Recommendations for Novel Antiplatelets

Prof. Khaing Khaing Shein
Department of Cardiology
Yangon General Hospital

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1. Introduction

- Acute coronary syndrome affects 1 in 5 patients, leading to a second ischemic event within 5 years.

- Antiplatelet therapy is crucial for treating patients with acute coronary syndrome (ACS) or percutaneous coronary intervention (PCI).

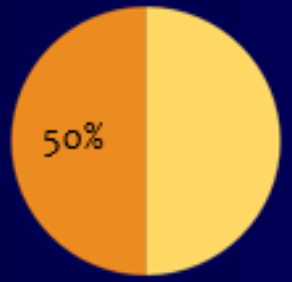
- Antiplatelet therapy, including acetylsalicylic acid (ASA), is crucial for managing the condition.

- Dual antiplatelet therapy, combining ASA with a P2Y12 receptor inhibitor, is now preferred.

Acute Coronary Syndromes: High Burden of Mortality

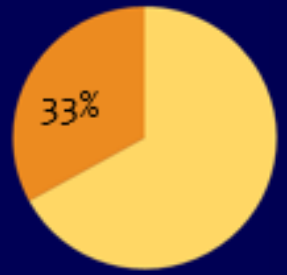
ACS incidence and mortality rates

ACS (ST and non-ST elevation) are responsible for half of all deaths due to CV disease[1]



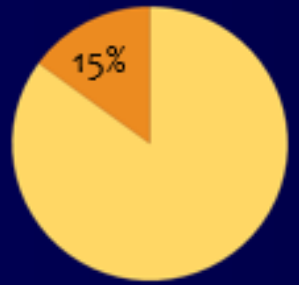
CV disease deaths due to ACS

One third of STEMI patients die within 24 hours of onset of ischaemia2



Death in STEMI patients at 24 hours

15% of NSTE patients die or have a nonfatal MI within 30 days [3,4]



Death or MI in NSTE patients within 30 days

1. Kolansky DM. Am J Manag Care. 2009;15:536–541.
2. Antman EM, et al. Circulation. 2004;110:e82–e292.
3. Braunwald E, et al. Circulation. 2002;106:1893–1900.
4. Boersma E, et al. Circulation 2000;101:2557–2567.

- Many patients still experience atherothrombotic events, even in dual antiplatelet therapy with aspirin and clopidogrel, possibly due to inadequate platelet inhibition.

- More potent antithrombotic strategies, including novel P2Y12 receptor antagonists and adjunctive agents, are needed for acute and long-term treatment.

What are the Types of antiplatelet drugs?

1. Cyclo-oxygenase (COX-1) inhibitor (aspirin)

2. Adenosine diphosphate (ADP) receptor inhibitors (clopidogrel, ticagrelor, ticlopidine, prasugrel)

3. Adenosine reuptake inhibitors (dipyridamole)

4. Glycoprotein platelet inhibitors (abciximab, eptifibatide, tirofiban)

5. Phosphodiesterase inhibitors (cilostazol)

6. Protease-activated receptor (PAR-1) antagonist (vorapaxar)

- The novel oral P2Y purinoceptor 12 (P2Y12)-receptor inhibitors prasugrel and ticagrelor were approved by the FDA for clinical use in 2009 and 2011, respectively.

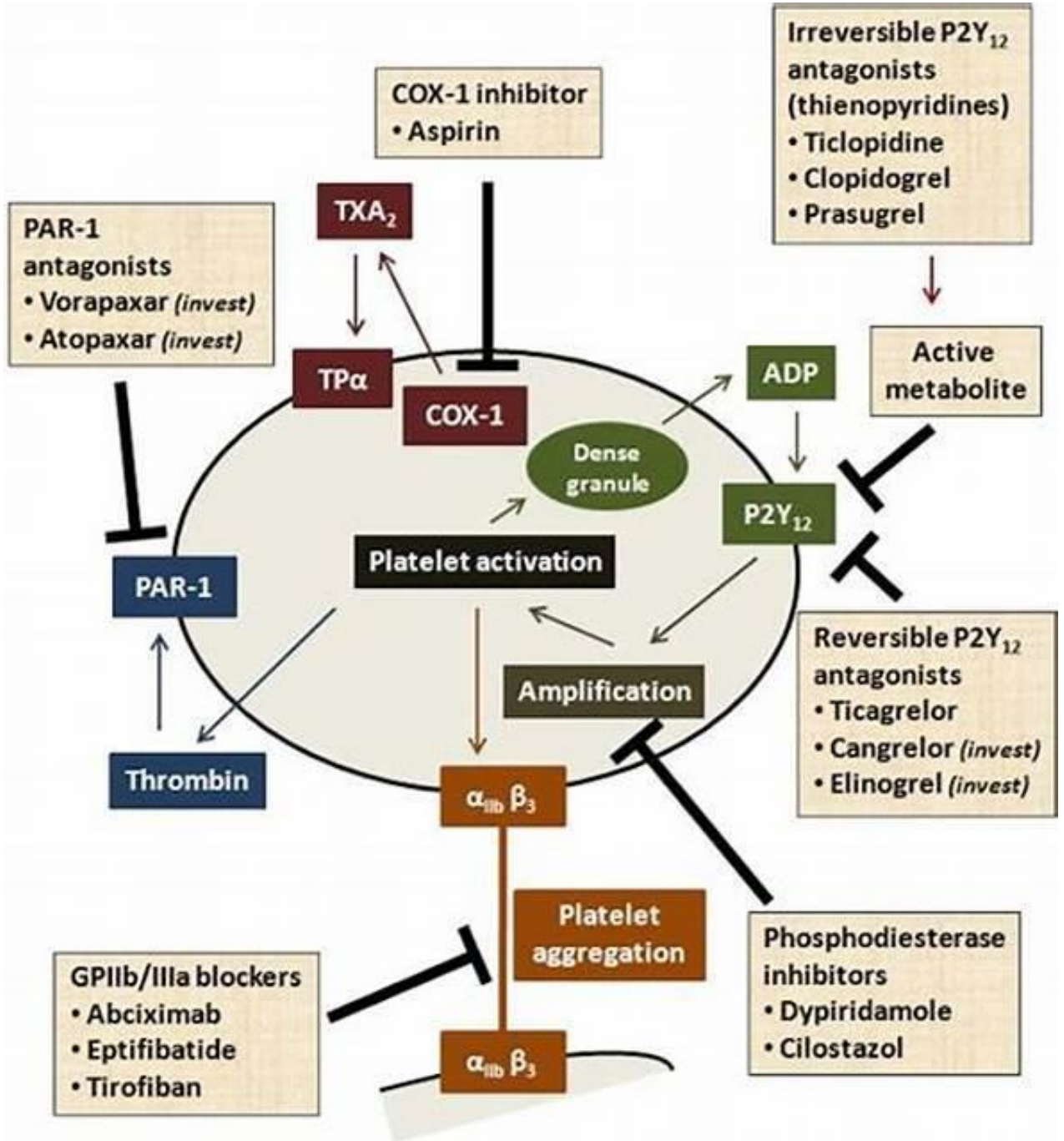
  - a faster-acting, more-potent, and more-predictable antiplatelet effect than clopidogrel
  - improved clinical outcomes in patients with ACS, but increased risk of bleeding

- Antiplatelet therapy is vital.

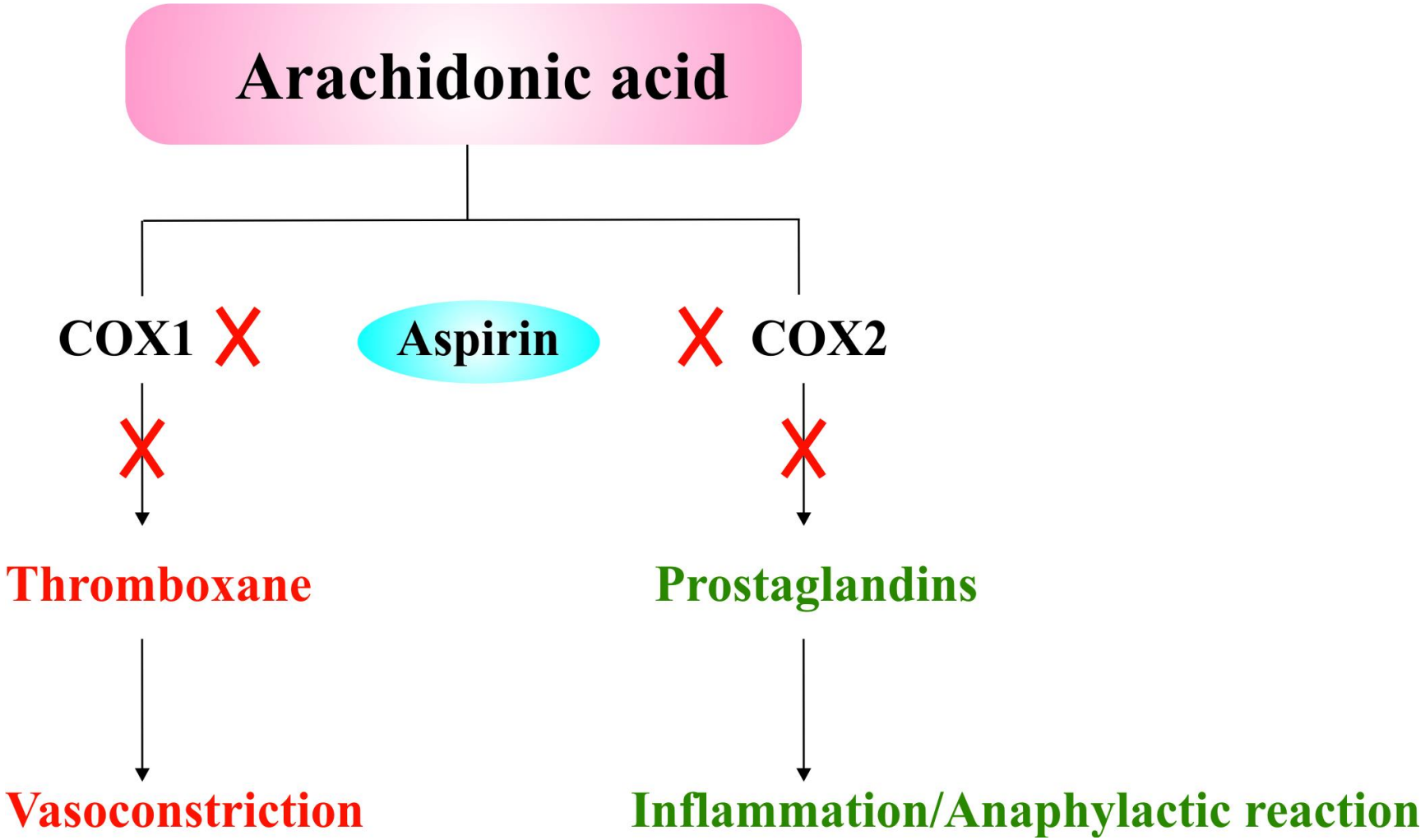
- After plaque rupture or erosion, platelet adhesion, activation, and aggregation are the major determinants of arterial thrombosis leading to ACS.

- Dual antiplatelet therapy with a combination of aspirin and either P2Y12-receptor inhibitors should be the treatment of choice in patients with ACS

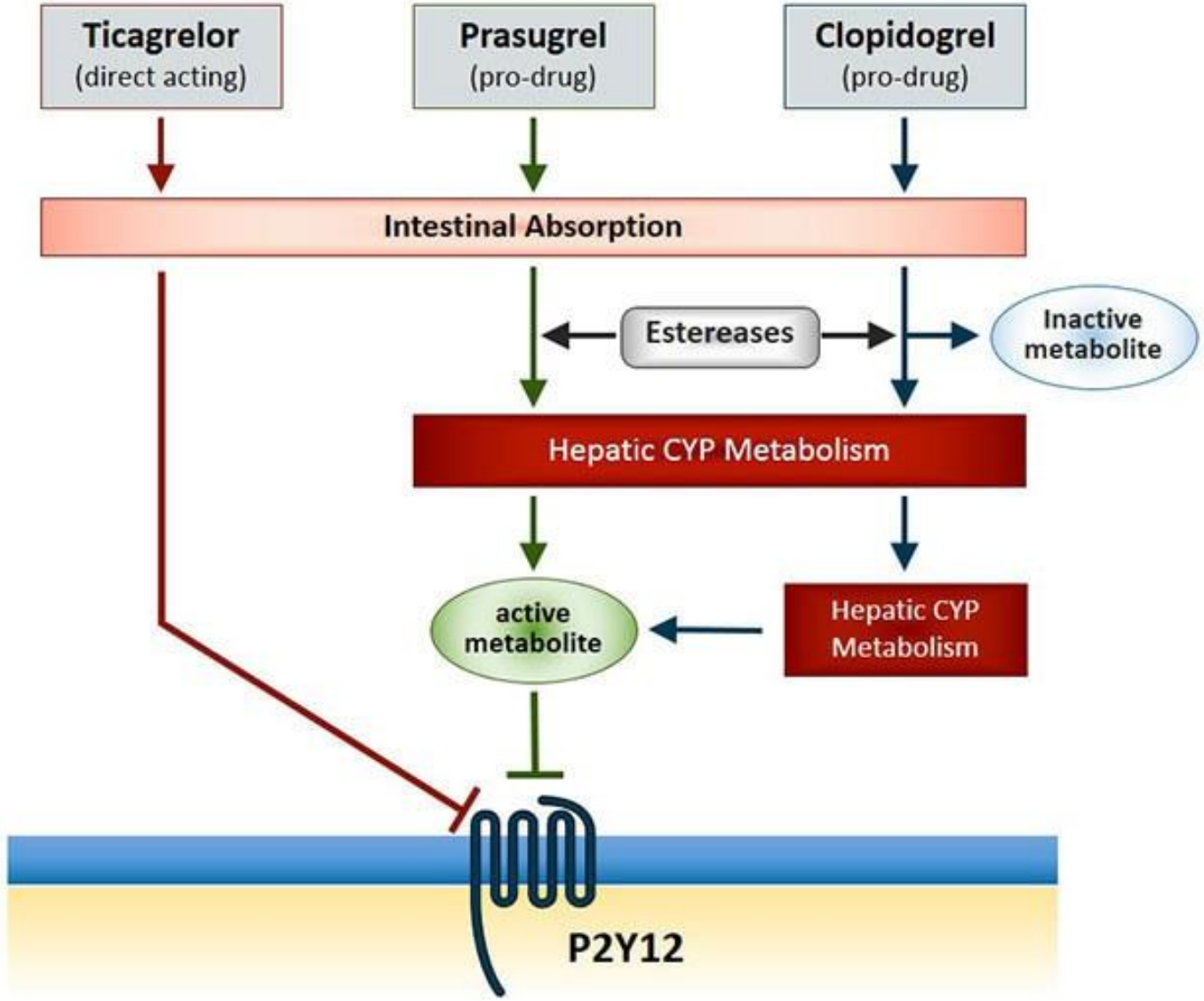
2. Mechanism of Action of Antiplatelets and Targets


COX-1 inhibitor
• Aspirin
Irreversible P2Y12 antagonists (thienopyridines)
• Ticlopidine
• Clopidogrel
• Prasugrel
PAR-1 antagonists
• Vorapaxar (invest)
• Atopaxar (invest)
TXA2
TPα
COX-1
ADP
Active metabolite
Dense granule
P2Y12
Platelet activation
PAR-1
Amplification
Reversible P2Y12 antagonists
• Ticagrelor
• Cangrelor (invest)
• Elinogrel (invest)
Thrombin
αIIb β3
Platelet aggregation
GPIIb/IIIa blockers
• Abciximab
• Eptifibatide
• Tirofiban
αIIb β3
Phosphodiesterase inhibitors
• Dypiridamole
• Cilostazol

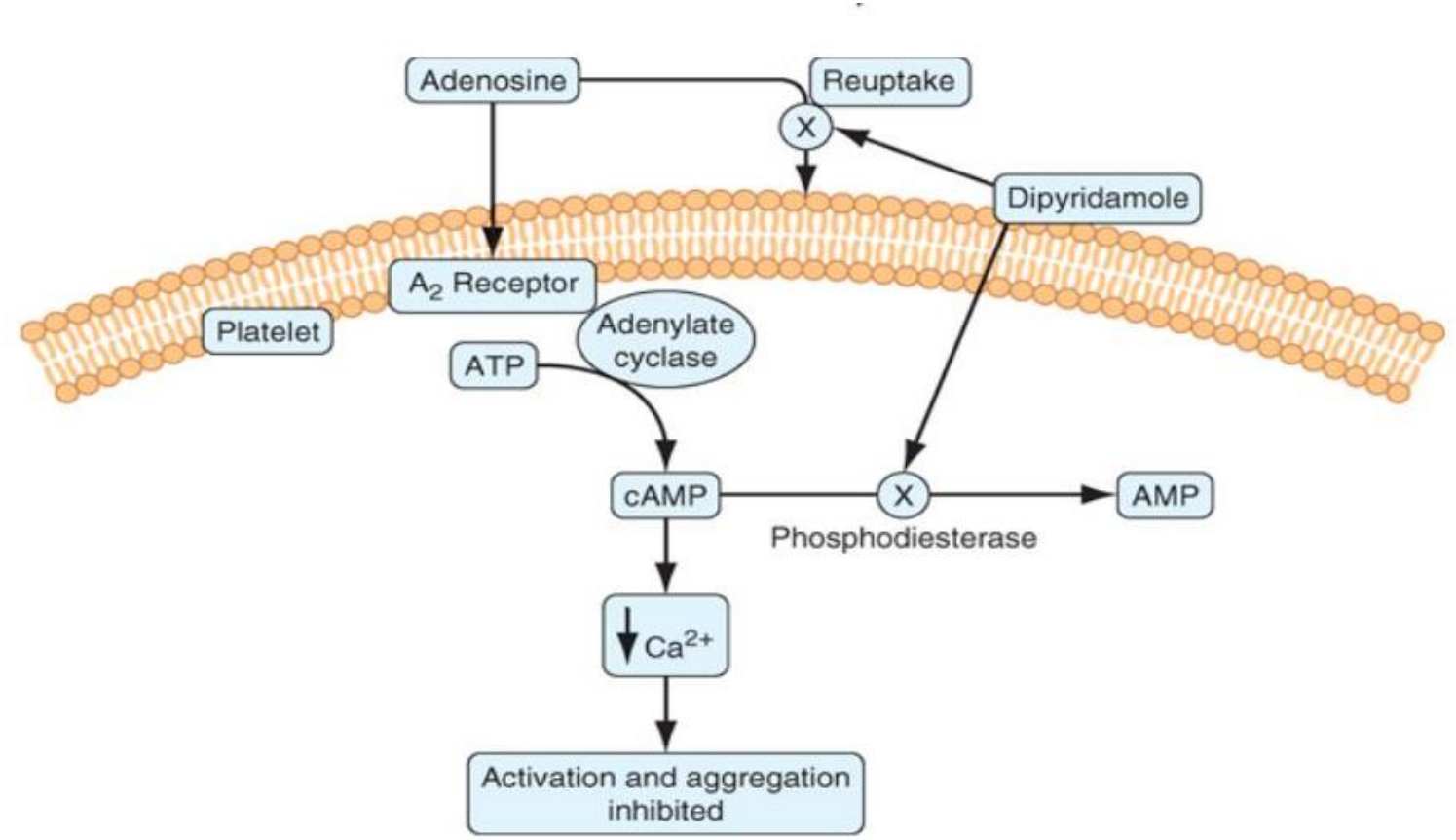
Cyclo-oxygenase (COX-1) inhibitor (aspirin)



Adenosine diphosphate (ADP) receptor inhibitors (clopidogrel, ticagrelor, ticlopidine, prasugrel)



Adenosine reuptake inhibitors (dipyridamole)



a) inhibition of platelet cAMP-phosphodiesterase
b) potentiation of adenosine inhibition of platelet function by **blocking reuptake by vascular and blood cells, and subsequent degradation of adenosine**
c) potentiation of PGI2 antiaggregatory activity and enhancement of PGI2 biosynthesis

Glycoprotein platelet inhibitors (abciximab, eptifibatide, tirofiban)

Glycoprotein IIb/IIIa Inhibitors

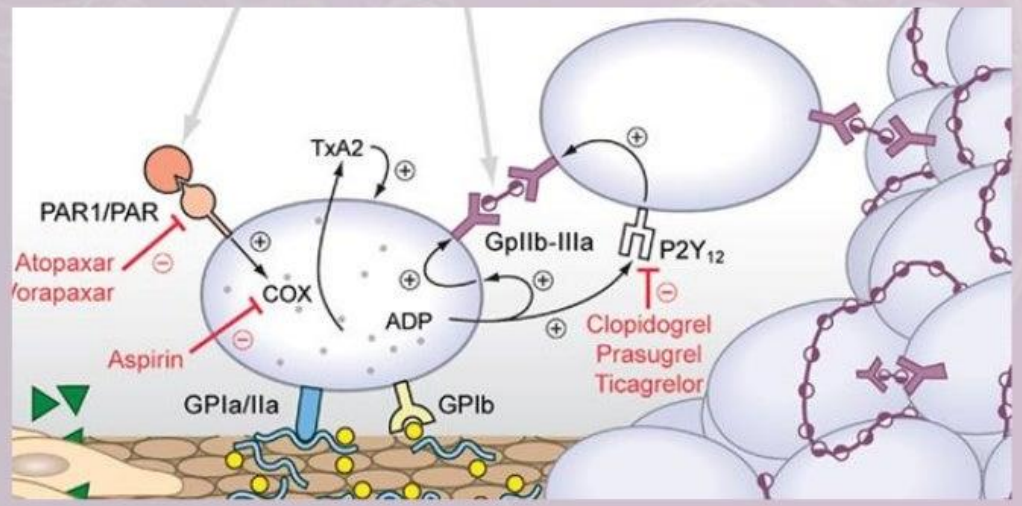
- The platelet integrin receptor GPIIb/IIIa mediates interactions between platelets and several ligands, primarily fibrinogen, leading to platelet aggregation
- GPIIb/IIIa antibodies and receptor antagonists inhibit this binding by antagonizing or binding to the receptor.

Abciximab (ReoPro®)

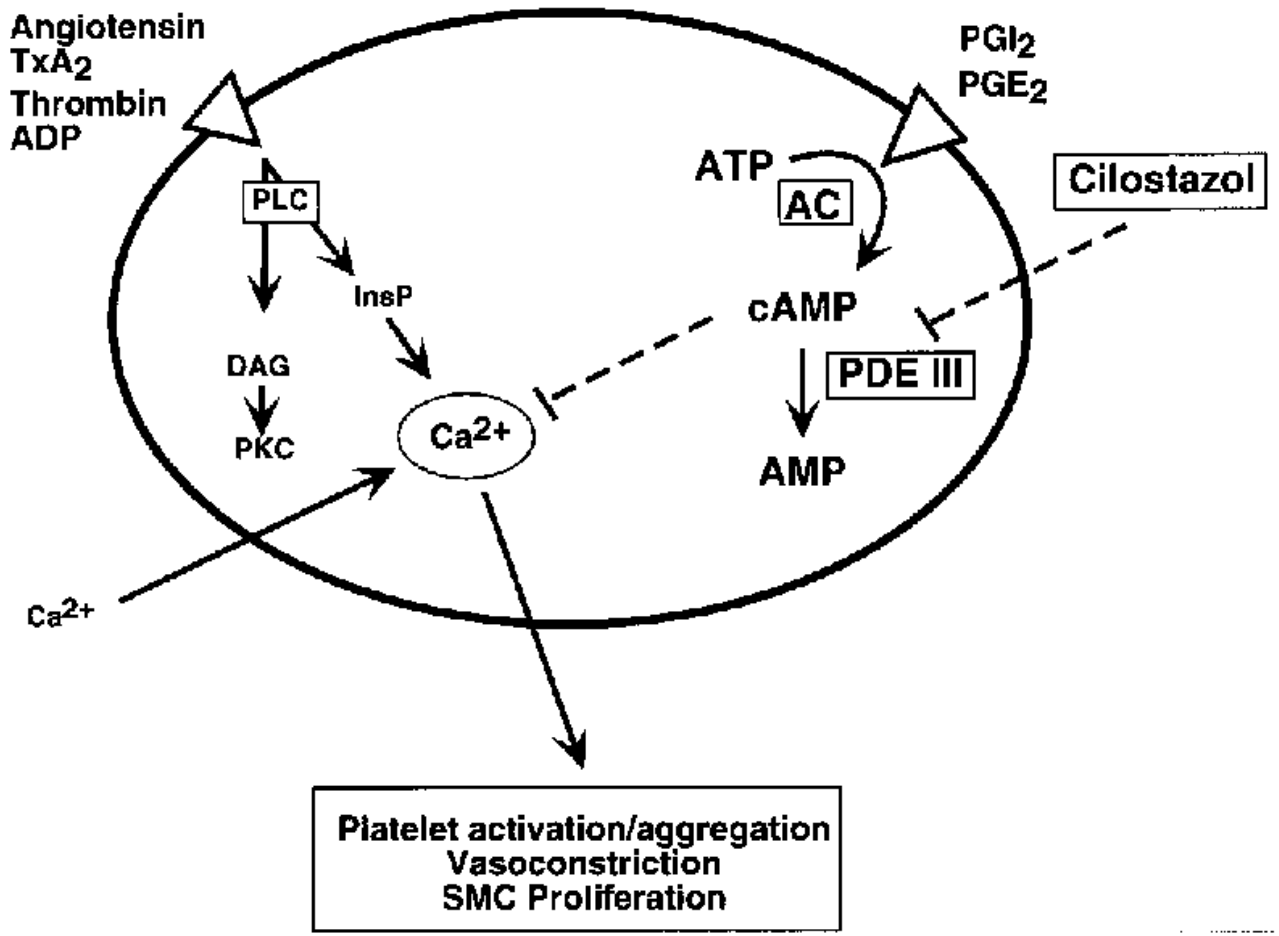
Noncompetitive irreversible inhibitor of intact GPIIb/IIIa receptor

Tirofiban (Aggrastat®)
Eptifabatide (Integrilin)

Competitive and reversible antagonists that act specifically on the α_{IIb}-subunit of GPIIb/IIIa



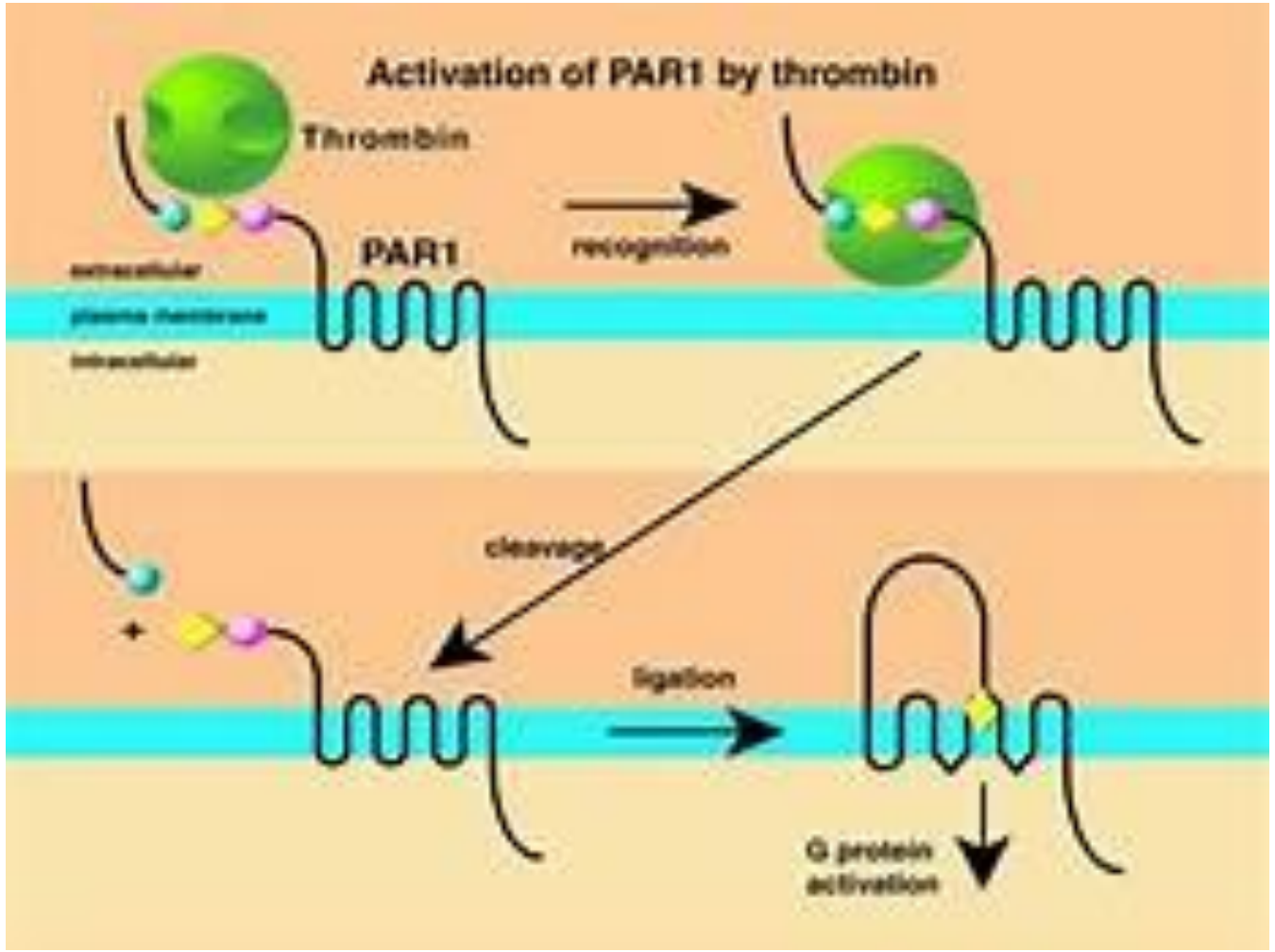
Phosphodiesterase inhibitors (cilostazol)



Cilostazol is a selective inhibitor of phosphodiesterase type 3 (PDE 3) with therapeutic focus on **increasing cAMP**.

An increase in cAMP results in an increase in the active form of protein kinase A (PKA), which is directly related with an inhibition in platelet aggregation.

Protease-activated receptor (PAR-1) antagonist (Vorapaxar)



Vorapaxar, a thrombin receptor antagonist acts by **reversible inhibition** of the protease-activated receptor-1 (PAR-1). PAR-1 is expressed on platelets, and it inhibits platelet aggregation, both thrombin-induced and thrombin receptor agonist peptide (TRAP)-induced.

Antiplatelet Therapy

Drug	Target	Half-life	Use
Ticlopidine	P2Y12 receptor	12 hours	Transient ischemic attacks, patients undergoing PCI
Clopidogrel	P2Y12 receptor	6–8 hours	NSTEMI, STEMI, PCI, recent stroke, or established PAD
Prasugrel	P2Y12 receptor	8 hours	Patients with ACS undergoing PCI
Ticagrelor	P2Y12 receptor	6–12 hours	STEMI, ACS
Abciximab	GPIIb-IIIa	< 10–30 minutes	PCI
Eptifibatide	GPIIb-IIIa	~2.5 hours	NSTEMI, PCI, unstable angina
Tirofiban	GPIIb-IIIa	2 hours	NSTEMI, PCI, unstable angina
Cilostazol	PDE3	11–13 hours	Intermittent claudication, PAD, PCI
Dipyridamole	PDE3 and inhibition of adenosine uptake	10 hours	Transient ischemic attacks

Journal of Blood Medicine 2012:3 33–42

Pharmacological properties of antiplatelets

Property	Clopidogrel	Prasugrel	Ticagrelor	Cangrelor	Elinogrel
Receptor blockade	Irreversible	Irreversible	Reversible	Reversible	Reversible
Route of administration	Oral	Oral	Oral	Intravenous	Intravenous and oral
Frequency	Once daily	Once daily	Twice daily	Bolus plus infusion	Bolus plus twice daily
Prodrug	Yes	Yes	No*	No	No
Onset of action	2–8 h	30 min–4 h‡	30 min–4 h‡	2 min	<15 min
Offset of action	7–10 days	7–10 days	3–5 days	30–60 min	Intravenous 50 min Oral 12 h
Interactions with CYP-targeted drugs	CYP2C19	No	CYP3A4/5	No	No
Indications	ACS and stable CAD undergoing PCI	ACS undergoing PCI	ACS (full spectrum)	Not approved Phase III stage	Not approved Phase II stage

3. Guidelines for Antiplatelet Therapy

Aspirin Dosing in Patients treated with DAPT

COR	LOE	Recommendation
I	B-NR	In patients treated with DAPT, a daily aspirin dose of 81 mg (range 75 mg–100 mg) is recommended

- Large overviews, including studies of nearly 200 000 persons, have consistently shown that lower aspirin doses (≤100 mg daily) are associated with less major and total bleeding than higher doses, either when used as monotherapy or when combined with the $P2Y_{12}$ inhibitor clopidogrel
- Studies comparing lower (75 mg to 150 mg) with higher aspirin doses have consistently found comparable ischemic event rates with either dose when used as monotherapy or when combined with the $P2Y_{12}$ inhibitor clopidogrel

2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease developed in collaboration with the EACTS*

*: European Association for Cardio-Thoracic Surgery

ESC
European Society of Cardiology

$P2Y_{12}$ inhibitor selection and timing

ESC European Society of Cardiology

Recommendations	Class	Level
In patients with ACS, ticagrelor (180 mg loading dose, 90 mg twice daily) on top of aspirin is recommended, regardless of initial treatment strategy, including patients pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced) unless there are contra-indications.	I	B
In patients with ACS undergoing PCI, prasugrel (60 mg loading dose, 10 mg daily dose) on top of aspirin is recommended for $P2Y_{12}$ inhibitor-naïve patients with NSTE-ACS or initially conservatively managed STEMI if indication for PCI is established, or in STEMI patients undergoing immediate coronary catheterization unless there is a high-risk of life-threatening bleeding or other contra-indications.	I	B

2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

Switching between oral $P2Y_{12}$ inhibitors

ESC European Society of Cardiology

Recommendations	Class	Level
In patients with ACS who were previously exposed to clopidogrel, switching from clopidogrel to ticagrelor is recommended early after hospital admission at a loading dose of 180 mg irrespective of timing and loading dose of clopidogrel, unless contra-indications to ticagrelor exist.	I	B
Additional switching between oral $P2Y_{12}$ inhibitors may be considered in cases of side effects/drug intolerance according to the proposed algorithms.	IIb	C

2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS
(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

ESC
European Society of Cardiology

Periprocedural and postprocedural antithrombotic therapyc in patients undergoing primary percutaneous coronary intervention

ESC European Society of Cardiology

Recommendations	Class	Level
Antiplatelet therapy		
A potent $P2Y_{12}$ inhibitor (prasugrel or ticagrelor), or clopidogrel if these are not available or are contra-indicated, is recommended before (or at latest at the time of) PCI and maintained over 12 months unless there are contra-indications such as excessive risk of bleeding.	I	A
Aspirin (oral or i.v, if unable to swallow) is recommended as soon as possible for all patients without contra-indications.	I	B
GP IIb/IIIa inhibitors should be considered for bailout if there is evidence of no-reflow or a thrombotic complication.	IIa	C
Cangrelor may be considered in patients who have not received $P2Y_{12}$ receptor inhibitors.	IIb	A

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www.escardio.org/guidelines 2017 ESC Guidelines for the Management of AMI-STEMI (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx095)

Maintenance antithrombotic strategy after ST-elevation myocardial infarction

ESC European Society of Cardiology

Recommendations	Class	Level
Antiplatelet therapy with low-dose aspirin (75–100 mg) is indicated.	I	A
DAPT in the form of aspirin plus ticagrelor or prasugrel (or clopidogrel if ticagrelor or prasugrel is not available or is contra-indicated) is recommended for 12 months after PCI unless there are contra-indications such as excessive risk of bleeding.	I	A
A PPI in combination with DAPT is recommended in patients at high risk of gastrointestinal bleeding.	I	B
In patients with an indication for oral anticoagulation, oral anti-coagulants are indicated in addition to antiplatelet therapy.	I	C

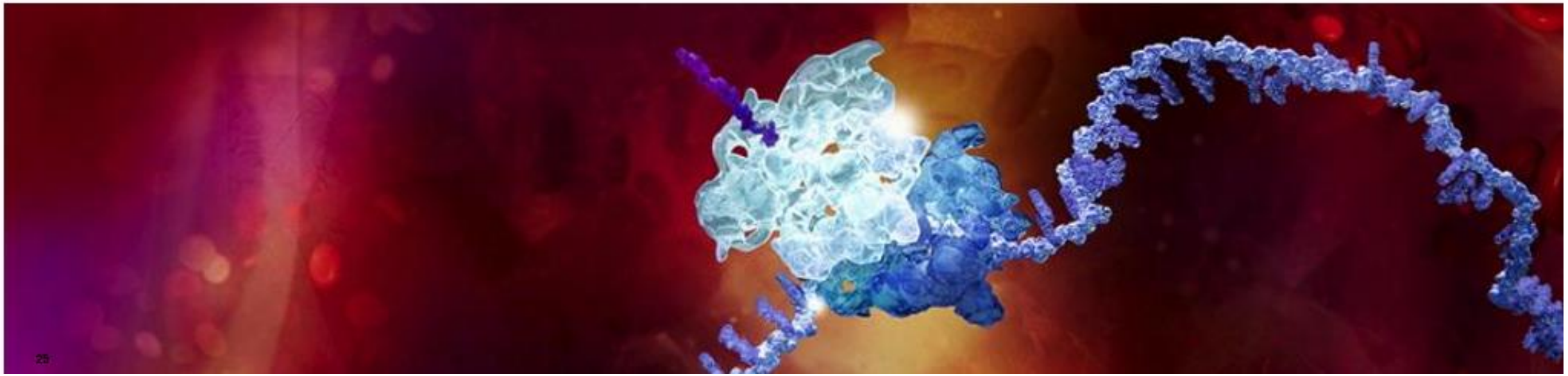
2014 ACC/AHA Non-ST-segment Elevation-ACS Guidelines

P2Y12 Inhibitors -- PCI

Recommendation *(to be given before the procedure)*	COR	LOE
Clopidogrel, 600-mg load dose → 75 mg/d	I	B
Prasugrel, 60-mg loading dose → 10 mg/d	I	B
Ticagrelor, 180-mg loading dose → 90 mg twice daily	I	B
Reasonable to use ticagrelor in preference to clopidogrel	**IIa**	**B**
Reasonable to use prasugrel in preference to clopidogrel	**IIa**	**B**

Amsterdam EA, et al. *Circulation.* 2014;130:2354-2394.[5]

2023 ESC guidelines for the management of acute coronary syndromes



Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome

Recommendation	Class	Level
Aspirin is recommended for all patients without contraindications at an initial oral LD of 150–300 mg (or 75–250 mg i.v.) and an MD of 75–100 mg o.d. for long-term treatment.	I	A
In all ACS patients, a P2Y12 receptor inhibitor is recommended in addition to aspirin, given as an initial oral LD followed by an MD for 12 months unless there is HBR	I	A
A proton pump inhibitor in combination with DAPT is recommended in patients at high risk of gastrointestinal bleeding	I	A

2023 ESC ACS guidelines

Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome

Recommendation	Class	Level
Prasugrel is recommended in P2Y12 receptor inhibitor-naïve patients proceeding to PCI (60 mg LD, 10 mg o.d. MD, 5 mg o.d. MD for patients aged ≥75 years or with a body weight	I	B
Ticagrelor is recommended irrespective of the treatment strategy (invasive or conservative) (180 mg LD, 90 mg b.i.d. MD).	I	B
Clopidogrel (300–600 mg LD, 75 mg o.d. MD) is recommended when prasugrel or ticagrelor are not available, cannot be tolerated, or are contraindicated.	I	C
If patients presenting with ACS stop DAPT to undergo CABG, it is recommended they resume DAPT after surgery for at least 12 months.	I	C

2023 ESC ACS guidelines

Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome

Recommendation	Class	Level
Prasugrel should be considered in preference to ticagrelor for ACS patients who proceed to PCI.	IIa	B
GP IIb/IIIa receptor antagonists should be considered if there is evidence of no-reflow or a thrombotic complication during PCI.	IIa	C
In P2Y12 receptor inhibitor-naïve patients undergoing PCI, cangrelor may be considered.	IIb	A
In older ACS patients, especially if HBR, clopidogrel as the P2Y12 receptor inhibitor may be considered.	IIb	C

2023 ESC ACS guidelines

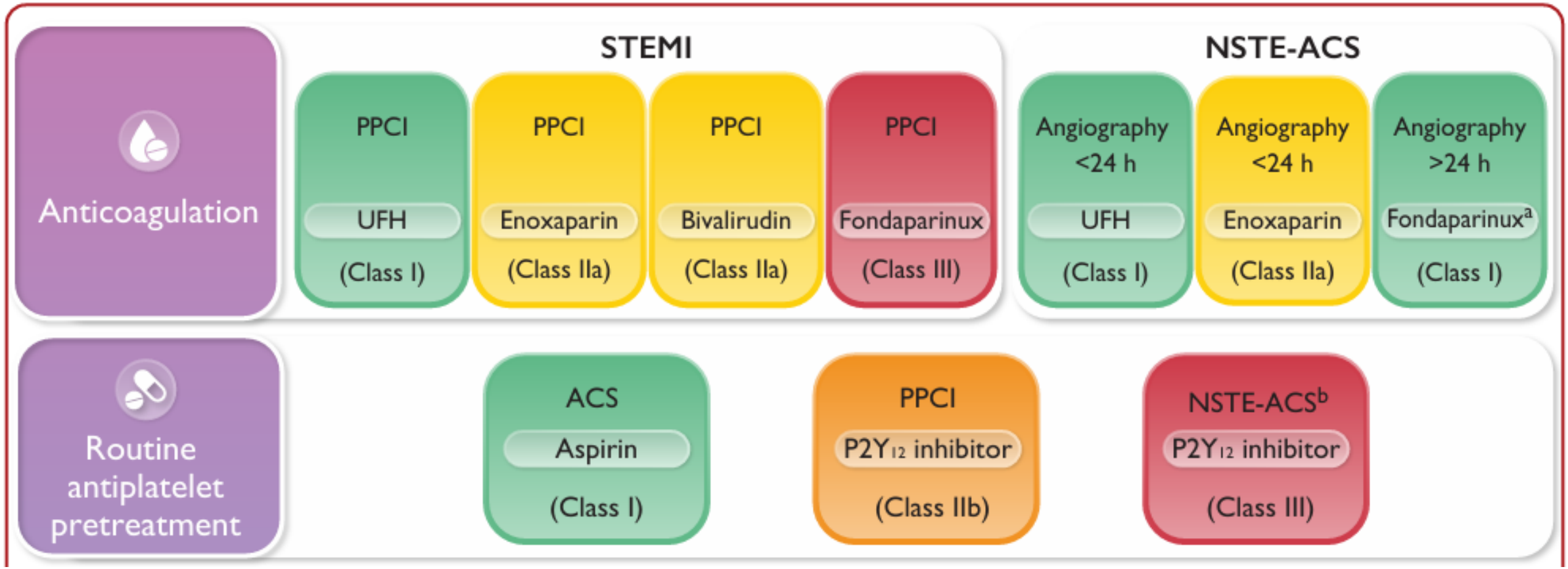
Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome

Recommendation	Class	Level
Pre-treatment with a P2Y12 receptor inhibitor may be considered in patients undergoing a primary PCI strategy.	IIa	B
Pre-treatment with a P2Y12 receptor inhibitor may be considered in NSTE-ACS patients who are not expected to undergo an early invasive strategy (<24hr) and do not have HBR.	IIa	C
Pre-treatment with a GP IIb/IIIa receptor antagonist is not recommended.	IIb	A
Routine pre-treatment with a P2Y12 receptor inhibitor in NSTE-ACS patients in whom coronary anatomy is not known and early invasive management (<24hr) is planned is not recommended.	IIb	C

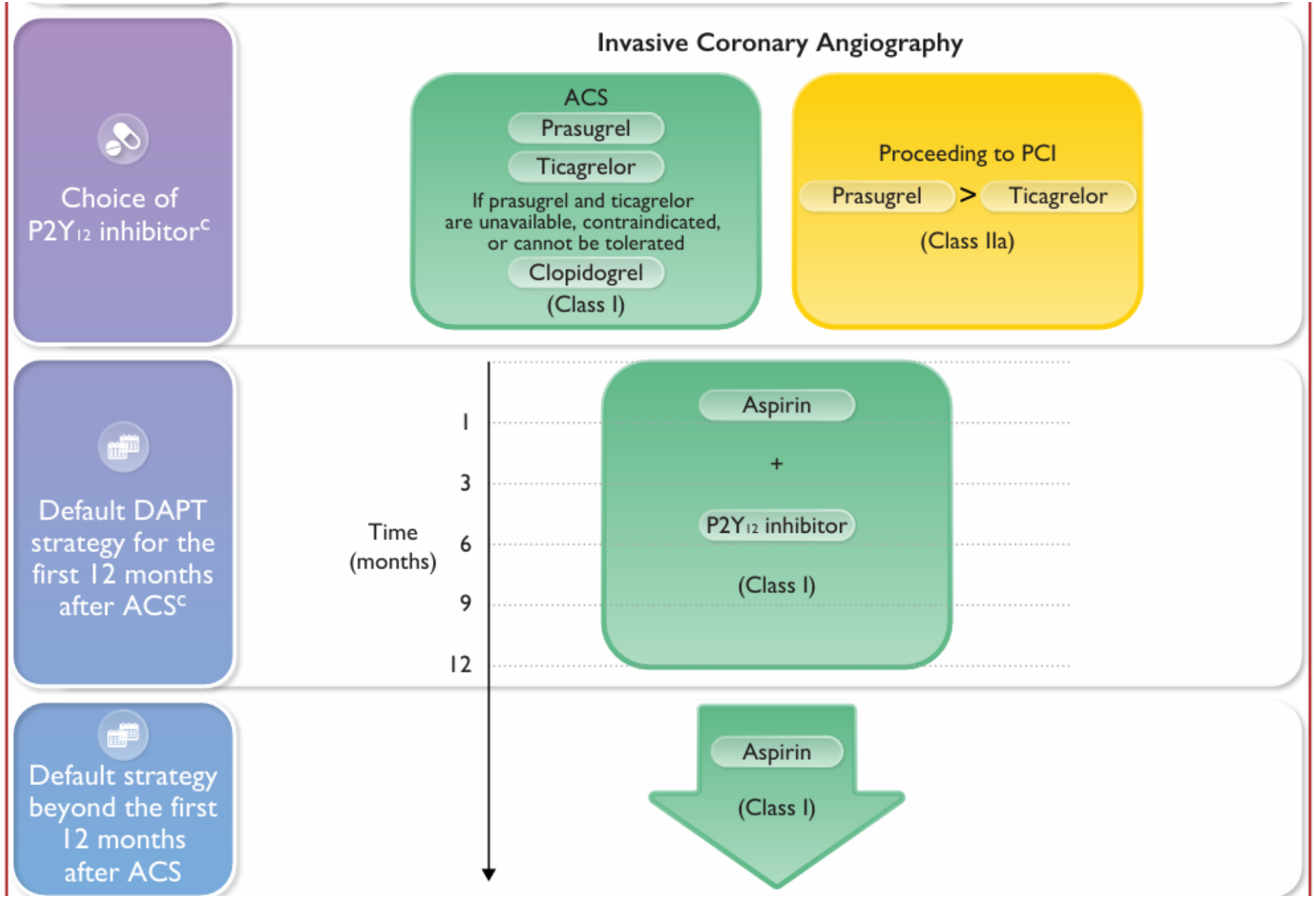
2023 ESC ACS guidelines

Recommended default antithrombotic therapy regimens in acute coronary syndrome patients without an indication for oral anticoagulation.

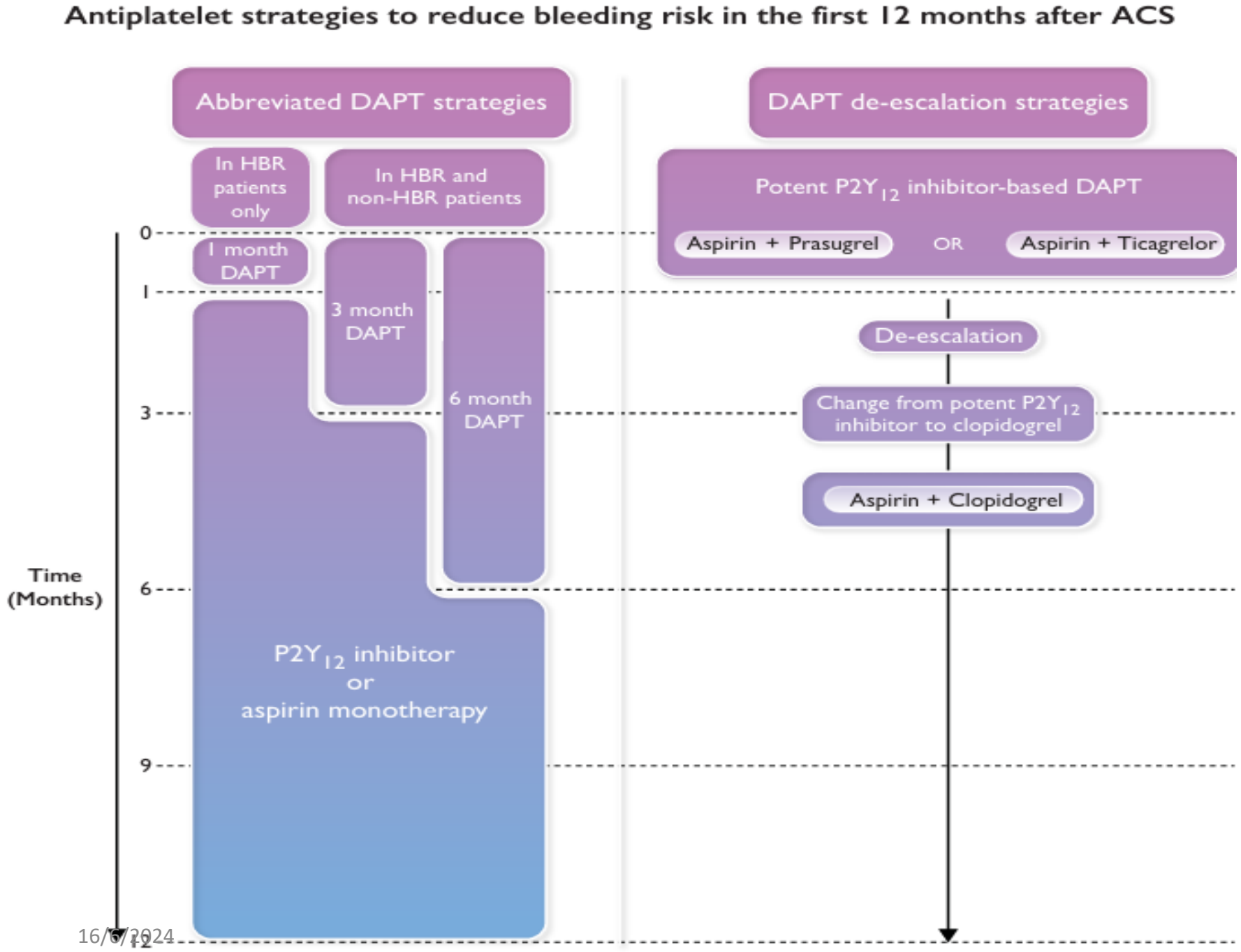
Recommended default antithrombotic therapy regimens in acute coronary syndrome patients without an indication for oral anticoagulation



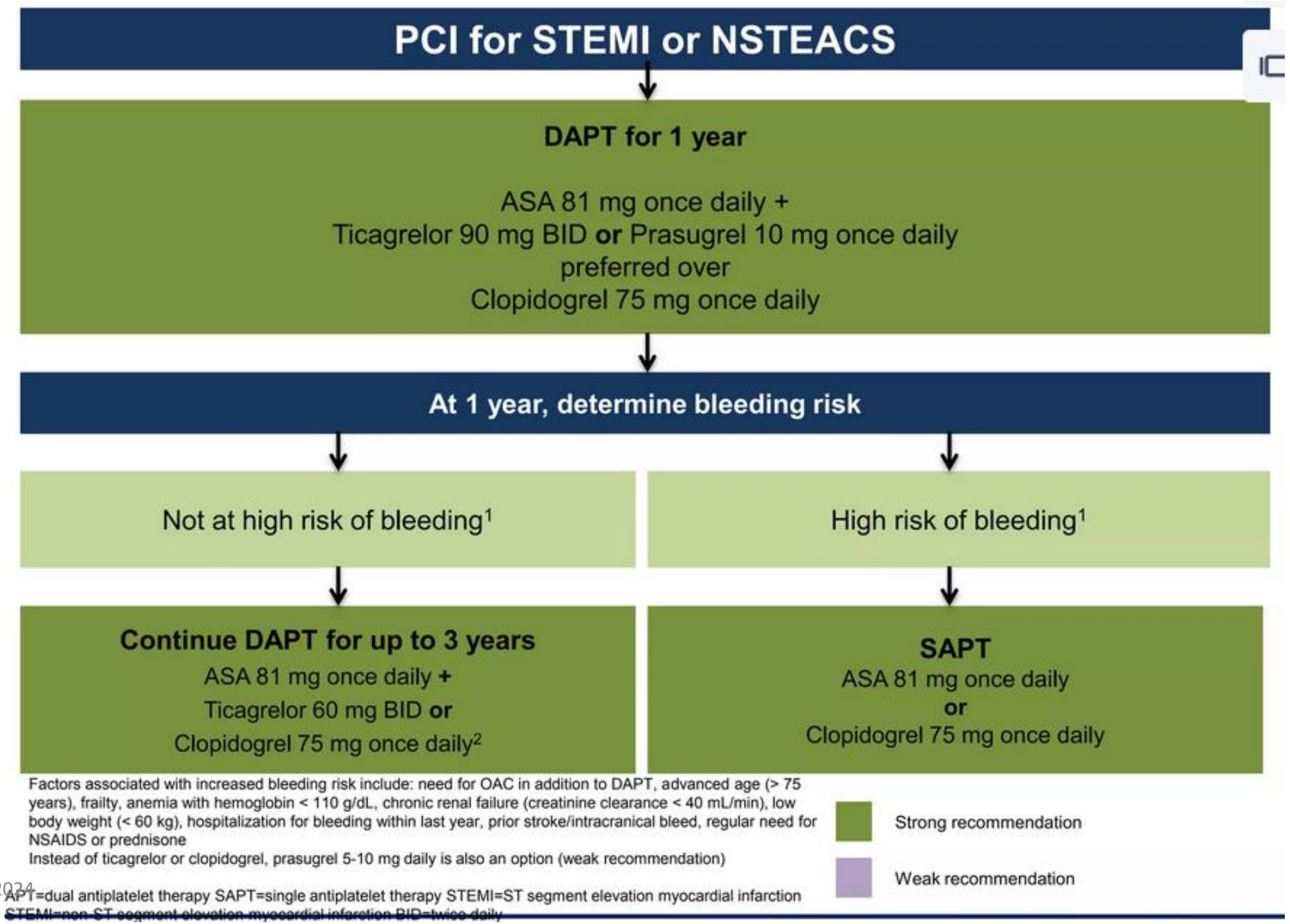
2023 ESC ACS guidelines

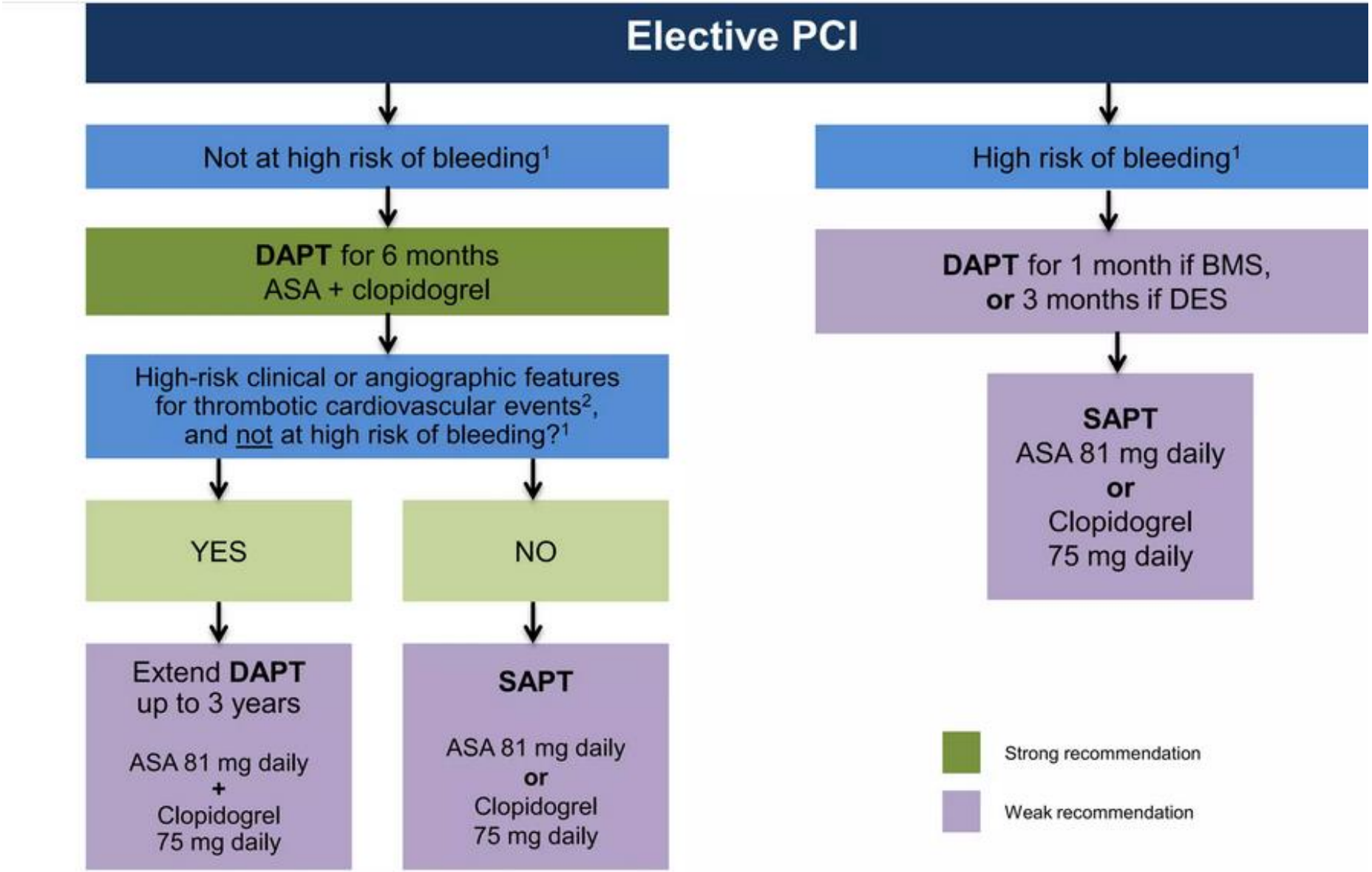


2023 ESC ACS guidelines



2023 ESC Guidelines for the management of ACS


PCI for STEMI or NSTEACS
DAPT for 1 year
ASA 81 mg once daily +
Ticagrelor 90 mg BID or Prasugrel 10 mg once daily
preferred over
Clopidogrel 75 mg once daily
At 1 year, determine bleeding risk
Not at high risk of bleeding1
High risk of bleeding1
Continue DAPT for up to 3 years
ASA 81 mg once daily +
Ticagrelor 60 mg BID or
Clopidogrel 75 mg once daily2
SAPT
ASA 81 mg once daily
or
Clopidogrel 75 mg once daily
Factors associated with increased bleeding risk include: need for OAC in addition to DAPT, advanced age (> 75 years), frailty, anemia with hemoglobin < 110 g/dL, chronic renal failure (creatinine clearance < 40 mL/min), low body weight (< 60 kg), hospitalization for bleeding within last year, prior stroke/intracranical bleed, regular need for NSAIDS or prednisone
Instead of ticagrelor or clopidogrel, prasugrel 5-10 mg daily is also an option (weak recommendation)
APT=dual antiplatelet therapy SAPT=single antiplatelet therapy STEMI=ST segment elevation myocardial infarction
STEMI=non-ST segment elevation myocardial infarction BID=twice daily
Strong recommendation
Weak recommendation



1 Factors associated with increased bleeding risk include: need for OAC in addition to DAPT, advanced age (> 75 years), frailty, anemia with hemoglobin < 110 g/dL, chronic renal failure (creatinine clearance < 40 mL/min), low body weight (< 60 kg), hospitalization for bleeding within last year, prior stroke/intracranical bleed, regular need for NSAIDS or prednisone.

2 Clinical and angiographic features associated with increased risk of thrombotic events include: age > 65, diabetes mellitus, prior myocardial infarction, chronic renal dysfunction (creatinine clearance < 60 mL/min), multi-vessel disease, multiple stents implanted, complex bifurcation lesion, total stent length > 60 mm, chronic total occlusion intervention or bioabsorbable vascular scaffold (BVS) implantation.

DAPT=dual antiplatelet therapy SAPT=single antiplatelet therapy BMS=bare metal stent DES=drug eluting stent

4. Duration of DAPT

Choosing Who Should be Considered for Prolonged (or Shorter) Duration DAPT

- Factors Associated with Increased Ischemic and Bleeding Risk
- Risk Score Calculators

Risks Stratification for Ischaemic and Bleeding Risks

- The ACC/AHA and ESC updates emphasize the importance of characterization for ischemic or bleeding complications.
- The DAPT score, derived from the DAPT trial, is used to assess the risk/benefit of prolonging DAPT beyond 12 months from PCI.
- The score assigns positive integer values to factors like diabetes, cigarette use, prior PCI, MI, congestive heart failure, MI at presentation, vein graft PCI, and stent diameter.
- The 2016 ACC/AHA update focused on bleeding risk factors, while the 2017 ESC update suggests using the PRECISE-DAPT score for out-of-hospital bleeding hazard prediction.

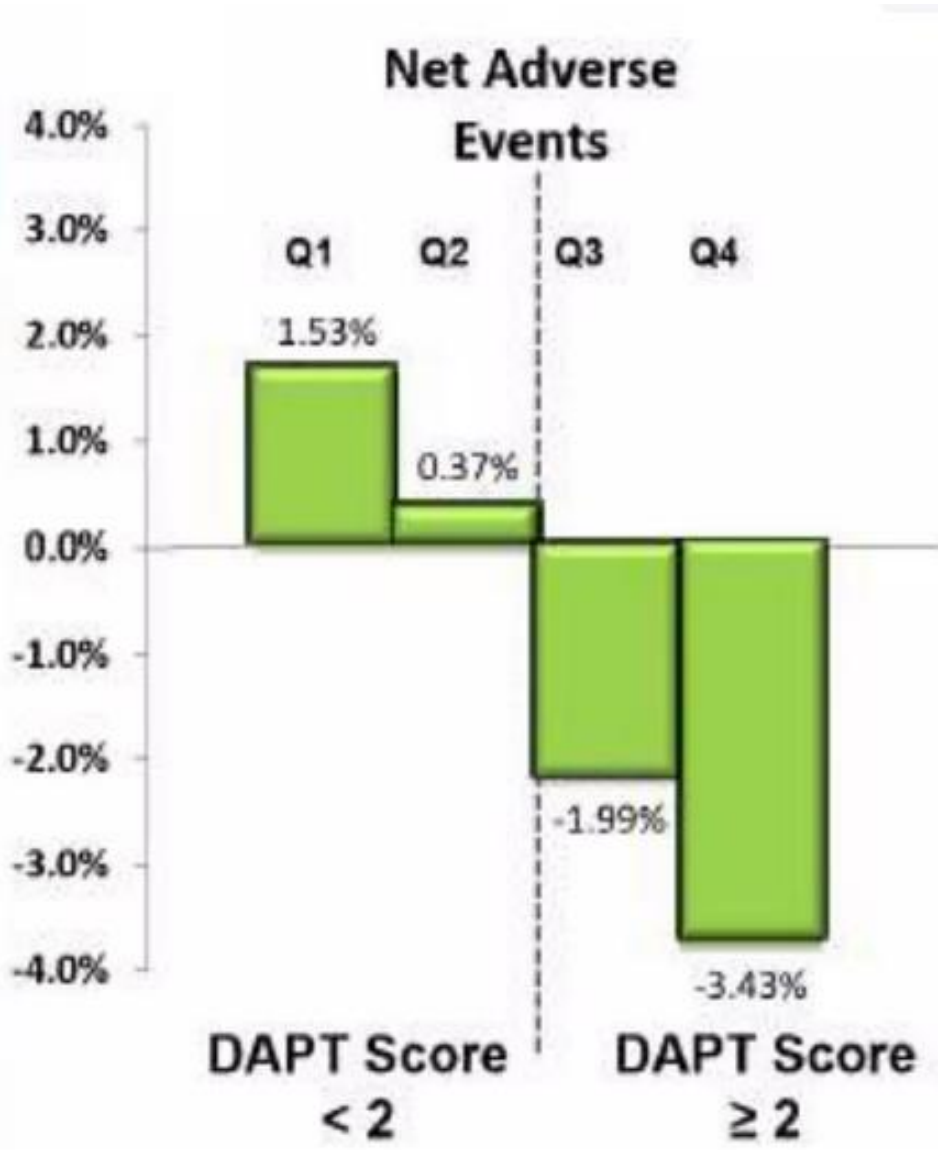
Clinical and Procedural Factors Associated with Increased Ischemic Risk or Increased Bleeding Ri

Increased Ischemic Risk/ Risk of Stent Thrombosis (May favor longer duration DAPT)	Increased Bleeding Risk (May favor shorter duration DAPT)
Increased Ischemic Risk • Advanced age • ACS presentation • Multiple prior MI • Extensive CAD • Diabetes mellitus • CKD **Increased Risk of Stent Thrombosis** • ACS presentation • Diabetes mellitus • Left ventricular ejection fraction <40% • First generation drug-eluting stent • Stent under-sizing or under-deployment • Small stent diameter or greater stent length • Bifurcation stents • In-stent restenosis	• History of prior bleeding • Oral anticoagulant therapy • Female sex • Advanced age • Low body weight • CKD • Diabetes mellitus • Anemia • Chronic steroid or NSAID therapy

Levine GN. et al. *Circulation*. 2016.

Dual Antiplatelet Therapy Study (DAPT Score)

Variable	Points
Age ≥75	-2
Age 65 - <75	-1
Age <65	0
Current cigarette smoker	+1
Diabetes mellitus	+1
MI at presentation	+1
Stent diameter <3mm	+1
Paclitaxel-eluting stent	+1
CHF or LVEF<30%	+2
Saphenous vein graft PCI	+2



How long should dual antiplatelet therapy be continued?

- Current guidelines recommend DAPT for 1 year after an acute coronary syndrome, particularly in patients with heightened ischemic risk

Features of patients at high risk of ischemic events

- Previous stent thrombosis on adequate antiplatelet therapy
- Stenting of the last remaining patent coronary artery
- Diffuse multivessel disease, especially in patients with diabetes
- Chronic kidney disease (i.e., creatinine clearance < 60 mL/min)
- At least 3 stents implanted
- At least 3 lesions treated
- Bifurcation with 2 stents implanted
- Total stented length greater than 60 mm
- Treatment of a chronic total occlusion
- History of ST-segment elevation myocardial infarction

5. Types of P2Y12i and Time of Initiation

- The American Heart Association and European Society of Cardiology (ESC) recommend P2Y 12 inhibitor selection and timing for patients with non-stent-embolic coronary artery disease (NSTEM-ACS) or STEMI.

- They prefer aspirin therapy with ticagrelor or prasugrel over clopidogrel.

- The 2017 ESC update favors prasugrel or ticagrelor over clopidogrel.

- Pre-treatment with P2Y 12 inhibitors is specific to the P2Y 12 inhibitor and clinical setting.

- In NSTE-ACS, ticagrelor and clopidogrel should be considered early, regardless of the initial management strategy.

- For STEMI patients, prasugrel can be given before coronary angiography if the indication to primary PCI is established.

- The 2017 ESC focused update also provides indications regarding DAPT for patients with stable CAD undergoing PCI, with clopidogrel being the drug of choice.

6. Platelet Function Testing and Genetic Testing

- The American Heart Association and European Society of Cardiology (ESC) do not recommend routine platelet function testing for adjusting antiplatelet therapy before or after elective stenting due to neutral results from multiple randomized trials.

- However, the 2018 ESC guidelines suggest de-escalation of P2Y 12 inhibitors guided by platelet function testing, particularly in patients unsuitable for 12-month DAPT.

- This recommendation follows the results of the TROPICAL ACS trial.

7. Switching of P2Y12 Inhibitor

- The 2016 ACC/AHA update did not address the issue of switching P2Y 12 inhibitors due to lack of randomized studies.

- The 2017 ESC update provides two CORs for early upgrading from clopidogrel to ticagrelor in ACS and switching between P2Y 12 inhibitors if side-effects or drug intolerance occur.

- A practical algorithm for switching between oral P2Y 12 inhibitors in acute and chronic settings is provided, with reloads recommended to avoid gaps in inhibitory effects.

- The ticagrelor dose should be adjusted when switching from ticagrelor to prasugrel or clopidogrel in the chronic setting to avoid drug-to-drug interactions, in line with expert consensus recommendations.

Antiplatelet Therapy Switching Clinician Guide in ACS

- From clopidogrel to prasugrel/ticagrelor - high risk of coronary/stent thrombosis
  - intolerance to clopidogrel
- From prasugrel to clopidogrel - cost
  - high bleeding risk
  - requiring concurrent treatment with an oral anticoagulant
  - Decision for medical management
- From prasugrel to ticagrelor - intolerance to prasugrel
  - decision for medical management
- From ticagrelor to clopidogrel - cost
  - high bleeding risk
  - requiring concurrent treatment with an oral anticoagulant
- From ticagrelor to prasugrel - intolerance to ticagrelor (e.g. dyspnea, ventricular pauses)
  - nonadherence to medications
  - CYP3A4 drug interactions

Switching between oral $P2Y_{12}$ inhibitors

From Clopidogrel to Ticagrelor

- In the presence of high risk of coronary thrombosis, give a 180 mg loading dose of ticagrelor, followed by the maintenance dose of 90 mg twice daily (irrespective of timing of the last dose of clopidogrel).

- In the maintenance or low risk phase, there is generally no need to administer a loading dose of ticagrelor; one can switch directly to ticagrelor maintenance dose 24 hours after the last dose of clopidogrel.

From Ticagrelor to Clopidogrel

- Loading dose of clopidogrel 300 mg is generally advisable, followed by the maintenance dose of 75 mg daily.
- Give the clopidogrel loading dose 12 hours after the last dose of ticagrelor.

Prasugrel to clopidogrel

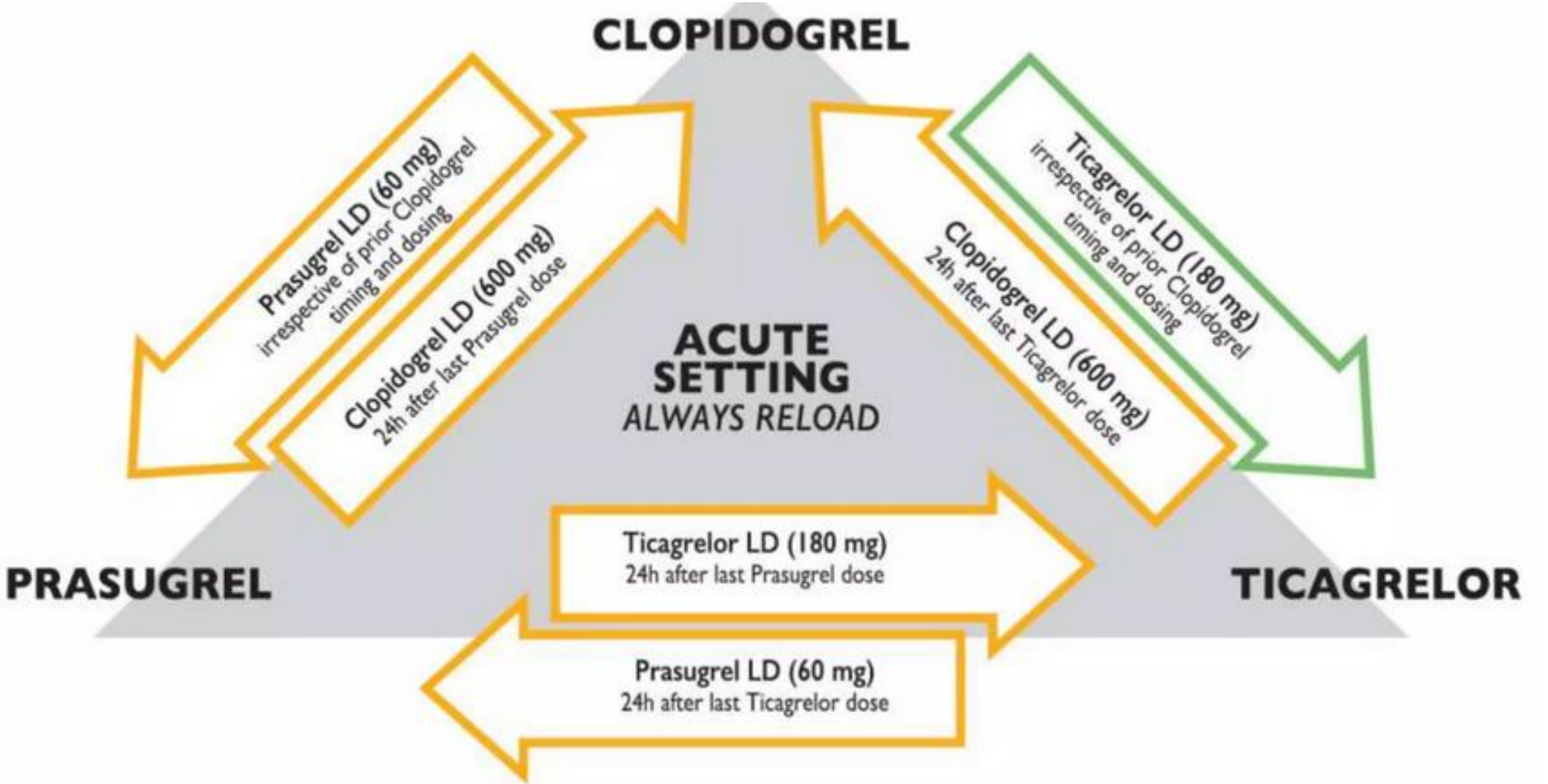
- The usual clopidogrel maintenance dose of 75 mg daily should be started 24 hours after the last dose of prasugrel.

Ticagrelor to prasugrel

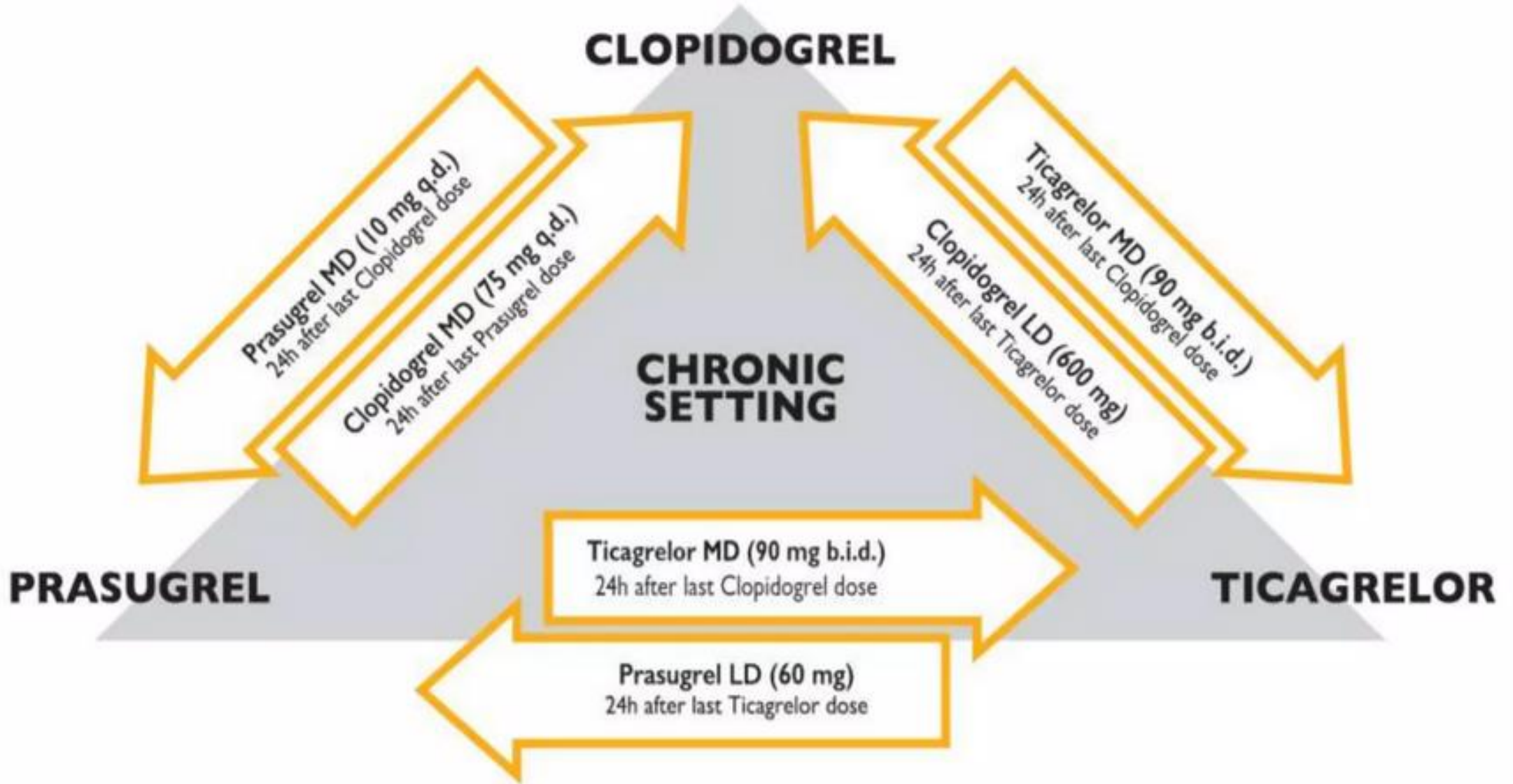
- A 60 mg loading dose of prasugrel should be administered 24 hours after the last dose of ticagrelor.

Prasugrel to ticagrelor

- A 90 mg maintenance dose of ticagrelor should be administered twice daily 24 hours after the last prasugrel dose.
- If it has been fewer than 30 days since the patient's PCI, a loading dose of 180 mg ticagrelor should be considered.



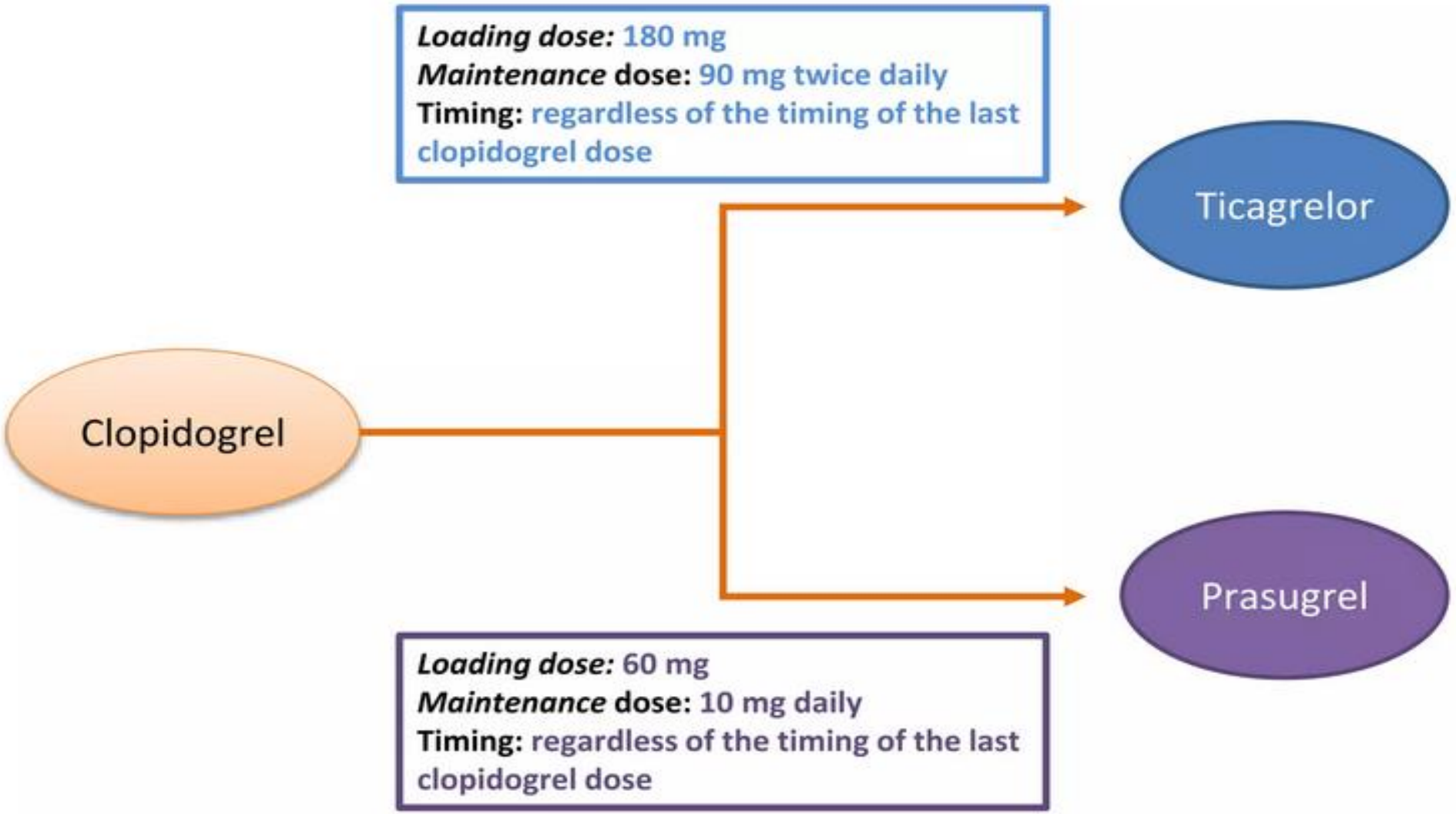
European Heart Journal (2017) 0, 1–48



European Heart Journal (2017) 0, 1–48

8. Intensification strategies

Intensification strategies



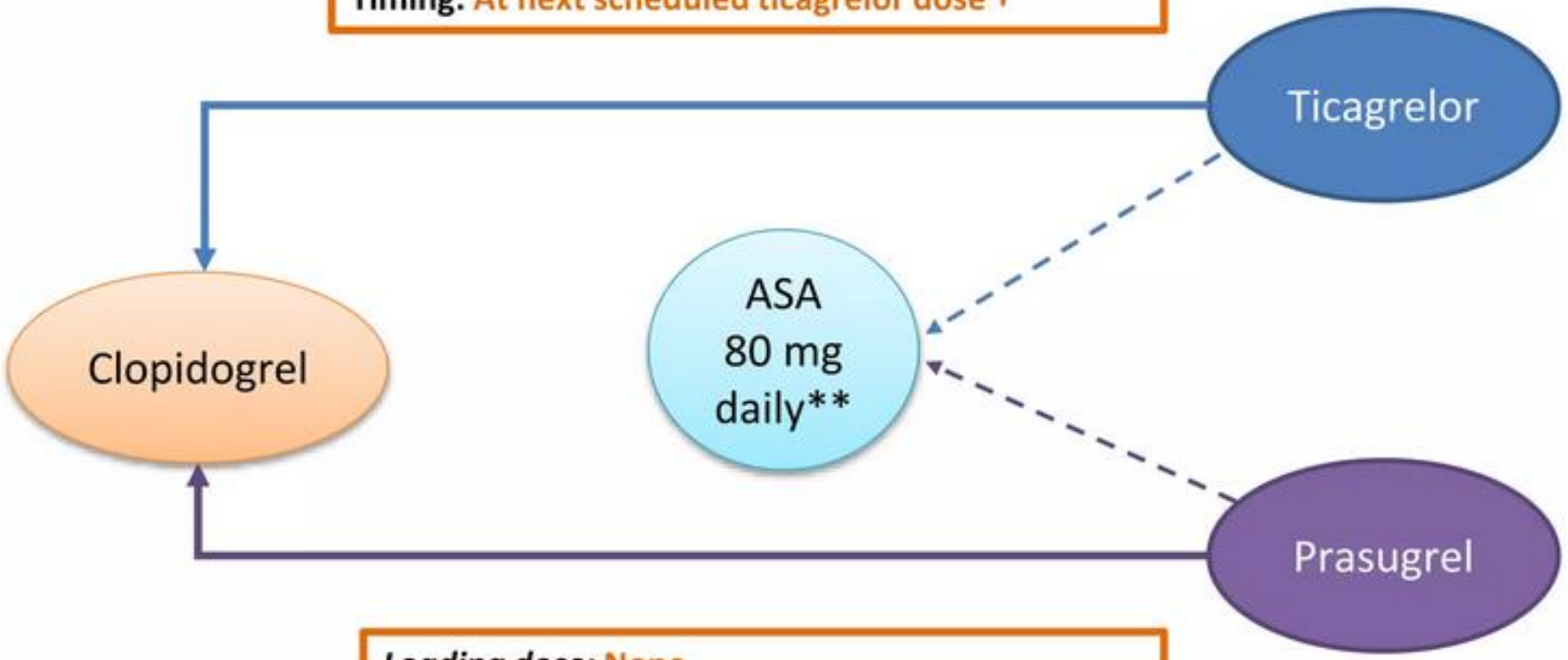
9. De-escalating strategies

- De-escalation from a more potent $P2Y_{12}$ inhibitor to clopidogrel occurs in up to 28% of patients with acute coronary syndromes, most often because of bleeding or high risk of bleeding.

- Similarly, switching between potent $P2Y_{12}$ inhibitors may be required if specific adverse effects such as shortness of breath or gout develop in patients receiving ticagrelor.

De-escalation strategies

Loading dose: Optional loading 300-600 mg *
Maintenance **dose:** 75 mg daily
Timing: At next scheduled ticagrelor dose †



Loading dose: None
Maintenance **dose:** 75 mg daily
Timing: At next scheduled dose

* Short-term (48h) PD advantage, might be relevant in the early post-ACS/PCI period, if no bleeding risk
† Extending to 24h post last ticagrelor dose may also be reasonable
** Consider monotherapy with ASA if switch because of bleeding

10. Points to be considered

Points To Be Considered

- Newer antiplatelet drugs have addressed some but not all the limitations of current therapy.
- Prasugrel and ticagrelor is more efficacious in preventing ischemic events in patients with ACS undergoing PCI, but with increased bleeding complications.
- Dual antiplatelet treatment has only been efficacious in ACS and post-PCI patients.
- Newer thienopyridines did not show advantages over and above those of ticlopidine or clopidogrel as to reduction of stroke.

Thank You for Your Kind Attention