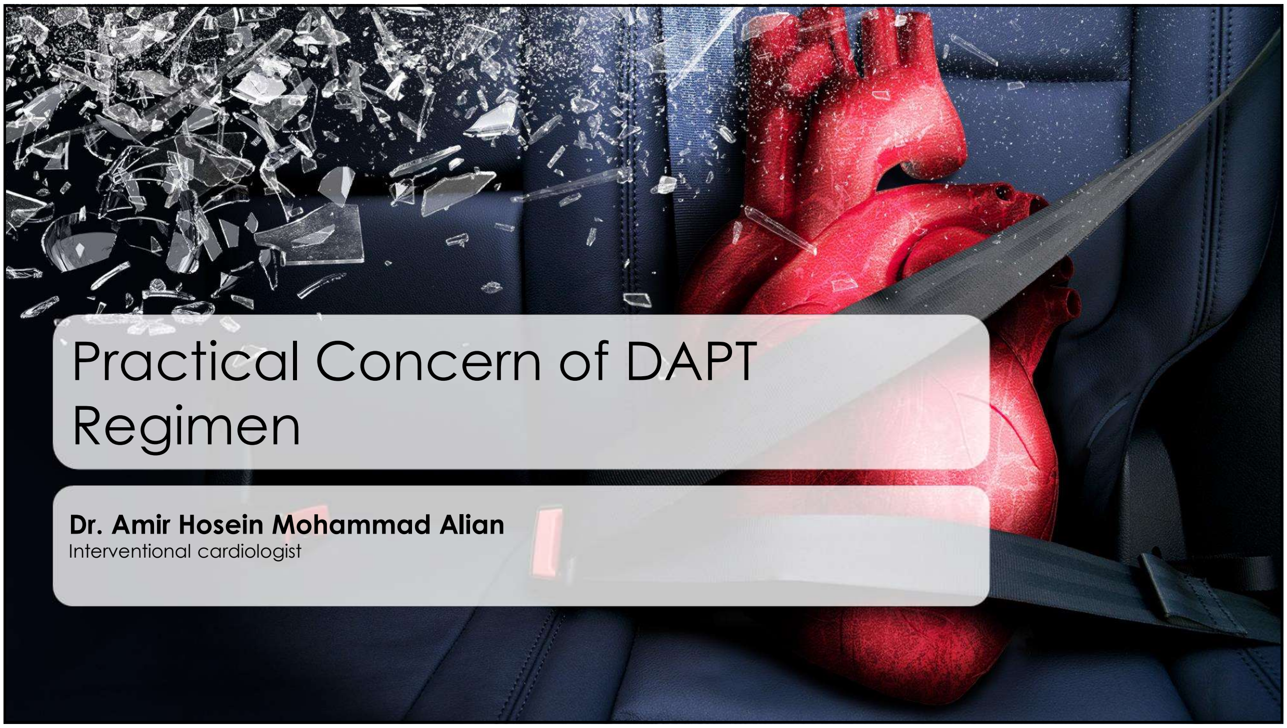

Practical Concerns of Prescribing Ticagrelor

- ✓ Switching
- ✓ Dyspnea
- ✓ Bleeding
  - intracranial Hemorrhage
  - Gastrointestinal bleeding
- ✓ Inconvenience (twice-daily dosing)

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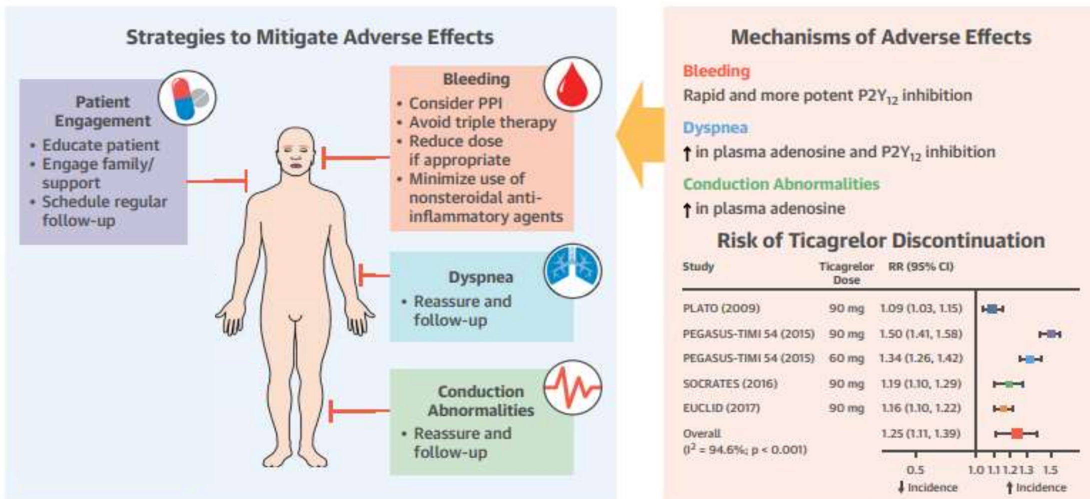
Ticagrelor's Adverse Effects and the Risk of Premature Discontinuation



IR-0922-BRL-7030-SP

J Am Coll Cardiol. 2019;73(19):2454–64

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ESC European Society of Cardiology

2017 DAPT Guidelines

Switching between oral P2Y12 inhibitors

RECOMMENDATION	COR	LOE
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 contraindications* to ticagrelor exist.	I	B
Additional switching between oral P2Y12 inhibitors may be considered in cases of side effects/drug intolerance according to the proposed algorithms.	IIb	C

* Contraindications for ticagrelor: previous intracranial hemorrhage or ongoing bleeds.

European Heart Journal (2018) 39, 213–254

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Switching Therapy

Switching therapy[2,5]

Reasons for escalating from Clopidogrel to Ticagrelor	Reasons for de-escalation from Ticagrelor to Clopidogrel
ACS patients, who are initially treated with Clopidogrel at presentation: • Patients with either moderate- to high-risk non-ST elevation ACS (NSTE-ACS) (planned for either conservative or invasive management) • STEMI planned for primary PCI	**Need for Oral Anticoagulant (OAC)**
Admitted with thrombotic event (e.g., stent thrombosis or ACS), who have been treated with Clopidogrel	**Bleeding, intolerance**
Who are known poor metabolizer of Clopidogrel (e.g., CYP2C19 loss-of-function)	**Dyspnea, intolerance**
	Triple therapy : OAC + DAPT
	Intolerable side effects

European Heart Journal (2018) 39, 213–254

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Switching Between Oral P2Y12 Inhibitors

Acute setting:

Clopidogrel → Ticagrelor: **Ticagrelor LD(180mg)** Irrespective of prior clopidogrel timing & dosing

Ticagrelor → Clopidogrel: **Clopidogrel LD(600mg)** 24h after last ticagrelor dose

Chronic setting:

Clopidogrel → Ticagrelor: **Ticagrelor MD(90mg bd)** 24h after last clopidogrel dose

Ticagrelor → Clopidogrel: **Clopidogrel LD(600mg)** 24h after last ticagrelor dose

Eur Heart J. 2018;39(3):213-260

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Dyspnea in ACS patients

The most common causes are:

- Heart failure exacerbation
- Pneumonia or acute bronchitis
- Worsening of pre-existing chronic pulmonary disease
- Recurrent ischemia
- Pulmonary thromboembolism
- Anemia
- Side effects of beta-blockers or ticagrelor

✓ **Ticagrelor-related dyspnea diagnosis is based on exclusion**

Clin Med Insights Case Rep. 2020;13:1179547620956634

IR-0122-BRL-6365-SP

Dyspnea in PLATO study

	Ticagrelor 90mg + Aspirin (N=9235)	Clopidogrel + Aspirin (N=9186)
Overall rate of dyspnea	14%	8%
Mild dyspnea	9.6%	5.5%
Moderate dyspnea	4.5%	2.4%
Severe dyspnea	0.4%	0.2%
Discontinuation of dyspnea	0.9%	0.1%

HIGHLIGHTS OF PRESCRIBING INFORMATION Reference ID: 4697813

IR-0122-BRL-6365-SP

Dyspnea in PLATO sub-study

199 subjects in a substudy of PLATO

After 1 month/ at least 6 months of chronic treatment

Pulmonary function testing irrespective of reported dyspnea

No indication of an adverse effect on pulmonary function

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Management Of Ticagrelor-related Dyspnea

Evaluation for the most common causes+

Symptoms like wheezing*, orthopnea**, paroxysmal nocturnal dyspnea***, or chest tightness or pain****

Yes: Treatment of the main reason

No

It usually occurs at rest, and is typically not related to exertion and does not limit exercise capacity

Watch and wait for 3-4 Days

Self limited

If does not resolve spontaneously

It is tolerable for the patient in the context of the benefit>risk profile of Ticagrelor treatment

Continue Ticagrelor and follow up

Persistent and intolerable

Drug discontinuation :
when dyspnea is persistent & cannot be tolerated

+Heart failure exacerbation, Pneumonia or acute bronchitis, Worsening of pre-existing chronic pulmonary disease, Recurrent ischemia, Pulmonary thromboembolism, Anemia

Eur Heart J Acute Cardiovasc Care 2015; 4(6): 555–560.

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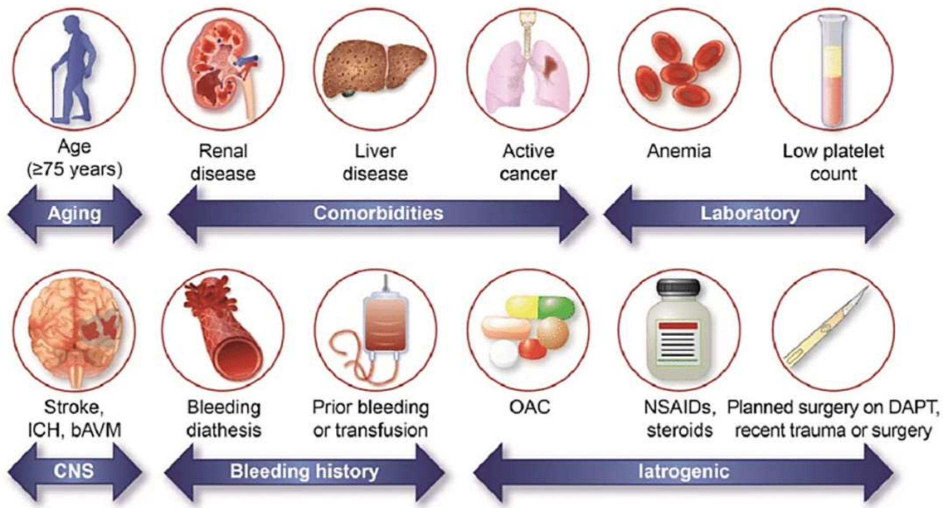
Increased Bleeding Risk



Circulation. 2019;140:240–26

IR-0922-BRL-7030-SP

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DAPT & Bleeding

- GI hemorrhage is the most common serious bleeding complication from the use of long-term antiplatelet therapy
- Omeprazole & esomeprazole have the highest propensity for clinically relevant interactions with clopidogrel & lansoprazole an intermediate probability
- No interaction between concomitant use of PPIs and prasugrel or ticagrelor

IR-0122-BRL-63665-SP

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Eur Heart J. 2018;39(3):213-260.

Management GI bleeding in DAPT therapy

Measures to minimize bleeding while on dual antiplatelet therapy

Recommendations	Class[a]	Level[b]
Radial over femoral access is recommended for coronary angiography and PCI if performed by an expert radial operator.[43,44]	I	A
In patients treated with DAPT, a daily aspirin dose of 75 - 100 mg is recommended.[45–47,51,52]	I	A
A PPI in combination with DAPT[c] is recommended.[70,79,80,86,87]	I	B
Routine platelet function testing to adjust antiplatelet therapy before or after elective stenting is not recommended.[58–60]	III	A

- PPIs have been recommended for reducing the risk of GI bleeding associated with DAPT.
- Aspirin plus Clopidogrel However, studies have found decreased efficacy of clopidogrel when concurrently administered with a PPI.
- Ticagrelor does not have drug interactions with PPIs.

European Heart Journal (2018) 39, 213–254

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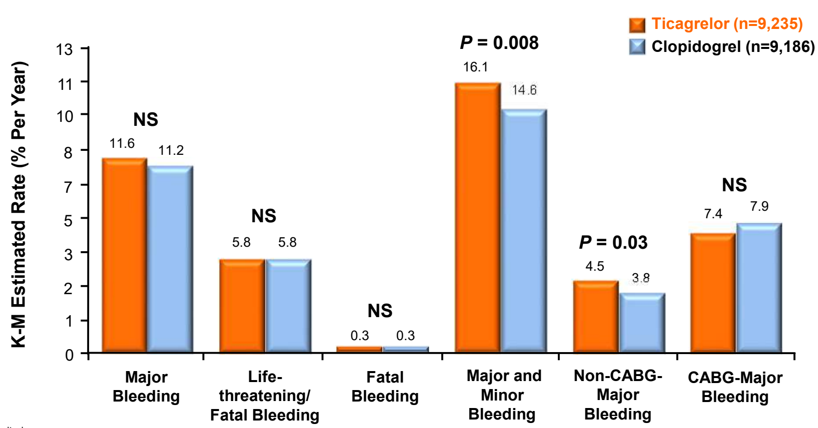
No significant difference in major fatal/life-threatening **bleeding** with Ticagrelor vs. Clopidogrel

PLATO Study



All values presented by PLATO criteria.
Both groups included aspirin.

N Engl J Med. 2009;361:1045–1057.

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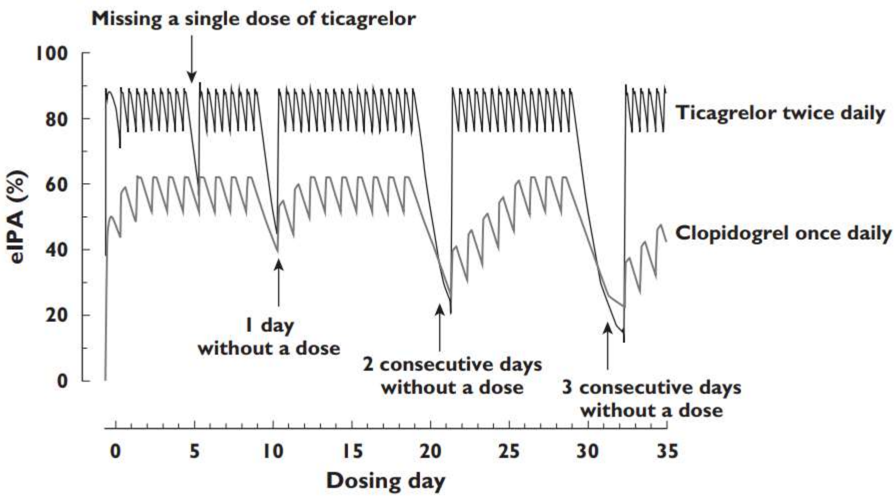
Twice-daily dosing



British Journal of Clinical Pharmacology 2013; 77(5),: 746-755.