

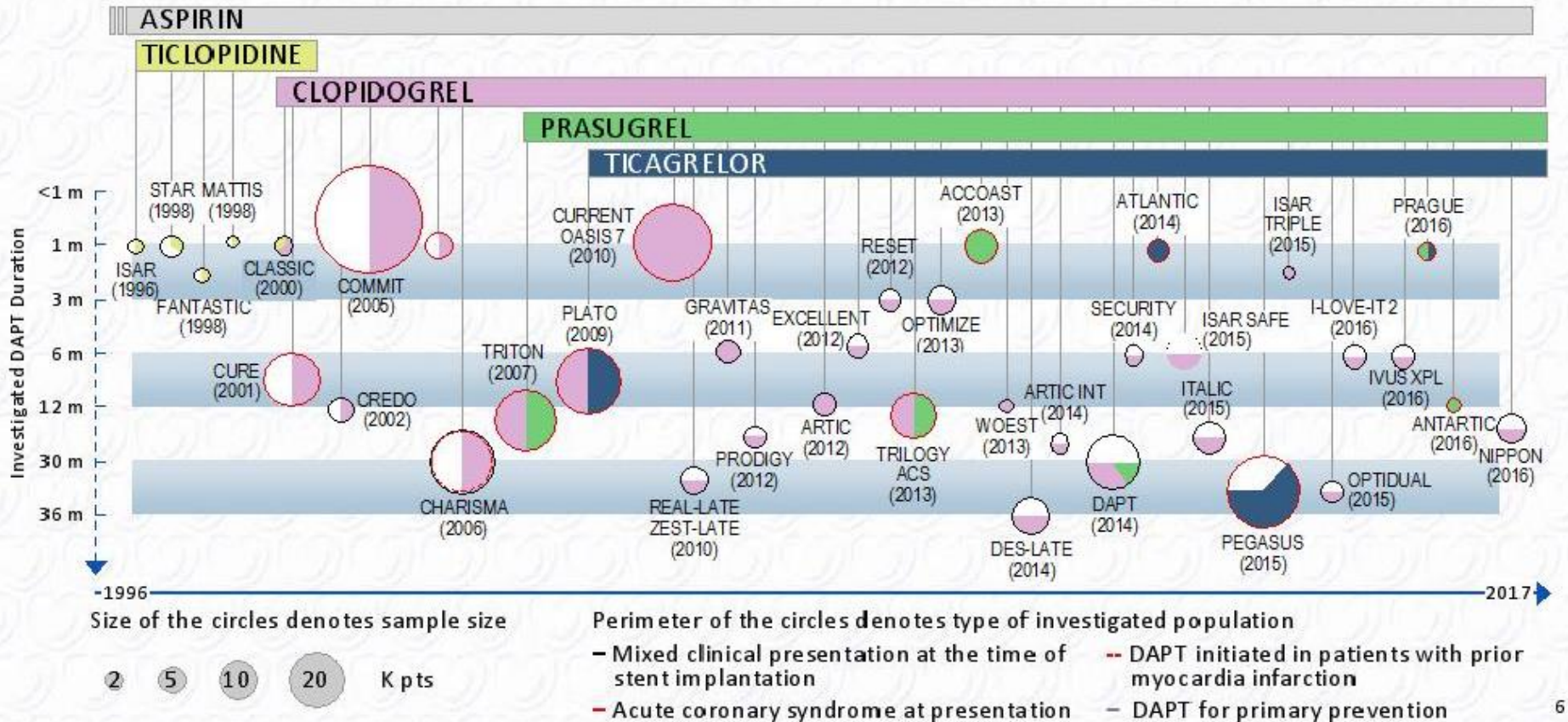
Tailored P2Y12 Strategy for CHIP Patients : **the TAILORED-CHIP Trial**

Pil Hyung Lee, MD

Division of Cardiology, Department of Internal Medicine
Asan Medical Center

Antiplatelet Therapy in CAD

A Daunting Dilemma



www.escardio.org/guidelines 2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

Antithrombotic Strategy after PCI Guidelines

Clinical presentation

Percutaneous Coronary Intervention

Stents

HBR

Intensity

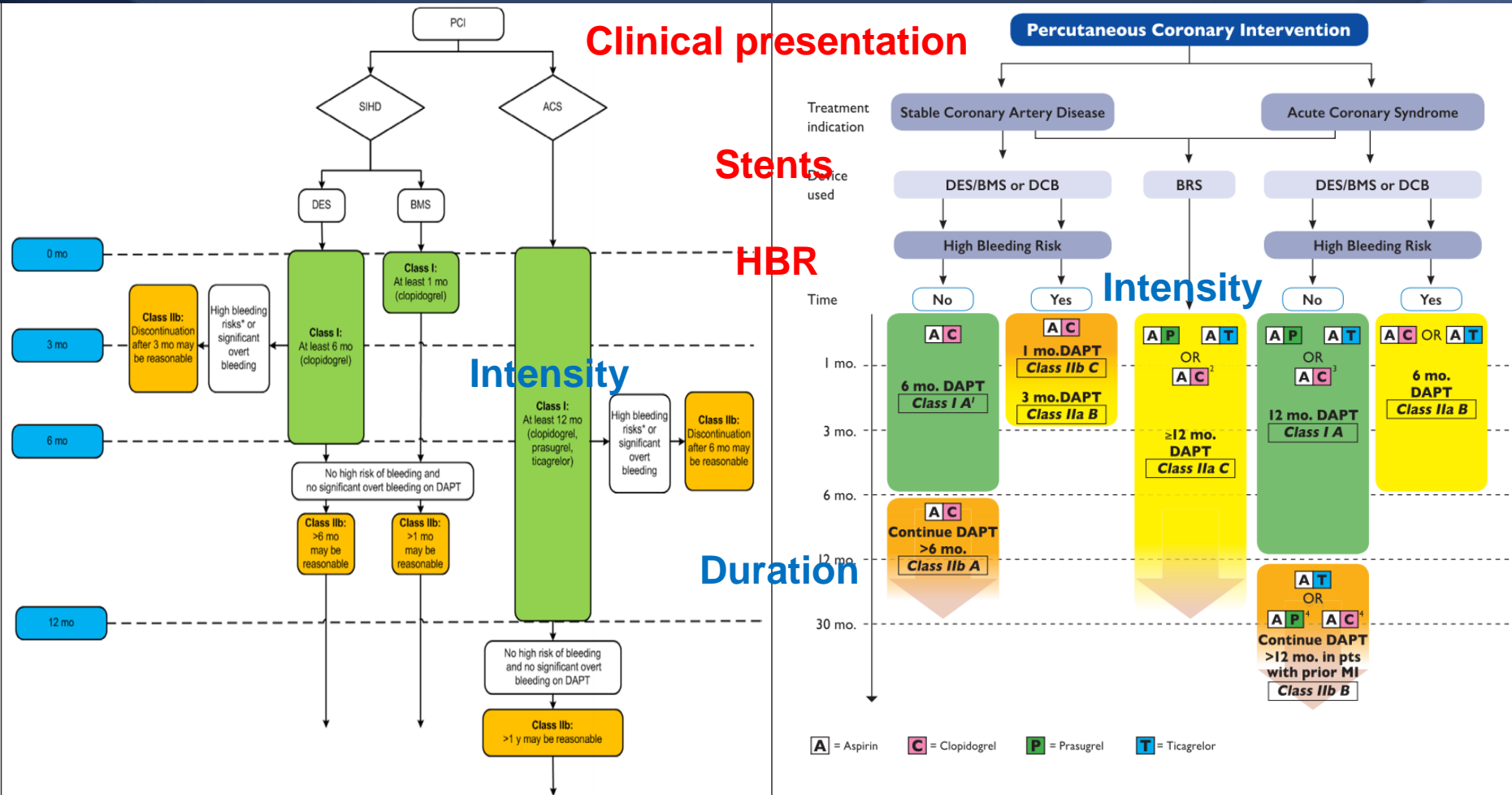
Duration

Treatment indication

Device used

Time

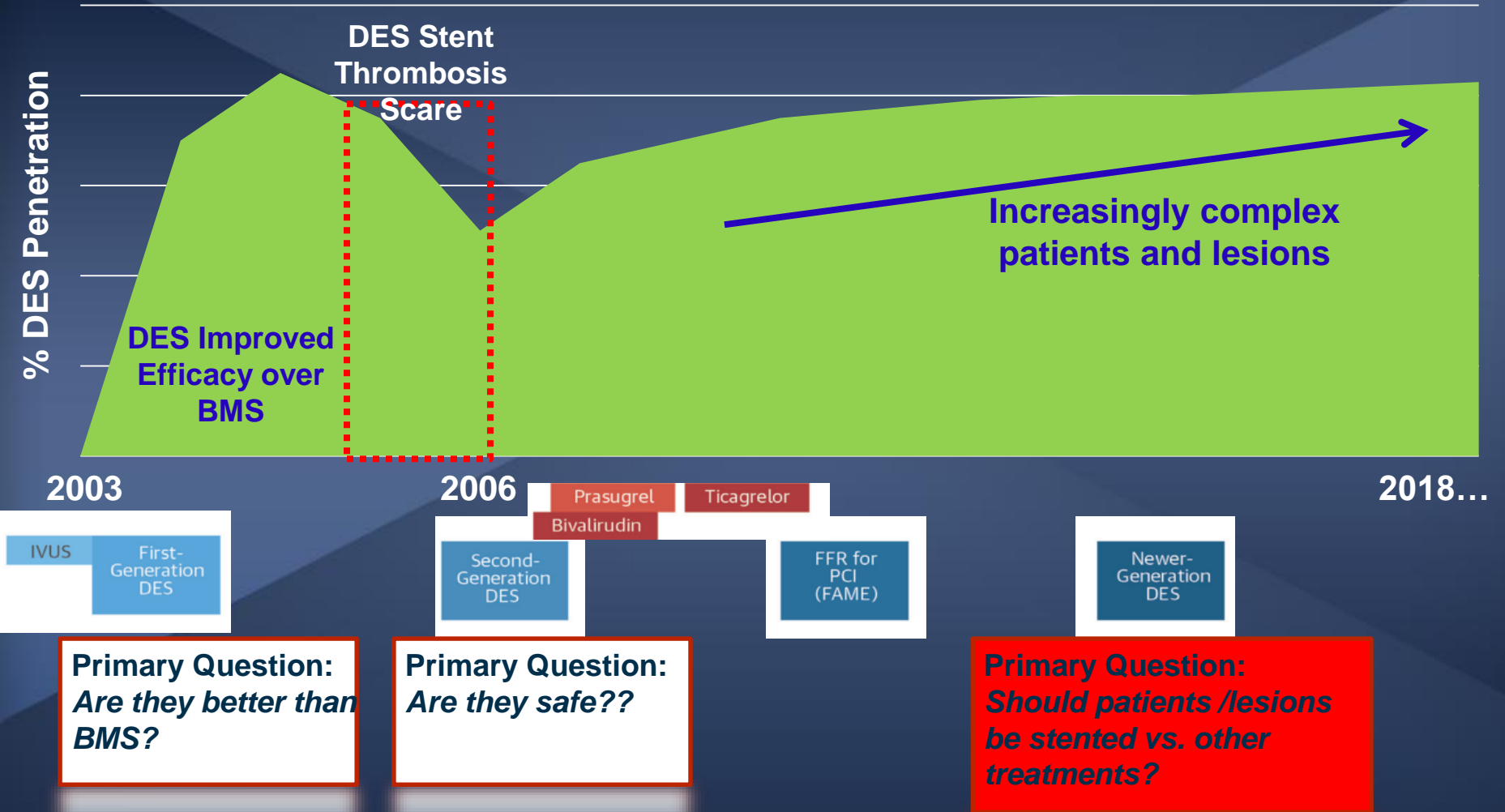
A = Aspirin **C** = Clopidogrel **P** = Prasugrel **T** = Ticagrelor



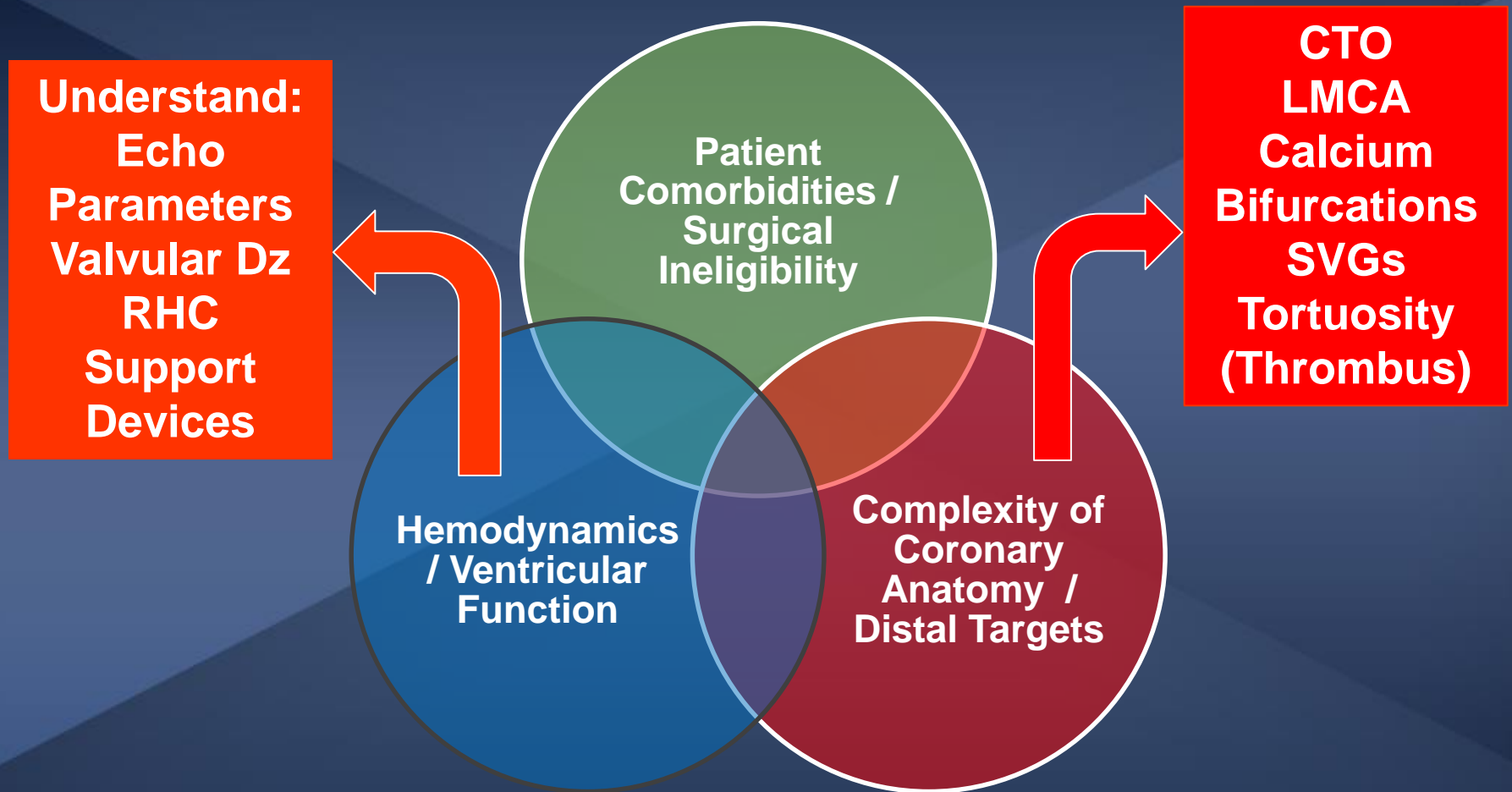
2016 ACC/AHA

2017 ESC

Evolution of DES Safety



The CHIP Population: Post-PCI; *High Ischemic Risk*



Treat the undertreated!

Lesion/Procedural Complexity

Duration of DAPT

Efficacy and Safety of
Dual Antiplatelet Therapy After Complex PCI



Complex target lesion anatomy or procedure is associated with increased ischemic event

DAPT duration after DES correlates with a lower incidence of ischemic events at the expense of increase bleeding

Prolonged (i.e. >6 months) DAPT duration^d may be considered in patients who underwent complex PCI.²⁴⁷

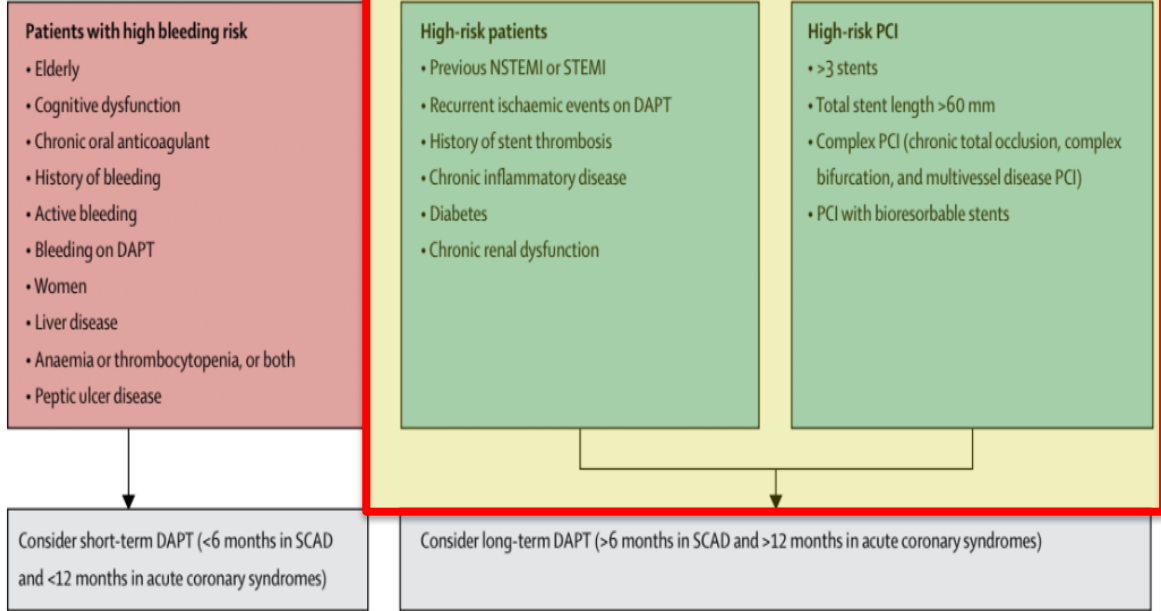
IIb

B

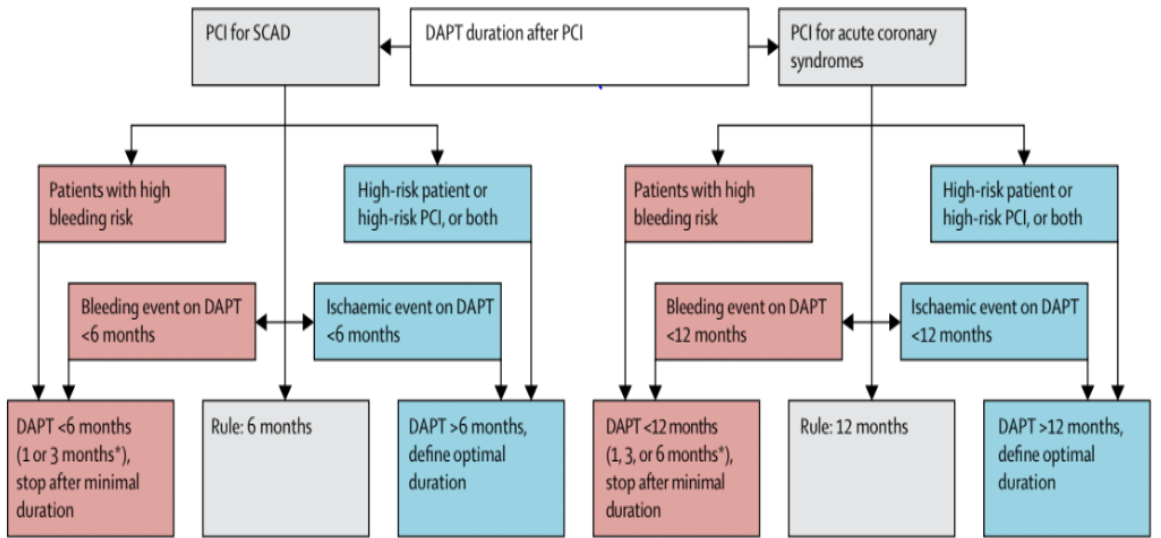
PhD,^f

Lorenz Räber, MD, PhD,^u Thomas Pilgrim, MD,^v Myeong-Ki Hong, MD,^z Hyo-Soo Kim, MD,^u Antonio Colombo, MD,ⁱ Philippe Gabriel Steg, MD,^{l,k} Deepak L. Bhatt, MD, MPH,^l Gregg W. Stone, MD,^{m,n} Stephan Windecker, MD,^b Ewout W. Steyerberg, PhD,^c Marco Valgimigli, MD, PhD,^b for the PRECISE-DAPT Study Investigators

A



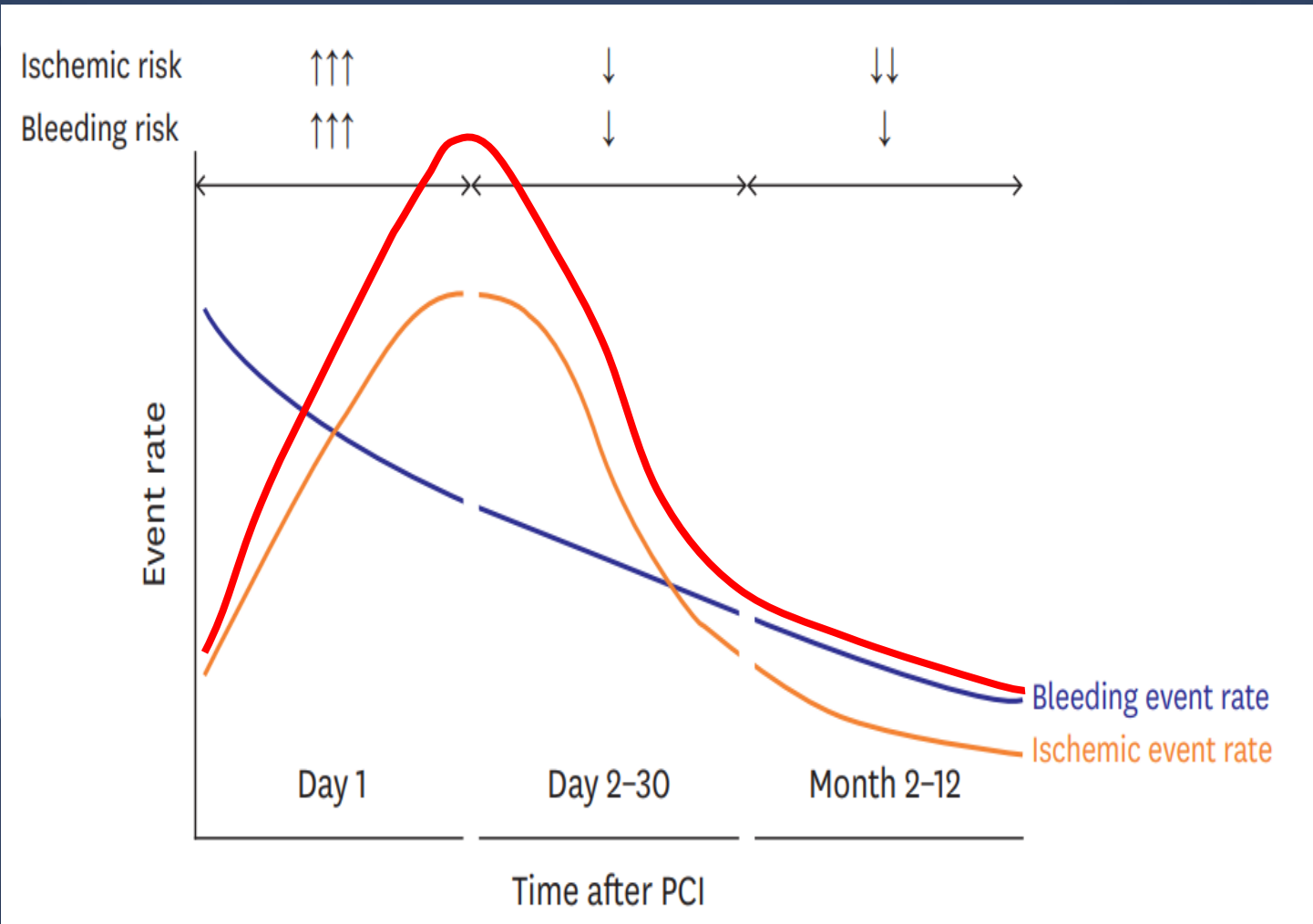
B



Complex High-Risk PCI ; HIR

Complex High-Risk PCI

May need alternative APT regimen



Ticagrelor With Aspirin or Alone in High-Risk Patients After Coronary Intervention (TWILIGHT) trial

PCI subjects at high risk for bleeding or ischemic complications*
N = 9000

*At least one clinical criteria: Age \geq 65, female, tn+ PVD, DM, CrCl $<$ 60 ml/min.
At least one angiographic criteria: Multivessel dz, $>$ 30 mm stenting, thrombus, bifurcation with 2 stents, LM \geq 50% or proximal LAD \geq 70%, calcified requiring atherectomy

3 MONTHS

DAPT: Ticagrelor + ASA

R

N = 8200

TICAGRELOR
+ ASA

TICAGRELOR
ALONE

12 MONTHS

SITE SPECIFIC
THERAPY

SITE SPECIFIC
THERAPY

3 MONTHS

Primary Endpoint: BARC Types 2, 3 or 5 bleeding
Secondary Endpoint: Composite of cardiovascular death, non-fatal myocardial infarction, ischemic stroke or ischemia-driven revascularization

TAILORED-CHIP trial

Alternative APT regimen for CHIP

2,000 Patients Undergoing Complex High-Risk PCI*

Stratified randomization by (1) trial center or (2) diabetes

Conventional Arm (N=1,000)

Clopidogrel + Aspirin
12 months

Tailored Arm (N=1,000)

Low-dose (60 mg) Ticagrelor + Aspirin
Early 6 months (**Early Escalation**)

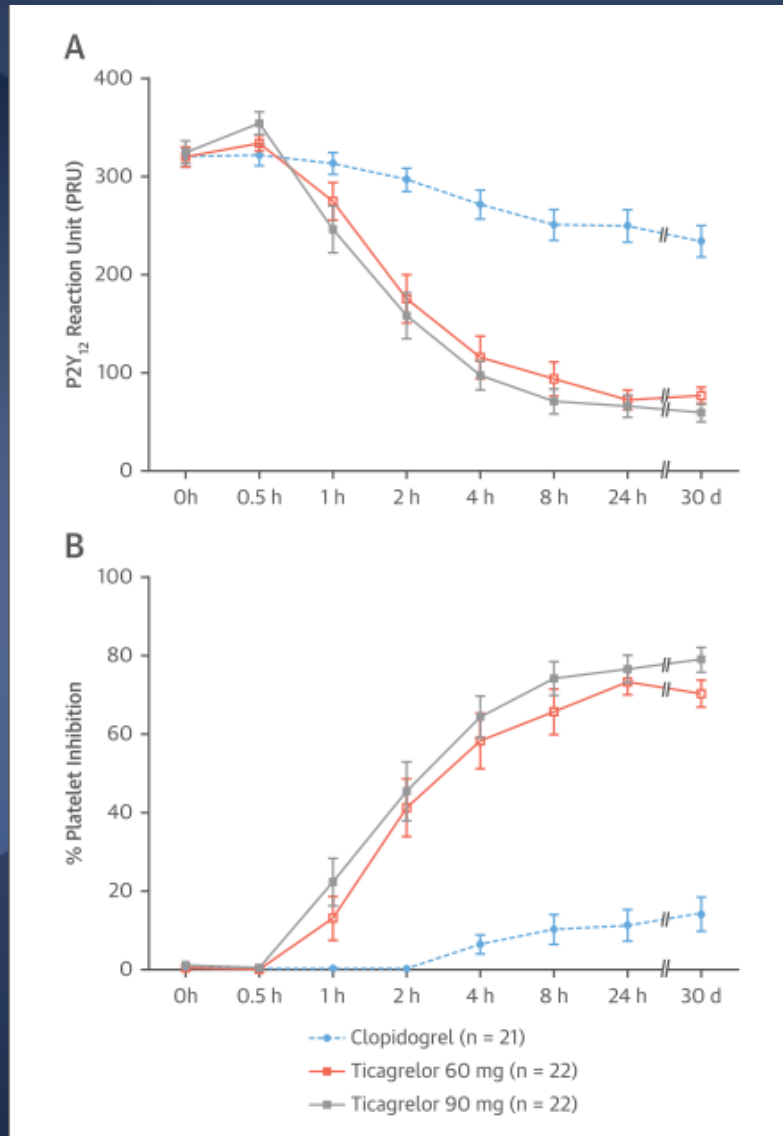
Clopidogrel alone
Late 6 months (**Late De-Escalation**)

The primary endpoint was a composite outcome of death, MI, stroke, stent thrombosis, urgent revascularization, and clinically relevant bleeding (BARC 2, 3, or 5) at 12 months

*Complex High-Risk PCI

: Left main PCI, chronic total occlusion, bifurcation requiring two-stent technique, severe calcification, diffuse long lesion (lesion length ≥ 30 mm), multivessel PCI (≥ 2 vessels requiring stent implantation), ≥ 3 requiring stents implantation, ≥ 3 lesions will be treated, predicted total stent length for revascularization >60 mm, diabetes, CKD (Cr-clearance <60 ml/min) or severe LV dysfunction (EF $<40\%$).

Early Course of Intense DAPT Concept (1)



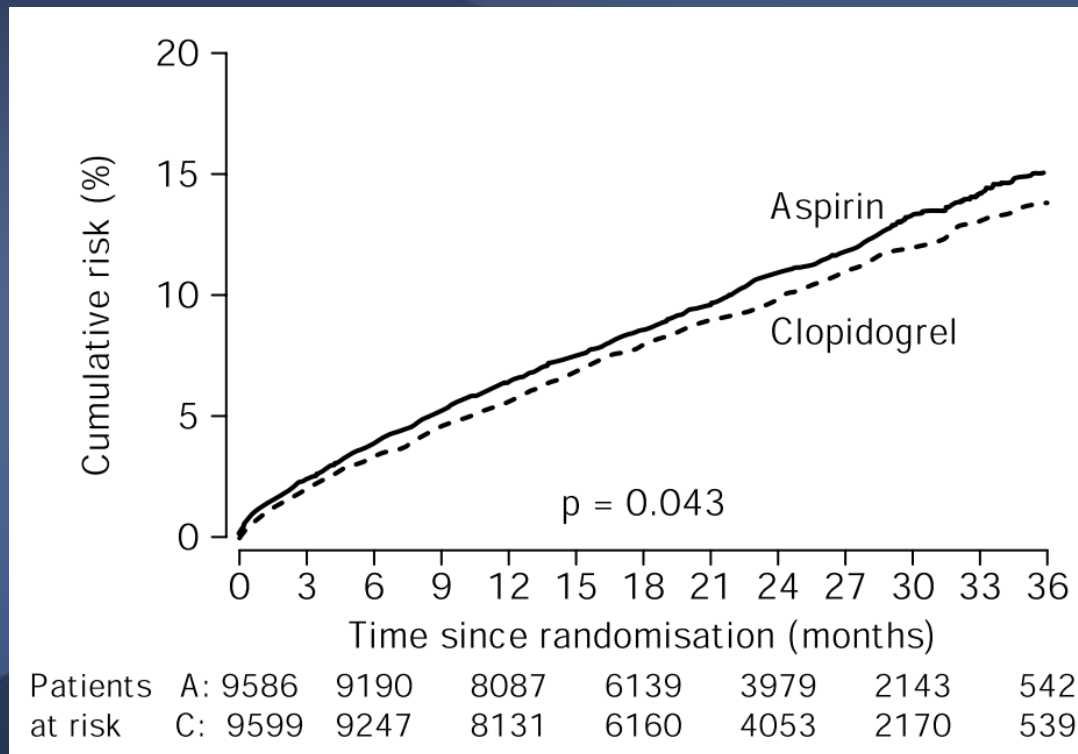
Effect of Low-Dose Versus Standard-Dose Ticagrelor and Clopidogrel on Platelet Inhibition in Acute Coronary Syndromes

DAPT with a 60mg of ticagrelor

Late monotherapy with clopidogrel

Concept (2)

Patients with recent ischemic stroke, recent MI, or symptomatic PAD (N = 19,185)



Cumulative Event Rate
(Ischemic stroke, MI,
vascular death)

8.7% Relative risk
reduction
(p=.043)

Aspirin = 5.83%
Clopidogrel = 5.32%

CAPRIE: Superior efficacy of clopidogrel versus aspirin

Late monotherapy with clopidogrel

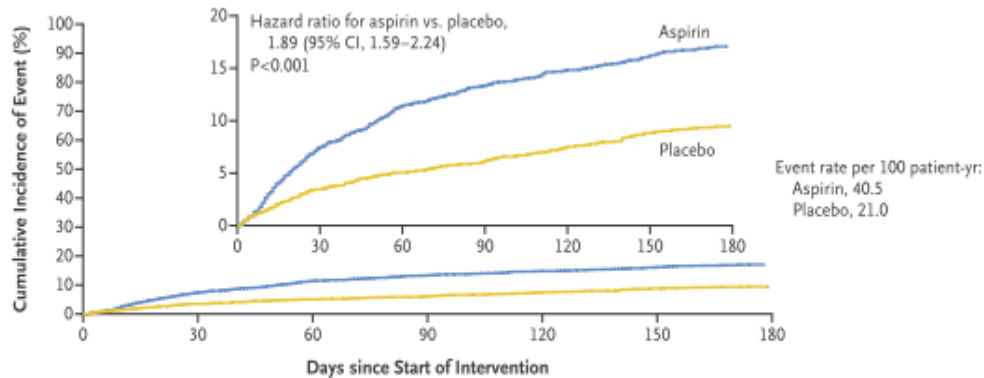
Concept (2)

Clinical Issues with Aspirin

- **Treatment Failure** (“Aspirin Resistance”)
 - Aspirin preparation (ie, enteric coated formulations)
 - Drug-drug interactions (ie, NSAIDs)
 - COX-1 related pathways
 - Medication noncompliance
 - Premature discontinuation
- **Irreversible platelet inhibition**
- **Bleeding risk**
- **Gastrotoxicity**

Late monotherapy with clopidogrel Concept (2)

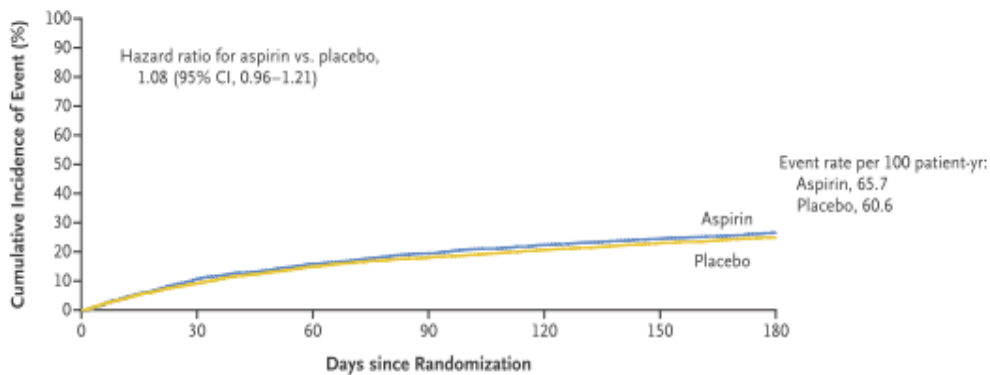
B Primary Outcome — Aspirin vs. Placebo



No. at Risk

Aspirin	2277	2003	1863	1789	1717	1674	962
Placebo	2279	2095	2006	1941	1880	1824	1079

B Death or Hospitalization — Aspirin vs. Placebo



No. at Risk

Aspirin	2307	2042	1909	1822	1752	1699	951
Placebo	2307	2083	1941	1864	1801	1746	997

Drop out aspirin
AUGUSTUS
STOPDAPT-2
SMART-CHOICE

Inclusion/Exclusion

Inclusion: Features of complex high-risk anatomic, procedural and clinical-related factors

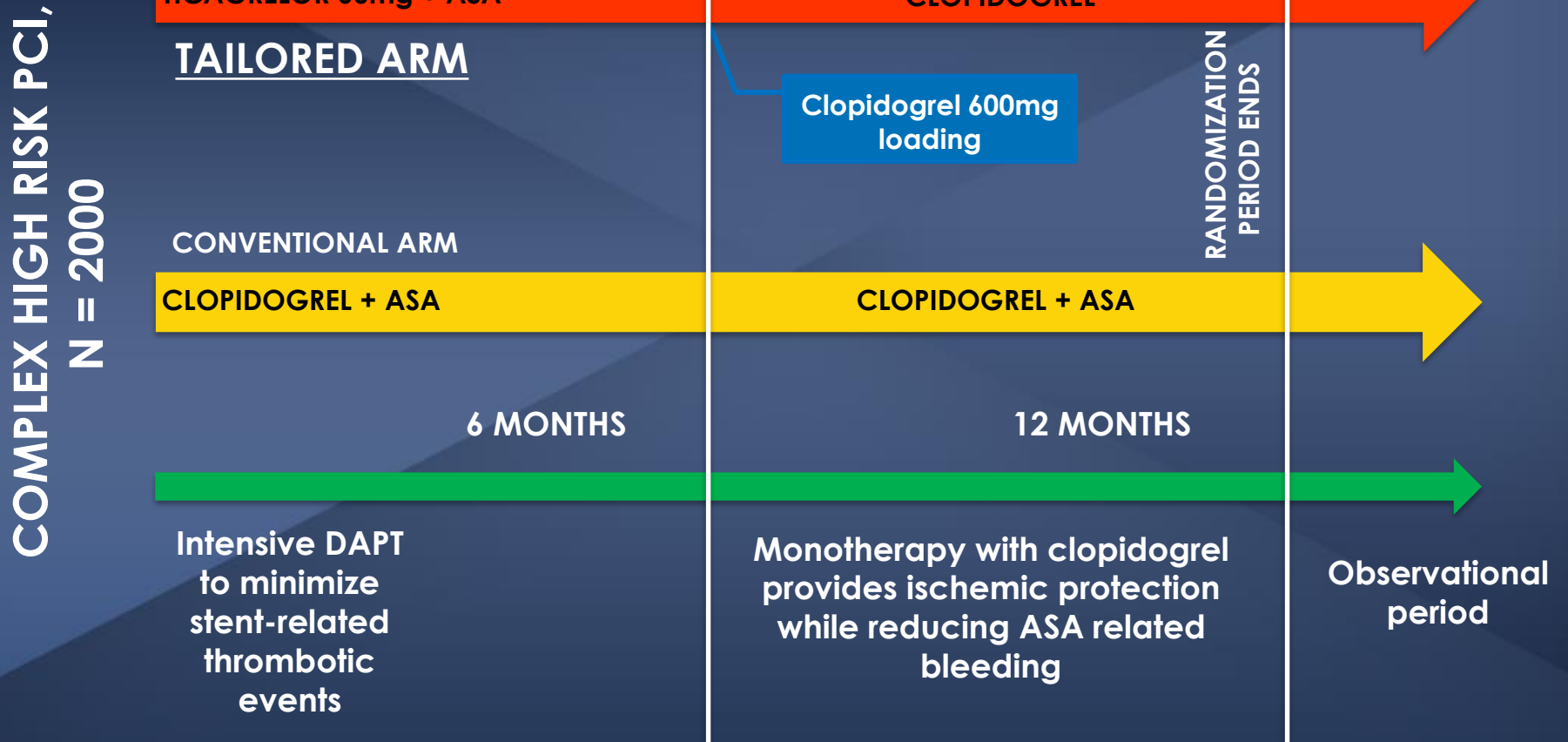
- ✓ Clinical criteria; diabetes, chronic kidney disease (CrCl <60 mL/min), LVEF <40%
- ✓ Lesional or procedural criteria; left main lesion, bifurcation lesion requiring two stent-technique, CTO lesion, severe calcification, long lesion (lesion length \geq at least 30mm), multi-vessel PCI, ≥ 3 stents implanted, ≥ 3 lesions treated, total stent length ≥ 60 mm

Exclusion:

- ✓ Enzyme-positive ACS (NSTEMI or STEMI)
- ✓ Contraindication to aspirin or P2Y12 inhibitors
- ✓ Need for chronic oral anticoagulation (warfarin or NOAC)
- ✓ History of ICH

Study Design

A Net Clinical Outcome of *all-cause death, MI, stroke, ST, urgent revascularization and clinical relevant bleeding (BARC 2,3, or 5)*



Conclusions

- A trend in PCI is toward performing in high-risk patients with increasingly complex lesions and procedure.
- Alternative DAPT regimens (early escalation, late de-escalation) may be reasonable in this complex, high-risk patient subset to achieve a balance between timely sufficient platelet inhibition and acceptable bleeding risk.
- TAILORED CHIP will help to inform this concept.