Platelet-ing It Safe:
Dual Antiplatelet Therapy for Special Populations with Coronary Artery Disease

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A Presentation for HealthTrust Members, June 7, 2023

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Disclosure

The presenter and her preceptors have no relevant financial relationships with ineligible companies to disclose.

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Objectives

Pharmacists & Nurses

- Recall **advantages**, potential **risks**, and **characteristics** of P2Y12 inhibitors
- Recognize **guideline recommendations** for the efficacy and bleeding risks associated with P2Y12 inhibitors used in dual antiplatelet therapy for special populations
- Identify appropriate **recommendations for P2Y12 inhibitor selection** in an antiplatelet regimen based on patient-specific recommendations

Objectives

Pharmacy Technicians

- Recall available **P2Y12 inhibitors** used in dual antiplatelet therapy after percutaneous coronary intervention
- Identify **safety considerations** with P2Y12 inhibitors
- Recognize potential **access barriers** for patients receiving P2Y12 inhibitors

01

Introduction

Role of dual antiplatelet therapy in percutaneous coronary intervention

Coronary Artery Disease (CAD)

- **Most common** type of heart disease, affecting 18.2 million American adults
- In the U.S., a myocardial infarction (MI) occurs nearly **every 40 seconds**
- Caused by **plaque buildup** in arteries (atherosclerosis)

Risk factors

- Hypertension
- Hypercholesterolemia
- Diabetes
- Smoking
- Obesity
- Physical inactivity
- Family history

Symptoms

- Chest pain or discomfort (angina)
- Shortness of breath
- Lightheadedness
- Nausea, vomiting
- Diaphoresis

Atherosclerosis

Stable ischemic heart disease (SIHD)

chest pain on exertion

Acute coronary syndrome (ACS)

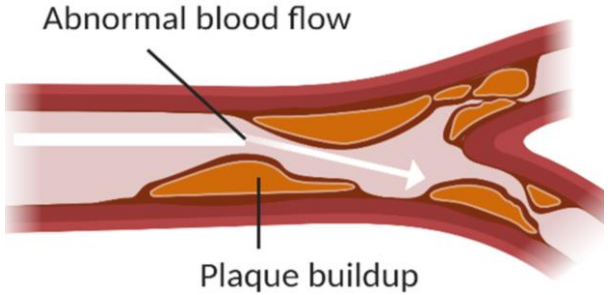
abrupt onset of chest pain

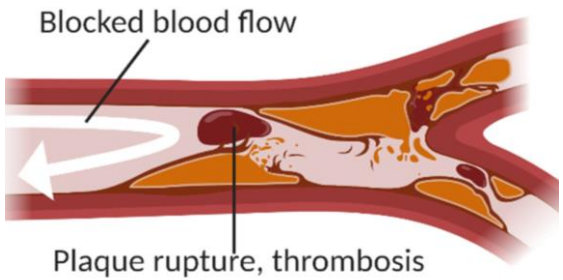
Sources: Libby P, et al. *Circulation*. 2005;111:3481-88.
National Heart, Lung, and Blood Institute. Coronary Heart Disease. 2022.
Fihn SD, et al. *J Am Coll Cardiol*. 2022;60(24):e44-e164.

CAD Pathophysiology

Plaque build-up inside coronary arteries → Partially or completely occluded blood flow → Angina

Plaque build-up inside coronary arteries → Plaque ruptures → Thrombus formation → ACS





Sources: National Heart, Lung, and Blood Institute. Coronary Heart Disease. 2022.
Fihn SD, et al. *J Am Coll Cardiol*. 2022; 60(24):e44-e164.
Images from: Surendran A, et al. *Metabolites*. 2021;11(10):685.

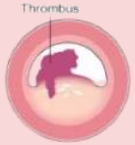
CAD Classification

Atherosclerosis

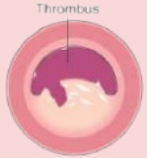
SIHD
no active thrombosis

ACS
sudden thrombotic blockage

NSTE-ACS
ST-segment depression, T-wave inversion, or no ECG changes



STEMI
ST segment elevation



UA
persistent chest pain despite medication and rest

NSTEMI
myocardial damage (elevated troponin)

Complications

- Cardiogenic shock
- Heart failure
- Arrhythmias
- Valvular dysfunction
- Mortality

Goals of therapy

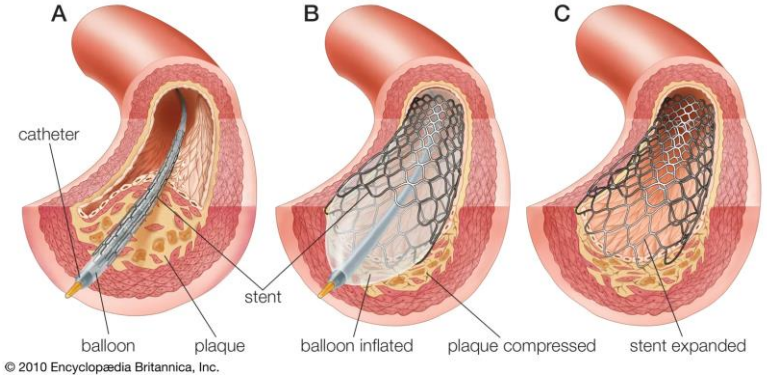
- Restore blood flow to infarct
- Relieve ischemic chest pain
- Reduce risk of recurrent major adverse cardiovascular events (MACE)

Sources: Lawton JS, et al. *Circulation*. 2021;145:e18-e114.
Fihn SD, et al. *J Am Coll Cardiol*. 2022;60(24):e44-e164.
Tsao CW, et al. *Circulation*. 2023;147:e93-e621.
Images from: Blanchaert R, et al. *Curr Opin Cardiol*. 1994;9(4):129-64.

NSTE-ACS: Non-ST-elevation acute coronary syndrome
UA: unstable angina
NSTEMI: non-ST-segment elevated myocardial infarction
STEMI: ST-segment elevated myocardial infarction

Percutaneous Coronary Intervention (PCI)

- **Stent placement** with balloon angioplasty
- Relieves coronary artery occlusion
  - Increases blood flow to ischemic myocardial tissue
- Reduces MI and cardiovascular mortality risks
- Indications
  - **STEMI**: primary PCI
  - **NSTE-ACS**: early invasive approach for intermediate-high TIMI risk scores



TIMI Risk Score *Assess risk of mortality and MACE (1 point each)*		
• Age ≥ 65 years • ≥ 3 CAD risk factors (hypertension, diabetes, family history, current smoker, hypercholesterolemia) • Known CAD (stenosis ≥ 50%) • Aspirin use in past 7 days • Severe angina (≥ 2 episodes in 24 hours) • EKG ST changes • Positive cardiac marker		
Low risk: 0 – 2 points	Intermediate risk: 3 – 4 points	High risk: ≥ 5 points

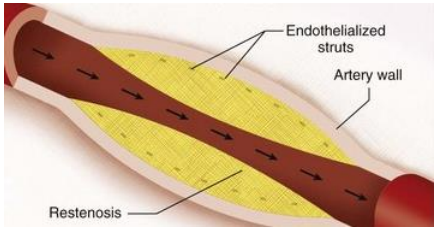
Sources: Lawton JS, et al. *Circulation*. 2021;145:e18-e114.
Bonaa KH, et al. *N Engl J Med*. 2016;375:1242-52.
Bangalore S, et al. *BMJ* . 2013;347:f6625.
Image from: DeBakey ME, et al. *Encyclopedia Britannica*. 2023.

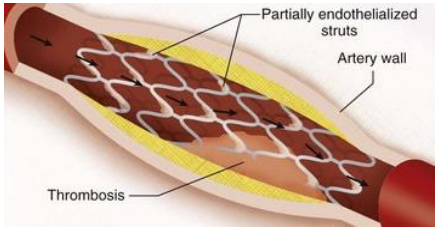
Coronary Artery Stents

Complications

Stent restenosis: growth of chronic, scar tissue
- Gradual narrowing of lumen
- Caused by vessel wall injury

Stent thrombosis: sudden, acute clotting of stent
- Early: within 1 month
- Late: between 1 and 12 months
- Very late: more than 12 months





BMS: Bare metal stent
DES: Drug-eluting stent

Types of Stents

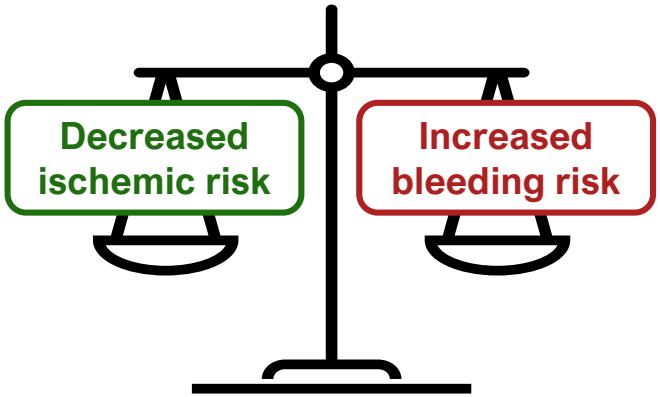
	BMS	First-generation DES	Second-generation DES
Definition	Made of metal mesh	Coated with antiproliferative drug (sirolimus, paclitaxel)	Coated with antiproliferative drug (zotarolimus, everolimus)
Stent restenosis risk	High	Low	Lower than first-generation
Stent thrombosis risk	Early	Late	Late (lower than first-generation)

Sources: Lawton JS, et al. *Circulation*. 2021;145:e18-e114.
Bonaa KH, et al. *N Engl J Med*. 2016;375:1242-52.
Images from: Imaging of Coronary Revascularization. Radiology Key. 2015.

Sources: Bangalore S, et al. *BMJ* . 2013;347:f6625.
Lai CH, et al. *Acta Cardiol Sin*. 2015;31(5):381-9.

Role of Dual Antiplatelet Therapy (DAPT) after PCI

Aspirin + P2Y12 inhibitor



- Synergistic antiplatelet effect
- Decreases stent thrombosis risk
- Reduces recurrence of cardiovascular-related ischemic events, including MI and mortality
- Prevents long-term systemic ischemic events caused by atherosclerotic progression

Sources: Angiolillo DJ, et al. *Eurointervention*. 2022;17:e1371-96.
Park TK, et al. *Circ Cardiovasc Interv*. 2016;9:e002816.
Koski R, et al. *PT*. 2018;43(6):352-57.
Navarese EP, et al. *Circulation*. 2020;142:150-160.

DAPT: Aspirin

	Aspirin
Brand name	Ecotrin®
Mechanism	Inhibits COX-1 and COX-2 activation, which suppresses thromboxane A2 production, preventing platelet aggregation
Binding	Irreversible
Dosing	Once daily
Metabolism	Hepatic hydrolysis
% Inhibition of Platelet Aggregation	30 – 50%
Bleeding risk	↑↑
Clinical pearls	Use with caution in non-steroidal anti-inflammatory drugs (NSAID) allergy
Affordability	Generic; OTC

- Inhibits platelet aggregation to reduce thrombus formation
- Benefit seen in patients with ACS regardless of PCI
  - Reduces incidence of MI and mortality
- Optimal dosing range: 75 mg to 100 mg daily
  - Minimizes bleeding risk
  - Similar protection from ischemic events compared to 325 mg daily

Sources: Angiolillo DJ, et al. *Eurointervention*. 2022;17:e1371-96.
Park TK, et al. *Circ Cardiovasc Interv*. 2016;9:e002816.
Collyer TC, et al. *Br J Anaesth*. 2009;102(4):492-98.

Sources: Koski R, et al. *PT*. 2018;43(6):352-57.
Navarese EP, et al. *Circulation*. 2020;142:150-60.
McQuaid KR, et al. *Am J Med*. 2006;119(8):624-38.

DAPT: Oral P2Y12 Inhibitors

	Clopidogrel	Prasugrel	Ticagrelor
Brand name	Plavix®	Effient®	Brilinta®
Mechanism	Binds to P2Y12 receptor on platelets to inhibit ADP-stimulation platelet activation		
Binding	Irreversible	Irreversible	Reversible
Loading dose	600 mg PO	60 mg PO	180 mg PO
Maintenance dose	75 mg PO once daily	10 mg PO once daily	90 mg PO twice daily
Dose adjustments	None	5 mg PO once daily if < 60 kg Not recommended if ≥ 75 years old	None
Metabolism	Prodrug; CYP2C19	Prodrug; esterases in intestinal tract	CYP3A4
% Inhibition of Platelet Aggregation	40 – 60%	70 – 80%	60 – 80%
Bleeding Risk	↑↑	↑↑↑	↑↑↑
Clinical pearls	Reduced efficacy with inhibitors and poor metabolizers of CYP2C19	Contraindicated with history of prior stroke or transient ischemic attack	May cause dyspnea and bradycardia; limit concomitant aspirin dose to 100 mg/day max
Affordability	Generic	Generic	Brand only

Note: clopidogrel is the recommended P2Y12 inhibitor for DAPT after PCI for SIHD

Sources: Koski R, et al. *PT*. 2018;43(6):352-57.
Navarese EP, et al. *Circulation*. 2020;142: 50-160.
Westman PC, et al. *Cardiovasc Revasc Med*. 2017;18(2):79-85.

Sources: Angiolillo DJ, et al. *Eurointervention*. 2022;17:e1371-96.
Park TK, et al. *Circ Cardiovasc Interv*. 2016;9.
Butler K, et al. *Br J Clin Pharmacol*. 2010;70(1):65-77.

Landmark Trials: P2Y12 Inhibitors in DAPT after PCI for ACS

Trial	Population	Intervention	Control	Major bleeding	MACE	Key results
TIMI-TRITON 38 (2007)	N = 13,608 ACS PCI: 99%	**Prasugrel** LD: 60 mg MD: 10 mg daily	**Clopidogrel** LD: 300 mg MD: 75 mg daily	HR 1.32 (1.03-1.68), **p = 0.03**	HR 0.81 (0.73-0.90), **p < 0.001**	↑ bleeding ↓ MACE
PLATO (2009)	N = 18,624 ACS PCI: ~60%	**Ticagrelor** LD: 180 mg MD: 90 mg BID	**Clopidogrel** LD: 300 mg MD: 75 mg daily	HR 1.04 (0.95-1.13), p = 0.43 Major or minor bleeding: HR 1.11 (1.03-1.20), **p = 0.008**	HR 0.84 (0.77-0.92), **p < 0.001**	↑ bleeding ↓ MACE
ISAR-REACT 5 (2019)	N = 4,018 ACS PCI: ~83%	**Ticagrelor** LD: 180 mg MD: 90 mg BID	**Prasugrel** LD: 60 mg MD: 10 mg daily	HR 1.12 (0.83-1.51), p = 0.46	HR 1.36 (1.09-1.70) **p = 0.006**	No difference in bleeding ↑ MACE

2021 ACC/AHA/SCAI Coronary Artery Revascularization Guideline Recommendation
Consider ticagrelor or prasugrel in preference to clopidogrel to reduce ischemic events (Level 2a)

Sources: Wiviott SD, et al. *N Engl J Med*. 2007;357:2001-15. Wallentin L, et al. *N Engl J Med*. 2009;361:1045-57.

Sources: Schupke S, et al. *N Engl J Med*. 2019;381:1524-34. Lawton JS, et al. *Circulation*. 2021;145:e18-e114.

Assessment Question #1 – Pharmacy Techs

Which of the following medications is **NOT** a P2Y12 inhibitor used as part of dual antiplatelet therapy?

A. Apixaban (Eliquis®)
B. Clopidogrel (Plavix®)
C. Prasugrel (Effient®)
D. Ticagrelor (Brilinta®)

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C. Prasugrel (Effient®)
D. Ticagrelor (Brilinta®)

Assessment Question #2 – Pharmacy Techs

Prasugrel is contraindicated in patients with a history of...?

A. Diabetes
B. Peptic ulcer disease
C. Stroke or transient ischemic attack
D. Myocardial infarction

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Assessment Question #3 – Pharmacists / Nurses

Which of the following is ranked correctly from **highest to lowest potency**?

A. Clopidogrel > ticagrelor > prasugrel
B. Prasugrel = ticagrelor > clopidogrel
C. Prasugrel > clopidogrel > ticagrelor
D. Ticagrelor > prasugrel > clopidogrel

Assessment Question #3 – Pharmacists / Nurses

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B. **Prasugrel = ticagrelor > clopidogrel**
C. Prasugrel > clopidogrel > ticagrelor
D. Ticagrelor > prasugrel > clopidogrel

DAPT in Special Populations

Triple Therapy

High Bleeding Risk

- Prasugrel and ticagrelor are more potent compared with clopidogrel but have higher bleeding risk
- Many patients on DAPT, however, have **high bleeding risk** or indication(s) for **anticoagulation**
- DAPT regimens can be tailored to patient-specific bleeding and ischemic risks

What DAPT strategies can be used mitigate increased bleeding risk?

DAPT in Special Populations

Genetic Polymorphisms

- Clopidogrel demonstrates **interpatient variability in platelet inhibition**
  - Inadequate platelet inhibition and reduced antiplatelet efficacy
  - **Risk of increased ischemic events**

- In contrast, prasugrel and ticagrelor have consistent platelet inhibition

Which patients should undergo genetic testing prior to DAPT?

02

High Bleeding Risk

Strategies for dual antiplatelet therapy in high bleed risk

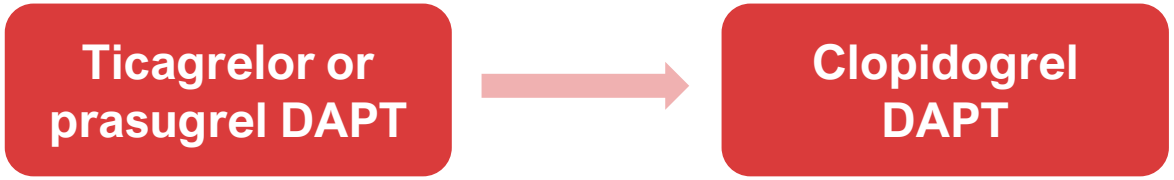
Bleeding & Ischemic Risk Assessment

↑ bleeding risk	↑ ischemic risk	↑ stent thrombosis risk
• Advanced age • Diabetes • History of prior bleeding • Female sex • Low body weight • Oral anticoagulant therapy • Chronic kidney disease • Anemia • Chronic steroid or NSAID therapy	• Advanced age • Diabetes • ACS presentation • Multiple prior myocardial infarctions • Extensive CAD • Chronic kidney disease	• ACS presentation • Diabetes • LVEF < 40% • First-generation DES • Small stent diameter • Greater stent length • Bifurcation stents • In-stent restenosis

- Choice of antiplatelet medication is a modifiable factor to reduce bleeding risk
  - **Clopidogrel has the lowest bleeding risk** of the P2Y12 inhibitors

Sources: Angiolillo DJ, et al. *Eurointervention*. 2022;17:e1371-96.
Levine GN, et al. *Circulation*. 2016;134:e123-e155.

P2Y12 Inhibitor De-escalation



- Not routinely recommended
- Can be considered for patients with **high bleeding risk**
- Avoid de-escalating within 1 month of PCI due to high risk of stent thrombosis

Sources: Angiolillo DJ, et al. *Eurointervention*. 2022;17:e1371-96.
Levine GN, et al. *Circulation*. 2016;134:e123-e155.
Musa T, et al. *J Am Coll Cardiol*. 2021.

Randomized Controlled Trials: P2Y12 Inhibitor De-escalation

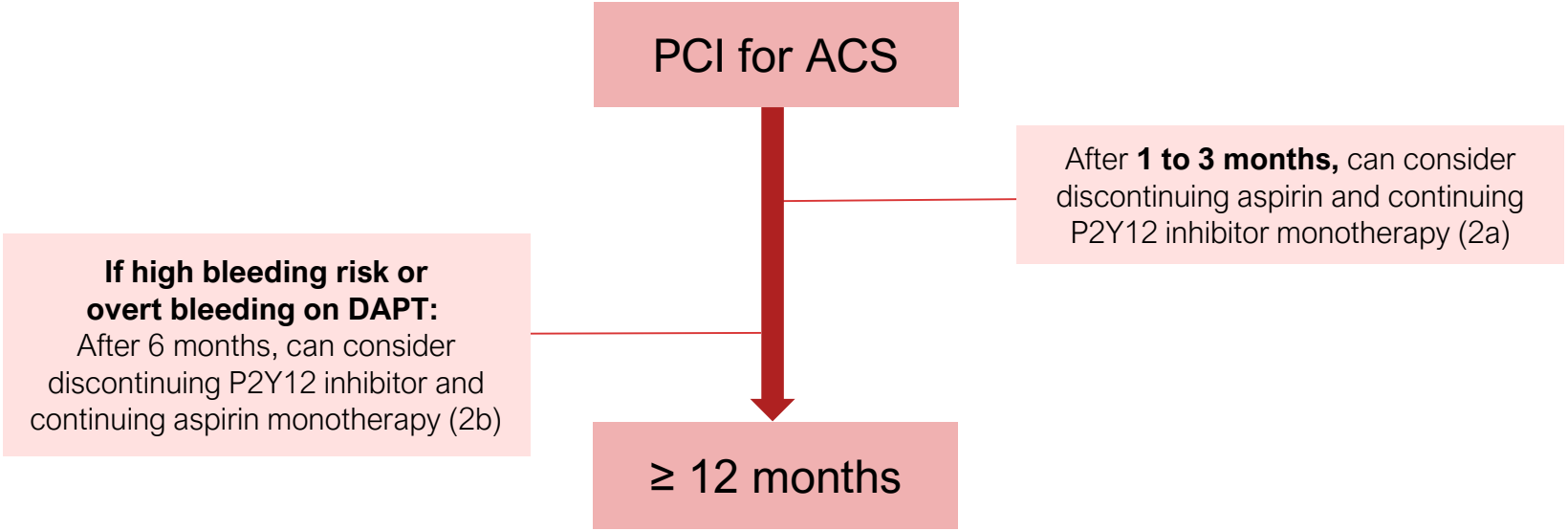
Trial	Patients	Intervention	Control	Major bleeding	MACE	Net clinical benefit*	Key results
TOPIC (2017)	N = 646 ACS: 100%	**De-escalation at 1 month** Prasugrel or ticagrelor to clopidogrel	Clopidogrel DAPT	HR 0.39 (0.27-0.57), **p < 0.01**	HR 0.48 (0.34-0.68), p = 0.36	HR 0.48 (0.34-0.68), **p < 0.01**	↓ bleeding No difference in MACE Greater net clinical benefit
TALOS-AMI (2021)	N = 2,697 ACS: 100%	**De-escalation at 1 month** Ticagrelor to clopidogrel	Ticagrelor DAPT	HR 0.52 (0.35 - 0.77), **p = 0.0012**	HR 0.69 (0.42 - 1.14), p = 0.15	HR 0.55 (0.40 - 0.76), **p = 0.0001**	↓ bleeding No difference in MACE Greater net clinical benefit

*Composite of ischemic and bleeding events

Sources: Cuisset T, et al. *Eur Heart J*. 2017;38(41):3070-78.
Kim CJ, et al. *Lancet*. 2021;398(10308):1305-16.

Post-PCI DAPT Duration

2021 ACC/AHA/SCAI Guideline Recommendations



- Consider **shorter-duration DAPT (1 - 3 months)** with transition to P2Y12 inhibitor monotherapy in select patients **to reduce bleeding risk** (Level 2a)

Source: Lawton JS, et al. *Circulation*. 2021;145:e18-e114.

Randomized Controlled Trials: Shortened Duration

Trial	Patients	Intervention	Control	MACE	Bleeding
SMART CHOICE (2019)	N = 2,993 STEMI: 10% NSTE-ACS: 48%	**3 months DAPT**, then P2Y12 inhibitor monotherapy	12 months DAPT	2.9% in short DAPT vs 2.5% in control **(p < 0.001 for noninferiority)**	HR 0.58 (0.36 - 0.92), **p = 0.02**
TWILIGHT (2019)	N = 9,006 STEMI: 0% NSTE-ACS: 63%	**3 months DAPT**, then P2Y12 ticagrelor monotherapy	12 months DAPT (ticagrelor)	3.9% in short DAPT vs 3.9% in control **(p < 0.001 for noninferiority)**	HR 0.56 (0.45 - 0.68), **p < 0.001**
TICO (2020)	N = 3,056 **STEMI: 36%** NSTE-ACS: 64%	**3 months DAPT**, then ticagrelor monotherapy	12 months DAPT (ticagrelor)	2.3% in short DAPT vs 3.4% in control (p = 0.09)	HR 0.56, (0.34 - 0.91), **p = 0.02**
STOP-DAPT2 (2019)	N = 3,045 STEMI: 19% NSTE-ACS: 20%	**1 month DAPT** (clopidogrel, prasugrel), then clopidogrel monotherapy	12 months DAPT (clopidogrel), then aspirin monotherapy	1.96% in short DAPT vs 2.51% in control **(p = 0.005 for noninferiority)**	HR 0.26 (0.11 - 0.64), **p = 0.004**

Sources: Hahn JY, et al. *JAMA*. 2019;321(24):2428-37.
Mehran R, et al. *N Engl J Med*. 2019;381:2032-42.
Kim BK, et al. *JAMA*. 2020;323(23):2407-16.
Watanabe H, et al. *JAMA*. 2019;321(24):2414-27.

Key findings:
Shortened durations of DAPT reduced bleeding risk without increasing MACE

MASTER-DAPT, 2021

Open-label RCT

N = 4579 patients with high bleeding risk who underwent PCI using sirolimus DES (2nd gen)
STEMI: 12% NSTE-ACS: 37%

DAPT for 1 month, then either aspirin or P2Y12 inhibitor monotherapy*

*If on oral anticoagulation, aspirin or P2Y12 inhibitor for up to 6 months

DAPT for 6 months, then either aspirin or P2Y12 inhibitor monotherapy¥

¥If on oral anticoagulation, DAPT for 3 months

	Composite of cardiovascular or bleeding events	MACE	Major bleeding
DAPT for 1 month vs 6 months	HR 0.97 (0.78 - 1.2), **p < 0.001 for noninferiority**	HR 1.02 (0.8 - 1.3), **p = 0.001 for noninferiority**	HR 0.68 (0.55 - 0.84), **p < 0.001**

- In patients with **high bleeding risk**, 1-month DAPT was **noninferior** to 6-month DAPT
- Reduction in major bleeding events without increased MACE
- Considerations:
  - 36% of study population were on oral anticoagulation
  - Control group had large variability in DAPT duration (2 to 12 months)

Source: Valgimigli M, et al. *N Engl J Med*. 2021;385(18):1643-55.

STOPDAPT-2 ACS, 2022

Open-label RCT

N = 4136 patients with ACS and underwent PCI using everolimus DES (2nd gen)
STEMI: 56% NSTE-ACS: 20%

1-to-2-month DAPT*, then clopidogrel monotherapy

12-month DAPT*

*clopidogrel (52%) or prasugrel (47%) in first 1 to 2 months, then switched to clopidogrel

Results	**Composite of cardiovascular or bleeding events**	**MACE**	**Major bleeding**
Shortened vs standard duration	HR 1.14 (0.80 - 1.62), p = 0.06 for noninferiority	HR 1.50 (0.99 - 2.26)	HR 0.46 (0.23 - 0.94)

- Shortened DAPT of 1 to 2 months **failed to show noninferiority** to 12 months of DAPT for composite of cardiovascular or bleeding events
- Reduced major bleeding events but trend towards increased MACE
- **Inconclusive findings**
- Considerations: clopidogrel resistance not evaluated (Japanese population)

Source: Watanabe H, et al. *JAMA Cardiol*. 2022;7(4):407-417.

Strategies for High Bleeding Risk after PCI

Key Takeaways

P2Y12 inhibitor selection

- **Clopidogrel** is most supported by studies for patients at high bleeding risk
- Prasugrel and ticagrelor have higher bleeding risks

De-escalation of P2Y12 inhibitor

- **After 1 month**, consider switching from DAPT with **ticagrelor or prasugrel to clopidogrel**
  - Associated with reduced bleeding risk without increasing ischemic risk

Shortened Duration

- **After 1 to 3 months,** consider discontinuing aspirin and continuing **clopidogrel or ticagrelor monotherapy**
  - Less bleeding risk associated with shorter DAPT durations
  - In **patients with STEMI** prior to PCI, early aspirin discontinuation is **NOT** strongly supported
- **If high bleeding risk or overt bleeding after 6 months**, consider discontinuing P2Y12 inhibitor and continuing **aspirin monotherapy**

Triple Therapy

Risks and benefits of dual antiplatelet therapy with long-term anticoagulation

Patient Case

Patient AB is a 75-year-old male (87 kg) with a past medical history of osteoarthritis, type 2 diabetes, and **nonvalvular atrial fibrillation**.

AB was hospitalized **3 weeks ago** for **NSTEMI**. He underwent percutaneous coronary intervention with a **second-generation drug-eluting stent** and was discharged on dual antiplatelet therapy.

AB presents to the clinic today for a follow-up visit. He reports adherence to all current medications.

Current Medications

- **Aspirin 81 mg PO daily**
- **Ticagrelor 90 mg PO BID**
- **Apixaban 5 mg PO BID**
- Atorvastatin 40 mg PO daily
- Metoprolol succinate 25 mg PO daily
- Ibuprofen 400 mg PO TID
- Semaglutide 1 mg subcutaneous weekly

Assessment Question #4 – Pharmacists / Nurses

Which of these factors increase AB's thrombotic risk? *Select all that apply.*

A. Diabetes
B. Osteoarthritis
C. Second-generation drug-eluting stent
D. History of NSTEMI
E. Semaglutide use

Assessment Question #4 – Pharmacists / Nurses

Which of these factors increase AB's thrombotic risk? *Select all that apply.*

A. **Diabetes**
B. Osteoarthritis
C. Second-generation drug-eluting stent
D. **History of NSTEMI**
E. Semaglutide use

Assessment Question #5 – Pharmacists / Nurses

Which of these factors increase AB's bleeding risk? *Select all that apply.*

A. Chronic ibuprofen use
B. Advanced age
C. Anticoagulant use
D. Male sex

Assessment Question #5 – Pharmacists / Nurses

Which of these factors increase AB's bleeding risk? *Select all that apply.*

A. **Chronic ibuprofen use**
B. **Advanced age**
C. **Anticoagulant use**
D. Male sex

Triple Therapy

Aspirin + P2Y12 inhibitor + oral anticoagulant (OAC)

- Two- to three-fold increased bleeding risk
- Indications for anticoagulation
  - **Atrial fibrillation** – most evidence
  - Venous thromboembolism
  - Prosthetic heart valves

Available OAC agents

	Warfarin	Apixaban	Rivaroxaban	Edoxaban	Dabigatran
Brand name	Coumadin®	Eliquis®	Xarelto®	Savaysa®	Pradaxa®
Class	Vitamin K antagonist (VKA)	Direct-acting oral anticoagulant (DOAC)			
Mechanism	Inhibits VKORC1 enzyme, which reduces synthesis of clotting factors II, VII, IX, and X	Directly inhibits factor Xa, preventing thrombin production and clot formation			Directly binds thrombin and prevents activation of clotting factors

Sources: Angiolillo DJ, et al. *Circulation*. 2018;138:527-36.
Sharma R, et al. *Cardiol Ther*. 2020;9(2):349-61.
Lawton JS, et al. *Circulation*. 2021;145:e18-e114.

Atrial Fibrillation (AF) on Anticoagulation after PCI

2021 ACC/AHA/SCAI Guideline Recommendations

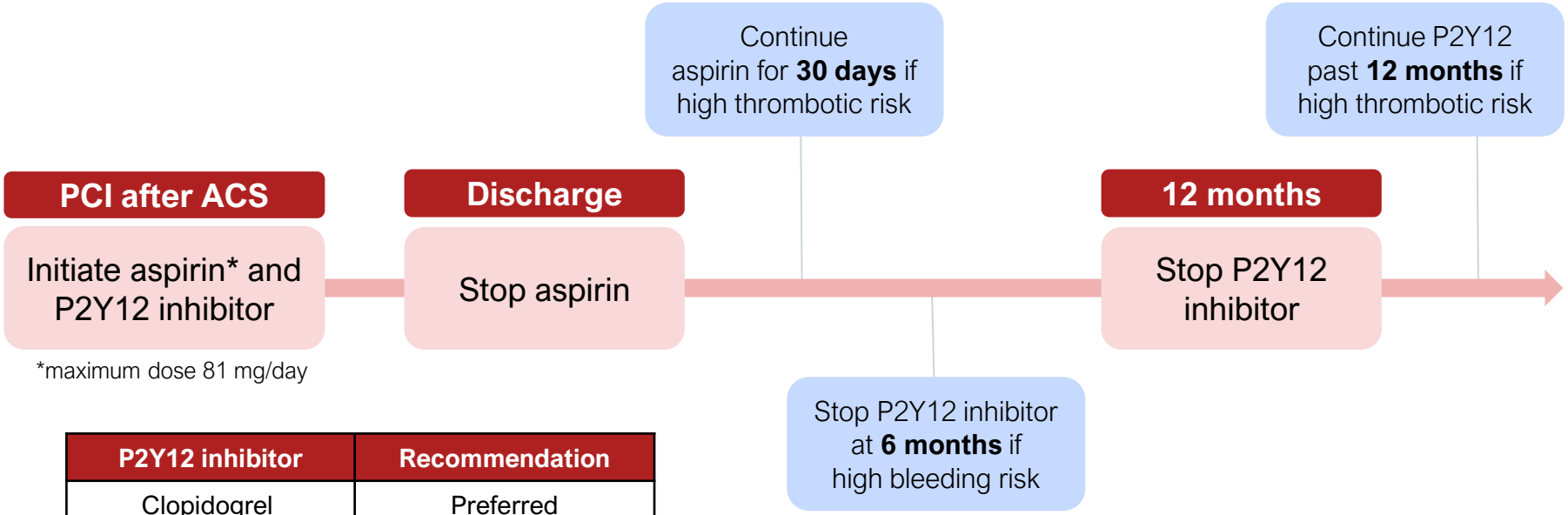
- **Discontinue aspirin treatment after 1 to 4 weeks** (Level 1)
  - Maintain P2Y12 inhibitor and anticoagulant to reduce bleeding risk (Level 1)

- **Consider DOAC over warfarin** to reduce bleeding risk (Level 2a)
  - Apixaban, rivaroxaban, edoxaban, dabigatran

Source: Lawton JS, et al. *Circulation*. 2021;145:e18-e114.

Atrial Fibrillation (AF) on Anticoagulation after PCI

2020 ACC Expert Consensus Decision Pathway



*maximum dose 81 mg/day

P2Y12 inhibitor	Recommendation
Clopidogrel	Preferred
Ticagrelor	Consider for ACS
Prasugrel	Avoid

Source: Khumbani DJ, et al. *J Am Coll Cardiol.* 2021;77(5):629-58.

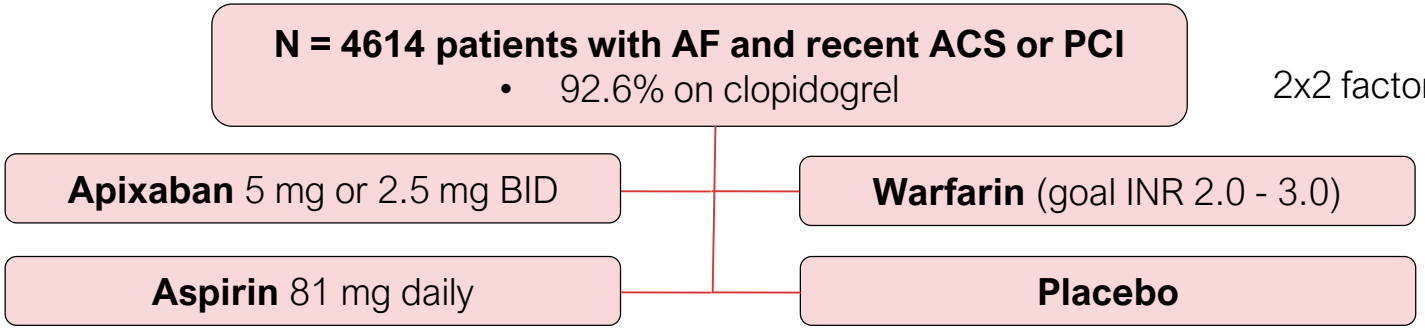
Randomized Controlled Trials: Triple Therapy in AF after PCI

Trial	Population	Intervention	Control	Major Bleeding	MACE
WOEST (2013)	N = 563 AF: 69%	**Warfarin** + clopidogrel	Warfarin triple therapy	HR 0.36 (0.26-0.50), **p < 0.0001**	HR 0.60 (0.38-0.94), **p = 0.025**
PIONEER AF-PCI (2016)	N = 2124 AF: 100%	**Rivaroxaban 15 mg daily** + clopidogrel*	Warfarin triple therapy*	HR 0.59 (0.47-0.76), **p < 0.001**	HR 1.08 (0.69-1.68), p = 0.75
		Rivaroxaban 2.5 mg BID + DAPT*		HR 0.63 (0.50-0.80), **p < 0.001**	HR 0.93 (0.59-1.48), p = 0.76
RE-DUAL PCI (2017)	N = 2725 AF: 100%	**Dabigatran 110 mg BID** + clopidogrel*	Warfarin triple therapy*	HR 0.52 (0.42-0.63), **p < 0.001**	HR 1.04, (0.84-1.29), P = 0.25
		Dabigatran 150 mg BID + clopidogrel*		HR 0.72 (0.58-0.88), **p < 0.002**	
ENTRUST AF-PCI (2019)	N = 1506 AF: 100%	**Edoxaban 60 mg (or 30 mg) daily** + clopidogrel*	Warfarin triple therapy*	HR 0.83 (0.65-1.05), **p = 0.0010 for noninferiority**	HR 1.06 (0.71-1.69), not significant

**Use of alternative P2Y12 inhibitor (ticagrelor or prasugrel) was < 15%*

Sources: Dewilde WJM, et al. *Lancet*. 2013;381(9872):1107-15.
Gibson CM, et al. *N Engl J Med*. 2016;375:2423-34.
Cannon CP, et al. *N Engl J Med*. 2017;377:1513-24.
Vranckx P, et al. *Lancet*. 2019;394(10206):1335-43.

AUGUSTUS, 2019



2x2 factorial design

Results	Major bleeding	MACE	Death or hospitalization
Apixaban vs warfarin	HR 0.69 (0.58-0.81), **p < 0.001**	0.93 (0.75-1.16), not significant	0.83 (0.74-0.93), **p = 0.002**
Aspirin vs placebo	HR 1.89 (1.59-2.24), **p < 0.001**	0.89 (0.71-1.11), not significant	1.08 (0.96-1.21), not significant

Major bleeding events per 100 patient years:

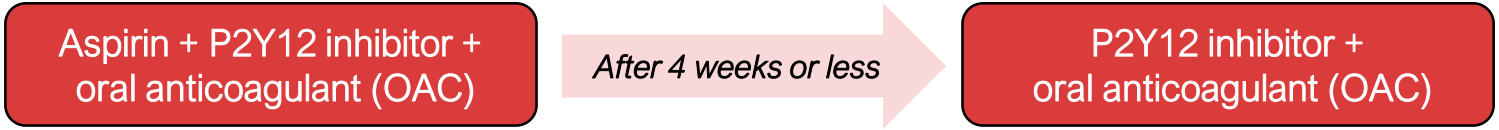
49.1 - warfarin + aspirin
33.6 - apixaban + aspirin
26.7 - warfarin + placebo
16.8 - apixaban + placebo

Source: Lopes RD, et al. *N Engl J Med*. 2019;380:1509-24.

Atrial Fibrillation (AF) on Anticoagulation after PCI

Key Takeaways

Duration of aspirin



Anticoagulant selection

- **DOAC** use is more supported in studies compared to warfarin

P2Y12 inhibitor selection

- **Clopidogrel** is preferred in most situations involving triple therapy
- Ticagrelor can be considered for PCI in the setting of ACS
- Avoid prasugrel use with concomitant OAC

Duration of P2Y12 inhibitor

- Continue for **12 months** for most patients with ACS and DES
- Consider shortened duration of **6 months if high bleeding risk**
- Can prolong past 12 months if high thrombotic risk and low bleeding risk

Patient Case

Patient AB is a 75-year-old male (87 kg) with a past medical history of osteoarthritis, type 2 diabetes, and **nonvalvular atrial fibrillation**.

AB was hospitalized **3 weeks ago** for **NSTEMI**. He underwent percutaneous coronary intervention with a **second-generation drug-eluting stent** and was discharged on dual antiplatelet therapy.

AB presents to the clinic today for a follow-up visit. He reports adherence to all current medications.

Current Medications

- **Aspirin 81 mg PO daily**
- **Ticagrelor 90 mg PO BID**
- **Apixaban 5 mg PO BID**
- Atorvastatin 40 mg PO daily
- Metoprolol succinate 25 mg PO daily
- Ibuprofen 400 mg PO TID
- Semaglutide 1 mg subcutaneous weekly

Assessment Question #6 – Pharmacists / Nurses

Based on AB's bleeding and thrombotic risks, how could his triple therapy regimen of apixaban, ticagrelor, and aspirin be adjusted?

A. Reduce ticagrelor dose and continue triple therapy
B. Discontinue aspirin only and continue ticagrelor and apixaban
C. Reduce apixaban dose and continue triple therapy
D. Continue aspirin, ticagrelor, and apixaban indefinitely

Assessment Question #6 – Pharmacists / Nurses

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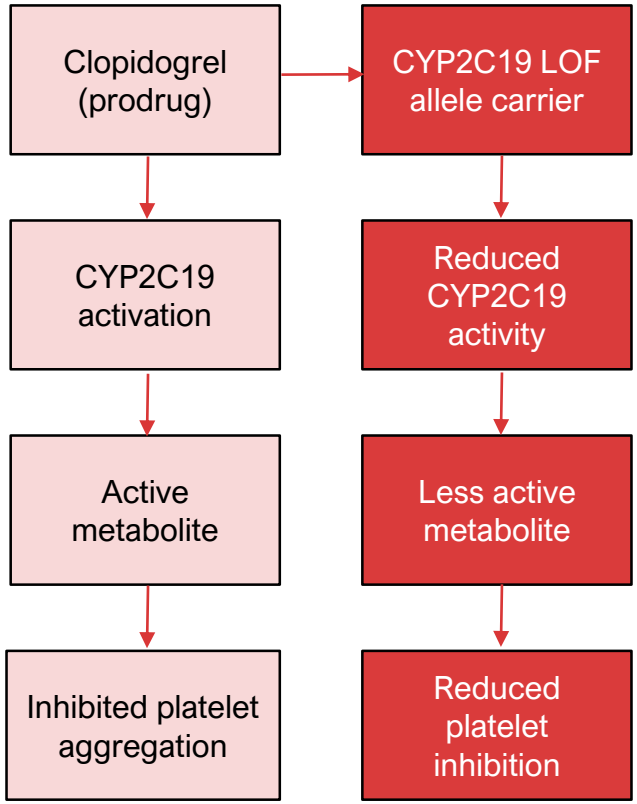
04

Genetic Polymorphisms

Dual antiplatelet therapy in CYP2C19 polymorphisms

CYP2C19 Genetic Polymorphisms



- CYP2C19 metabolizer phenotype responses to clopidogrel
  - **Intermediate (IMs)** - reduced
  - **Poor (PMs)** - significantly reduced
- More than 30% of individuals in the U.S. carry a **CYP2C19 loss-of-function (LOF) allele**
  - IMs: 20 – 30%
  - PMs: 1 – 5%
- East Asians have a higher prevalence of CYP2C19 LOF allele
- **Clopidogrel Black Box Warning**
  - Significantly reduced antiplatelet efficacy in CYP2C19 PMs
- Genotype-guided therapy may be reasonable in certain patients

Sources: Klein MD, et al. *Arterioscler Thromb Vasc Biol.* 2019;39:647-52.
Sibbing D, et al. *JACC Cardiovasc Interv*. 2019;12(16):1521-37.

CYP2C19 Genotype-Guided Therapy

2022 Clinical Pharmacogenetics Implementation Consortium Guideline Recommendations

CYP2C19 phenotype	Genotype	Clopidogrel metabolism	Clinical implication	Recommendation
Normal metabolizer	Two normal function alleles	Normal	--	Clopidogrel 75 mg daily
Intermediate metabolizer	One LOF allele	Reduced	Increased risk for ischemic events	Use prasugrel or ticagrelor* if no contraindication
Poor metabolizer	Two LOF alleles	Significantly reduced		

**Prasugrel 10 mg daily or ticagrelor 90 mg BID*

Source: Lee CR, et al. *Clin Pharmacol Ther.* 2022;112(5):959-67.

CYP2C19 Genotype Testing after PCI

ACC/AHA/SCAI Guideline Recommendations

2011 PCI	Consider genetic testing if high risk for poor clinical outcomes (Class 2b) • Urgent PCI for an ACS event • Elective high-risk PCIs for left main bifurcation or last patent artery
2016 Duration of DAPT in CAD	Routine genetic testing NOT recommended due to insufficient evidence that supports improved outcomes (Class 3: No Benefit)
2021 Coronary Artery Revascularization	Not discussed

- More recent evidence suggests that CYP2C19 genotype-guided therapy can improve risk of MACE

Sources: Levine GN, et al. *Circulation*. 2011;124:e574-651.
Levine GN, et al. *Circulation*. 2016;134:e123-e155.
Lawton JS, et al. *Circulation*. 2021;145:e18-e114.

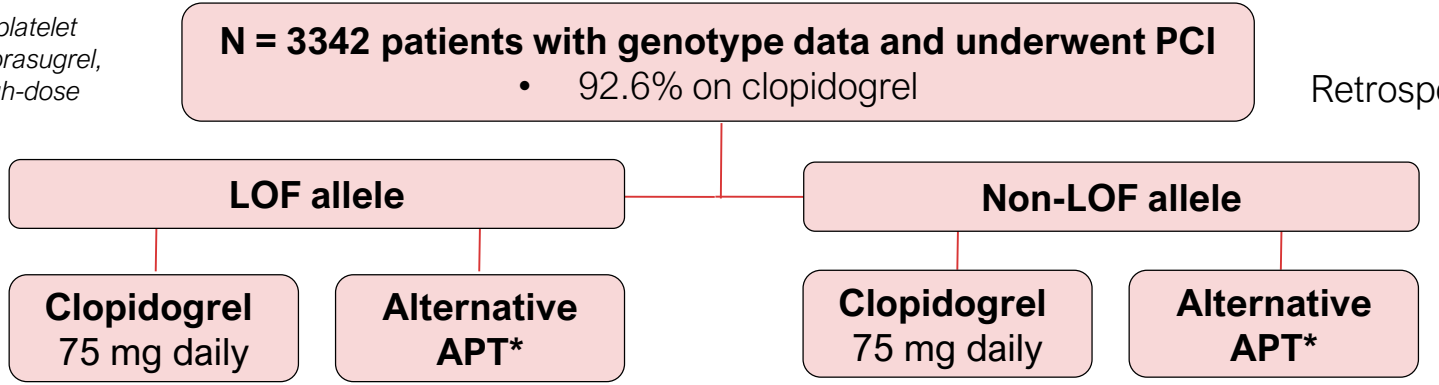
Randomized Controlled Trials: CYP2C19 Genotype-Guided Therapy after PCI

Trial	Patients	Intervention	Control	MACE	Bleeding	Considerations
PHARMCLO (2018)	N = 888	**Genotype-guided** LOF: ticagrelor or prasugrel Non-LOF: clopidogrel, ticagrelor, prasugrel	Standard therapy (clopidogrel, ticagrelor, prasugrel)	HR 0.58 (0.43-0.78), **p < 0.001**	HR 0.62 (0.35-1.1), p = 0.1	MACE in patients on clopidogrel: HR 0.68 (0.47-0.97), **p = 0.03** Prasugrel: < 10% per group
POPular Genetics (2019)	N = 2488	**Genotype-guided** LOF: ticagrelor or prasugrel non-LOF: clopidogrel	Standard therapy (ticagrelor, prasugrel)	HR 0.87 (0.62-1.21), p = 0.40	HR 0.78 (0.61-0.98), **p = 0.04**	Prasugrel: < 2% per group
TAILOR-PCI (2020)	N = 1849	**Genotype-guided** LOF: ticagrelor non-LOF: clopidogrel	Standard therapy (clopidogrel)	HR 0.66 (0.43-1.02), p = 0.06	HR 1.22 (0.60-2.52), p = 0.58	MACE at 90 days: HR 0.21 (0.08-0.54), **p = 0.001**

Sources: Notarangelo FM, et al. *J Am Coll Cardiol.* 2018;71(17):1869-77.
Claassens DMF, et al. *N Engl J Med*. 2019;381:1621-31.
Pereira NL, et al. *JAMA*. 2020;324(8):761-71.

Beitelshees et al, 2022

**Alternative antiplatelet therapy (APT): prasugrel, ticagrelor, or high-dose clopidogrel*



Results	MACE	MACE at 90 days	Clinically significant bleeding events
LOF: Alternative APT vs clopidogrel	HR 0.56 (0.39-0.82), **p = 0.002**	HR 0.40 (0.23-0.71), **p = 0.002**	HR 1.15 (0.60-2.20), p = 0.685
Non-LOF: Alternative APT vs clopidogrel	HR 1.08 (0.72-1.62), p = 0.715	HR 1.09 (0.64-1.86), p = 0.752	HR 1.30 (0.71-2.38), p = 0.397
Clopidogrel: LOF vs non-LOF	HR 1.67 (1.27-2.19), **p < 0.001**	--	--

Source: Beitelshees AL, et al. *J Am Heart Assoc*. 2022;11:e024159.

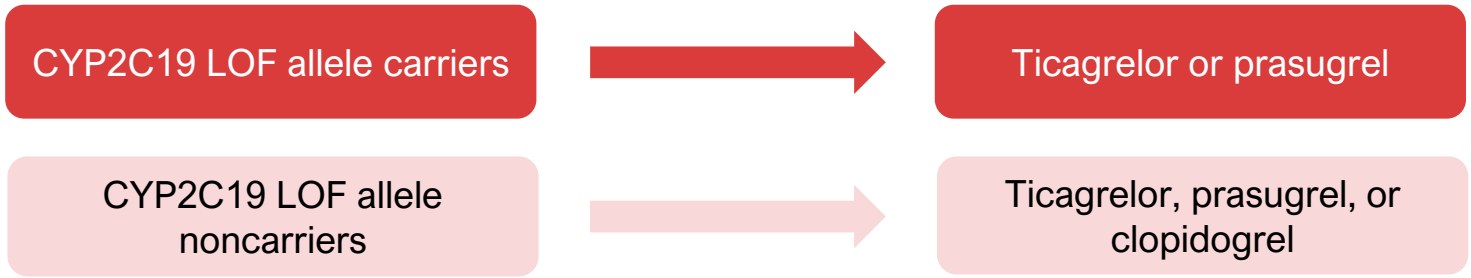
CYP2C19 Genotype Testing after PCI

- No strong recommendations to support or oppose genotype-guided therapy
  - Recent studies add to existing evidence that validates clinical utility of genetic testing
- Point-of-care genotype testing being considered outside of U.S.
  - Proposed place in therapy: replace laboratory testing
  - Insufficient evidence to show point-of-care testing improves outcomes
- Emerging pharmacist role in pharmacogenomics-based therapy

Sources: Owusu-Obeng A, et al. *Pharmacotherapy.* 2014;34(10):1102-12.
Klein MD, et al. *Arterioscler Thromb Vasc Biol*. 2019;39:647-52.
Sibbing D, et al. *JACC Cardiovasc Interv*. 2019;12(16):1521-37.

CYP2C19 Genotype-Guided Therapy after PCI

Key Takeaways



- Genotype-guided therapy reduced ischemic events without significantly increasing major bleeding
- Genetic testing not routinely recommended but can be considered in high-risk patients

P2Y12 inhibitor selection

- Consider **ticagrelor or prasugrel** in patients who are **CYP2C19 LOF allele carriers**
- Majority of randomized controlled trial populations were on ticagrelor

Assessment Question #7 – Pharmacists / Nurses

KZ is a 54-year-old female who underwent PCI and will be started on DAPT. Genotype testing results indicate KZ is a **poor CYP2C19 metabolizer**. Based on the **2022 Clinical Pharmacogenetics Implementation Consortium Guidelines**, which of the following is true regarding P2Y12 inhibitor therapy?

A. Clopidogrel therapy can increase KZ's bleeding risk
B. Clopidogrel therapy can increase KZ's ischemic risk
C. Ticagrelor therapy can increase KZ's ischemic risk
D. Clopidogrel is the recommended P2Y12 inhibitor therapy for KZ because metabolism is not affected

Assessment Question #7 – Pharmacists / Nurses

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05

Conclusions

Roles in Practice

Pharmacist's Role

Understand

- Factors that influence P2Y12 inhibitor choice in DAPT
- Advantages and disadvantages to each P2Y12 inhibitor

Assess

- Appropriateness of DAPT regimen based on a patient's bleed risk, use of an oral anticoagulant, and pharmacogenomics

Intervene

- Potential safety issues, contraindications, drug interactions
- Alternative P2Y12 inhibitors based on evidence-based efficacy and affordability

Factors to consider when selecting P2Y12 inhibitor:

- Bleeding and thrombotic risks
- Antiplatelet responsiveness
- Medication accessibility

Assessment Question #8 – Pharmacy Techs

Which products are only available as **brand name** medications? *Select all that apply.*

A. Aspirin (Ecotrin®)
B. Clopidogrel (Plavix®)
C. Prasugrel (Effient®)
D. Ticagrelor (Brilinta®)

Assessment Question #8 – Pharmacy Techs

Which products are only available as **brand name** medications? *Select all that apply.*

A. Aspirin (Ecotrin®)
B. Clopidogrel (Plavix®)
C. Prasugrel (Effient®)
D. Ticagrelor (Brilinta®)

Summary

- Certain patient populations are at higher bleeding risk or higher ischemic risk
- P2Y12 inhibitor selection should be tailored to patient-specific factors and concomitant medical conditions
- Pharmacists and pharmacy technicians can help optimize DAPT, increase medication accessibility, and provide patient education

References

1. Libby P, Theroux P. Pathophysiology of coronary artery disease. *Circulation*. 2005;111:3481-88.
2. National Heart, Lung, and Blood Institute. Coronary Heart Disease. 2022.
3. Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease. *J Am Coll Cardiol*. 2022;60(24):e44-e164.
4. Surendran A, Atefi N, Zhang H, et al. Defininingacute coronary syndrome through metabolomics. *Metabolites*. 2021;11(10):685.
5. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI Guideline for coronary artery revascularization. *Circulation*. 2022;145(3):e18-e114.
6. Tsao CW, Aday AW, Almarzooq ZI, et al. Heart disease and stroke statistics 2023 update. *Circulation*. 2023;147:e93-e621.
7. Blanchaert R. Ischemic heart disease. *Curr Opin Cardiol*. 1994;9(4):129-64
8. Bønaa KH, Mannsverk J, Wiseth R, et al. Drug-eluting or bare-metal stents for coronary artery disease. *N Engl J Med*. 2016;375(13):1242-52.
9. Bangalore S, Toklu B, Amoroso N, et al. Bare metal stents, durable polymer drug eluting stents, and biodegradable polymer drug eluting stents for coronary artery disease: mixed treatment comparison meta-analysis. *BMJ*. 2013;347:f6625.
10. DeBakey ME. Balloon angioplasty. *Encyclopedia Britannica*. 2023.
11. Lai CH, Lee WL, Sung SH, et al. Comparison of bare-metal stent and drug-eluting stent for the treatment of patients undergoing percutaneous coronary intervention for unprotected left main coronary artery disease - long-term result from a single center experience. *Acta Cardiol Sin*. 2015;31(5):381-9.
12. Imaging of Coronary Revascularization. Radiology Key. 2015.
13. Angiolillo DJ, Galli M, Collet JP, et al. Antiplatelet therapy after percutaneous coronary intervention. *Eurointervention*. 2022;17:e1371-96.
14. Park TK, Song YB, Ahn J, et al. Clopidogrel versus aspirin as an antiplatelet monotherapy after 12-month dual-antiplatelet therapy in the era of drug-eluting stents. *Circ Cardiovasc Interv*. 2016;9:e002816.
15. Koski R, Kennedy B. Comparative review of oral P2Y12 inhibitors. *P T*. 2018;43(6):352-57.
16. Navarese EP, Khan SU, Kołodziejczak M, et al. Comparative efficacy and safety of oral P2Y12 inhibitors in acute coronary syndrome: network meta-analysis. *Circulation*. 2020;142(2):150-160.
17. Collyer TC, Gray DJ, Sandhu R, et al. Assessment of platelet inhibition secondary to clopidogrel and aspirin therapy in preoperative acute surgical patient. *Br J Anaesth*. 2009;102(4):492-98.
18. McQuaid KR, Laine L. Systematic review and meta-analysis of adverse events of low-dose aspirin and clopidogrel in randomized controlled trials. *Am J Med*. 2006;119(8):624-38.
19. Westman PC, Lipinski MJ, Torguson R, et al. A comparison of cangrelor, prasugrel, ticagrelor, and clopidogrel in patients undergoing percutaneous coronary intervention: A network meta-analysis. *Cardiovasc Revasc Med*. 2017;18(2):79-85.
20. Butler K, Teng R. Pharmacokinetics, pharmacodynamics, safety, and tolerability of multiple ascending doses of ticagrelor in healthy volunteers. *Br J Clin Pharmacol*. 2010;70(1):65-77.
21. Wiviott SD, Braunwald E, McCabe CH, et al. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. 2007;357(20):2001-15.
22. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. 2009;361(11):1045-57.
23. Schupke S, Neumann FJ, Menichelli M, et al. Ticagrelor or prasugrel in patients with acute coronary syndromes. *N Engl J Med*. 2019 Oct 17;381(16):1524-1534.
24. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA Guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: *Circulation*. 2016 Sep 6;134(10):e123-55.
25. Musa T, Mgbemena O, Franchi F. De-escalation of P2Y12-inhibiting therapies to reduce the risk of bleeding after PCI. *J Am Coll Cardiol*. 2021.
26. Cuisset T, Deharo P, Quilici J, et al. Benefit of switching dual antiplatelet therapy after acute coronary syndrome: the TOPIC (timing of platelet inhibition after acute coronary syndrome) randomized study. *Eur Heart J*. 2017;38(41):3070-78.
27. Kim CJ, Park MW, Kim MC, et al. Unguided de-escalation from ticagrelor to clopidogrel in stabilized patients with acute myocardial infarction undergoing percutaneous coronary intervention (TALOS-AMI): an investigator-initiated, open-label, multicentre, non-inferiority, randomised trial. *Lancet*. 2021;398(10308):1305-1

References

28. Hahn JY, Song YB, Oh JH, et al. Effect of P2Y12 inhibitor monotherapy vs dual antiplatelet therapy on cardiovascular events in patients undergoing percutaneous coronary intervention: The SMART-CHOICE Randomized Clinical Trial. *JAMA*. 2019;321(24):2428-2437.
29. Mehran R, Baber U, SHarma SK, et al. Ticagrelor with or without aspirin in high-risk patients after PCI. *N Engl J Med*. 2019;381:2032-42.
30. Kim BK, Hong SJ, Cho YH, et al. Effect of ticagrelor monotherapy vs ticagrelor with aspirin on manjor bleeding and cardiovascular events in patients with acute coronary syndrome: TICO randomized clinical trial. *JAMA*. 2020;323(23):2407-16.
31. Watanabe H, Domei T, Morimoto T, et al. Effect of 1-month dual antiplatelet therapy followed by clopidogrel vs 12-month dual antiplatelet therapy on cardiovascular and bleeding events in patients receiving PCI: STOPDAPT-2 randomized clinical trial. *JAMA*. 2019;321(24):2414-27.
32. Valgimigli M, Frigoli E, Heg D, et al. Dual antiplatelet therapy after PCI in patients at high bleeding risk. *N Engl J Med*. 2021;385(18):1643-55.
33. Watanabe H, Morimoto T, Natsuaki M, et al. Comparison of clopidogrel monotherapy after 1 to 2 months of dual antiplatelet therapy with 12 months of dual antiplatelet therapy in patients with acute coronary syndrome: STOPDAPT-2 ACS. *JAMA Cardiol*. 2022:7(4):407-417.
34. Angiolillo DJ, Goodman SG, Bhatt DL, et al. Antithrombotic therapy in patients with atrial fibrillation treated with oral anticoagulation undergoing percutaneous coronary intervention. *Circulation*. 2018;138:527-36.
35. Sharma R, Kumar P, Prashanth SP, et al. Dual antiplatelet therapy in coronary artery disease. *Cardiol Ther*. 2020;9(2):349-61.
36. Khumbhani DJ, Cannon CP, Beavers CJ, et al. 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. *J Am Coll Cardiol*. 2021;77(5):629-58.
37. Dewilde WJM, Oirbans T, Verheugt FWA, et al. Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomized, controlled trial. *Lancet*. 2013;381(9872):1107-15.
38. Gibson CM, Mehran R, Bode C, et al. Prevention of bleeding in patients with atrial fibrillation undergoing PCI. *N Engl J Med.* 2016;375:2423-34.
39. Cannon CP, Bhatt DL, Oldgren J, et al. Dual antithrombotic therapy with dabigatran aftre PCI in atrial fibrillation. *N Engl J Med*. 2017;377:1513-24.
40. Vranckx P, Valgimigli M, Eckardt L, et al. Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI). *Lancet*. 2019;394(10206):1335-43.
41. Lopes RD, Heizer G, Aronson R, et al. Antithrombotic therapy after acute coronary syndrome or PCI in atrial fibrillation. *N Engl J Med*. 2019;380:1509-24.
42. Klein MD, Williams AK, Lee CR, Stouffer GA. Clinical utility of CYP2C19 genotyping to guide antiplatelet therapy in patients with an acute coronary syndrome or undergoing percutaneous coronary intervention. *Arterioscler Thromb Vasc Biol*. 2019;39:647-52.
43. Sibbing D, Aradi D, Alexopoulos D, et al. Updated expert consensus statement on platelet function and genetic testing for guiding P2Y12 receptor inhibitor treatment in percutaneous coronary intervention. *JACC Cardiovasc Interv.* 2019;12(16):1521-37.
44. Lee CR, Luzum JA, Sangkuhl K, et al. Clinical pharmacogenetics implementation consortium guideline for CYP2C19 genotype and clopidogrel therapy: 2022 update. *Clin Pharmacol Ther*. 2022;112(5):959-67.
45. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guidleline for percutaneous coronary intervention. *Circulation*. 2011;124:e574-651.
46. Notarangelo FM, Maglietta G, Bevilacqua P, et al. Pharmacogenomic approach to selecting antiplatelet therapy in patients with acute coronary syndromes: PHARMCLO trial. *J Am Coll Cardiol*. 2018;71(17):1869-77.
47. Claassens DMF, Vos GJA, Bergmeijer TO, et al. A genotype-guided strategy for oral P2Y12 inhibitors in primary PCI. *N Engl J Med*. 2019;381:1621-31.
48. Pereira NL, Farkouh ME, So D, et al. Effect of genotype-guided oral P2Y12 inhibitor selection vs conventional clopidogrel therapy on ischemic outcomes after percutaneous coronary intervention: TAILOR-PCI trial. *JAMA*. 2020;324(8):761-71.
49. Beitelshees AL, Thomas CD, Empey PE, et al. CYP2C19 genotype-guided antiplatelet therapy after percutaneous coronary intervenition in diverse clinical settings. *J Am Heart Assoc.* 2022;11:e024159.
50. Owusu-Obeng A, Weitzel KW, Hatton RC, et al. Emerging roles for pharmacists in clinical implementation of pharmacogenomics. *Pharmacotherapy*. 2014;34(10):1102-12.

Thank you!

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