

ACS and Acute MI: Brand New Issues

Antithrombotic Therapy in ACS-PCI

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Presenter Disclosure Information

Name: Dominick J Angiolillo

Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization listed below.

Received payment as an individual for:

- a) Consulting fee or honorarium from: Abbott, Amgen, Astra-Zeneca, Bayer, Biosensors, Boehringer Ingelheim, Bristol-Myers Squibb, Chiesi, CSL Behring, Daiichi-Sankyo, Eli Lilly, Faraday, Haemonetics, Janssen, Merck, Novartis, Novo Nordisk, PhaseBio, PLx Pharma, Pfizer, Sanofi and Vectura;
- b) Honorarium for participation in review activities (DSMB member) from National Institute of Health (NIH).
- c) Honorarium from the American Board of Internal Medicine (Interventional Cardiology Subspecialty Exam Writing Committee Member)

Institutional payments for:

- a) Grant support industry from: Amgen, AstraZeneca, Bayer, Biosensors, Celo-Nova, CSL Behring, Daiichi-Sankyo, Eisai, Eli Lilly, Faraday, Gilead, Idorsia, Janssen, Matsutani Chemical Industry Co., Merck, and Novartis.
- b) Grant in gift: Spartan; Scott R. MacKenzie Foundation
- c) Federal agency: NIH

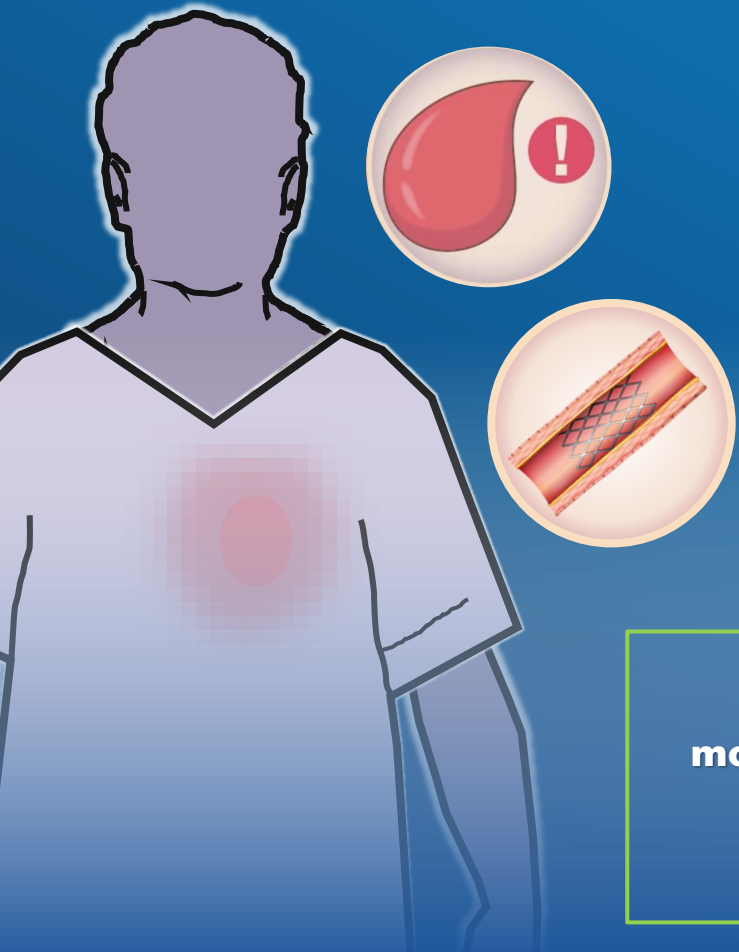
Historical perspective and “current” status

- Twelve months of dual antiplatelet therapy (DAPT) with aspirin and the adjunctive use of a P2Y12 inhibitor has represented for over 2 decades the cornerstone of treatment for the prevention of thrombotic complications in ACS patients (CURE, TRITON, PLATO) – Class I recommendation.
- Prasugrel (ACS-PCI only; TRITON) and ticagrelor (invasive and non-invasively managed ACS; PLATO) are preferred over clopidogrel as P2Y12 inhibitor of choice in the absence of contraindications – Class I recommendation.
- Prasugrel preferred over ticagrelor (ISAR-REACT 5; ESC guideline only)

Considerations

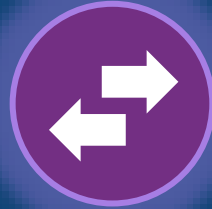
- Prevention strategies of cardiovascular events post-ACS have changed over the past 10-20 years (e.g., aggressive LDL lowering), resulting in a reduction in ischemic event rates.
- Evolution in stent technology with safer platforms.
- Better understanding of the prognostic implications of bleeding complications (ie., increased mortality), shifting attention towards bleeding reduction strategies.

Re-Consideration: Is twelve month of intensified DAPT necessary in all patients?



De-Escalation Strategies

ARC Definition



By
Switch



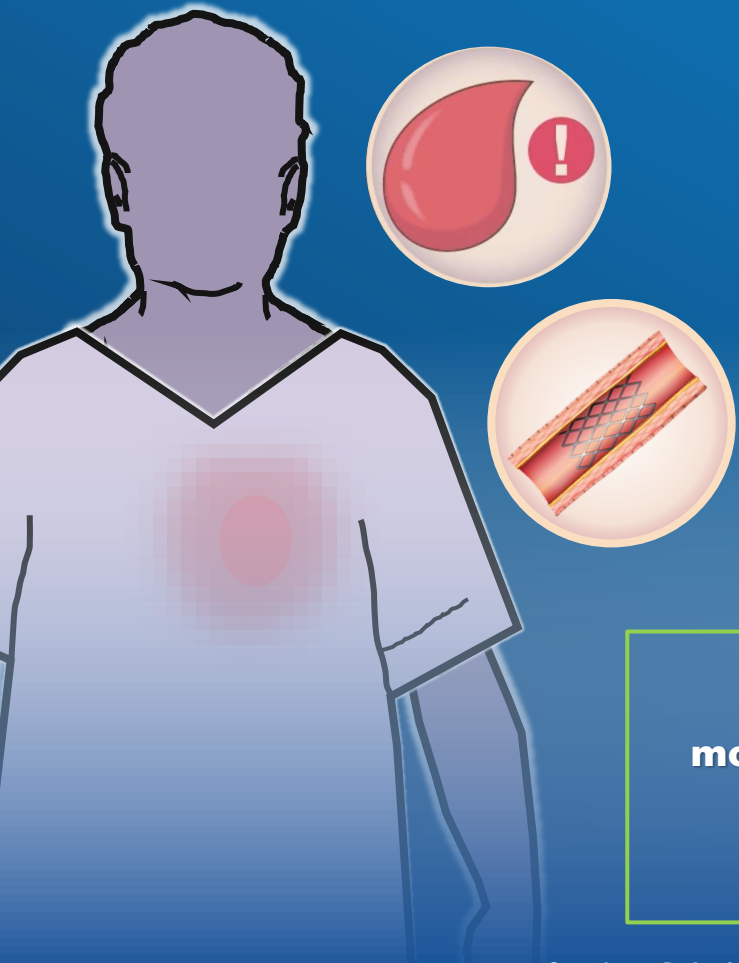
By Dose
Reduction



By
Discontinuation

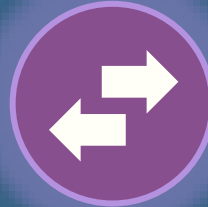
De-escalation: Modulation of antiplatelet therapy consisting in changes in the antiplatelet effect by modification of: a) drug, b) dose or c) number aimed at reducing the intensity of platelet inhibition.

Goal: reduce bleeding while preserving efficacy



De-Escalation Strategies

ARC Definition



By
Switch



By Dose
Reduction

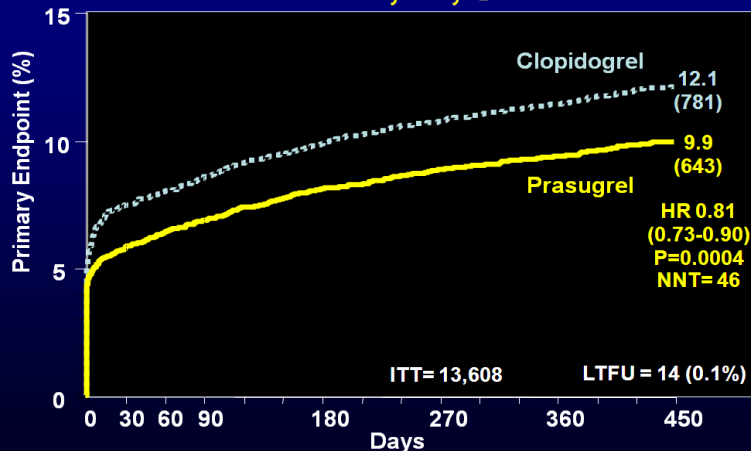


By
Discontinuation

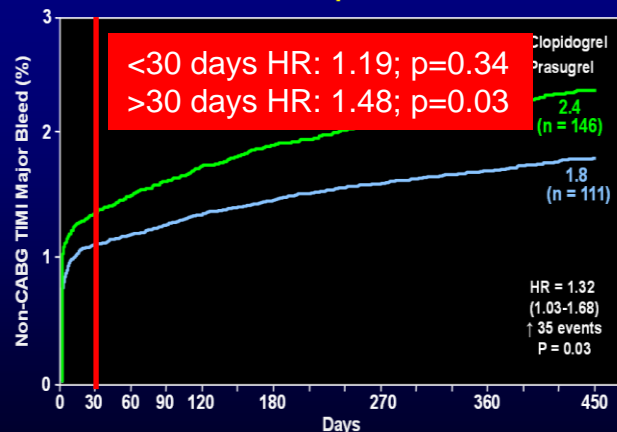
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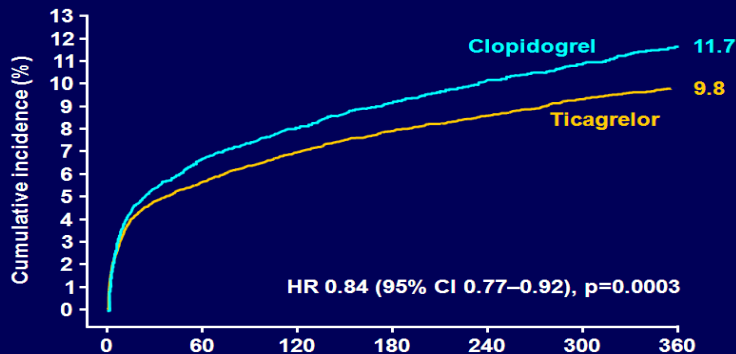
Primary Endpoint CV Death, MI, Stroke



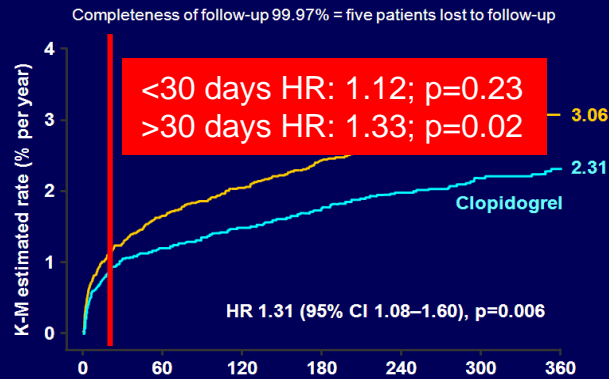
Non-CABG TIMI Major Bleed All ACS Population



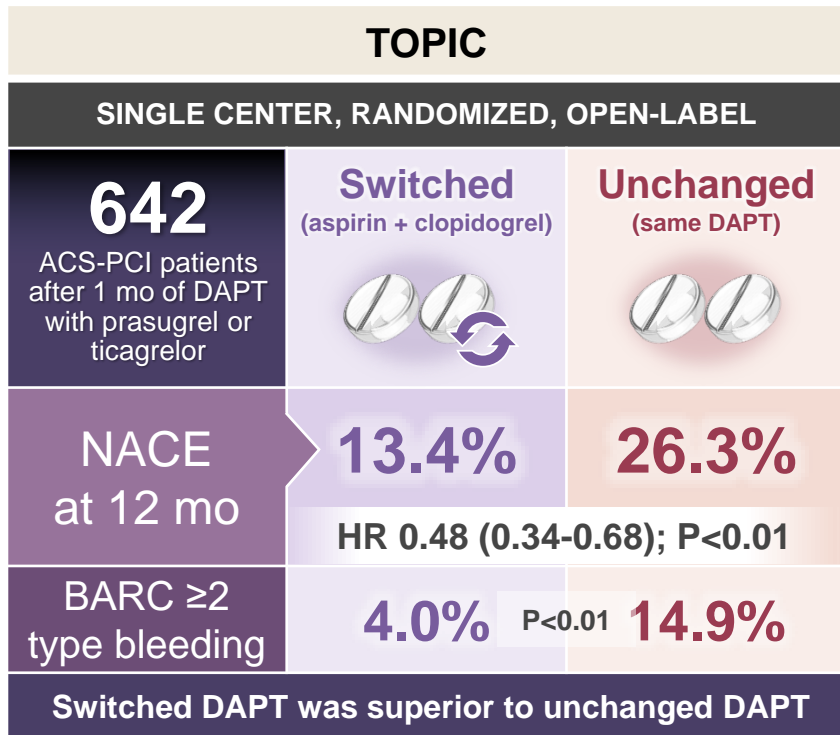
K-M estimate of time to first primary efficacy event (composite of CV death, MI or stroke)



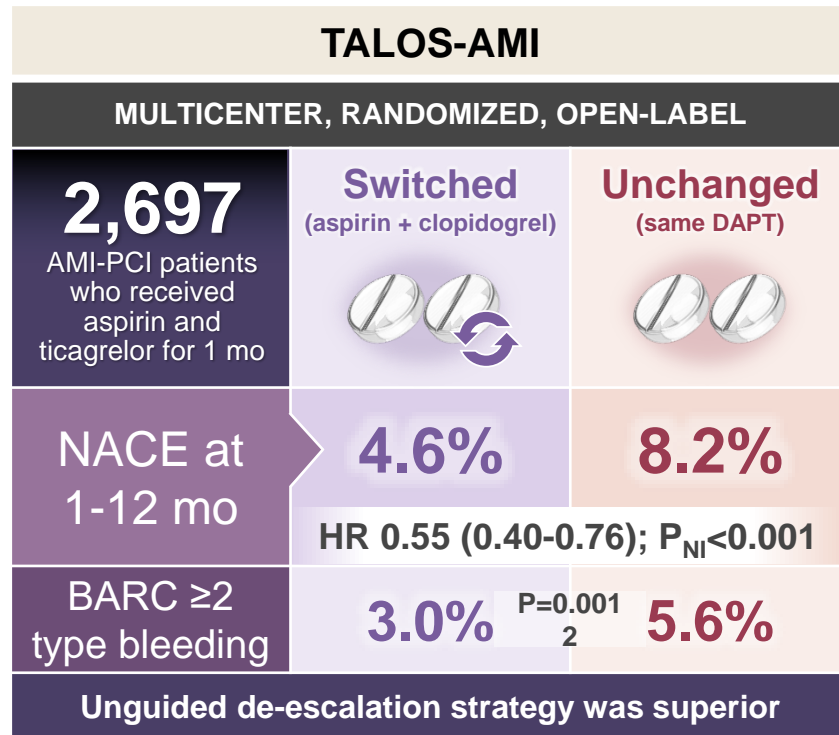
Time to non-procedure-related PLATO major bleeding



Unguided de-escalation

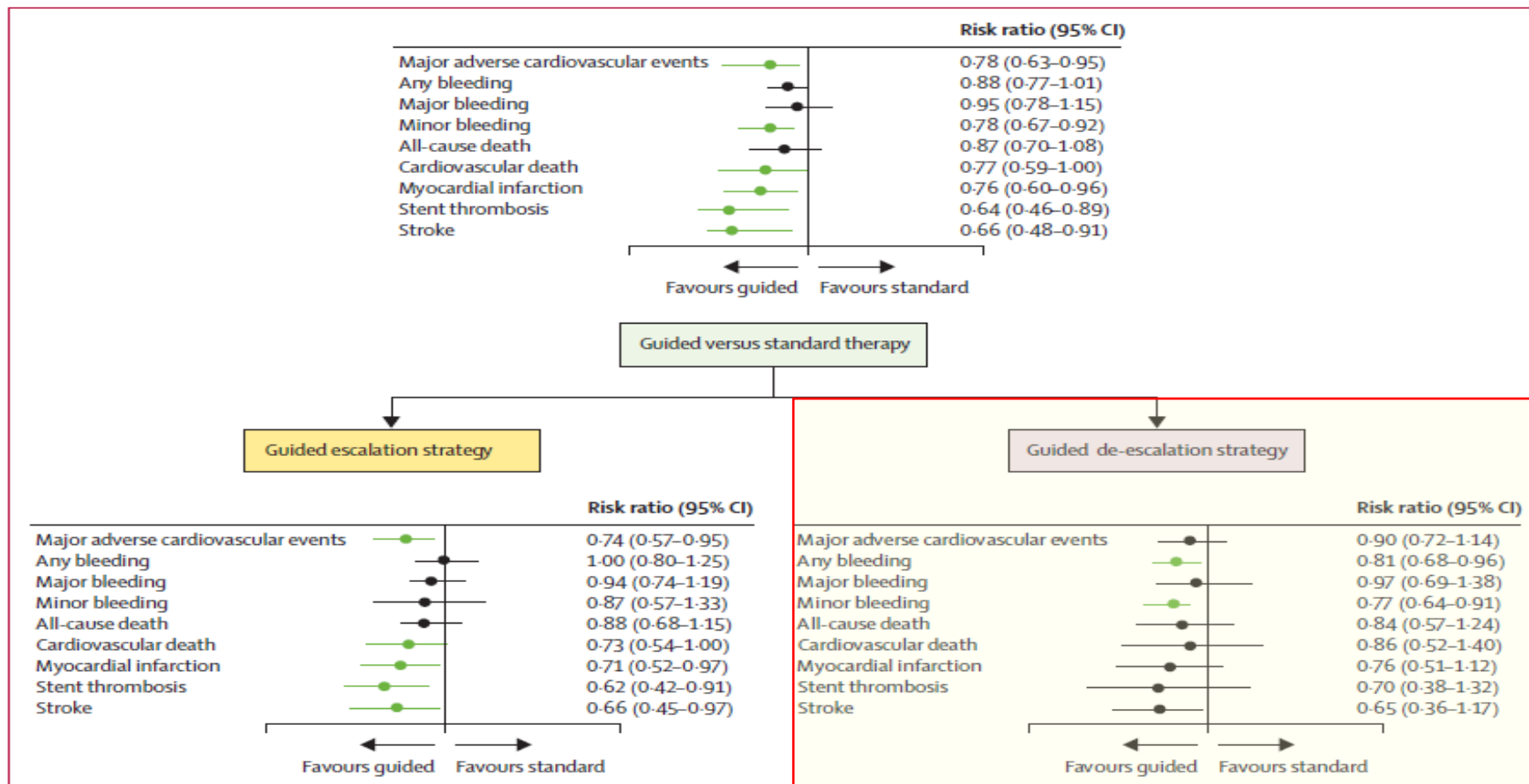


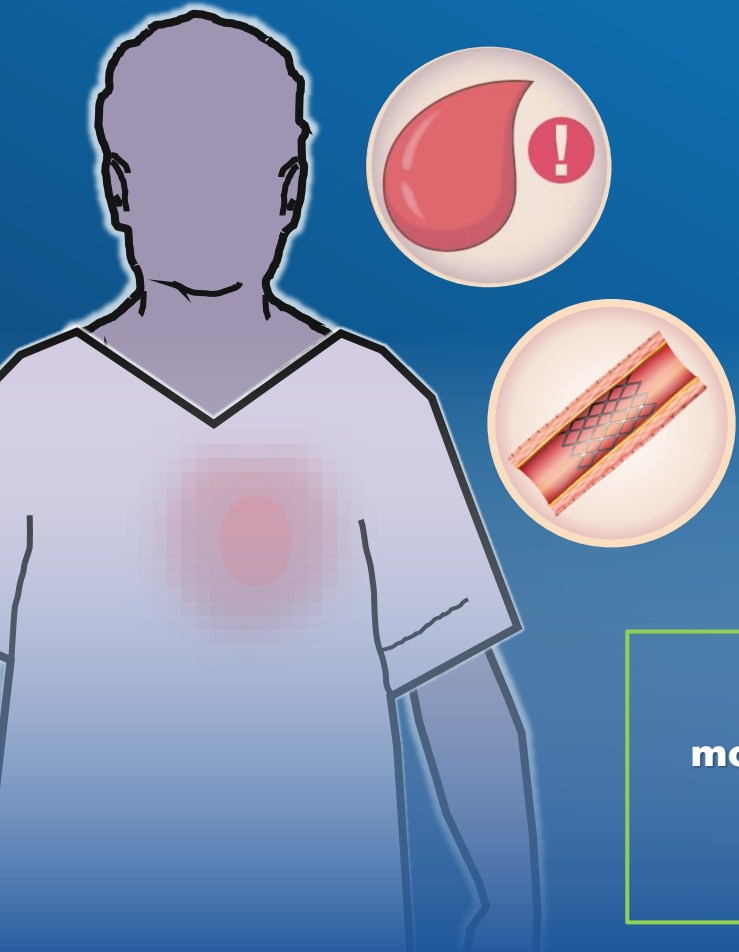
Cuisset T, et al. Eur Heart J. 2017;38:3070-3078



Kim CJ, et al. Lancet. 2021;398:1305-1316

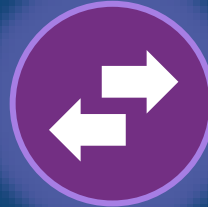
Guided (Platelet Function/Genetic Testing) vs Standard Antiplatelet Therapy in Patients Undergoing PCI: A Systematic Review and Meta-analysis (n=20743)





De-Escalation Strategies

ARC Definition



By
Switch



By Dose
Reduction



By
Discontinuation

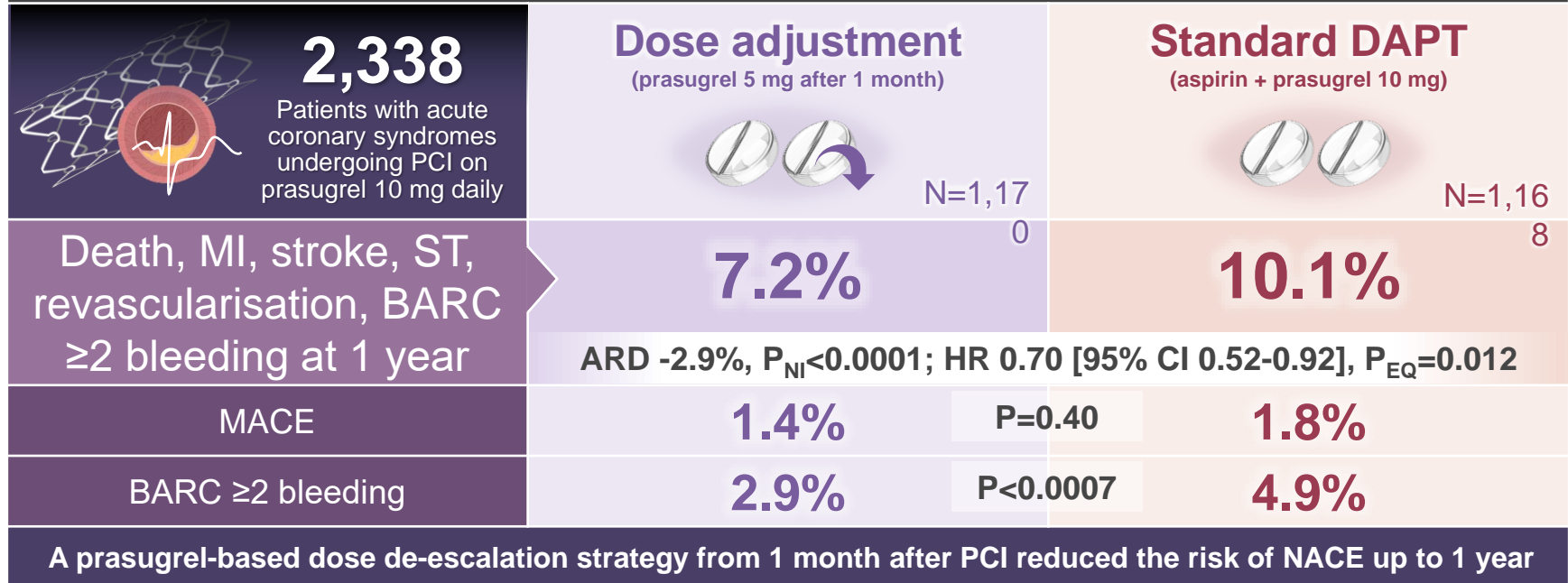
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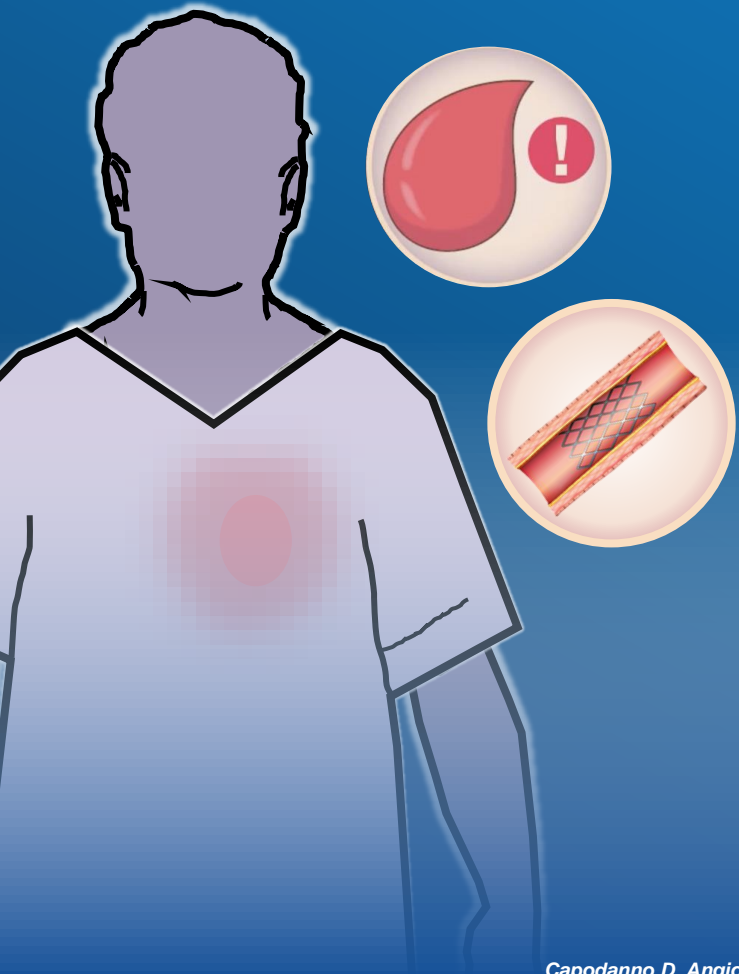
Goal: reduce bleeding while preserving efficacy

Halving the dose

Prasugrel-based de-escalation of DAPT after PCI in patients with ACS

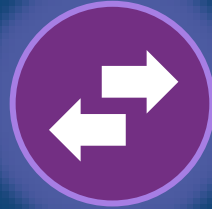
HOST-REDUCE-POLYTECH-ACS | OPEN-LABEL, MULTICENTER, NONINFERIORITY RANDOMIZED TRIAL





De-Escalation Strategies

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By Dose
Reduction



By
Discontinuation







Short DAPT

ASA P2Y12-i
Monotherapy



Numerous studies have shown that shortening DAPT by stopping the P2Y12 inhibitor at 6 months or sooner and maintaining aspirin monotherapy reduces bleeding without “apparent” trade-off in efficacy –but the devil is in the details.

Trials of P2Y₁₂-i discontinuation in ACS

SMART-DATE			REDUCE-ACS			DAPT-STEMI		
MULTICENTER, RANDOMIZED, OPEN-LABEL			MULTICENTER, RANDOMIZED, OPEN-LABEL			MULTICENTER, RANDOMIZED, OPEN-LABEL		
2,712 Patients with UA, NSTEMI or STEMI	Short DAPT (P2Y ₁₂ -i 6-mo) 	Standard (P2Y ₁₂ -i 12-mo) 	1,496 Patients with UA, NSTEMI or STEMI	Short DAPT (P2Y ₁₂ -i 3-mo) 	Standard P2Y ₁₂ -i 12-mo 	870 Patients with STEMI on DAPT, event- free at 6 mo	SAPT (aspirin only) 	DAPT (P2Y ₁₂ -i 18-mo) 
	MACE at 18 mo	4.7%		4.2%	NACE at 12 mo		8.2%	8.4%
P_{NI}=0.03			P_{NI}<0.001			P_{NI}=0.004		
MI	1.8%	0.8%	ST	1.6%	0.8%	MI	1.8%	1.8%
Short DAPT was NI (but unsafe?)			Short DAPT was NI (but unsafe?)			Short DAPT was NI (large NI margin)		

Lancet 2018;391:1274-1284

EuroIntervention 2019;15:e990-e998

BMJ 2018;363:k3793

P2Y₁₂ inhibitor SAPT after PCI

Safety and Efficacy of P2Y₁₂ Inhibitor Monotherapy Versus DAPT in Patients After PCI

STUDY-LEVEL META-ANALYSIS OF GLOBAL LEADERS, SMART-CHOICE, STOPDAPT-2, TWILIGHT, TICO

32,145 Patients who received short DAPT after PCI	P2Y₁₂ inhibitor SAPT (n=16,057)		Standard DAPT (n=16,088)	
Primary bleeding outcome	2.0%	HR 0.60 (0.45–0.79)	3.1%	
Major bleeding (BARC 3 or 5)	1.2%	HR 0.60 (0.42–0.86)	1.8%	
Primary MACE outcome	2.7%		3.1%	
Death	1.3%		1.5%	
Myocardial infarction	1.1%		1.3%	
Stroke	0.6%		0.6%	
Stent thrombosis	0.5%		0.4%	

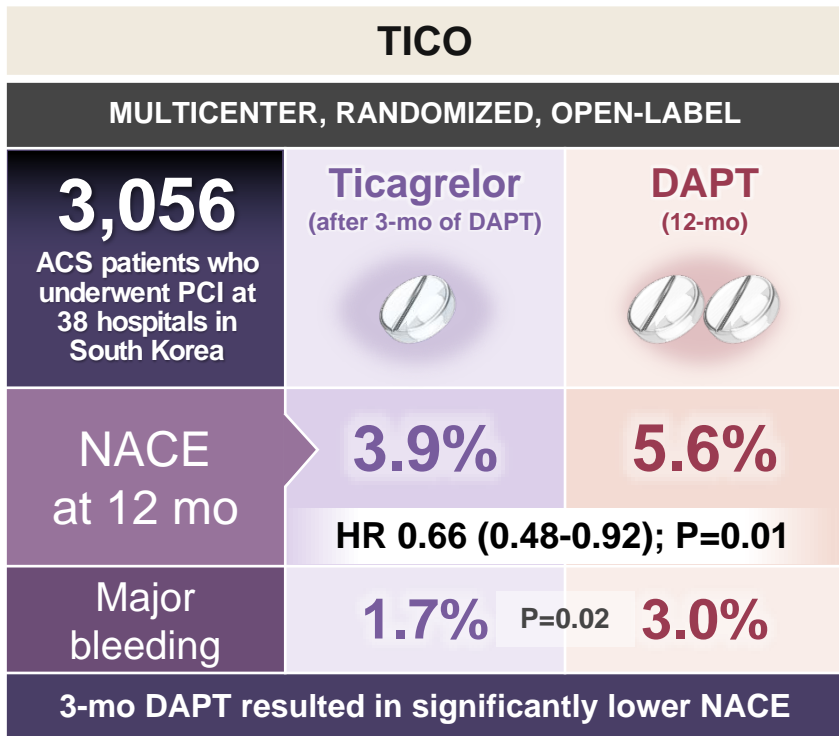
Long DAPT significantly reduced NACE in non-HBR patients undergoing complex PCI



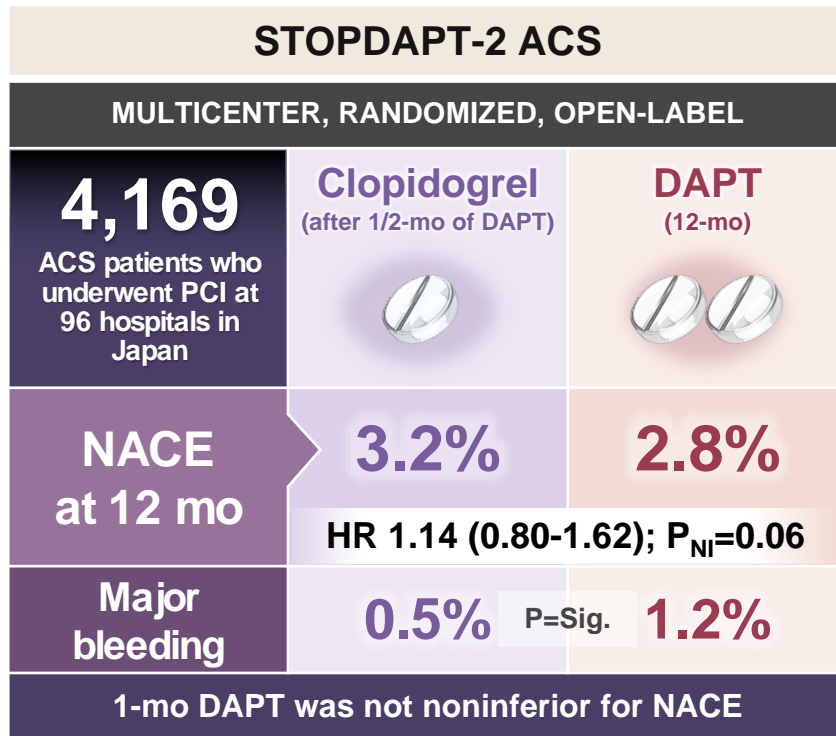
Not All P2Y12 Inhibitors are Created Equal!



Trials of aspirin discontinuation in ACS



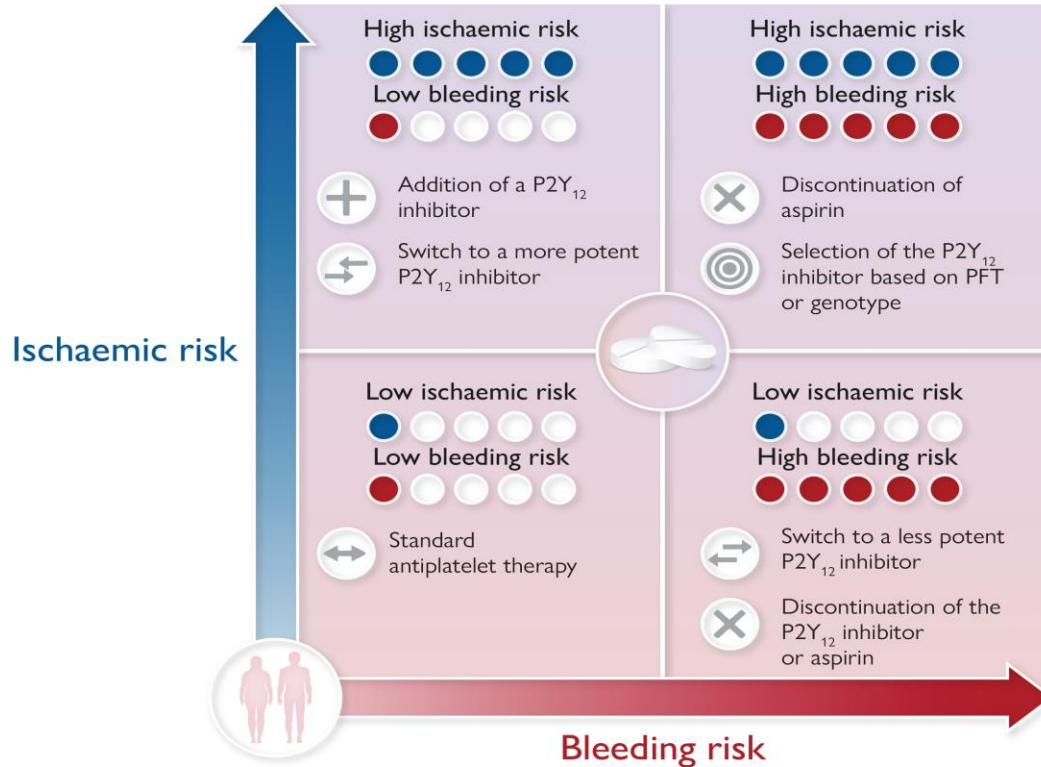
Kim BK, et al. JAMA. 2020;323:2407-2416



Watanabe H. JAMA. 2019;321:2414-2427

Strategies for tailoring antithrombotic therapy according to individual ischaemic and bleeding risk. ...

Personalized approach to antiplatelet therapy in coronary artery disease



One Size Does NOT Fit All

