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# **2012 Focused Update on the Canadian Cardiovascular Society Guidelines for the use of Antiplatelet Therapy**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

## Rationale for Antiplatelet Guidelines

- Clinicians need clear guidance on the use of all risk prevention strategies to reduce the burden of ischemic vascular disease.
- Guidelines have long been available to provide evidence based care for the management of:
  - Lipids – CCS
  - Hypertension – CHEP
  - Diabetes – CDA
  - Many other disease states, but none, prior to this document specifically directed to antiplatelet therapy

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

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**2012**

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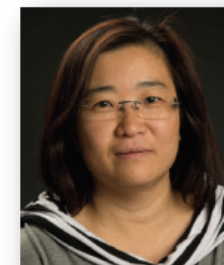
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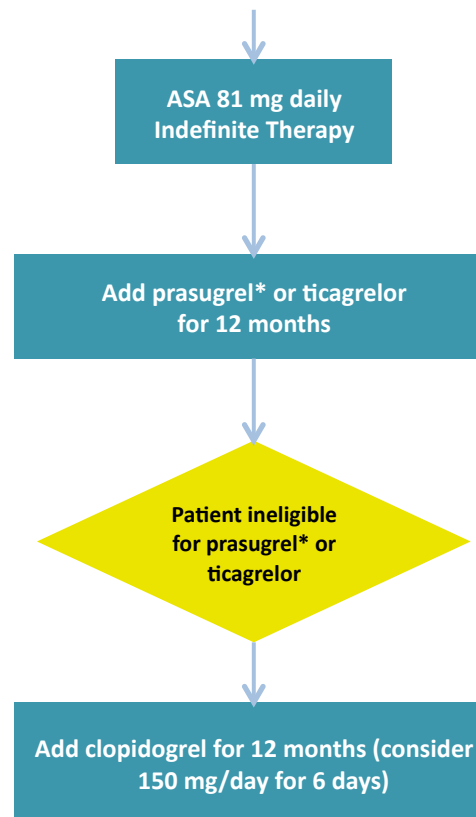
**Updated evidence for antiplatelet therapy post-ACS in patients treated with PCI, CABG, or medical therapy alone.**

## **RECOMMENDATIONS for NSTEMACS**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

# Recommendations for Non-ST-Elevation Acute Coronary Syndrome

Coronary anatomy defined and PCI planned



\*Prasugrel should be avoided in patients with prior TIA or stroke. In patients aged  $\geq 75$  years or body weight  $\leq 60$  kg, prasugrel should be used with caution and a 5 mg dose considered.

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## Antiplatelet Therapy for Secondary Prevention in the First Year Following NSTEMACS

1. We recommend ASA 81 mg daily indefinitely in all patients with NSTEMACS (Strong Recommendation, High Quality Evidence). For patients allergic to or intolerant of ASA, indefinite therapy with clopidogrel 75 mg daily is recommended (Strong Recommendation, High Quality Evidence) (Unchanged)
2. We recommend ticagrelor 90 mg twice daily over clopidogrel 75 mg daily for 12 months in addition to ASA 81 mg daily in patients with moderate to high risk NSTEMACS managed with either PCI, CABG surgery or medical therapy alone. (Strong Recommendation, High Quality Evidence) (New)

**New**

## Antiplatelet Therapy for Secondary Prevention in the First Year Following NSTEMACS

3. We recommend prasugrel 10 mg daily over clopidogrel 75 mg daily for 12 months in addition to ASA 81 mg daily in P2Y<sub>12</sub> inhibitor-naïve patients with NSTEMACS after their coronary anatomy has been defined and PCI planned  
(Strong Recommendation, High Quality Evidence)  
(New) **New**
4. We recommend avoiding prasugrel in patients with prior TIA or stroke or in patients who are not treated with PCI. Except in patients with a high probability of undergoing PCI, we recommend avoiding prasugrel before the coronary anatomy has been defined.  
(Strong Recommendation, Moderate Quality Evidence)  
(New) **New**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

## Antiplatelet Therapy for Secondary Prevention in the First Year Following NSTEMACS

5. We recommend clopidogrel 75 mg once daily for 12 months in addition to ASA 81 mg daily in patients with NSTEMACS managed with either PCI, CABG, or medical therapy and who are not eligible for ticagrelor or prasugrel  
(Strong Recommendation, High Quality Evidence)  
(New) **New**
6. We recommend that in patients where clopidogrel is to be used, a higher maintenance dose of 150 mg daily be considered for the first 6 days in patients with NSTEMACS treated with PCI  
(Strong Recommendation, Moderate Quality Evidence)  
(New) **New**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

**New**

## Antiplatelet Therapy for Secondary Prevention in the First Year Following NSTEMI/ACS

### Practical tips for ticagrelor and prasugrel

- In patients receiving DAPT, we suggest using ASA 81 mg daily.
- Ticagrelor can be used in patients managed with either PCI, CABG, or medical therapy alone, whereas prasugrel should be used only in patients undergoing PCI.
- In patients  $\geq 75$  years of age or weight  $\leq 60$  kg, when available, prasugrel 5 mg daily could be considered.

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

**Updated evidence for antiplatelet therapy post-ACS in patients treated with PCI, CABG, or medical therapy alone.**

## **RECOMMENDATIONS for STEMI**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

## Antiplatelet Therapy for Secondary Prevention in the First Year Following STEMI

1. We recommend ASA 81 mg daily indefinitely in all patients with STEMI (Strong Recommendation, High Quality Evidence).  
(Unchanged)
2. We recommend indefinite therapy with clopidogrel 75 mg daily for patients allergic to or intolerant of ASA (Strong Recommendation, High Quality Evidence)  
(Unchanged)
3. We recommend clopidogrel 75 mg daily for at least 1 month in addition to ASA 81 mg daily in patients with STEMI who were managed with either fibrinolytic therapy or no reperfusion therapy (Strong Recommendation, High Quality Evidence).  
Clopidogrel may be continued for 12 months (Weak Recommendation, Low Quality Evidence)  
(New)

**New**

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**New**

## Antiplatelet Therapy for Secondary Prevention in the First Year Following STEMI

4. We recommend either prasugrel 10 mg daily or ticagrelor 90 mg twice daily over clopidogrel 75 mg daily for 12 months in addition to ASA 81 mg daily after primary PCI

(Strong Recommendation, Moderate Quality Evidence)

(New)

**New**

5. We recommend clopidogrel 75 mg daily for 12 months in addition to ASA 81 mg daily after primary PCI in patients who are not eligible for prasugrel or ticagrelor (Strong Recommendation, Moderate Quality Evidence)

(New)

**New**

6. We recommend that in patients where clopidogrel is to be used, a higher maintenance dose of 150 mg daily be considered for the first 6 days in patients with STEMI treated with PCI

(Strong Recommendation, Moderate Quality Evidence)

(New)

**New**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

## Antiplatelet Therapy for Secondary Prevention in the First Year Following STEMI

7. We recommend avoiding prasugrel in patients with prior TIA or stroke and using a 5-mg dose if required in patients of age  $\geq 75$  years or weight  $\leq 60$  kg  
(Strong Recommendation, Low Quality Evidence)  
(New)

**New**

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# **Antiplatelet Therapy for Secondary Prevention in the First Year Following PCI**

## **RECOMMENDATIONS FOR PCI for a NON-ACS INDICATION**

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## Antiplatelet Therapy for Secondary Prevention in the First Year Following PCI: NON-ACS INDICATION

1. We recommend clopidogrel 75 mg daily for at least 12 months in addition to ASA 81 mg daily indefinitely in patients receiving PCI with BMS or DES for a non-ACS indication  
(Strong Recommendation, High Quality Evidence)  
(Unchanged)
2. We recommend that in patients receiving a BMS who are unable to tolerate clopidogrel for 12 months (e.g. increased risk of bleeding or scheduled non-cardiac surgery), the minimum duration of therapy should be 1 month  
(Strong Recommendation, High Quality Evidence).  
In patients at very high risk of bleeding, the minimum duration of treatment may be 2 weeks  
(Weak Recommendation, Low Quality Evidence)  
(New)

**New**

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## Antiplatelet Therapy for Secondary Prevention in the First Year Following PCI: NON-ACS INDICATION

3. We recommend ASA 81 mg daily indefinitely in all patients who have undergone PCI  
(Strong Recommendation, Moderate Quality Evidence).  
(Unchanged)
4. We recommend that all patients undergoing PCI be assessed for their ability to tolerate and comply with DAPT for 1 year. In patients unable to tolerate or comply with DAPT for 1 year (e.g. increased risk of bleeding, scheduled noncardiac surgery, or anticipated poor compliance), BMS rather than DES should be used.  
(Strong Recommendation, Low Quality Evidence) (Unchanged)

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## Antiplatelet Therapy for Secondary Prevention in the First Year Following PCI: NON-ACS INDICATION

5. We suggest that in patients receiving a second-generation DES who are unable to tolerate clopidogrel for 12 months (e.g. increased risk of bleeding or scheduled noncardiac surgery), the minimum duration of therapy may be 3 months.

(Weak Recommendation, Low Quality Evidence)

(New)

**New**

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**Updated evidence for antiplatelet  
therapy post-ACS  
in patients treated with PCI.**

**GENERAL RECOMMENDATIONS for  
ACS AND PCI**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

**New**

## Antiplatelet Therapy for Secondary Prevention in the First Year Following PCI: ACS AND PCI

1. We recommend that for patients who are compliant with clopidogrel and have experienced stent thrombosis, prasugrel 10 mg daily or ticagrelor 90 mg twice daily may be considered in addition to ASA 81 mg daily  
(Strong Recommendation, Low Quality Evidence)  
(New)

**New**

2. We suggest continuation of a P2Y<sub>12</sub> inhibitor with ASA beyond 12 months be considered in patients with a high thrombosis risk and a low bleeding risk  
(Weak Recommendation, Low Quality Evidence)  
(New)

**New**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

**New**

## Antiplatelet Therapy for Secondary Prevention in the First Year Following PCI: ACS AND PCI

3. We suggest that if patients require surgery (CABG or non-CABG), the P2Y<sub>12</sub> inhibitor be withheld, if possible, as follows: clopidogrel 5 days prior, ticagrelor 5 days prior, and prasugrel 7 days prior to the date of surgery (Weak Recommendation, Low Quality Evidence)

(New)

**New**

4. We suggest against switching the P2Y<sub>12</sub> inhibitor initially selected at discharge unless there is a compelling clinical reason (e.g. stent thrombosis, bleeding, or cardiovascular event)

(Weak Recommendation, Very Low Quality Evidence)

(New)

**New**

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# **Antiplatelet Therapy Regimen Following Coronary Artery Bypass Grafting**

## **RECOMMENDATIONS**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*



## Antiplatelet Therapy Regimen Following Coronary Artery Bypass Grafting

1. We recommend ASA 81 mg daily indefinitely in patients who undergo CABG with or without use of a saphenous vein graft  
(Strong Recommendation, Moderate Quality Evidence)  
(Unchanged)
2. We suggest the use of clopidogrel 75 daily indefinitely in patients undergoing CABG who are intolerant of ASA with or without use of saphenous vein graft  
(Weak Recommendation, Low Quality Evidence) (Unchanged)

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

**New**

## Antiplatelet Therapy Regimen Following Coronary Artery Bypass Grafting

3. We recommend that in patients with ACS requiring CABG, the risk of bleeding versus the benefit of continuing dual antiplatelet therapy be weighed in deciding the appropriate timing of intervention  
(Strong Recommendation, Low Quality Evidence)  
(New) **New**
4. We suggest that if possible in patients scheduled for CABG, clopidogrel and ticagrelor be discontinued for 5 days and prasugrel for 7 days before surgery  
(Weak Recommendation, Low Quality Evidence)  
(New) **New**
5. We recommend that DAPT be continued for 12 months in patients with ACS after CABG  
(Strong Recommendation, Moderate Quality Evidence).  
(New) **New**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

**New**

## **Antiplatelet Therapy Regimen Following Coronary Artery Bypass Grafting**

### **Practical Tips**

In stable patients with ACS without critical coronary anatomy who are clinically stabilized, clopidogrel and ticagrelor should be withheld for 5 days and prasugrel for 7 days before CABG. In patients with ACS, DAPT should be restarted at maintenance dose within 48-72 hours post-operatively when deemed safe by the cardiac surgical team.

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

## Change in Philosophy in Antiplatelet Therapy for ACS: 2012

- Choice of antiplatelet agent dependent on treatment modality
  - Medical: clopidogrel or ticagrelor
  - PCI: ticagrelor or prasugrel preferred over clopidogrel
  - CABG: clopidogrel or ticagrelor
  - Elective, non-ACS: clopidogrel
- Recommendation is for DAPT for 1 year for all ACS patients whether they are treated medically, with PCI (BMS OR DES) or with CABG

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# **Novel Oral Anticoagulants and Antiplatelet Therapy for the Secondary Prevention Following ACS**

## **RECOMMENDATIONS**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

**New**

## **Novel Oral Anticoagulants and Antiplatelet Therapy for Secondary Prevention Following ACS**

1. We recommend against the use of triple therapy with rivaroxaban, clopidogrel and ASA over the use of dual therapy with ticagrelor or prasugrel plus ASA for secondary prevention of ACS  
(Weak Recommendation, Very Low Quality Evidence)  
(New)

**New**

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**New**

## **Novel Oral Anticoagulants and Antiplatelet Therapy for Secondary Prevention Following ACS**

### **Practical Tip**

There may be patients in whom combining an oral anticoagulant with DAPT is warranted, such as patients with atrial fibrillation or a mechanical heart valve who develop ACS. Attention is needed to monitor and minimize the duration of “triple antithrombotic therapy” given the high risk for bleeding associated with such treatment.

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

**New**

## **Novel Oral Anticoagulants and Antiplatelet Therapy for Secondary Prevention Following ACS**

2. We recommend against the use of dabigatran and apixaban at any dose in combination with antiplatelet therapy for secondary prevention of ACS  
(Strong Recommendation, High Quality Evidence)  
(New)

**New**

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# Interaction between Clopidogrel and Proton Pump Inhibitors

## RECOMMENDATIONS

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**New**

## **Interaction between Clopidogrel and Proton Pump Inhibitors**

1. We recommend selective use of PPIs in patients receiving DAPT at high risk of upper gastrointestinal bleeding (Strong Recommendation, Moderate Quality Evidence). (New)

**New**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

## **Interaction between Clopidogrel and Proton Pump Inhibitors**

2. We suggest that prescribing a PPI that minimally inhibits CYP2C19 (e.g. pantoprazole) be considered in patients receiving a PPI with clopidogrel (Weak Recommendation, Low Quality Evidence). (Unchanged)

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

**New**

## **Interaction between Clopidogrel and Proton Pump Inhibitors**

### **Practical Tip**

PPIs should not be used routinely in all patients taking DAPT but should be considered in patients at higher risk of gastrointestinal bleeding.

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# **2012 Focused Update on the Canadian Cardiovascular Society Guidelines for the use of Antiplatelet Therapy**

## **GUIDELINE PEARLS**

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## Primary Prevention

DO	DON'T
<p>Consider ASA <b>only</b> where there is clear evidence of high risk.</p> <ul style="list-style-type: none"><li>• Asymptomatic carotid stenosis</li><li>• Asymptomatic coronary atherosclerosis</li><li>• Endstage CKD</li><li>• Reduced ABI</li></ul>	<p>Use antiplatelet therapy for primary prevention.</p>

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## Cerebrovascular disease

DO	DON'T
<p>Provide lifetime antiplatelet Rx to all patients post ischemic stroke or TIA.</p> <p>Consider DAPT with ASA + Clopidogrel in patients with high risk TIA or minor stroke for 30 days.</p>	<p>Use DAPT with ASA + Clopidogrel for long term secondary stroke prevention.</p>

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## ACS / PCI

DO	DON'T
Provide lifetime antiplatelet Rx to all patients post ACS with or without PCI.	Use doses of ASA above 81 mg.
Provide DAPT with ASA + P2Y12 inhibitor to all ACS patients.	Discontinue DAPT prior to 1 yr without a very good reason.
Know the type of stent your patient has inserted.	EVER discontinue DAPT in a patient with a Drug Eluting Stent prior to 1 yr, EVER (without a cardiology consult)
Consider DAPT beyond 1 year in patients with high risk of thrombosis and low risk of bleeding.	

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## Management of patients post ACS who require surgery, diagnostic or dental procedures

DO	DON'T
<p>Delay such procedures in patients taking DAPT.</p> <p>Stop clopidogrel for 7-10 days prior <b>if it can be done so safely.</b></p> <p>Stop ASA for 7 – 10 days for bleeding high risk surgical procedures.</p>	<p>Discontinue DAPT prior to 1 year in patients with Drug Eluting Stents EVER (without a cardiology consult)</p> <p>Stop ASA for minor procedures including:</p> <ul style="list-style-type: none"><li>• Arthrocentesis</li><li>• Dental procedures</li><li>• Cataract surgery</li><li>• Skin excisions</li></ul>

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## Minor Bleeding Management

DO	DON'T
<p>If persistent check:</p> <ul style="list-style-type: none"><li>• Complete blood count</li><li>• INR and activated Partial Thromboplastin Time (aPTT)</li></ul>	<p>Stop antiplatelet therapy for:</p> <ul style="list-style-type: none"><li>• Eccymosis</li><li>• Petechia</li><li>• Subconjunctival hemorrhage</li><li>• Epistaxis</li><li>• Dental / gingival bleeding</li></ul>

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## Drug Interactions

DO	DON'T
Use Coxibs over traditional NSAIDs in patients taking ASA for CV prevention <b>but only if absolutely necessary.</b>	Use PPI's that inhibit CYP2C19 in patients taking clopidogrel or prasugrel.  Use NSAIDs or Coxibs in patients at increased risk of vascular events.

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# **2012 Focused Update on the Canadian Cardiovascular Society Guidelines for the use of Antiplatelet Therapy**

## **DRUG SUMMARIES**

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## Drug Summaries

	Clopidogrel	Prasugrel	Ticagrelor
<b>Requires metabolic activation through CYP2C19</b>	Yes sensitive to polymorphisms and drug interactions	Yes but less sensitive to polymorphisms and drug interactions	
<b>Indications</b>	ACS, PCI, PAD, CVD	PCI	ACS, PCI
<b>Maintenance Dosing</b>	75 mg OD	10 mg OD	90 mg BID
<b>Reversible Inhibition</b>	No	No	Yes
<b>Efficacy</b>	++ • Further 2% ARR over ASA monotherapy	+++ • Further 2% ARR over clopidogrel + ASA	+++ • Further 2% ARR over clopidogrel + ASA
<b>Bleeding Risk</b>	+	+++	++
<b>Issues</b>	• Rash	• Bleeding risk in: Prior stroke / TIA < 60 Kg > 75 yrs • Increased fatal bleeding	• Dyspnea • Ventricular pause • Hyperuricemia • Slight increased Cr

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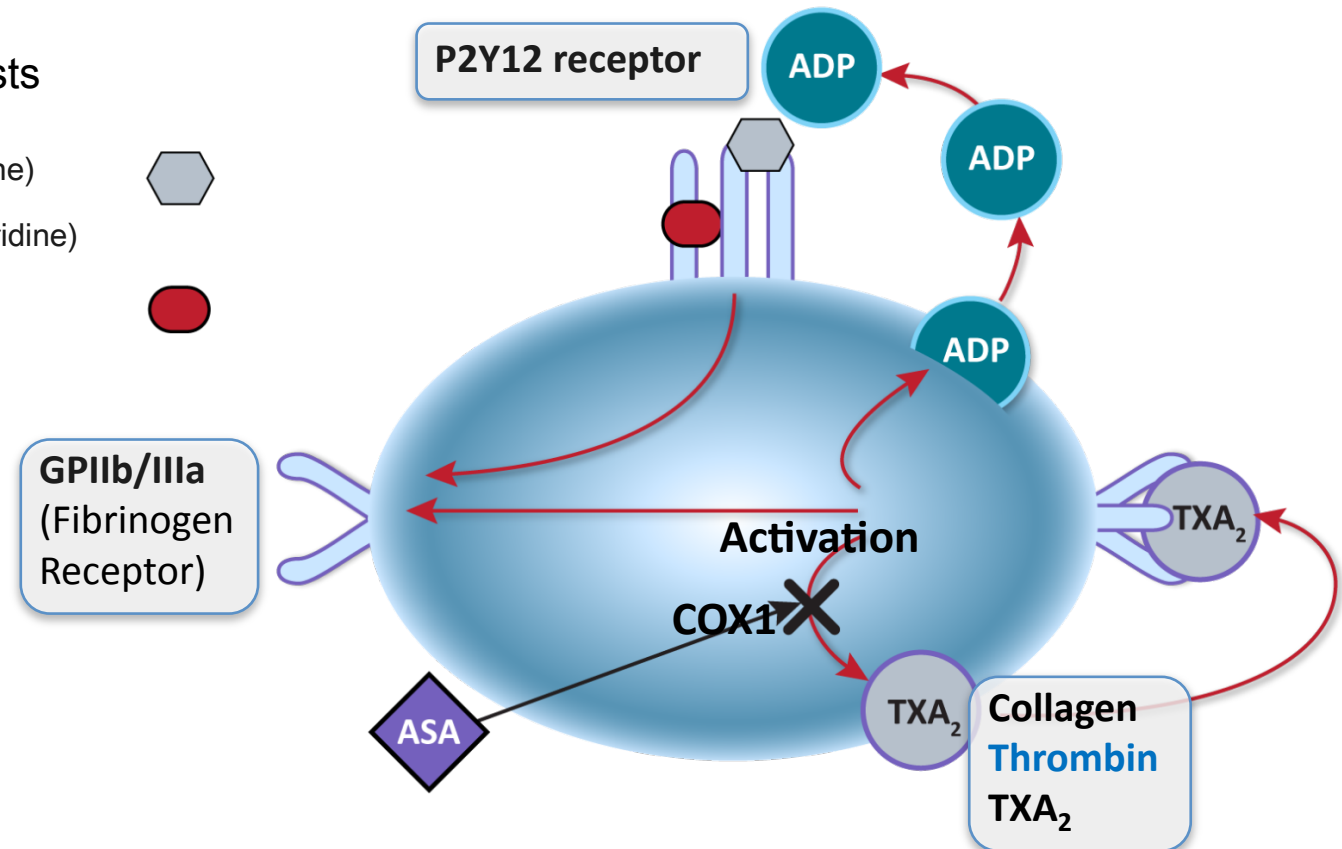
## Antiplatelet Mechanisms of Action

## P2Y12 Receptor Antagonists

# Prasugrel (thienopyridine)

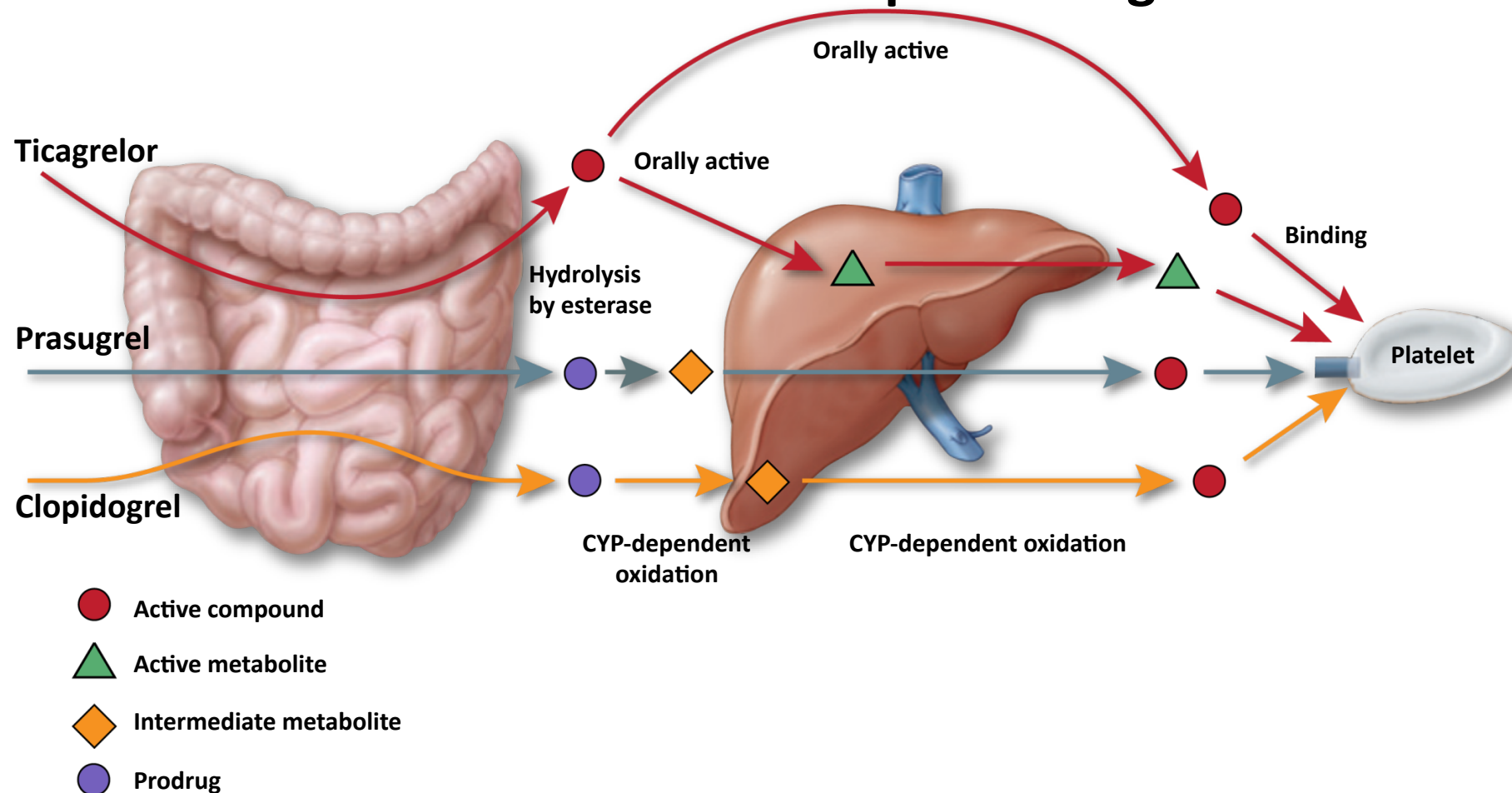
## Clopidogrel (thienopyridine)

# Ticagrelor (CPTP)



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## Metabolism of P2Y<sub>12</sub> Receptor Antagonists



Adapted from: Schomig A. NEJM. 2009;361(11):1108-1111. Effient (Prasugrel) Product Monograph March 11, 2011 version. Brilinta (Ticagrelor) Product Monograph May 26, 2011 version. Plavix (Clopidogrel) Product Monograph May 9, 2011 version.

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## **2012 Focused Update on the Canadian Cardiovascular Society Guidelines for the use of Antiplatelet Therapy**

### **CASES**

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## Case 1: Mr. Smith

- 63 yo male office worker presents complaining of shortness of breath intermittently since hospital discharge following heart attack 3 weeks ago
  - Describes intermittent feeling of breathless usually at rest
  - Not associated with:
    - Chest pain, palpitations, nausea/vomiting, ankle swelling, cough or wheeze
  - Able to continue with usual activities
  - Physical exam – normal

## Case 1: Mr. Smith

- NSTEMI 3 weeks prior to current visit
  - Managed with percutaneous intervention
  - Drug eluting stents x 2
  - Discharged after 3 days with uneventful course and preserved LV function
- Comorbid conditions
  - Hypertension
  - Hyperlipidemia
- Current meds
  - ECASA 81 mg OD
  - Ticagrelor 90 mg BID
  - Metoprolol 50 mg BID
  - Rosuvastatin 20 mg OD
  - Irbesartan / HCT 300/12.5 mg OD

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## Case 1: Mr. Smith

Which of the following are likely causes of his dyspnea?

- A. Recurrent cardiac ischemia
- B. Anxiety
- C. Medication side effect
- D. Cardiac arrhythmia
- E. Pulmonary disease

All are correct but the key point is that C is a correct response

## Case 1: Mr. Smith

Which of the following investigations would you order?

- A. EKG
- B. Cardiac echo
- C. Chest X ray
- D. Holter monitor
- E. Graded exercise stress test
- F. Cardiology consult

All responses are correct.

## Case 2: Mr. Brown

- 67 yr old sedentary male with history of DM, HTN, high cholesterol
- Meds: ramipril, ASA, simvastatin, metformin
- Presents with new onset crescendo typical CP x 3 days culminating in rest pain
- No bleeding diathesis
- No history of TIA or stroke
- Weight: 80kg
- Exam: BP 150/85, HR 80 (sinus). No CHF; +S4 otherwise normal

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## Case 2: Mr. Brown

- Normal CBC, electrolytes
- Creatinine: 112 mmol/L
- Troponin I: 1.2 µg/L (4<sup>th</sup> generation assay)
- ECG: NSR, 1mm horizontal ST depression V1-V3
- CXR: normal (no CHF)
- Admitted with Dx of high risk Non-ST Elevation Acute Coronary Syndrome (NSTEMACS)
- Undergoes coronary angiography and subsequent drug eluting stent implantation

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## Case 2: Mr. Brown

Which discharge antiplatelet regimens are preferred following NSTEMACS and coronary stent?

1.ASA + Clopidogrel

2.ASA + Ticagrelor



3.ASA + Prasugrel



4.Any of the above

5.None of the above

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## Case 2: Mr. Brown

How long should this patient receive dual antiplatelet therapy?

- 1.1 month
- 2.3 months
- 3.6 months
- 4.1 year
- 5.Indefinite



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## Case 2: Mr. Brown

What if he had instead received a BMS?

1. Same as with a drug eluting stent
2. Shorter than with a drug eluting stent
3. Longer than with a drug eluting stent



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## Case 3: Mr. Sanchez

- 56 year old man, stable CCS 3 angina referred for elective PCI after trial of medical therapy
- Cath: 80% mid RCA lesion; stented with 1 x DES (everolimus eluting stent)

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## Case 3: Mr. Sanchez

For elective PCI, the duration of dual anti platelet therapy should be:

1. Same duration as following ACS
2. Shorter duration than following ACS
3. Longer duration as following ACS



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## Case 3: Mr. Sanchez

Which discharge antiplatelet regimens are preferred following elective coronary stenting?

- 1.ASA + Clopidogrel
- 2.ASA + Ticagrelor
- 3.ASA + Prasugrel
- 4.Any of the above
- 5.None of the above



## Case 4: Mr. Price

- 3 months after receiving a DES, your patient has to undergo prostatectomy for cancer. He has been advised to discontinue his antiplatelet therapy for the surgery
- He asks you, his family doctor, if this is safe?

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## Case 4: Mr. Price

Your response:

1. Yes, you can interrupt the clopidogrel after 3 months post PCI but continue the ASA
2. No, you must continue clopidogrel along with ASA for a minimum of 1 year regardless of the surgery

1 is correct, however 2 is also correct if he has a 2<sup>nd</sup> generation DES (not specified)

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

## Case 4: Mr. Price

Your response:

What if he had received a bare metal stent?



1. Yes, you can stop the clopidogrel after 3 months post PCI but continue the ASA
2. No, you must continue clopidogrel along with ASA for a minimum of 1 year

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*

**Thank you and questions**

Tanguay JF, Bell AD et al. (in press), *Can J Cardiol*