukocyte count $13 \times 10^9/L$

Platelet count $89 \times 10^9/L$

Creatinine 84 $\mu\text{mol/L}$



Case 2, continued

What duration of anticoagulation do you recommend?

- A. Discontinue anticoagulation now
- B. Discontinue anticoagulation after 3 months
- C. Discontinue anticoagulation after 6 months
- D. Continue anticoagulation indefinitely

Recommendation

In **patients with active cancer and VTE**, the ASH guideline panel suggests long-term anticoagulation for secondary prophylaxis (longer than 6 months) rather than short term treatment alone (3-6 months) (*conditional recommendation based on low certainty in the evidence about effects*).

Outcomes* (Quality of Evidence)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with short term treatment (3-6 mos)	Risk difference with long term treatment (longer than 6 mos)
● Mortality	RR 1.38 (0.85 to 2.23)	24 per 1,000	9 more deaths per 1,000 (4 fewer to 30 more)
● PE	RR 0.66 (0.29 to 1.51)	50 per 1,000	17 fewer recurrent PE per 1,000 (35 fewer to 25 more)
● Recurrent VTE	RR 0.54 (0.23 to 1.27)	138 per 1,000	63 fewer recurrent events per 1,000 (106 fewer to 36 more)
● Major bleeding	RR 1.25 (0.68 to 2.30)	15 per 1,000	4 more bleeds per 1,000 (5 fewer to 20 more)

* Mean follow-up: 31 months

Recommendation

In **patients with active cancer and VTE receiving long-term anticoagulation for secondary prophylaxis**, the ASH guideline panel suggests continuing indefinite anticoagulation over stopping after completion of a definitive period of anticoagulation (*conditional recommendation based on very low certainty in the evidence about effects*).

Outcomes (Quality of Evidence)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with definite duration (< 12 mos)	Risk difference with indefinite duration of therapy
● Mortality	RR 0.70 (0.45 to 1.09)	15 per 1,000	5 fewer deaths per 1,000 (8 fewer to 1 more)
● PE	RR 0.23 (0.12 to 0.44)	27 per 1,000	21 fewer recurrent PE per 1,000 (24 fewer to 15 fewer)
● Recurrent VTE	RR 0.20 (0.11 to 0.38)	95 per 1,000	76 fewer recurrent events per 1,000 (85 fewer to 59 fewer)
● Major bleeding	RR 2.21 (1.32 to 3.44)	7 per 1,000	9 more bleeds per 1,000 (3 more to 18 more)

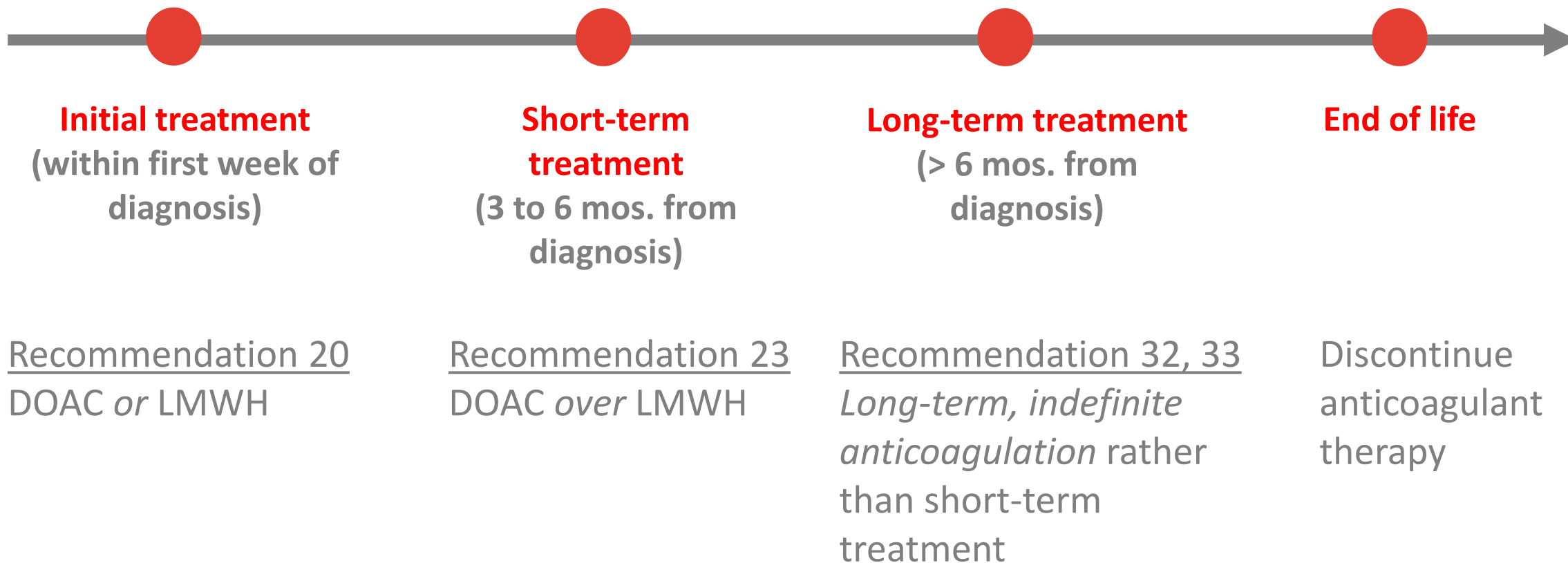
Remarks

- Long-term anticoagulation can be discontinued **when patients are no longer at high risk of recurrent VTE or if patients are entering the last weeks of life.**
- The decision to anticoagulate for a prolonged period will be dependent on the type and stage of cancer (e.g., metastatic cancer or not), long-term prognosis, and periodic re-evaluation of risk of thrombosis and bleeding, comorbidities, costs and patient preferences and values.
- The choice of anticoagulant must also be based on the specific clinical setting to minimize risk, after careful consideration of bleeding risk, drug-drug interactions, patient's preference, and the availability of treatment options including cost considerations.

Anticoagulation at the end of life

- Observational data support stopping anticoagulants and antithrombotic drugs as death approaches.
- Observational data have shown:
 - A high risk of clinically relevant bleeding (**7-10%**) in the last weeks of life
 - That bleeding is strongly associated with use of anticoagulants (**HR 1.48**, 95% CI 1.02-2.15) and antiplatelet drugs (**HR 1.67**, 95% CI 1.15-2.44)

Case 2, Summary



Case 3: Treatment of incidental PE

53 year old male with **metastatic renal cell carcinoma (to bones, liver)**

Past Medical History: Hypothyroidism, depression

Medications: Levothyroxine, escitalopram, **cabozantinib (TKI drug)**

Seen in outpatient clinic:

Routine staging CT shows **bilateral segmental/subsegmental pulmonary emboli**

Bilateral leg doppler ultrasound negative for DVT

He is asymptomatic with normal vital signs

Laboratory investigations:

Hemoglobin 129 g/L

Leukocyte count $12 \times 10^9/L$

Platelet count $330 \times 10^9/L$

Creatinine 94 $\mu\text{mol/L}$

What is your treatment recommendation?

- A. Clinical observation only
- B. IVC filter insertion
- C. Start apixaban 10mg BID x 1 week, followed by apixaban 5mg BID
- D. Start warfarin (target INR 2.5)



Recommendation

In **patients with cancer and incidental (unsuspected) PE**, the ASH guideline panel suggests short-term anticoagulation treatment rather than observation (*conditional recommendation based on very low certainty in the evidence about effects*).

Outcomes (Quality of Evidence)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with observation	Risk difference with treatment
● Mortality	RR 0.81 (0.67 to 0.98)	369 per 1,000	70 fewer deaths per 1,000 (122 fewer to 7 fewer)
● Symptomatic PE*	RR 0.36 (0.18 to 0.72)	60 per 1,000	39 fewer recurrent PE per 1,000 (49 fewer to 17 fewer)
● Symptomatic recurrent DVT*	RR 0.19 (0.08 to 0.48)	48 per 1,000	39 fewer recurrent events per 1,000 (44 fewer to 25 fewer)
● Major bleeding*	RR 3.00 (1.21 to 7.47)	22 per 1,000	44 more bleeds per 1,000 (5 more to 414 more)

* Follow-up: 3 months

Remarks

- Clinicians should use clinical judgment when considering anticoagulation for incidental PE, sub-segmental PE or splanchnic vein thrombosis.
- Factors that should be considered include diagnostic certainty, chronicity (age of thrombus), extent of thrombosis, associated symptoms and bleeding risks.
- If therapeutic anticoagulation is warranted, the ASH guideline panel recommends use of the same anticoagulants recommended for treatment of cancer-associated thrombosis.



Other guideline recommendations that were not covered in this session

- Primary prophylaxis in hospitalized *medical* patients with cancer
- Primary prophylaxis for patients with cancer and a central venous catheter
- Treatment versus observation for patients with cancer and SSPE or visceral/splanchnic vein thrombosis
- Treatment of patients with cancer and recurrent VTE despite anticoagulation

Some future priorities for research

- Optimal choice, dosing and duration of parenteral anticoagulation to prevent VTE in hospitalized patients with cancer
- Cost effectiveness of primary prophylaxis for ambulatory patients with cancer
- Primary prophylaxis for patients with cancer and a central venous catheter (treatment duration, agent of choice)
- Comparative safety, efficacy and cost effectiveness of oral agents versus parenteral therapy for VTE in patients with cancer
- Treatment versus observation for patients with cancer and incidental/subsegmental PE or splanchnic vein thrombosis

In Summary: Back to our Objectives

1. Describe recommendations for primary prophylaxis in patients with cancer undergoing surgery
 - Prophylaxis with LMWH or fondaparinux recommended over UFH
 - Extended thromboprophylaxis (4 weeks) for major abdominal/pelvic surgery
2. Describe recommendations for primary prophylaxis in ambulatory patients with cancer receiving systemic therapy
 - Pharmacological prophylaxis (DOACs) for patients at moderate to high risk of VTE
3. Select appropriate anticoagulant therapy for VTE in patients with cancer
 - Initial treatment (within 1 week): LMWH or DOACs
 - Short-term treatment (3-6 months): DOACs over LMWH
 - Long-term treatment (> 6 months): Indefinite anticoagulation
4. Describe recommendations for treatment of incidental PE in patients with cancer
 - Anticoagulation rather than observation



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- Author of this ASH VTE Slide Set:
Siraj Mithoowani MD, MHPE (McMaster University)

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