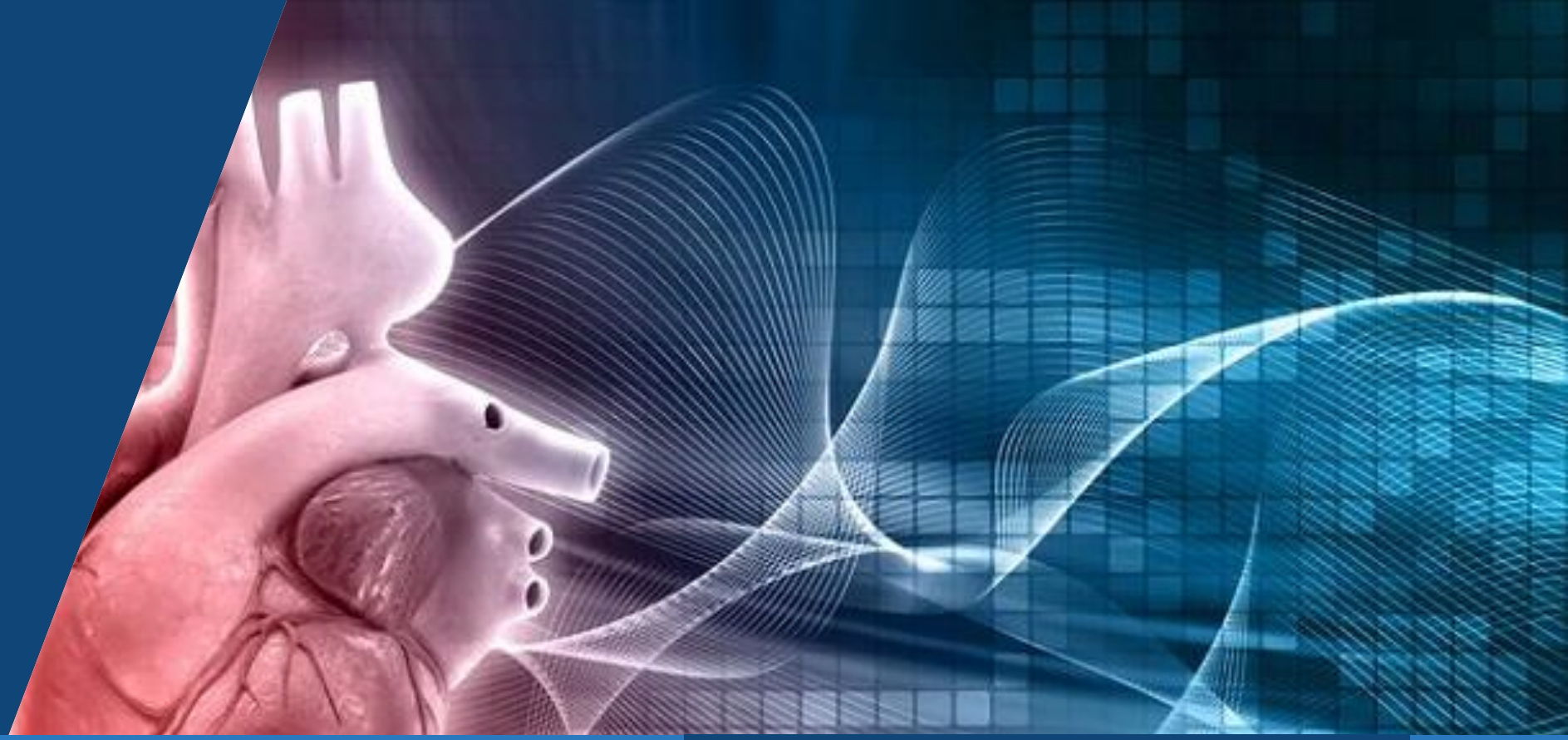
TCTAP
DIGITAL

Seoul
South Korea



Escalation Antithrombotic Strategy: When and How?

UNIVERSITÀ degli STUDI di CATANIA

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Disclosures

Within the past 12 months, with respect to the content of this presentation, I, **Davide Capodanno**, have had a financial interest/arrangement or affiliation with the organization(s) listed below:

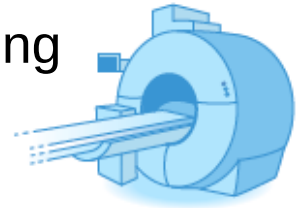
Affiliation/Financial Relationship	Company
Consulting or lecturing fees (minor)	Biotronik, Daiichi Sankyo, Sanofi, Terumo

Optimizing PCI outcomes

Before the procedure

- Bleeding risk stratification

- Non-invasive testing if applicable



- Appropriateness criteria for revascularization

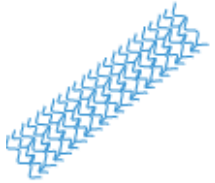
- Avoid routine pretreatment with antiplatelet therapy

During the procedure

- Radial access

- Optimal anticoagulation

- Appropriate stent selection



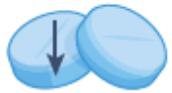
- Intravascular imaging-guided stent optimization

After the procedure

- Choice of DAPT

- Short duration of DAPT

- Modulation of DAPT



- Proton pump inhibitors

Capodanno D, et al. Nat Rev Cardiol. 2022;19:117-132

Optimizing PCI outcomes

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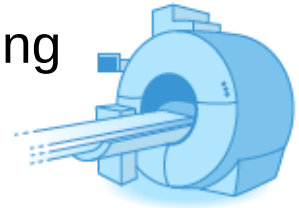

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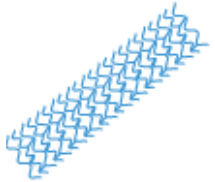

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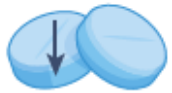
- **Modulation of DAPT**



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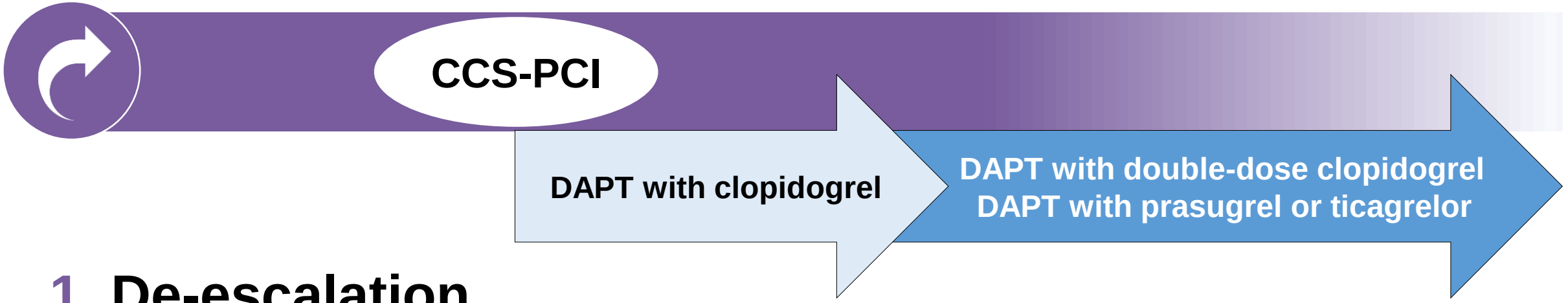
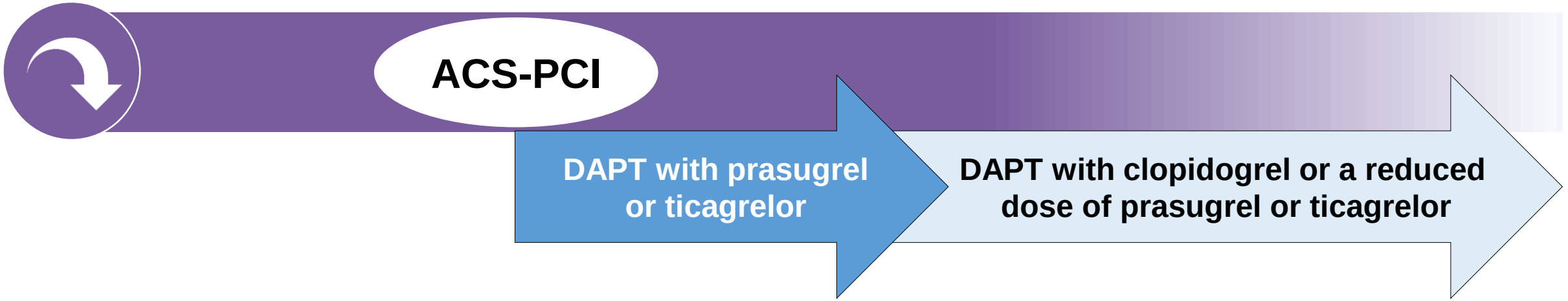
Modulating DAPT

1. Escalation

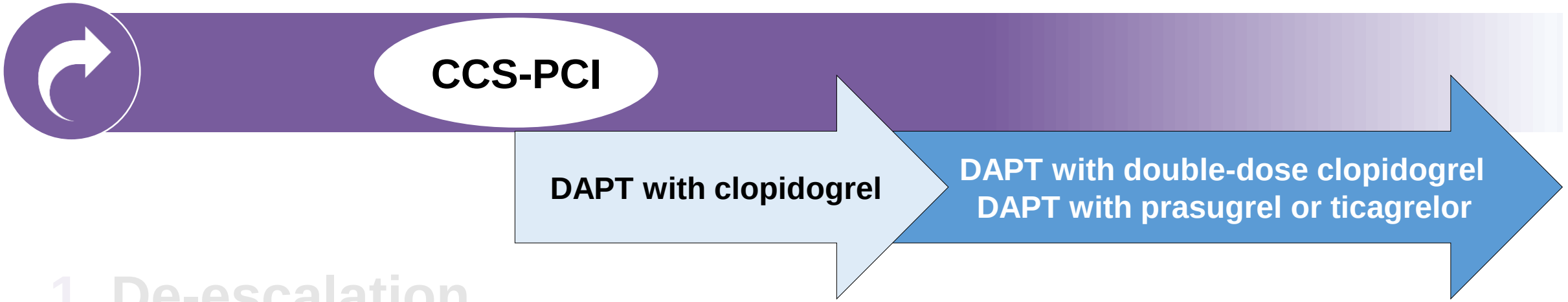


1. De-escalation



Modulating DAPT

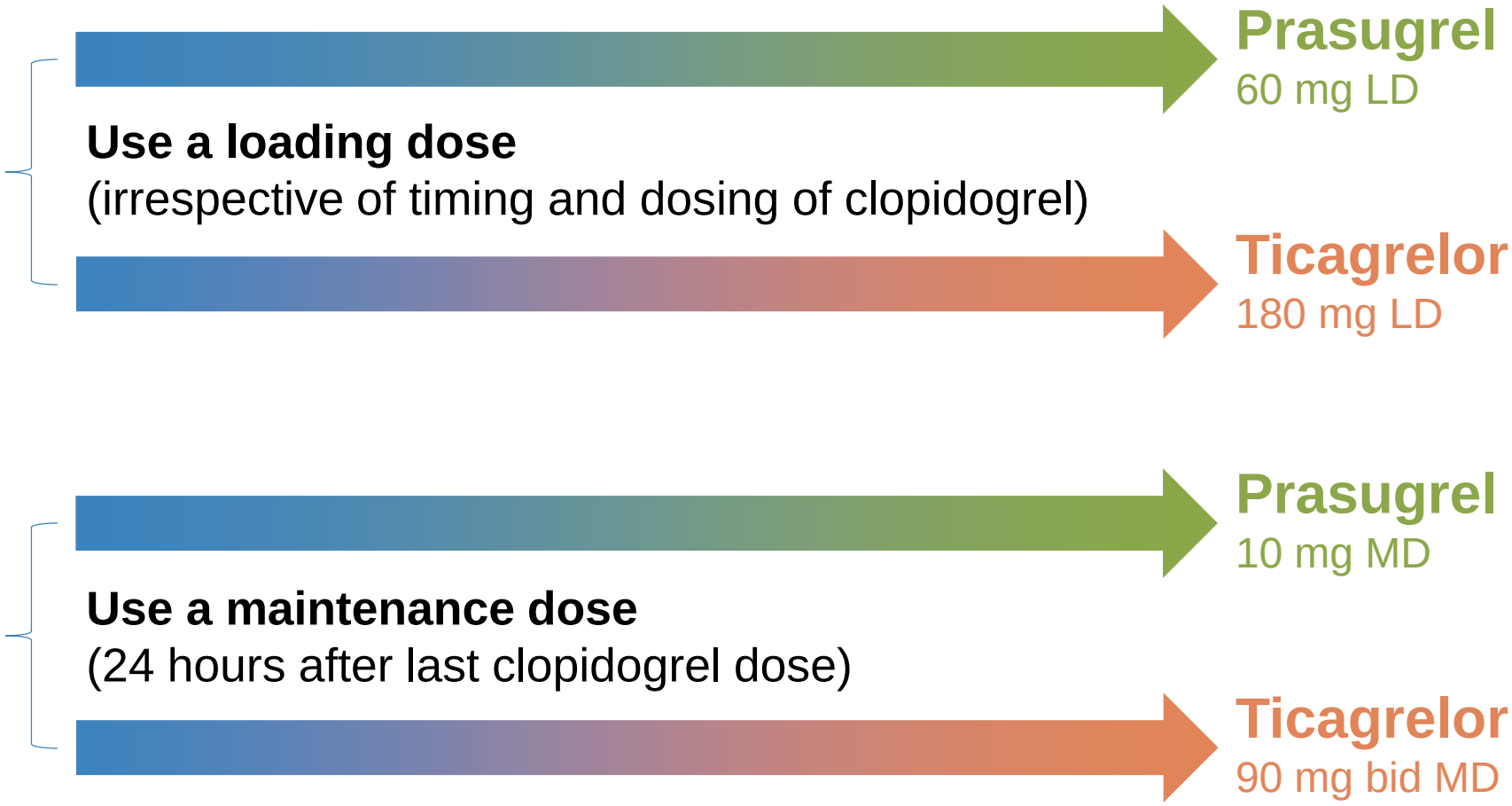
1. Escalation



1. De-escalation

How to escalate?

Switching strategies



Angiolillo DJ, et al. Circulation. 2017;136:1955–1975

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Who to escalate?

VerifyNow PFT

Step 1

When prompted, insert the test until it clicks

Step 2

When prompted, insert the tube into the test sample port

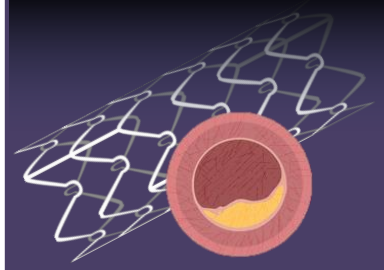
Step 3

Close the cover and read results within 2 to 5 minutes

PFT-guided escalation

Bedside Monitoring to Adjust Antiplatelet Therapy for Coronary Stenting

ARCTIC | OPEN-LABEL, MULTICENTER, RANDOMIZED TRIAL



2,440
Participants undergoing PCI for ACS or stable CAD

	PFT-guided adjustment (double-dose clopidogrel or prasugrel if HPR)	Standard treatment (standard clopidogrel therapy)
	N=1,227	N=1,213
Death, MI, stroke, ST, or urgent revascularization at 12 months	34.6%	31.1%
	Hazard ratio 1.13; 95% CI 0.98-1.29; P=0.10	
ST or urgent revascularization	4.9%	4.6%
	P=0.77	

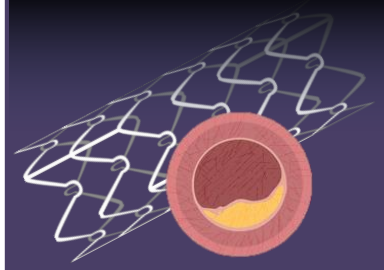
No significant improvements in clinical outcomes with platelet-function monitoring and treatment adjustment

Collet JP, et al. N Engl J Med 2012;367:2100-2109

PFT-guided escalation

Personalized antiplatelet therapy in stable CAD patients undergoing PCI

PATH-PCI | OPEN-LABEL, MULTICENTER, RANDOMIZED TRIAL



2,337
Participants undergoing PCI for stable CAD

	PFT-guided adjustment (ticagrelor in case of HPR)	Standard treatment (standard clopidogrel therapy)
	N=1,123	N=1,114
Cardiac death, MI, stroke, ST, revascularization, and bleeding at 6 months	5.1%	7.5%
	Hazard ratio 0.68; 95% CI 0.49-0.95; P=0.023	
Major bleeding at 30 days	0.5%	0.3%
	P=0.32	

Personalized antiplatelet therapy can significantly improve the net clinical benefit 180 days after PCI

Zheng JJ, et al. Eur Heart J Cardiovasc Pharmacother. 2020;6:211-221

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Side by side

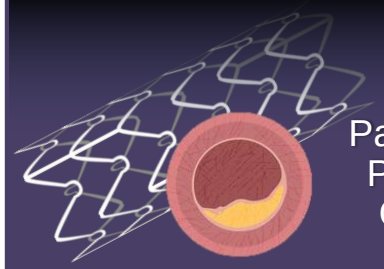
	ARCTIC	PATH-PCI
Patients, no	2,400 (Caucasians)	2,237 (Asians)
Population	DES-PCI (27% NSTE-ACS)	DES-PCI (stable CAD)
Patient follow-up, mo	12	6
Study type	Open label	Open label
Monitoring group	VerifyNow ASA and $P2Y_{12}$i PFT at baseline and 2-4 weeks for adjustment	PL-12 after a DAPT loading dose
Adjustment, if any	i.v. ASA (PRU ≥550), double dose clopidogrel or prasugrel (if clop-HPR)	Ticagrelor (if clop-HPR)
HPR (monitoring arm)	34.5%	62.8%
P2Y12-i at FU (monitoring arm)	80% clopidogrel, prasugrel 11.9%	-
Primary endpoint	Death, MI, stroke, ST, uTVR	Cardiac death, MI, stroke, ST, urgent revascularization, and bleeding
Findings	Hazard ratio, 1.13; 95% CI, 0.98 to 1.29; P=0.10	Hazard ratio, 0.68; 95% CI, 0.49 to 0.95; P=0.0023
Bleeding	Similar	Similar

Spartan CYP2C19 genotyping

Genotype-guided escalation

Genotype-Guided Oral P2Y12 Inhibitor Selection vs Clopidogrel After PCI

TAILOR PCI | OPEN-LABEL, MULTICENTER, RANDOMIZED TRIAL



1,849
Participants undergoing PCI for ACS or stable CAD with CYP2C19 LOF variants

	Genotype-guided (aspirin + ticagrelor twice daily) N=903	Standard treatment (aspirin + clopidogrel) N=946
CV death, MI, stroke, ST, and severe recurrent ischemia at 12 months	4.0%	5.9%
	Hazard ratio 0.66; 95% CI 0.43-1.02; P=0.06	
Major or minor bleeding	1.9%	P=0.58 1.6%

Genotype-guided selection of an oral P2Y12 inhibitor resulted in no statistically significant difference

Pereira NL, et al. JAMA. 2020;324:761-771

Can we do any better?

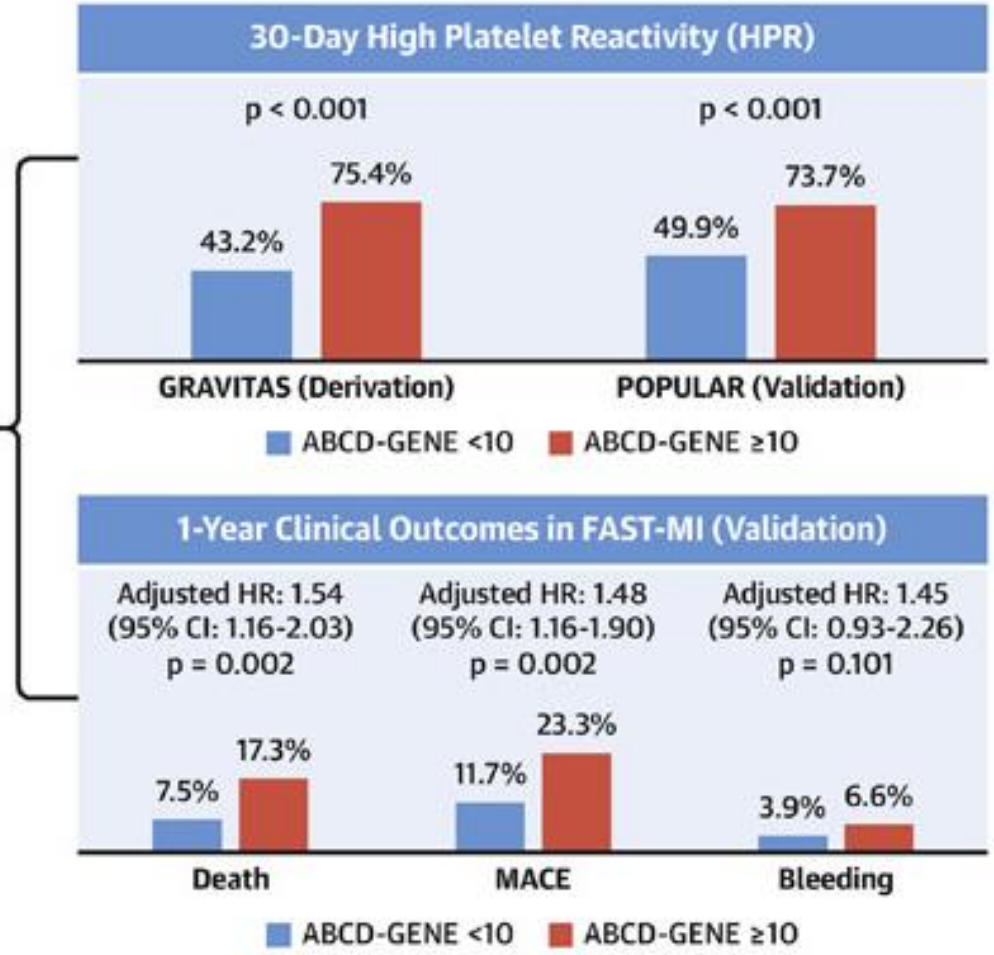
Integrating clinical factors

ABCD-GENE score

Clinical factors

Genetic factors

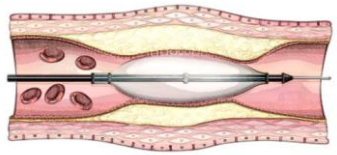
ABCD-GENE Score		Points
Clinical Factors		
	Age >75 years	+4
	Body mass index >30 kg/m²	+4
	CKD (GFR <60 ml/min)	+3
	Diabetes mellitus	+3
Genetic Factors		
	One *CYP2C19* LOF allele	+6
	Two *CYP2C19* LOF alleles	+24



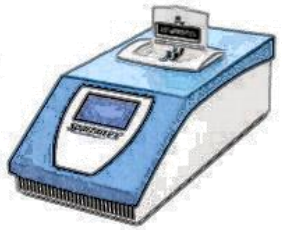
Angiolillo DJ, Capodanno D, et al. JACC Cardiovasc Interv. 2020;13:606-617

ABCD-GENE in TAILOR-PCI

PCI



Rapid genotyping



Risk factors


Age


BMI


CKD


Diabetes

Genotyping alone →

Death, MI or stroke at 1 year

1 LOF allele vs wild type
HR 0.97, 95% CI 0.62-1.53

2 LOF alleles vs wild type
HR 0.98, 95% CI 0.36-2.68

ABCD-GENE score (genotype + risk factors) →

Death, MI or stroke at 1 year

High vs low score
HR 2.02, 95% CI 1.34-3.04
p<0.001

Capodanno D, et al. J Am Heart Assoc. 2022;11:e024156

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Clinical outcomes of guided escalation

Guided escalation

Guided versus standard antiplatelet therapy in patients undergoing PCI		
META-ANALYSIS OF 14 STUDIES (RCTs AND OS; 20,743 PATIENTS; MEAN FOLLOW-UP 11 MONTHS)		
10 studies of escalation based on PFT or genotype testing, including ARCTIC, TAILOR PCI and PATH PCI	**Guided therapy** (escalation based on PFT or genotype testing)	**Standard therapy** (no use of PFY or genotype testing)
MACE	Risk ratio, 0.74; 95% CI 0.57-0.95	
Any bleeding	Risk ratio, 1.00; 95% CI 0.80-1.25	
Major bleeding	Risk ratio, 0.94; 95% CI 0.74-1.19	
Minor bleeding	Risk ratio, 0.87; 95% CI 0.57-1.33	
All-cause death	Risk ratio, 0.88; 95% CI 0.68-1.15	
Cardiovascular death	Risk ratio, 0.73; 95% CI 0.54-1.00	
Myocardial infarction	Risk ratio, 0.71; 95% CI 0.52-0.97	
Stent thrombosis	Risk ratio, 0.62; 95% CI 0.42-0.91	
Stroke	Risk ratio, 0.55; 95% CI 0.45-0.97	
Guided escalation reduced the risks of MACE, cardiovascular death, MI, stent thrombosis and stroke		

Galli M, et al. Lancet 2021;397:1470–83

Escalation Antithrombotic Strategy: When and How?

- Escalation guided by platelet function or genotype testing may have merits in reducing thrombotic complications. However, the benefit of escalation in the individual trials is more controversial than the benefit of de-escalation (e.g., mixed data for platelet function testing and neutral data for genetic testing).
- Both platelet function testing and genotyping are available as point-of-care assays, thus mitigating the complexity burden.
- In 2020, de-escalation has entered the list of practice recommendations included in the European guidelines for NSTE-ACS, but no corresponding recommendation currently exists for guided escalation in CCS guidelines.

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