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Optimal Antithrombotics for Complex Patients: Different Drugs, Dosing, or Duration?

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TCTAP • Seoul • April 28, 2019

WHAT MAKES A PATIENT "COMPLEX"?

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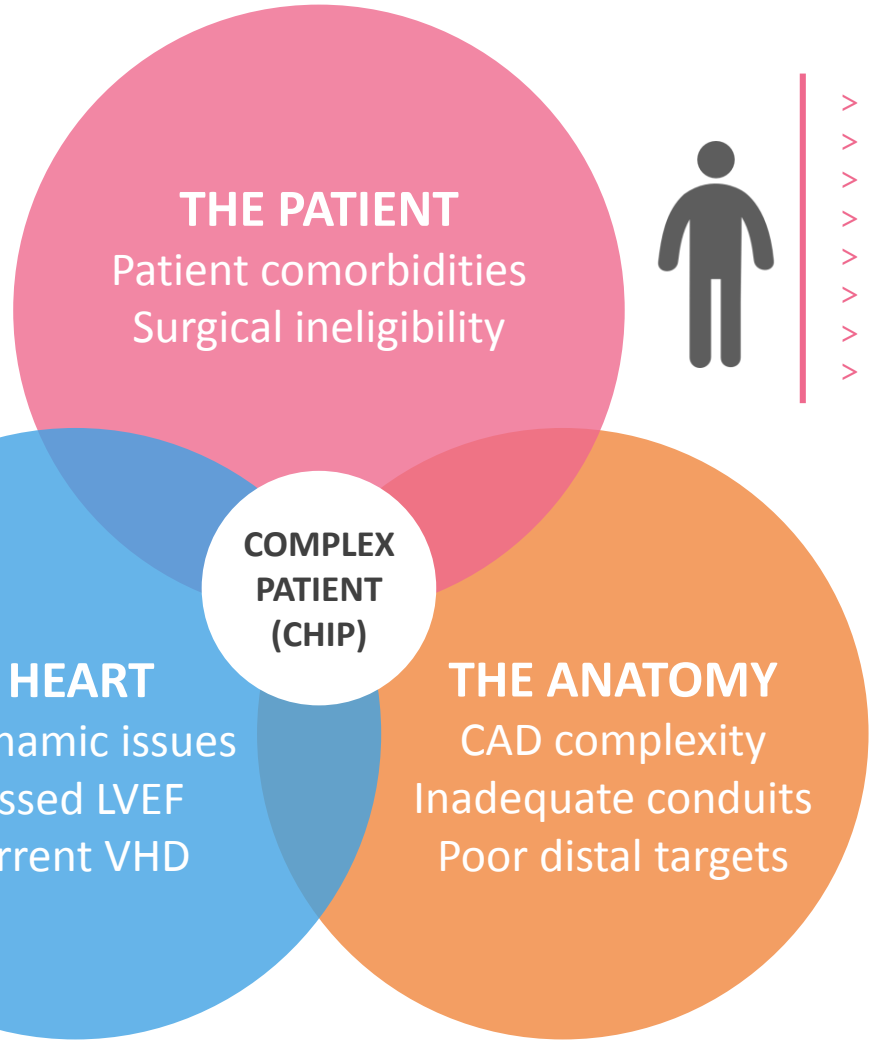
CHIP

COMPLEX HIGHER-RISK (AND INDICATED) PATIENT



- Oxygen-dependent COPD
- Severe liver disease
- Carotid artery disease
- Prior stroke
- Frailty
- Prior CABG
- Hostile chest
- Severe aortic calcification

- Poor hemodynamic status
- Impaired ventricular function
- Presence of concomitant valvular heart disease
- Pulmonary hypertension
- Right ventricular failure

- Unprotected left main CAD
- Complex bifurcation and trifurcation lesions
- Chronic total occlusions
- Heavily calcified lesions
- High SYNTAX score
- Inadequacy of conduits
- Poor distal targets

Kirtane AJ, et al. Circulation. 2016;134:422-31

WHAT MAKES PCI "COMPLEX"?

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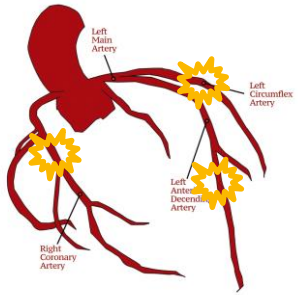
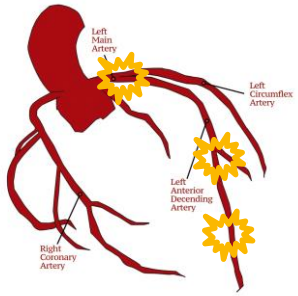
- 3 vessels treated

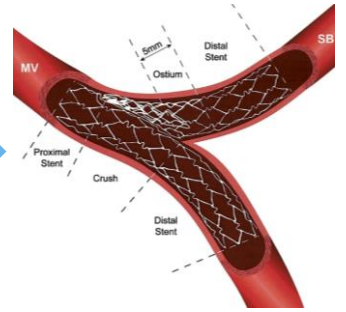


- At least 3 stents implanted

- At least 3 lesions treated

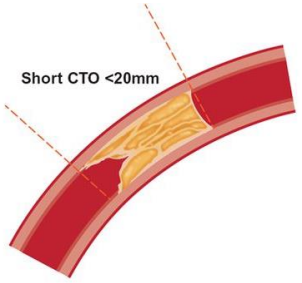


- Bifurcation with 2 stents implanted



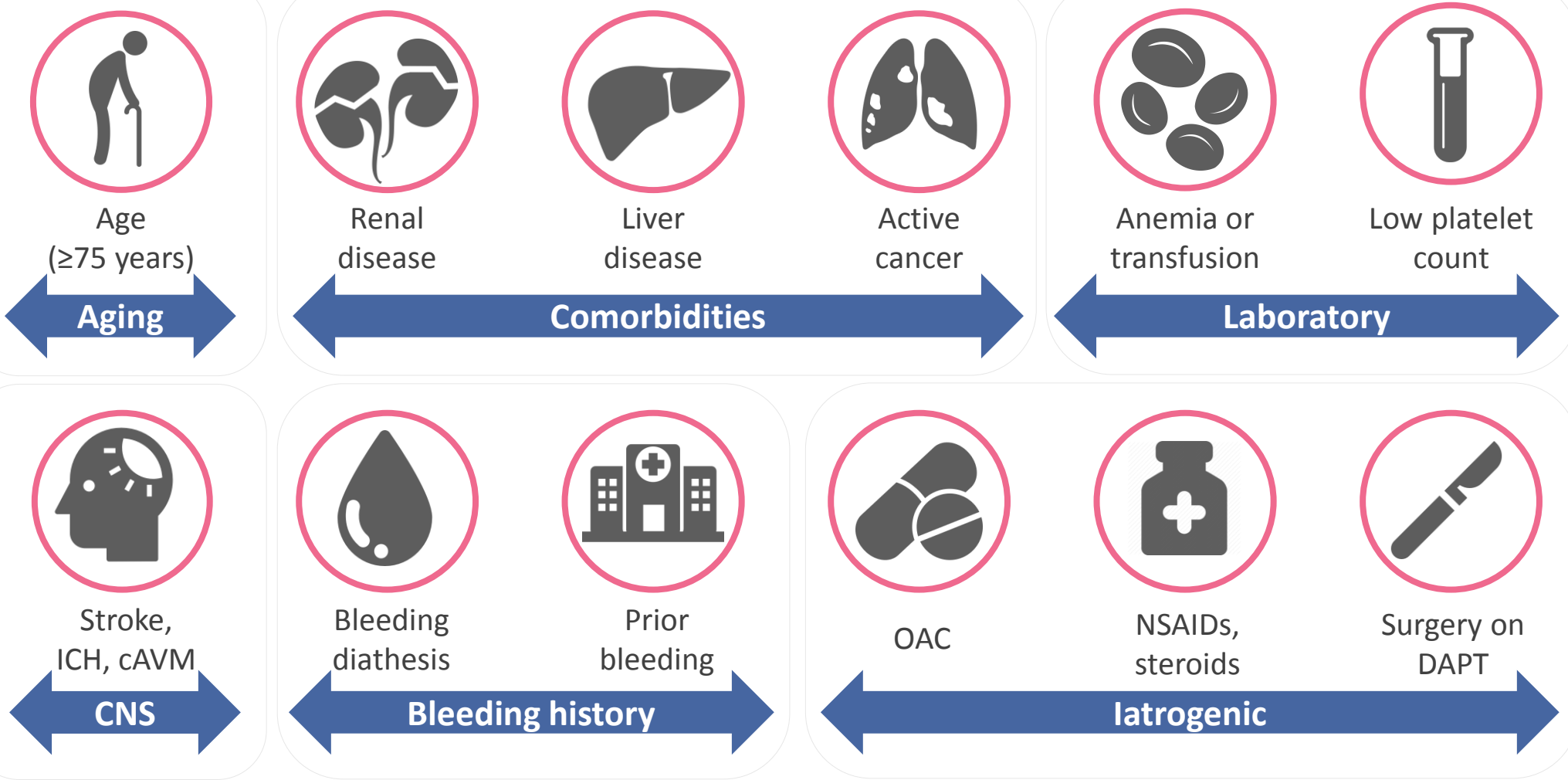
- Total stent length >60 mm

- Chronic total occlusion



Giustino G, et al. J Am Coll Cardiol. 2016;68:1851-1864

WHAT MAKES ANTIPLATELET THERAPY "COMPLEX"?



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COMPLEX PCI

Drug selection

CANGRELOR FOR COMPLEX PCI

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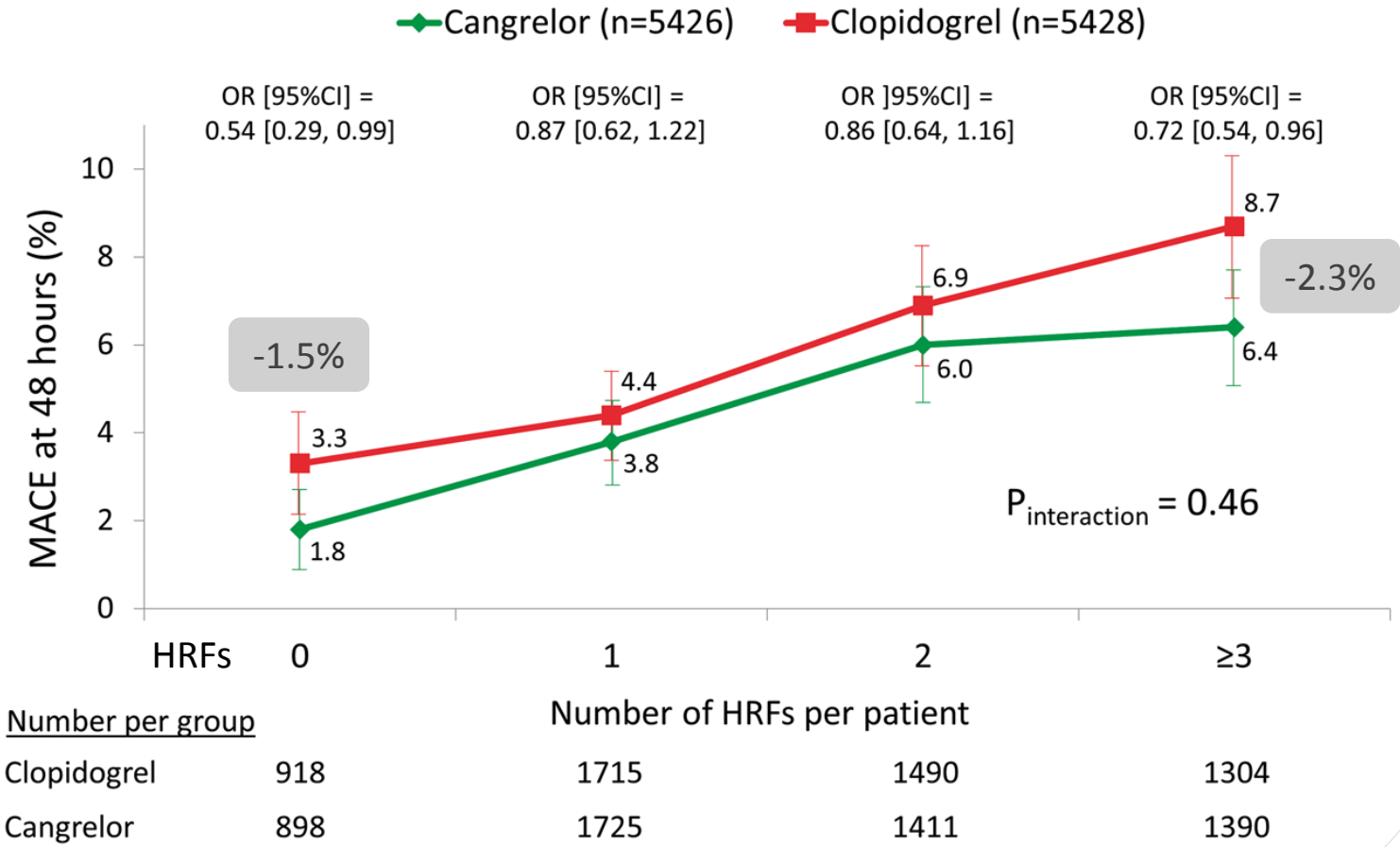
HIGH RISK FEATURES (HRFs)

- Long lesions
- Left main lesions
- Bifurcations lesions
- Thrombotic lesions
- Tortuous lesions
- Angulated lesions
- Eccentric lesions
- Calcified lesions
- Multi-lesion treatment

DEATH, MI, ST, OR ID-REVASCULARIZATION AT 48 HOURS



Number per group				
Clopidogrel	918	1715	1490	1304
Cangrelor	898	1725	1411	1390

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Stone GW, et al. Eur Heart J. 2018;39:4112–4121

CANGRELOR FOR COMPLEX PCI BY CLINICAL PRESENTATION

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HIGH RISK FEATURES (HRFs)

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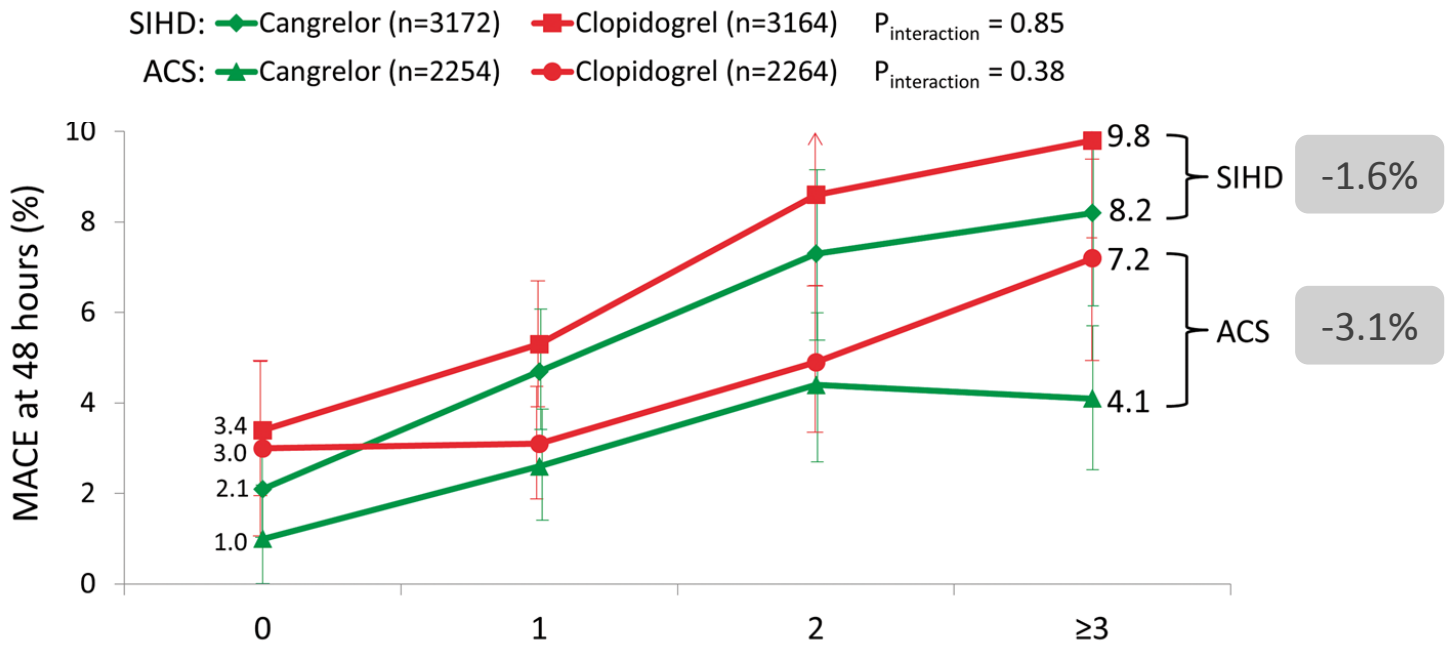


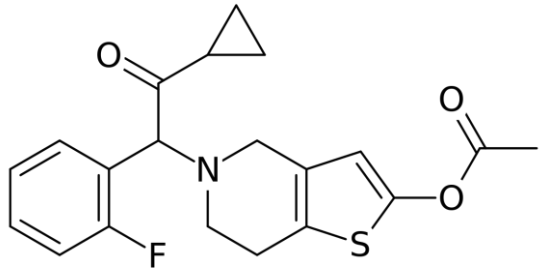
Number per group				
Clopidogrel SIHD	614	1006	798	745
Clopidogrel ACS	304	709	692	559
Cangrelor SIHD	606	991	792	782
Cangrelor ACS	292	734	619	608

Stone GW, et al. Eur Heart J. 2018;39:4112–4121

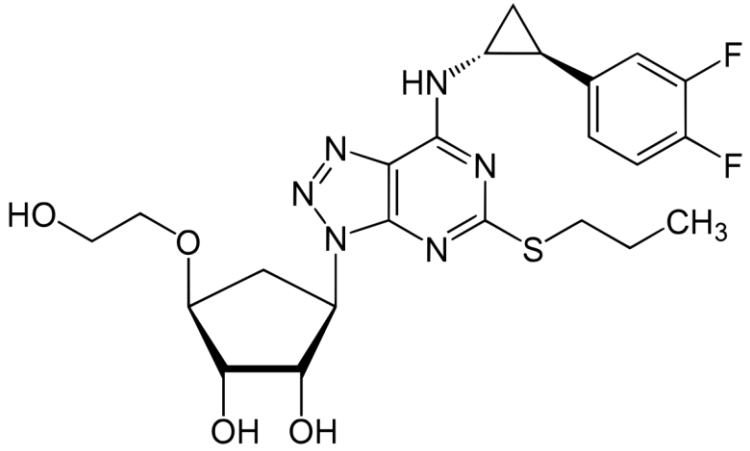
PRASUGREL AND TICAGRELOR FOR COMPLEX PCI

Recommendation	COR	LOE
Prasugrel or ticagrelor may be considered in specific high-risk situations of elective stenting (e.g. history of stent thrombosis or left main stenting)	IIb	C

PRASUGREL



TICAGRELOR



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Neumann FJ, et al. Eur Heart J. 2019;40:87-165

COMPLEX PCI

DAPT duration

DAPT DURATION AFTER DRUG-ELUTING STENTS

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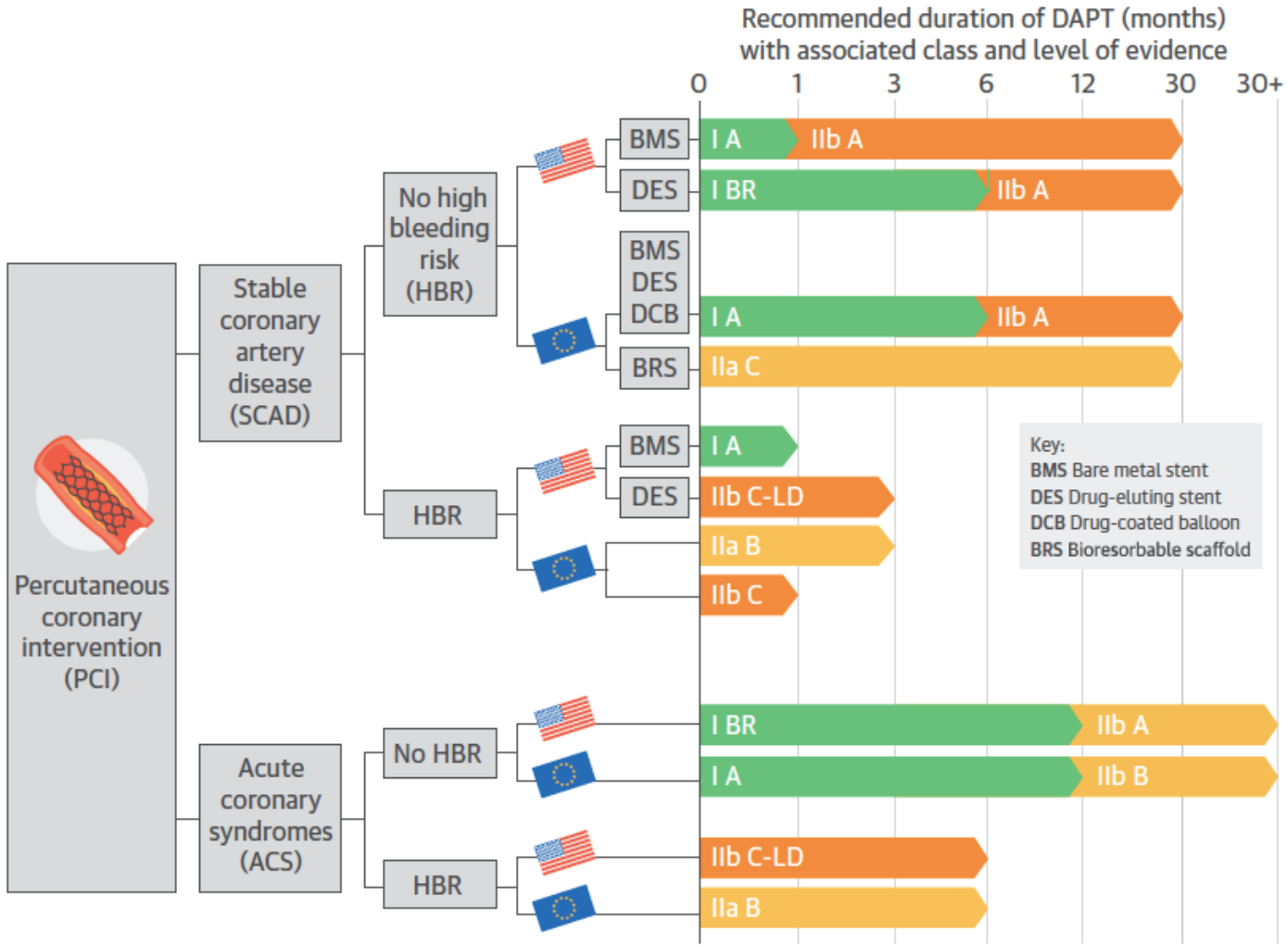

Stable CAD

No HBR	6 months or longer*
HBR**	3 months

ACS

No HBR	12 months or longer*
HBR**	6 months

* Consider longer duration based on PCI complexity, DAPT score ≥2 or risk profile

** e.g. PRECISE DAPT score ≥25

Capodanno D, Angiolillo DJ, et al. J Am Coll Cardiol. 2018;72:2915-2931

LONG VS. SHORT DAPT BY PCI COMPLEXITY

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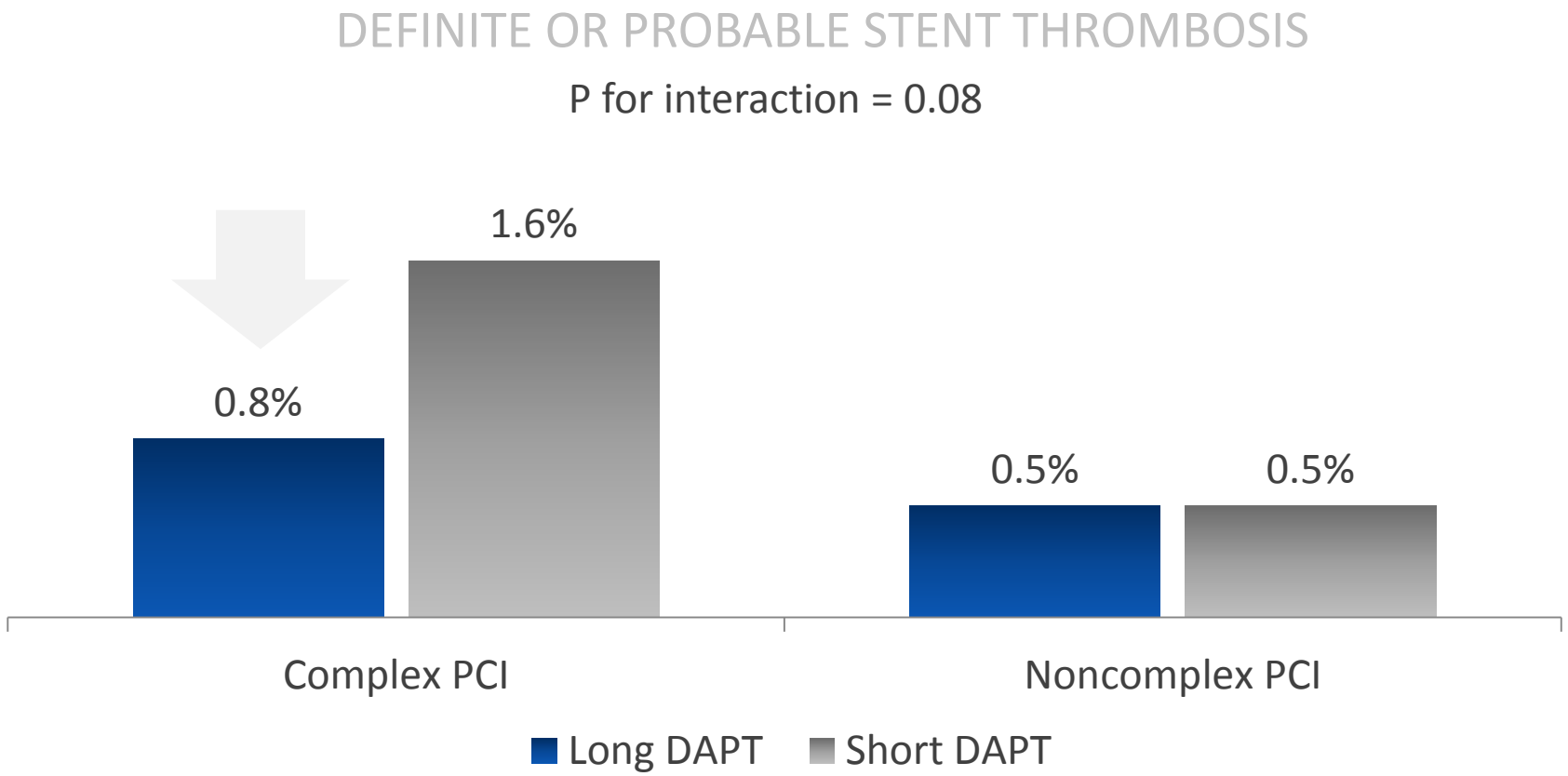

63% ↓ ST

with longer DAPT in complex PCI

(p_{int}=0.08)

81% ↑ Bleeding

with longer DAPT in complex PCI

(p_{int}=0.96)

Complex PCI was defined as having at least 1 of the following features: 3 vessels treated, ≥3 stents implanted, ≥3 lesions treated, bifurcation with 2 stents implanted, total stent length >60 mm, or chronic total occlusion

Giustino G, et al. J Am Coll Cardiol. 2016;68:1851-1864

DAPT, COMPLEXITY AND THE PRECISE-DAPT SCORE

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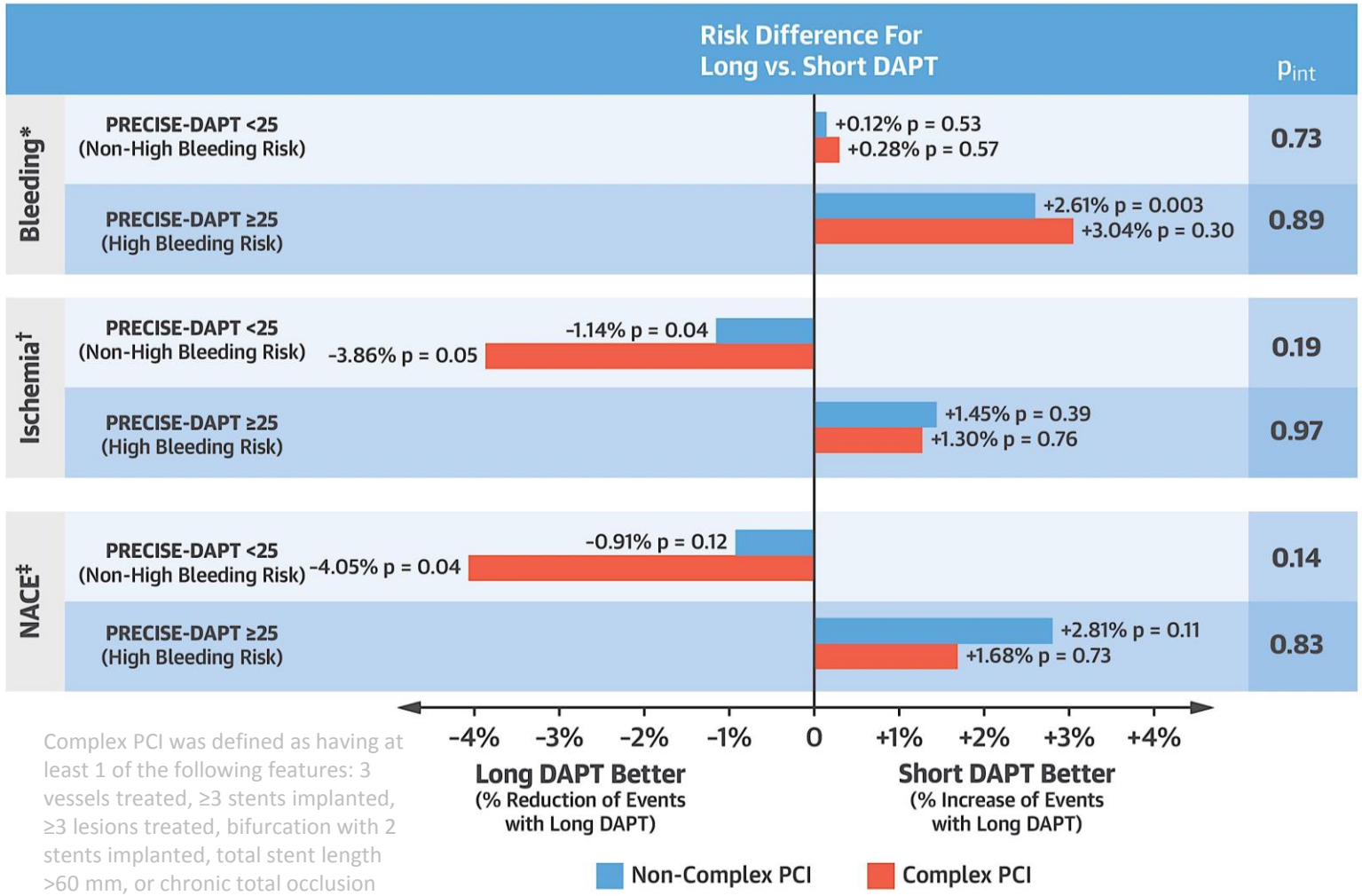

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COMPLEX PCI

Long DAPT increases bleeding in complex PCI if PRECISE-DAPT ≥25 (HBR)

Long DAPT reduces MACE in complex PCI if PRECISE-DAPT <25 (non-HBR)

NET BENEFIT
Non-HBR: long DAPT better
HBR: short DAPT better

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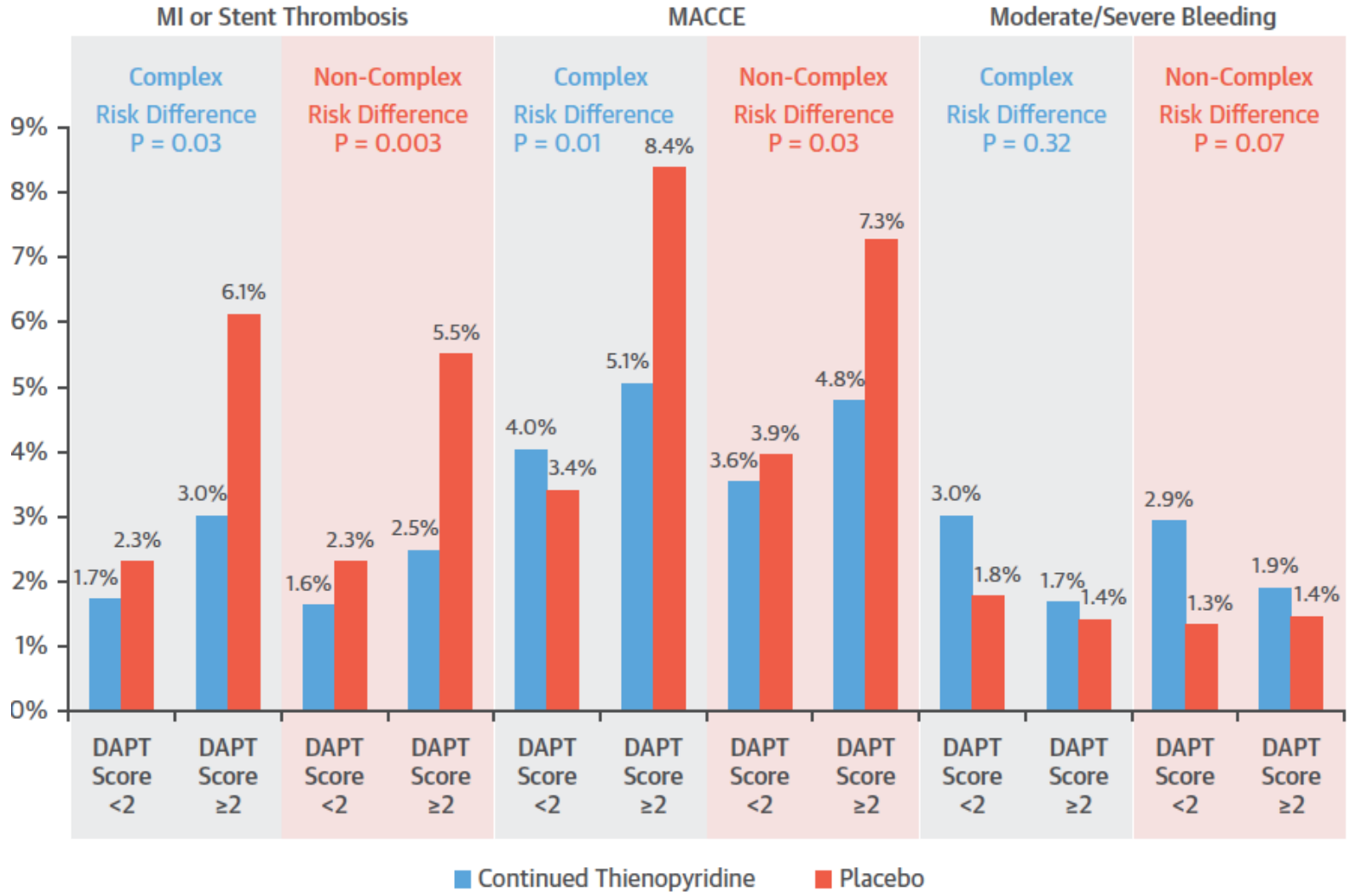
Costa F et al. J Am Coll Cardiol. 2019;73:741-754

DAPT, COMPLEXITY AND THE DAPT SCORE



Complex PCI was defined as having at least 1 of the following features: unprotected left main, >2 lesions per vessel, lesion length ≥ 30 mm, bifurcation lesion with side branch ≥2.5 mm, vein bypass graft (segment or anastomosis), or thrombus-containing lesion

Extended DAPT better with high DAPT score in patients with and without complex anatomy

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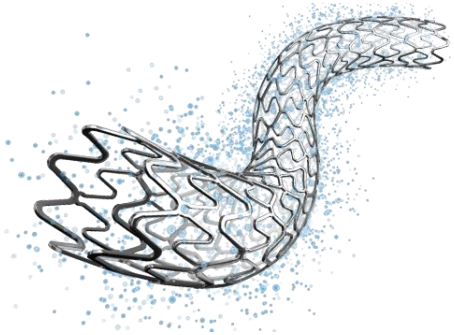
Yeh RW, et al. J Am Coll Cardiol 2017;70:2213–23

PROTECTING STENTS ≠ PROTECTING PATIENTS



HIGH RISK

PCI with DES | Mandatory DAPT | Extended DAPT

Prevention of stent-related thrombotic events

Secondary prevention of atherothrombotic events

Hospital discharge

3, 6 or 12 months

30 months, lifelong or until tolerated

PRECISE-DAPT SCORE

≥25 = SHORT DAPT

DAPT SCORE

≥2 = LONG DAPT

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Adapted from Chen H, et al. Expert Rev Cardiovasc Ther. 2018;16:735-748

COMPLEX PCI

New directions

ASPIRIN: TOO MUCH OR TOO LITTLE?

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TOO LITTLE!

Add rivaroxaban 2.5 mg bid in CAD patients or ticagrelor 60 mg bid in prior MI patients after the mandatory DAPT period

- PEGASUS
- COMPASS

TOO MUCH!

Go aspirin-free and use a potent $P2Y_{12}$ inhibitor

- GLOBAL LEADERS
- SHORT-DAPT 2
- SMART CHOICE
- TWILIGHT
- TICO

GLOBAL LEADERS: COMPLEX PCI POST-HOC ANALYSIS

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PRIMARY AND SECONDARY OUTCOMES AT 24 MONTHS (ITT)

	Experimental group N=7,980	Reference group N=7,988	Risk ratio (95% CI)	P-value
Death or Q-wave MI *	**3.81%**	**4.37%**	**0.87 (0.75-1.01)**	**0.073**
Death	2.81%	3.17%	0.88 (0.74-1.06)	0.18
Q-wave MI	1.04 %	1.29%	0.80 (0.60-1.07)	0.14
BARC 3 or 5 bleeding	**2.04%**	**2.12%**	**0.97 (0.78-1.20)**	**0.77**
BARC 3 bleeding	0.28%	0.30%	0.92 (0.52-1.64)	0.78
BARC 5 bleeding	1.88%	1.99%	0.95 (0.76-1.18)	0.63

* Primary endpoint

COMPLEX PCI post-hoc analysis

EuroPCR 2019
Hotlines and
Late-Breaking Trials

12 PM - 1:15 PM

May 21, 2019
Main arena

Vranckx P, et al. Lancet. 2018;392:940-949

TICAGRELOR MONOTHERAPY AFTER COMPLEX PCI

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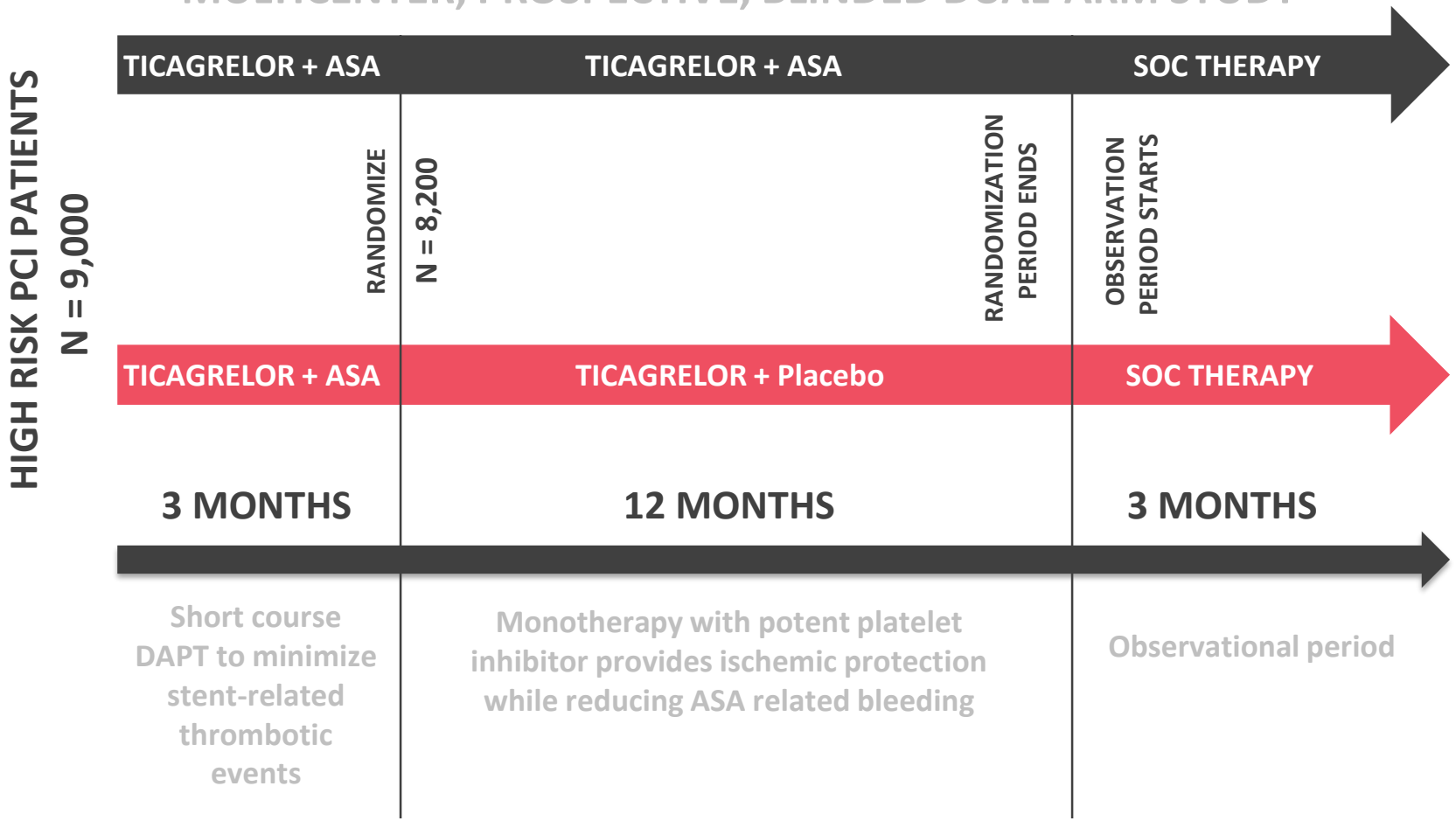
MULTICENTER, PROSPECTIVE, BLINDED DUAL-ARM STUDY



Primary Endpoint
BARC 2, 3, 5 bleeding between 3 and 15 months

Status
Enrollment completed
Expected at TCT 2019

Angiographic Inclusion Criteria: Multivessel coronary artery disease; Target lesion requiring total stent length >30 mm; Bifurcation lesions with Medina X,1,1 classification requiring at least 2 stents; Left main (≥50%) or proximal LAD (≥70%) lesion; Calcified target lesion requiring atherectomy.

Baber U, et al. Am Heart J. 2016;182:125-134

DIFFERENT DRUGS, DOSING OR DURATION?

- **MACE increase progressively with the number of high risk angiographic features**
  - > Prasugrel and ticagrelor are recommended for ACS and may be considered for elective complex PCI
  - > Cangrelor consistently reduces periprocedural MACE regardless of angiographic complexity
- **Complex PCI suggests an opportunity for extending DAPT beyond the mandatory period**
  - > However, HBR should inform decision-making on DAPT duration, even in complex PCI patients
  - > The PRECISE DAPT and DAPT scores work fine in both complex and noncomplex PCI patients
- **Emerging strategies to optimize the risk-benefit balance of antithrombotic therapy for complex patients are under investigation**

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