Review of the 2020 ACC Clinical Decision Pathway for Anticoagulant and Antiplatelet Therapy in Patients with Atrial Fibrillation or Venous Thromboembolism

Sarah A. Spinler, PharmD
FCCP, FAHA, FASHP, AACC, BCPS AQ-Cardiology
Professor and Department Chair
Department of Pharmacy Practice
sspinler@Binghamton.edu

COLLEGE of



Disclosures

- Financial: None
- I intend to reference unapproved/unlabeled indications for drugs in this presentation.



Objectives

After completion of this activity, pharmacists will be able to

- Describe the recommended antithrombotic management strategy of a patient with prior history of VTE receiving anticoagulation presenting for PCI
- Describe the recommended antithrombotic management strategy of a patient with AF receiving anticoagulation who now needs PCI
- Describe the recommended antithrombotic management strategy of a patient on antiplatelet therapy presenting with either new VTE or new diagnosis of AF

EXPERT CONSENSUS DECISION PATHWAY

2020 ACC Expert Consensus Decision
Pathway for Anticoagulant and
Antiplatelet Therapy in Patients With
Atrial Fibrillation or Venous
Thromboembolism Undergoing
Percutaneous Coronary Intervention
or With Atherosclerotic Cardiovascular Disease

A Report of the American College of Cardiology Solution Set Oversight Committee

Writing Committee Dharam J. Kumbhani, MD, SM, FACC, *Chair* Christopher P. Cannon, MD, FACC, *Vice-Chair*

Craig J. Beavers, PharmD, FACC Deepak L. Bhatt, MD, MPH, FACC Adam Cuker, MD, MS Ty J. Gluckman, MD, FACC Joseph E. Marine, MD, FACC Roxana Mehran, MD, FACC Steven R. Messe, MD Nimesh S. Patel, MD Benjamin E. Peterson, MD, MPH Kenneth Rosenfield, MD, FACC Sarah A. Spinler, PHARMD, AACC Vinod H. Thourani, MD, FACC



Determination of Need

- 1 in 4 individuals will develop AF in their lifetime.
- CAD occurs in 25% to 35% of individuals with AF.
- More than 10% of patients with AF require APT at some time.
- The incidence of VTE is 1 to 2 per 1000 person years.
- Pathophysiologic link between CAD and VTE with common need for antithrombotic therapy

Triple Antithrombotic Therapy

- Anticoagulation plus dual antiplatelet therapy (DAPT)
- DAPT is low-dose aspirin plus a P2Y₁₂ inhibitor (either clopidogrel, ticagrelor or prasugrel)
- Historical rationale was that oral anticoagulation (OAC) was not sufficient for preventing stent thrombosis following PCI and similarly antiplatelet therapy was not sufficient for early treatment of VTE

Triple Antithrombotic Therapy

- Adding a single antiplatelet therapy (SAPT) increases major bleeding risk
 - Meta-analysis of 10 studies (Dentali et al)
 - OR major bleeding1.43
 - No benefit in arterial TE reduction (except in mechanical heart valve)
- Addition of DAPT to OAC further increases the risk of major bleeding 2- to 3-fold
 - As high as 2.2% at one month and 4%-12% at one year
 - Double antithrombotic therapy with DOAC plus either aspirin or P2Y₁₂ inhibitor
 - Multiple published meta-analysis of 4 large DOAC PCI AF trials
 - Associated with increased risk of major bleeding (RR 1.69 Gargiulo et al.)
 - Nonsignificant excess of MACE
 - DOAC plus SAPT lower risk of bleeding than VKA plus DAPT (Capodanno et al.)

Dentali F, et al. Arch Intern Med. 2007 Jan 22;167(2):117-24. Gargiulo G, et al. Eur Heart J. 2019 Dec 7;40(46):3757-3767. Capodanno D, et al. J Am Heart Assoc. 2020 Aug 18;9(16):e017212.



TABLE 1 Randomized Trials of Dual Versus Triple Therapy for AF and PCI (29-33)

Trial Name	WOEST	PIONEER AF-PCI	RE-DUAL PCI	AUGUSTUS	ENTRUST-AF PCI
Patients enrolled	n = 573	n = 2,124	n = 2,725	n = 4,614	n = 1,506
Trial design	Open-label, Randomized	Open-label, Randomized	Open-label, Randomized	2 × 2 factorial randomized*	Open-label, Randomized
Treatment arms	Group 1: VKA (INR per indication) + P2Y ₁₂ i vs. Group 2: VKA (INR 2.0) + aspirin + P2Y ₁₂ i	Group 1: Rivaroxaban (15 mg daily) + P2Y ₁₂ i vs. Group 2: Rivaroxaban (2.5 mg twice daily) + aspirin + P2Y ₁₂ i vs. Group 3: VKA (INR 2-3) + aspirin + P2Y ₁₂ i [†]	Group 1: Dabigatran (110 mg twice daily) + P2Y ₁₂ i vs. Group 2: Dabigatran (150 mg twice daily) + P2Y ₁₂ i vs. Group 3: VKA (INR 2-3) + aspirin (1-3 months) + P2Y ₁₂ i	Group 1: Apixaban (5 mg twice daily) + P2Y ₁₂ i vs. Group 2: Apixaban (5 mg twice daily) + aspirin + P2Y ₁₂ i vs. Group 3: VKA (INR 2-3) + P2Y ₁₂ i vs. Group 4: VKA (INR 2-3) + aspirin + P2Y ₁₂ i [†]	Group 1: Edoxaban (60 mg daily) + P2Y ₁₂ i vs. Group 2: VKA (INR 2-3) + aspirin (1-12 months) + P2Y ₁₂ i ⁵
Predominant P2Y ₁₂ i	Clopidogrel	Clopidogrel	Clopidogrel	Clopidogrel	Clopidogrel
Duration of ASA use in dual therapy arm	4 hours	72 hours	1.6 days	7 days	5 days
Follow-up	12 months	12 months	14 months	6 months	12 months
Indication for OAC therapy	AF (69%) Mechanical valve (10%)	AF (100%)	AF (100%)	AF (100%)	AF (100%)
Indication for APT	PCI for ACS (≈28%) PCI for SIHD (≈72%)	PCI for ACS (≈50%) PCI for SIHD (≈49%)	PCI for ACS (≈50%) PCI for SIHD (≈50%)	PCI for ACS (≈37%) PCI for SIHD (≈39%) Medical treatment for ACS (≈24%)	PCI for ACS (≈52%) PCI for SIHD (≈48%)



TABLE 1 Randomized Trials of Dual Versus Triple Therapy for AF and PCI (29-33)

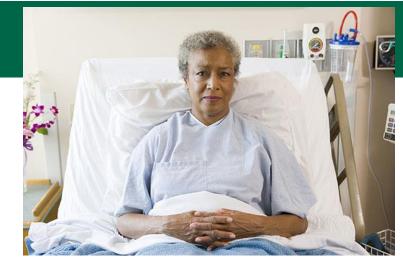
Trial Name	WOEST	PIONEER AF-PCI	RE-DUAL PCI	AUGUSTUS	ENTRUST-AF PO
Primary outcome event rate(s), (HR; 95% CI)	19.4% vs. 44.4%; (0.36; 0.26-0.50)	Group 1 vs. 3 16.8% vs. 26.7%; (0.59; 0.47-0.76) Group 2 vs. 3 18.0% vs. 26.7%; (0.63; 0.50-0.80)	Dabigatran 110 mg twice daily vs. WTT 15.4% vs. 26.9%; (0.52; 0.42-0.63) Dabigatran 150 mg twice daily vs. WTT 20.2% vs. 25.7%; (0.72; 0.58-0.88)	Apixaban vs. VKA 10.5% vs. 14.7%; (0.69; 0.58-0.81) Aspirin vs. placebo 16.1% vs. 9.0%; (1.89; 1.59-2.24)	17.0% vs. 20%; (0.83; 0.65-1.05)
Primary ischemic/ thrombotic endpoint	Death, MI, stroke, target vessel revascularization, and stent thrombosis	Death from cardiovascular causes, MI, or stroke	Death, Thromboembolic events (MI, stroke, or systemic embolism), or unplanned revascularization	Death or ischemic event (stroke, MI, stent thrombosis, or urgent revascularization)	Cardiovascular death, stroke, systemic embolic event, MI, or definite stent thrombosis
Event rate for primary ischemic/ thrombotic endpoint (HR; 95% CI)	11.1% vs. 17.6%; (0.60; 0.38-0.94)	Group 1 vs. 3 6.5% vs. 6.0%; (1.08; 0.69-1.68) Group 2 vs. 3 5.6% vs. 6.0%; (0.93; 0.59-1.48)	Dabigatran 110 mg twice daily vs. WTT 15.2% vs. 13.4%; (1.13; 0.90-1.43) Dabigatran 150 mg twice daily vs. WTT 11.8% vs. 12.8%; (0.89; 0.67-1.19)	Apixaban vs. VKA 6.7% vs. 7.1%; (0.93; 0.75-1.16) Aspirin vs. placebo 6.5% vs. 7.3%; (0.89; 0.71-1.11)	7% vs. 6%; (1.06; 0.71-1.69)
TIMI major bleeding (HR; 95% CI)	3.2% vs. 5.6%; (0.56; 0.25-1.27)	Group 1 vs. 3 2.1% vs. 3.3%; (0.66; 0.33-1.31) Group 2 vs. 3 1.9% vs. 3.3%; (0.57; 0.28-1.16)	Dabigatran 110 mg twice daily vs. WTT 1.4% vs. 3.8%; (0.37; 0.20-0.68) Dabigatran 150 mg twice daily vs. WTT 2.1% vs. 3.9%; (0.51; 0.28-0.93)	Apixaban vs. VKA 1.7% vs. 2.1%; (0.78; 0.51-1.20) Aspirin vs. placebo 2.4% vs. 1.3%; (1.93; 1.23-3.03)	2.0% vs. 3.2%; (0.62; 0.33-1.19)



TABLE 1 Continued							
Trial Name	WOEST	PIONEER AF-PCI	RE-DUAL PCI	AUGUSTUS	ENTRUST-AF PCI		
Stent thrombosis (HR; 95% CI)	1.4% vs. 3.2%; (0.44; 0.14-1.44)	Group 1 vs. 3 0.8% vs. 0.7%; (1.20; 0.32-4.45) Group 2 vs. 3 0.9% vs. 0.7%; (1.44; 0.40-5.09)	Dabigatran 110 mg twice daily vs. WTT 1.5% vs. 0.8%; (1.86; 0.79-4.40) Dabigatran 150 mg twice daily vs. WTT 0.9% vs. 0.9%; (0.99; 0.35-2.81)	Apixaban vs. VKA 0.6% vs. 0.8%; (0.77; 0.38-1.56) Aspirin vs. placebo 0.5% vs. 0.9%; (0.52; 0.25-1.08)	1.1% vs. 0.8%; (1.32; 0.46-3.79)		
Cardiovascular death (HR 95% CI)	1.1% vs. 2.5%; (0.43; 0.11-1.66)	Group 1 vs. 3 2.4% vs. 1.9%; (1.29; 0.59-2.80) Group 2 vs. 3 2.2% vs. 1.9%; (1.19; 0.54-2.62)	Dabigatran 110 mg twice daily vs. WTT 3.8% vs. 3.2% (1.17; 0.72-1.89) Dabigatran 150 mg twice daily vs. WTT 2.8% vs. 3.1% (0.84; 0.47-1.51)	Apixaban vs. VKA 2.5% vs. 2.3%; (1.05; 0.0.72-1.52) Aspirin vs. placebo 2.3% vs. 2.5%; (0.92; 0.63-1.33f)	2.3% vs. 2.1%; (1.06; 0.54-2.10)		



Patient Case: Patient on OAC who now needs PCI



• JS is a 71 year-old, 68 kg female with a past history of HTN and AF treated with apixaban 5 mg PO BID. CrCl estimated with actual body weight is 65 mL/min. She presents to the hospital with NSTE MI and undergoes uncomplicated PCI of the right coronary artery with bivalirudin and placement of a DES. The patient has no prior history of major bleeding with OAC and is at low risk of bleeding. She is not considered high-risk for stent thrombosis.

1. JS's hospital discharge antithrombotic regimen should be (Chose one)

- A. Apixaban, aspirin 81 mg, clopidogrel
- B. Apixaban, aspirin 81 mg, ticagrelor
- C. Apixaban, clopidogrel
- D. Bridged to warfarin (INR 2-2.5), aspirin 81 mg, clopidogrel
- E. I'm not sure.



2. The length of time JS should receive either dual or triple antithrombotic therapy (based on your response to the prior question) is

- A. 1 month
- B. 6 months
- C. 12 months
- D. Greater than 12 months
- E. I'm not sure.



General Principles

- Antithrombotic regimen should take into consideration bleeding and ischemic risk (SIHD versus ACS).
- "Overall, we recommend against the routine use of triple antithrombotic therapy for most patients."



Scenario 1: Patient on OAC requiring PCI

- Default strategy following PCI is dual antithrombotic therapy with OAC and P2Y₁₂ inhibitor.
- DOAC is preferred post PCI (even in patients originally on VKA)
 - Lower risk of major, fatal and ICH compared to VKA
 - Simplicity of regimen
 - · Lack of need for bridging
- For prior VKA with good INR control, consideration to continuing VKA (goal INR 2.0-2.5)
 - Especially for CKD
 - Continue aspirin until INR 2.0 or above.
 - If AF high thrombotic risk, consider bridging.
- Clopidogrel preferred over ticagrelor and prasugrel
 - Lower risk of bleeding
 - Scarce data wit ticagrelor: reserve for patient with high risk of stent thrombosis
 - Avoid prasugrel (4-fold increased risk of major bleeding as part of triple regimen)

Scenario: Patient on OAC requiring PCI

- Prior to PCI, the patient should receive 162-325 mg aspirin followed by 81 mg/day continued during hospitalization and discontinued at hospital discharge for most patients.
- Preferred stent type is DES
- Triple therapy reserved with aspirin for 30 days in patients at high risk of stent thrombosis with low bleeding risk.

Scenario: Patient on OAC requiring PCI

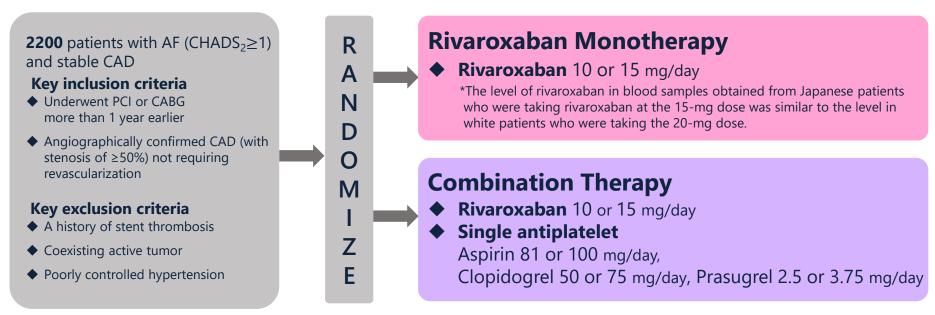
- For patients with AF and indefinite OAC
 - Continue antiplatelet therapy (P2Y12 inhibitor preferred) for one year post PCI
 - Use clopidogrel for 6 months then either clopidogrel or low-dose aspirin for another 6 months
 - AFIRE trial supports discontinuation of APT at 12 months





Atrial Fibrillation and Ischemic events with Rivaroxaban in patiEnts with stable coronary artery disease: AFIRE Study

A multicenter, prospective, randomized, open-label, parallel-group trial)



Yasuda S, Kaikita K, Akao M, Ako J, Matoba T, Nakamura M, Miyauchi K, Hagiwara N, Kimura K, Hirayama A, Matsui K, Ogawa H; AFIRE Investigators. Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease. N Engl J Med. 2019 Sep 19;381(12):1103-1113.





Primary End Points

Primary efficacy end point 1);

- > The composite of stroke, systemic embolism, myocardial infarction, unstable angina requiring revascularization, or death from any cause
- Assessed noninferiority of rivaroxaban monotherapy, as compared with combination therapy (noninferiority margin: 1.46 for the 95% CI, with a power of 80%)
- Performed in the modified ITT population

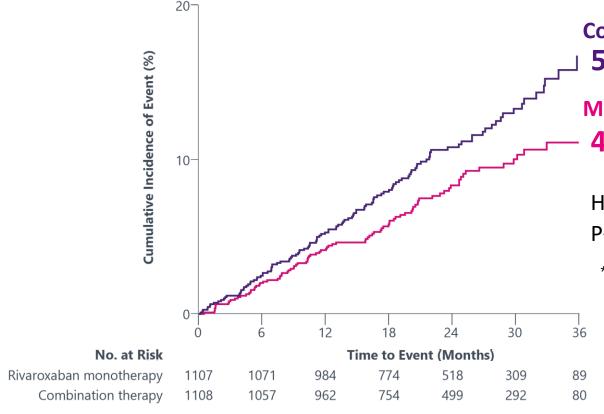
Primary safety end point 1);

- > A closed testing procedure was conducted after assessment of primary efficacy endpoint
- To determine superiority of rivaroxaban monotherapy, as compared with combination therapy
- Major bleeding, as defined according to the criteria of the ISTH*
- Performed in the safety population

Sample size; Estimated that the enrollment of 2200 patients and the occurrence of at least 219 primary efficacy end points were required. 1)



Kaplan-Meier Estimates of First Occurrence of Primary Efficacy Events



Combination therapy

5.75% per patient-year

Monotherapy

4.14% per patient-year

HR, **0.72** (**0.55** to **0.95**) P<0.001 (noninf.)

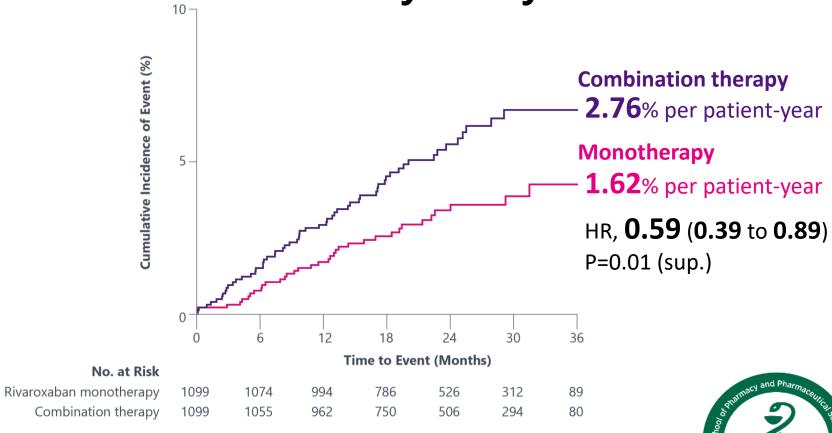
*In the assessment for superiority for the primary efficacy end point (that was not prespecified), the P value was 0.02.



Yasuda S, et al. N Engl J Med. 2019 Sep 19;381(12):1103-1113.



Kaplan-Meier Estimates of First Occurrence of Primary Safety Events

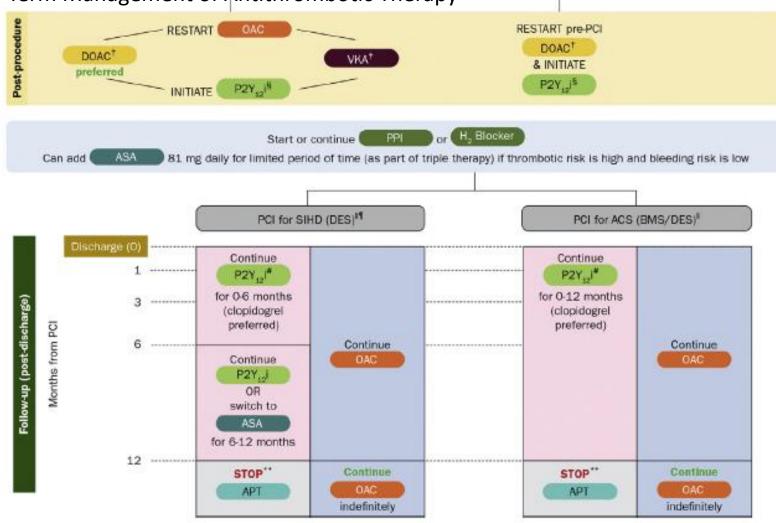


Yasuda S, et al. N Engl J Med. 2019 Sep 19;381(12):1103-1113.

Scenario 1: Patient on OAC requiring PCI

- For patients with AF and indefinite OAC
 - For patients at high risk of bleeding antiplatelet therapy may be discontinued
 - SIHD (no ACS for prior 12 months) after 3 months
 - ACS after 6 months
 - If BMS, at least one month of SAPT
- Add PPI or H2 blocker for patients taking ≥ 2 antithrombotic agent
 - Remember to discontinue when patient APT is discontinued.

Figure 2. Patient With AF on OAC Who Now Needs PCI: Post-Procedure and Long-Term Management of Antithrombotic Therapy



3. JS's hospital discharge antithrombotic regimen should be (Chose one)

- A. Apixaban, aspirin 81 mg, clopidogrel
- B. Apixaban, aspirin 81 mg, ticagrelor
- C. Apixaban, clopidogrel
- D. Bridged warfarin (INR 2-2.5), aspirin 81 mg, clopidogrel
- E. I'm not sure.



3. JS's hospital discharge antithrombotic regimen should be (Chose one)

- A. Apixaban, aspirin 81 mg, clopidogrel
- B. Apixaban, aspirin 81 mg, ticagrelor
- C. Apixaban, clopidogrel
- D. Bridged warfarin (INR 2-2.5), aspirin 81 mg, clopidogrel
- E. I'm not sure.



4. The length of time JS should receive dual antithrombotic is

- A. 1 month
- B. 6 months
- C. 12 months
- D. Greater than 12 months
- E. I'm not sure.



4. The length of time JS should receive dual antithrombotic therapy is

- A. 1 month
- B. 6 months
- C. 12 months
- D. Greater than 12 months
- E. I'm not sure.



Scenario 2: Patient on APT with new VTE

- If primary prevention of ASCVD, discontinue APT, use OAC
- For prior stroke/TIA, stop APT start OAC
- If cerebrovascular disease with carotid endarterectomy, carotid stent or PAD with peripheral stent, use APT for up to1-3 months post stent (in addition to OAC)
- If history of CABG, use APT plus OAC if CABG < 1 year ago.
- If SIHD
 - With DES stent ≥ 12 months ago, discontinue APT, use OAC
 - With stent ≤ 6 months use OAC plus clopidogrel
 - With stent 6-12 months use OAC plus either clopidogrel of aspirin 81 mg/day
- If ACS, use OAC plus clopidogrel

Patient Case: Patient with VTE on OAC who undergoes PCI



- LT is a 54 year-old obese male (110 kg, CrCl 88 mL/min) with a past history of well-controlled Crohn's disease on adalimumab who presented with femoral DVT 4 months ago. He was treated with rivaroxaban 15 mg PO BID for 21 days followed by 20 mg PO daily. He tested negative for antiphospholipid antibodies.
- He presents with STEMI and received a PCI with DES placement in the left anterior descending coronary artery
- He is low-risk for bleeding (other than injection site)

5. LT's hospital discharge antithrombotic regimen should be (Chose one)

- A. Rivaroxaban, aspirin 81 mg, clopidogrel
- B. Rivaroxaban, clopidogrel
- C. Aspirin 81 mg, ticagrelor
- D. None of the above.
- E. I'm not sure.



6. In the absence of a need for APT, how long is anticoagulation indicated for prevention of VTE in LT?

- A. 3 months
- B. 3-6 months
- C. 12 months
- D. Indefinitely
- E. I'm not sure.



7. The length of time LT should receive either dual or triple antithrombotic is

- A. 1 month
- B. 6 months
- C. 12 months
- D. Greater than 12 months
- E. I'm not sure.



8. If rivaroxaban is administered with APT, what would be the appropriate dose of rivaroxaban for LT at hospital discharge following PCI

- A. 15 mg PO daily with food
- B. 20 mg PO daily with food
- C. 10 mg PO daily with or without food



Scenario 3: Patient with VTE on OAC who now needs PCI

- Reassess the duration of OAC for VTE
 - 2020 ASH Guidelines: indefinite OAC for most patients with chronic risk factors, active cancer or unprovoked VTE
 - 3-6 months for transient risk factors (called "timelimited" course)
 - Balanced by risk factors for bleeding
- Reassess risk/benefits of indefinite OAC at least annually

Ortel TL, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. Blood Adv. 2020 Oct 13;4(19):4693-4738.

2020 ASH VTE Guidelines

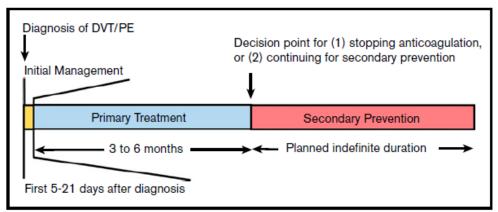


Figure 1. Time frame of the decisions. Initial management (yellow box) spans the first 5 to 21 days following diagnosis of a new VTE and includes issues concerning whether the patient can be treated at home or requires admission to the hospital, use of thrombolytic therapy, whether an IVC filter needs to be placed, and initial anticoagulant therapy. Primary treatment continues anticoagulant therapy for 3 to 6 months total and represents the minimal duration of treatment for the VTE. After completion of primary treatment, the next decision concerns whether anticoagulant therapy will be discontinued or if it will be continued for secondary prevention of recurrent VTE. Typically, secondary prevention is continued indefinitely, although patients should be reevaluated on a regular basis to review the benefits and risks of continued anticoagulant therapy. Our choice of terminology reflects the distinct clinical intentions of the different phases of VTE management, linking them to important clinical decisions addressed in the guidelines, rather than using terms reflecting the relative duration of therapy.



2020 ASH VTE Guidelines

- Primary treatment for
 3-6 months in all patients
- Discontinue anticoagulation after primary treatment in patients with a transient risk factor.
- Indefinite anticoagulation recommended for most patients with unprovoked
 VTE or chronic risk factors

Table 3. Risk factors and venous thromboembolism

Transient risk factors (risk factors that resolve after they have provoked VTE)*

Major transient risk factors (occur within 3 mo of VTE diagnosis); examples include:

Surgery with general anesthesia for ≥30 min

Confined to bed in hospital for ≥3 d with an acute illness ("bathroom privileges" only)

Cesarean section

Minor transient risk factors (occur within 2 mo of VTE diagnosis); examples include:

Surgery with general anesthesia for <30 min

Admission to hospital for <3 d with an acute illness

Estrogen therapy (eg, oral contraceptives, hormone replacement therapy)

Pregnancy and puerperium

Confined to bed out of hospital for ≥3 d with an acute illness

Leg injury associated with decreased mobility for ≥3 d

Chronic (persistent) risk factors (risk factors that persist after the development of VTE)†

Active cancer (eg, ongoing chemotherapy; recurrent or progressive disease)

Inflammatory bowel disease

Autoimmune disorders (eg, antiphospholipid syndrome, rheumatoid arthritis)

Chronic infections

Chronic immobility (eg, spinal cord injury)

Ortel TL, et al. Blood Adv. 2020 Oct 13;4(19):4693-4738.

9. In the absence of a need for APT, how long is anticoagulation indicated for prevention of VTE in LT?

- A. 3 months
- B. 3-6 months
- C. 12 months
- D. Indefinitely
- E. I'm not sure.



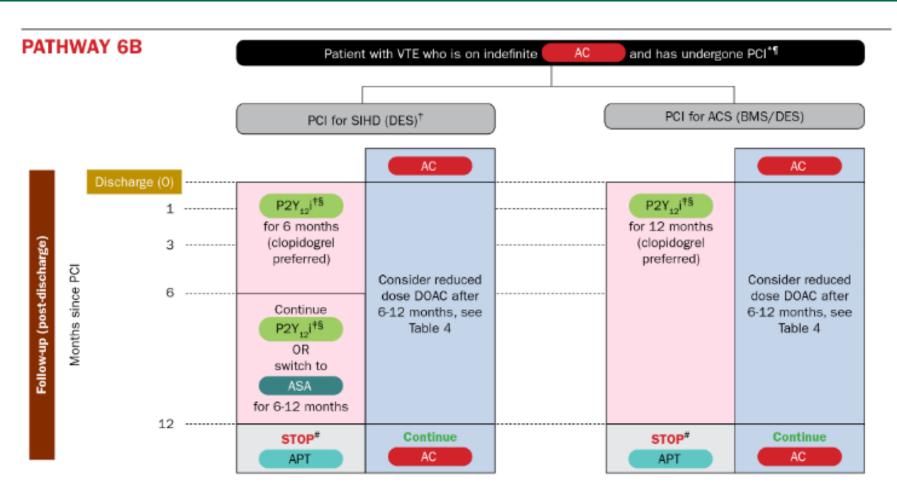
9. In the absence of a need for APT, how long is anticoagulation indicated for prevention of VTE in LT?

- A. 3 months
- B. 3-6 months
- C. 12 months
- D. **Indefinitely**
- E. I'm not sure.



Scenario 3: Patient with VTE on OAC who undergoes PCI

- DOAC preferred over VKA
 - Lower risk of major bleeding in VTE
 - Switch patient on VKA to DOAC
 - Rarely, AKI with resulting renal dysfunction post PCI could necessitate switch from DOAC to VKA
- For DOACs, if primary therapy complete (e.g. after 6 months) and indefinite therapy indicated, use appropriate DOAC dose.
 - Apixaban could be reduced to 2.5 mg PO BID
 - Rivaroxaban could be reduced to 10 mg PO day





10. LT's hospital discharge antithrombotic regimen should be (Chose one)

- A. Rivaroxaban, aspirin 81 mg, clopidogrel
- B. Rivaroxaban, clopidogrel
- C. Aspirin 81 mg, ticagrelor
- D. None of the above.
- E. I'm not sure.



10. LT's hospital discharge antithrombotic regimen should be (Chose one)

- A. Rivaroxaban, aspirin 81 mg, clopidogrel
- B. Rivaroxaban, clopidogrel
- C. Aspirin 81 mg, ticagrelor
- D. None of the above.
- E. I'm not sure.



11. The length of time LT should receive dual antithrombotic is

- A. 1 month
- B. 6 months
- C. 12 months
- D. Greater than 12 months
- E. I'm not sure.



11. The length of time LT should receive dual antithrombotic is

- A. 1 month
- B. 6 months
- C. 12 months
- D. Greater than 12 months
- E. I'm not sure.



12. What is the appropriate dose of rivaroxaban for LT at hospital discharge following PCI?

- A. 15 mg PO daily with food
- B. 20 mg PO daily with food
- C. 10 mg PO daily with or without food



12. What is the appropriate dose of rivaroxaban for LT at hospital discharge following PCI?

- A. 15 mg PO daily with food
- B. 20 mg PO daily with food
- C. 10 mg PO daily with or without food



Reduce to 15 mg PO daily with food in 2 months.

Questions?

