

Time to Consider Different P2Y12 Strategy for Complex PCI/CHIP Patients: From the OPTIMA to TAILORED-PCI Trial

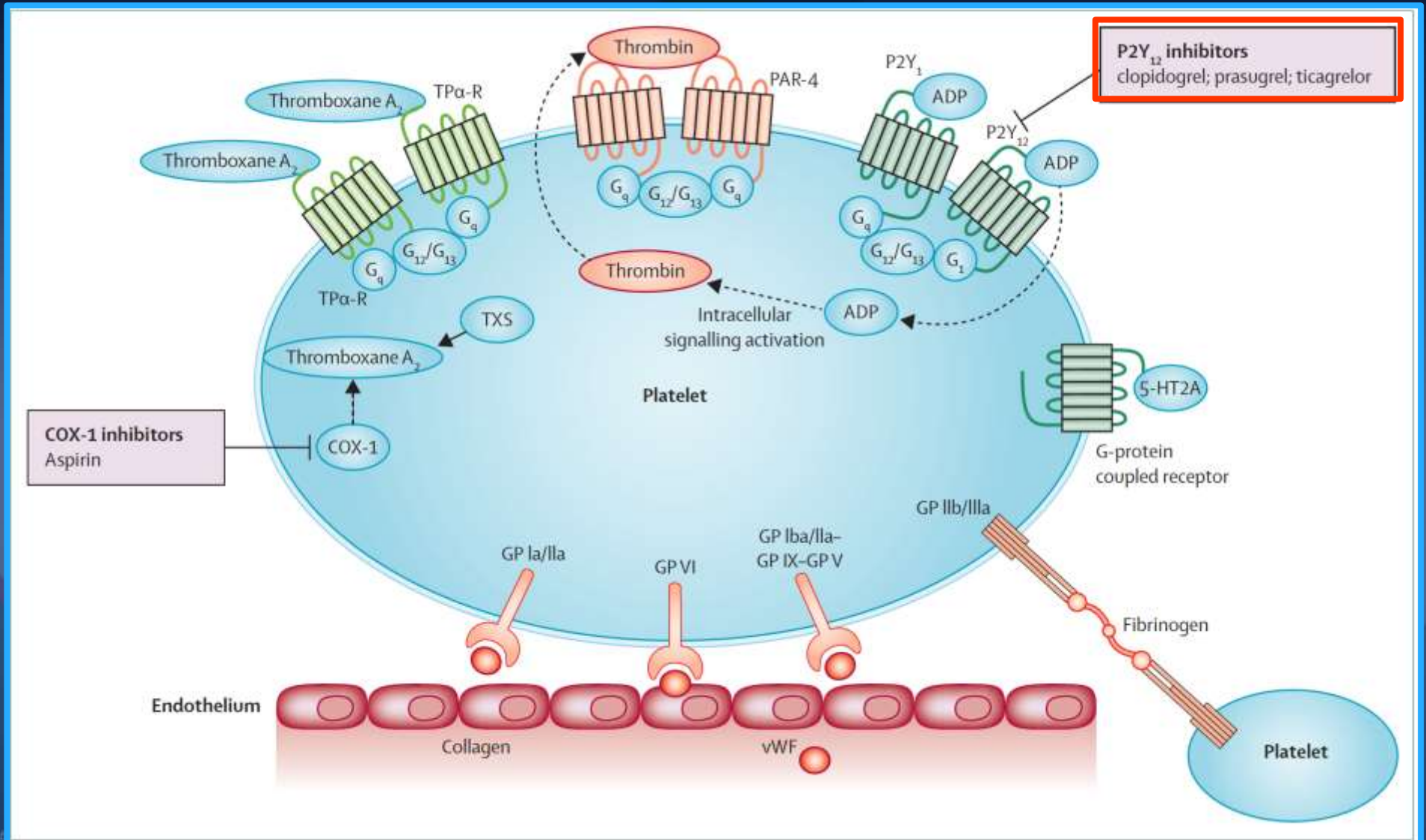
Duk-Woo Park, MD, PhD

Department of Cardiology, Ulsan College of Medicine,
Asan Medical Center

Disclosure

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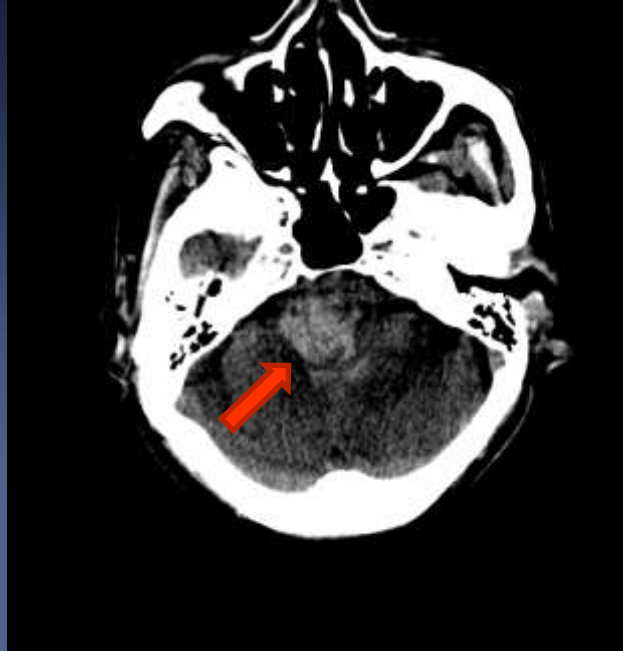
Contemporary P2Y₁₂ Inhibitors



Fatal Case Series



74/F, ACS, PCI
Extensive subdural
hemorrhage
after ticagrelor use
→ Expired



74/M, ACS, PCI
Acute ICH, pons
after ticagrelor use
→ Expired



70/M, ACS, PCI
Multiple SDH
after ticagrelor use
→ Vegetative state

East-Asian Paradox

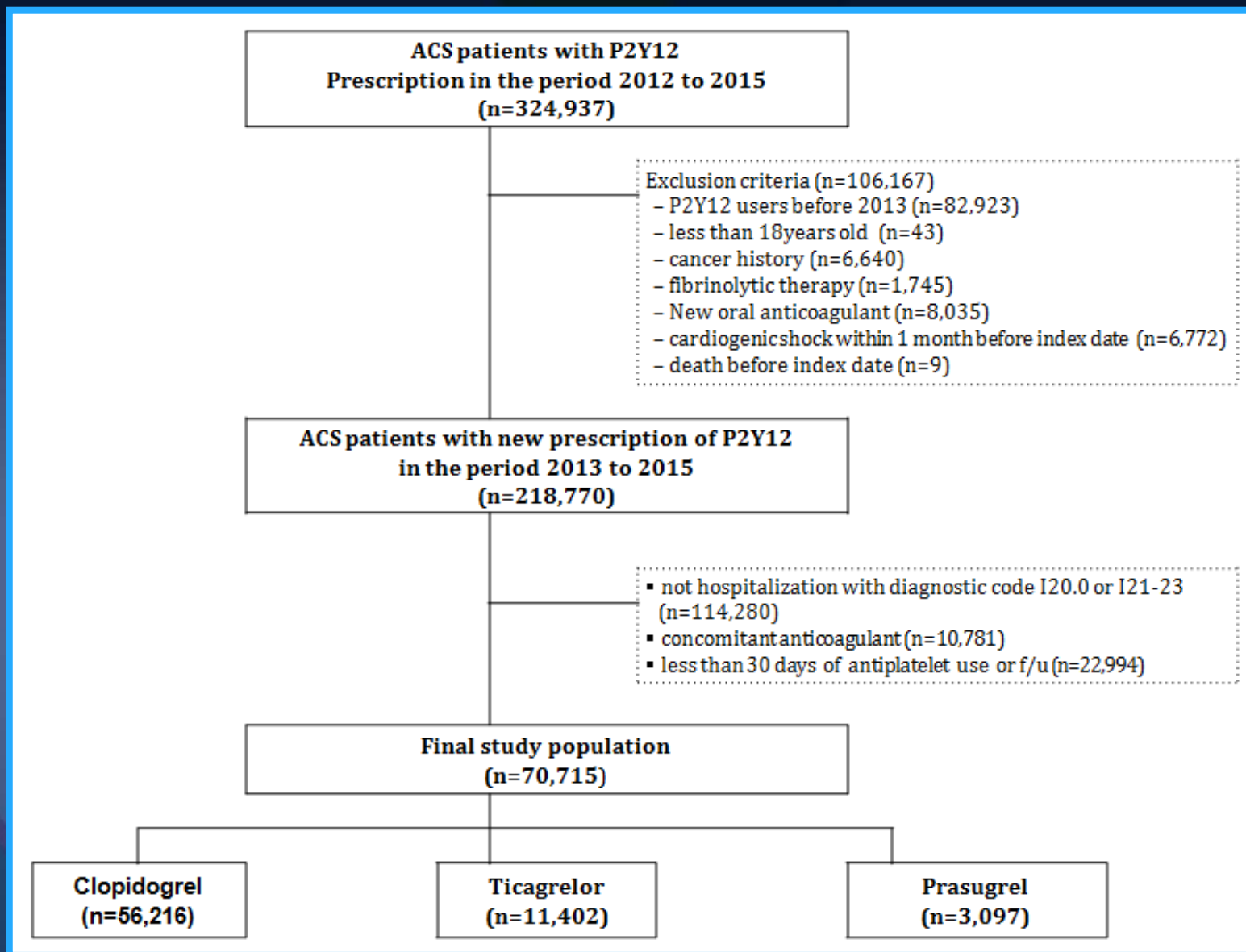
EXPERT CONSENSUS DOCUMENT

World Heart Federation expert consensus statement on antiplatelet therapy in East Asian patients with ACS or undergoing PCI

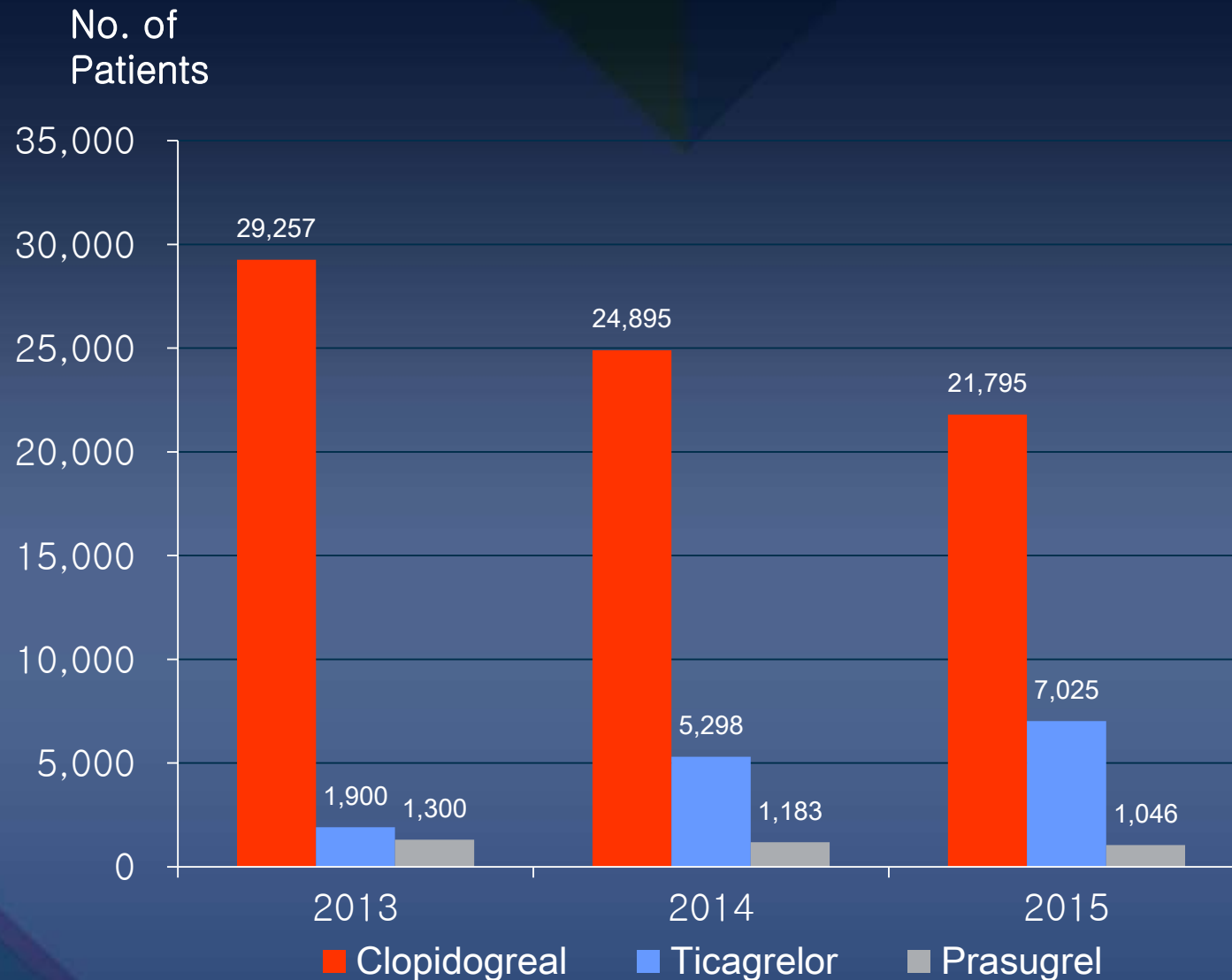
Glenn N. Levine, Young-Hoon Jeong, Shinya Goto, Jeffrey L. Anderson, Yong Huo, Jessica L. Mega, Kathryn Taubert and Sidney C. Smith Jr

Abstract | Guideline recommendations on the use of dual antiplatelet therapy (DAPT) in patients with acute coronary syndromes and in those undergoing percutaneous coronary intervention (PCI) have been formulated by both the ACC/AHA and the ESC. These recommendations are based primarily on large, phase III, randomized, controlled trials of the P2Y₁₂ inhibitors clopidogrel, prasugrel, and ticagrelor. However, few East Asian patients have been included in the trials to assess the use of these agents, particularly the newer agents prasugrel and ticagrelor. Additionally, an increasing body of data suggests that East Asian patients have differing risk profiles for both thrombophilia and bleeding compared with white patients, and that a different 'therapeutic window' of on-treatment platelet reactivity might be appropriate in East Asian patients. Furthermore, a phenomenon referred to as the 'East Asian paradox' has been described, in which East Asian patients have a similar or even a lower rate of ischaemic events after PCI compared with white patients, despite a higher level of platelet reactivity during DAPT. Recognizing these concerns, the World Heart Federation has undertaken this evidence-based review and produced this expert consensus statement to determine the antiplatelet treatment strategies that are most appropriate for East Asian patients.

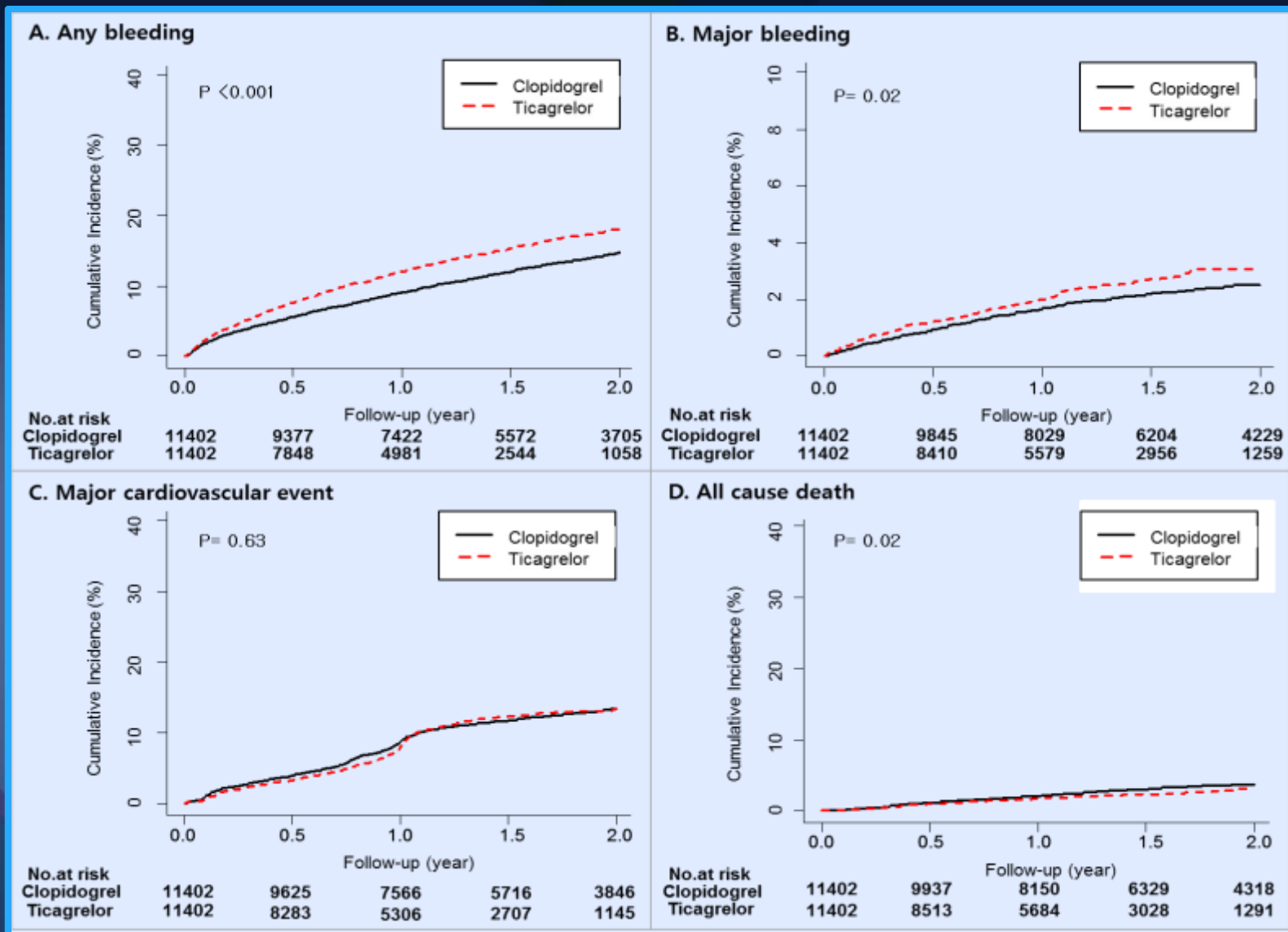
National Cohort Registry of ACS Patients



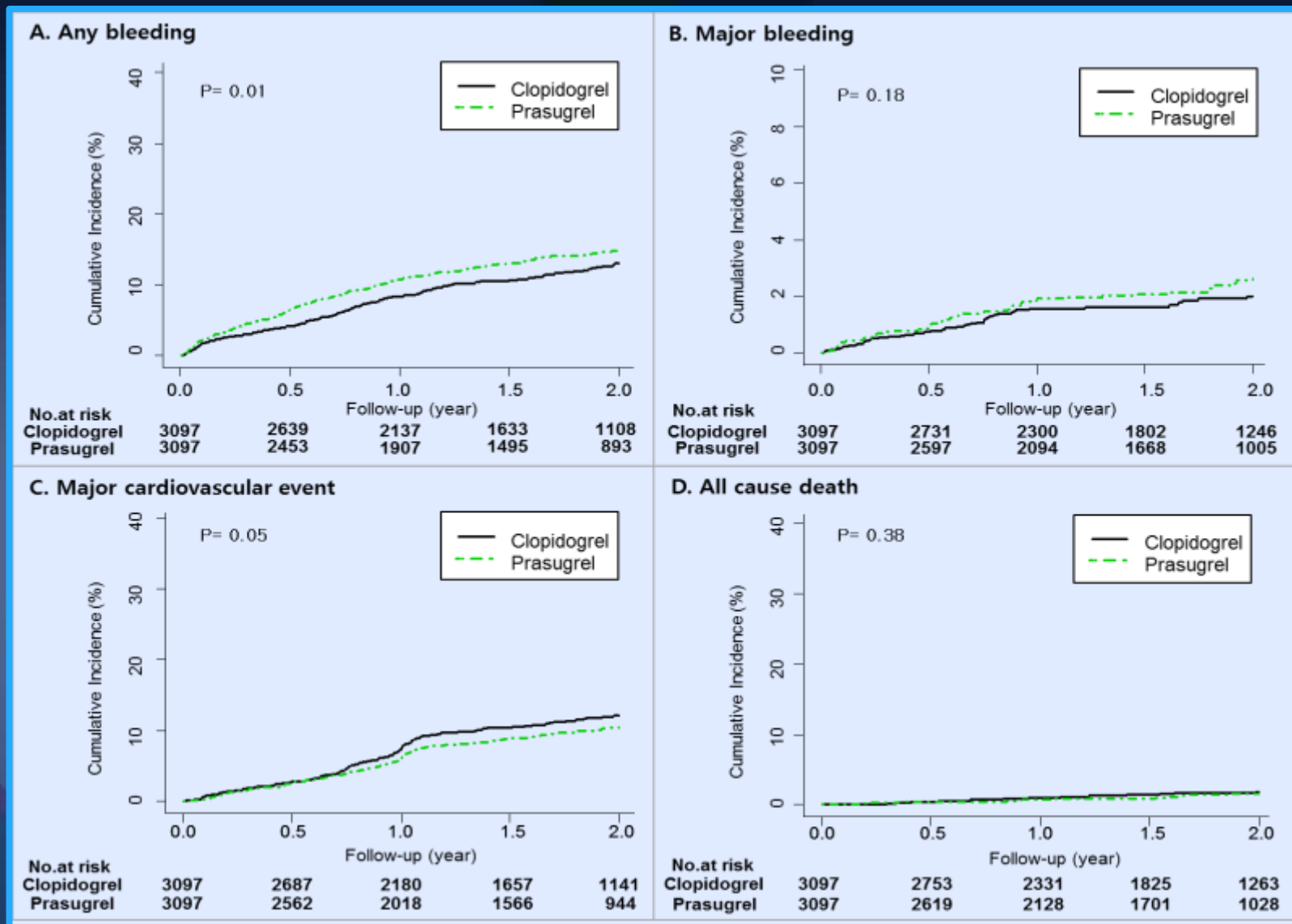
Temporal Trend of P2Y12 Inhibitors Use



PS-Matched Cohort of Ticagrelor and Clopidogrel (N=11,402)

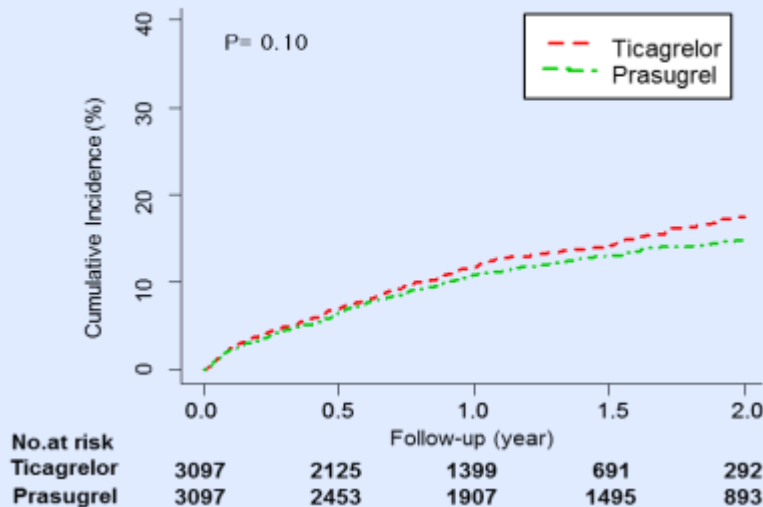


PS-Matched Cohort of Prasugrel and Clopidogrel (N=3,097)

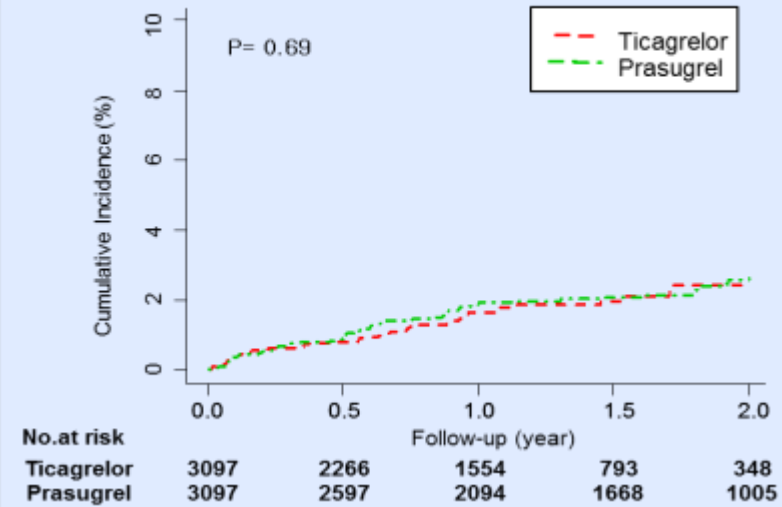


PS-Matched Cohort of Ticagrelor and Prasugrel (N=3,097)

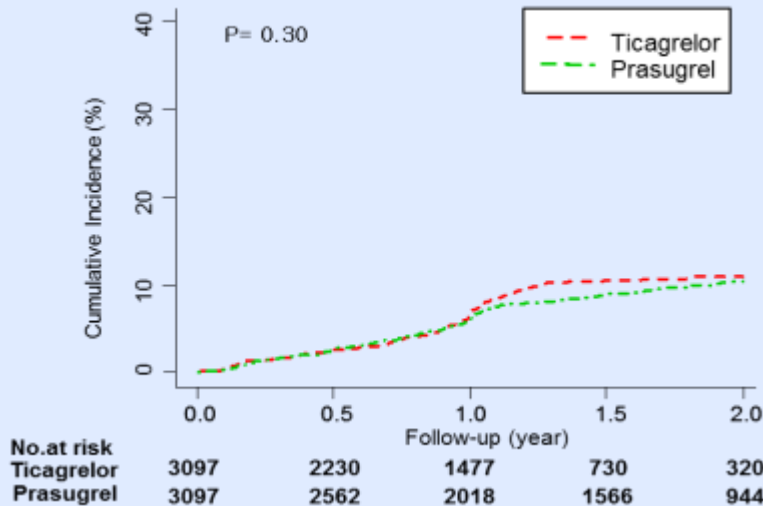
A. Any bleeding



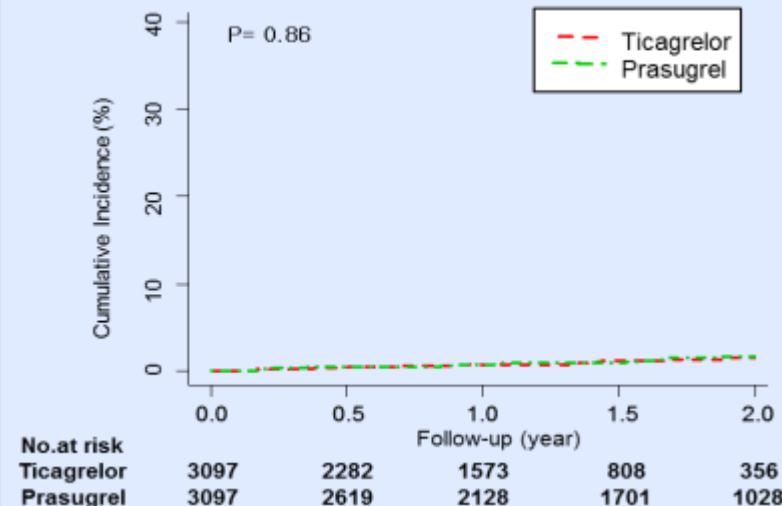
B. Major bleeding



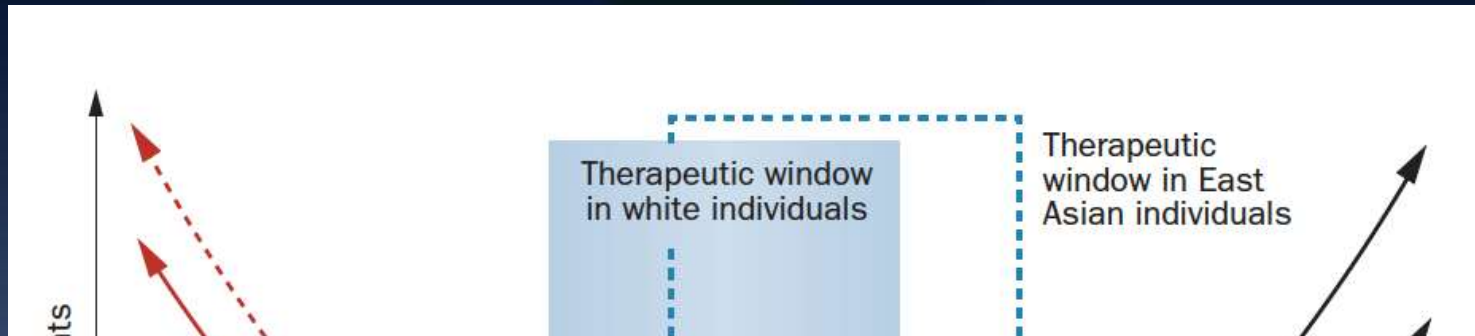
C. Major cardiovascular event



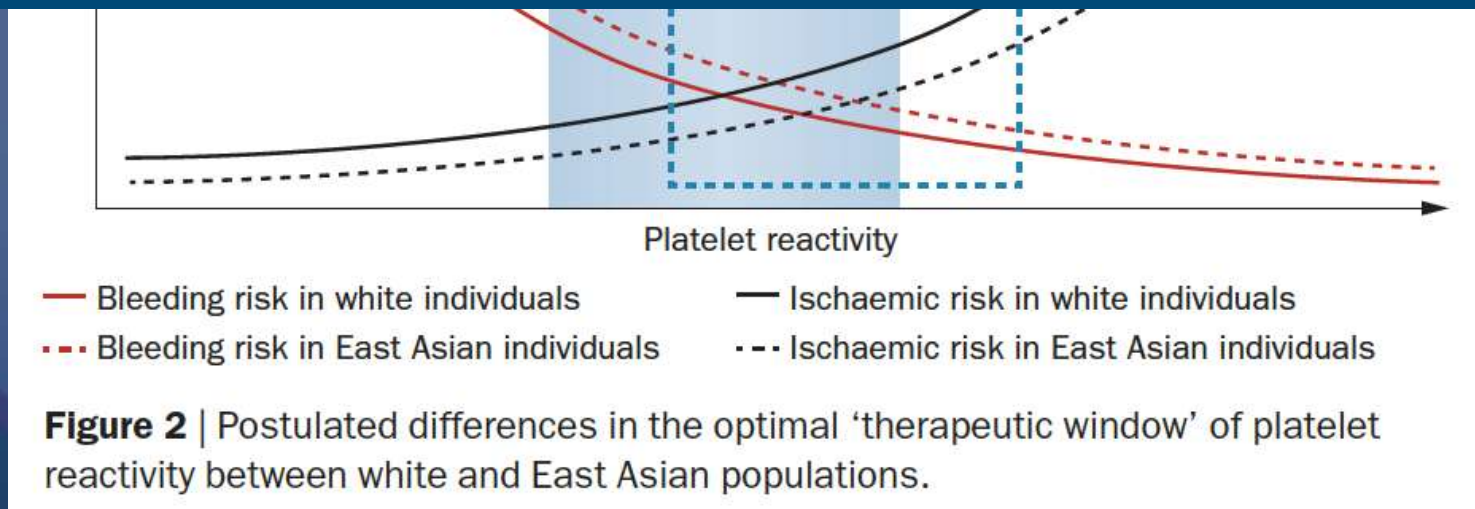
D. All cause death



East-Asian Paradox



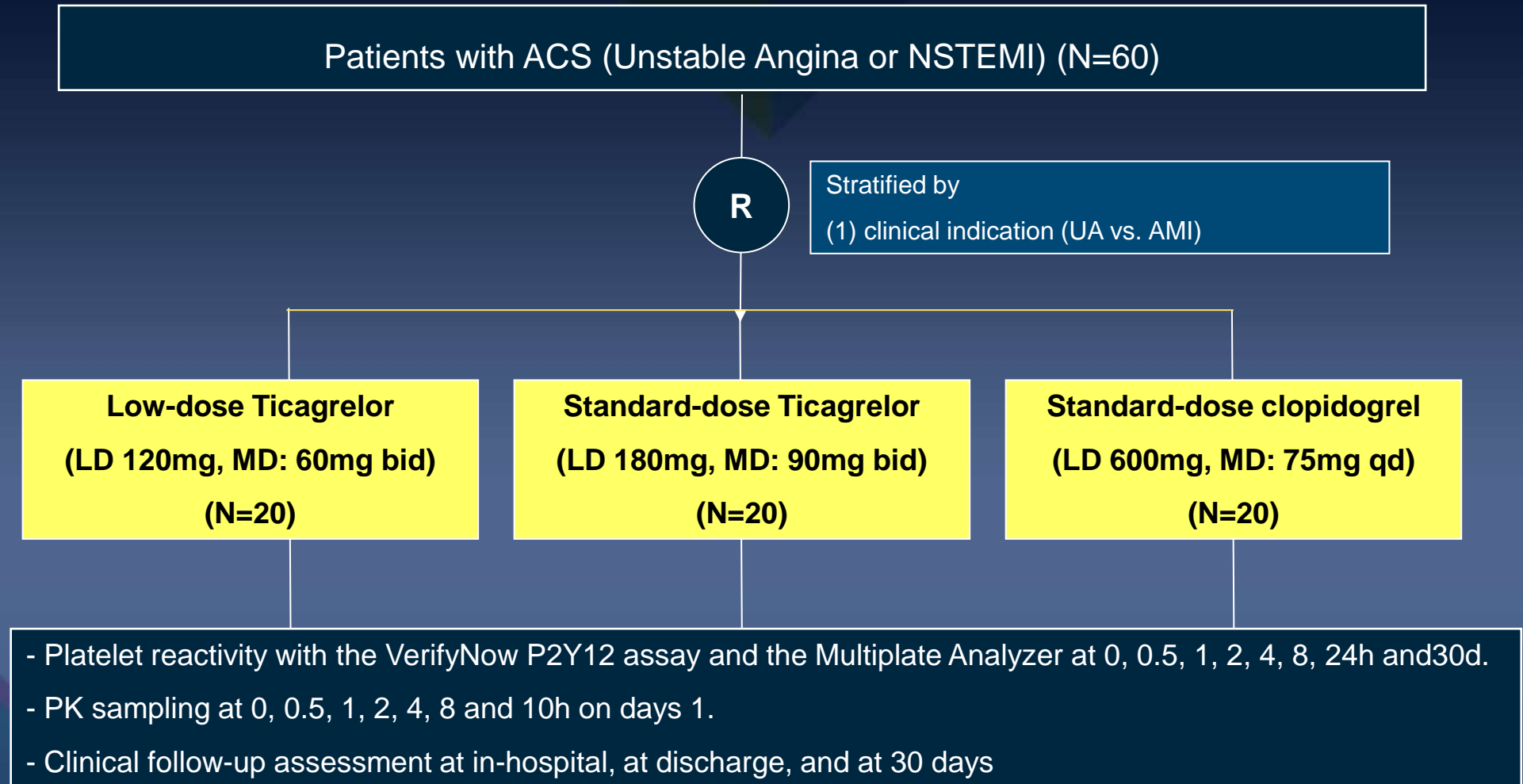
Which Dose Is Optimal for East-Asian Patients?



A Randomized Double-Blind Trial Evaluating
Platelet Inhibition with Low-Dose Ticagrelor
versus Standard-Dose Ticagrelor and
Clopidogrel in Acute Coronary Syndromes:

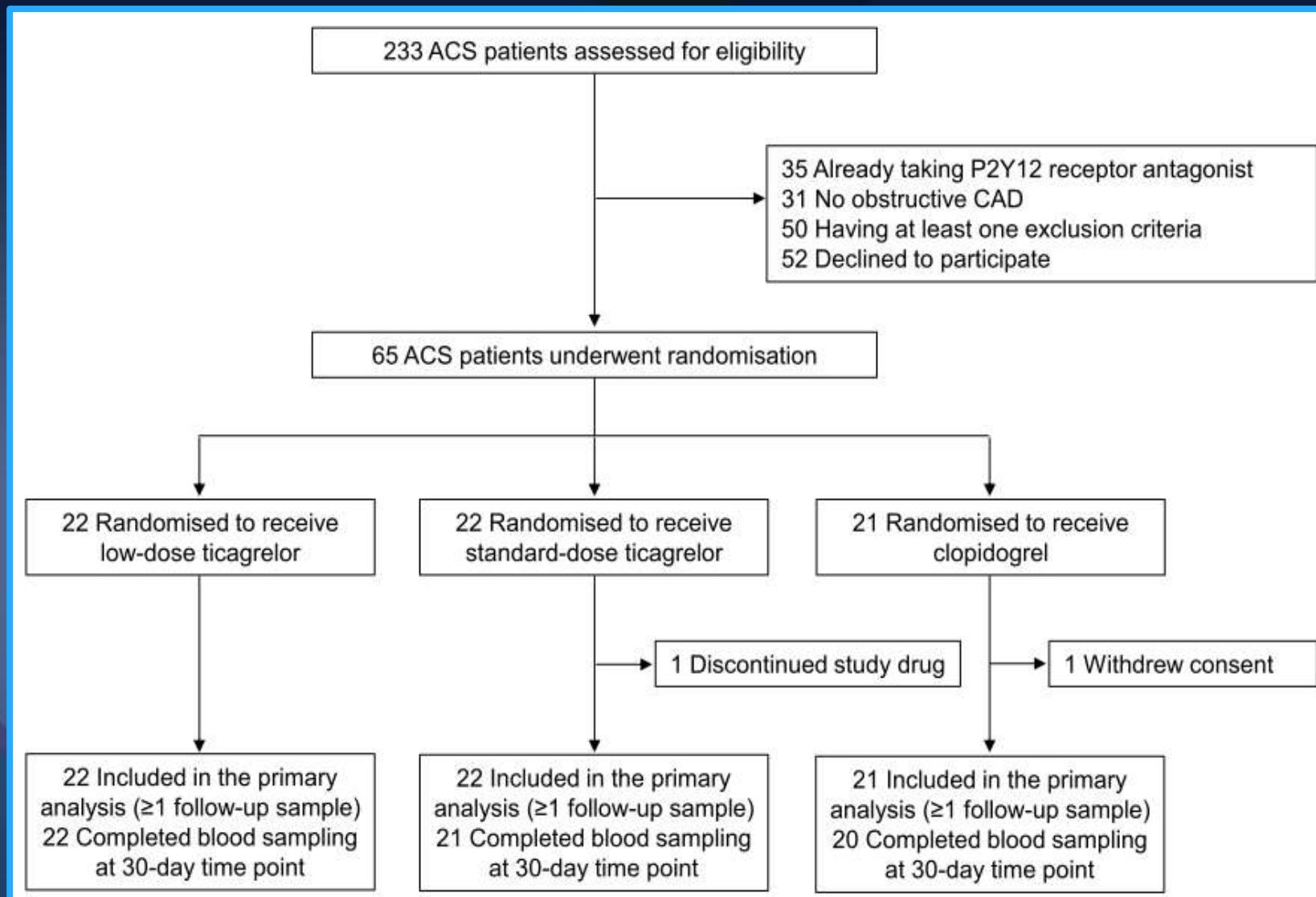
The OPTIMA Trial

Trial Design

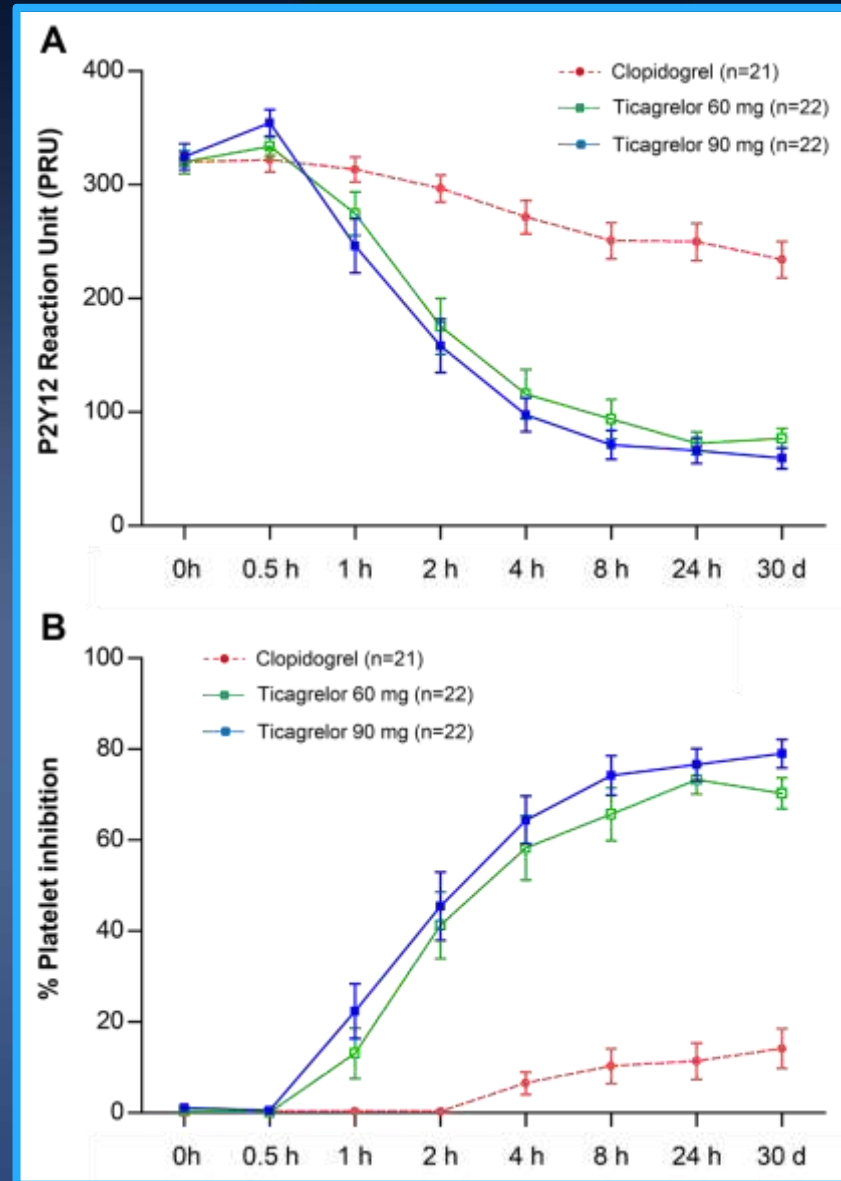


****Primary end point: PRU at 8hrs after loading and at 30 days during maintenance**

Patient Flow Diagram



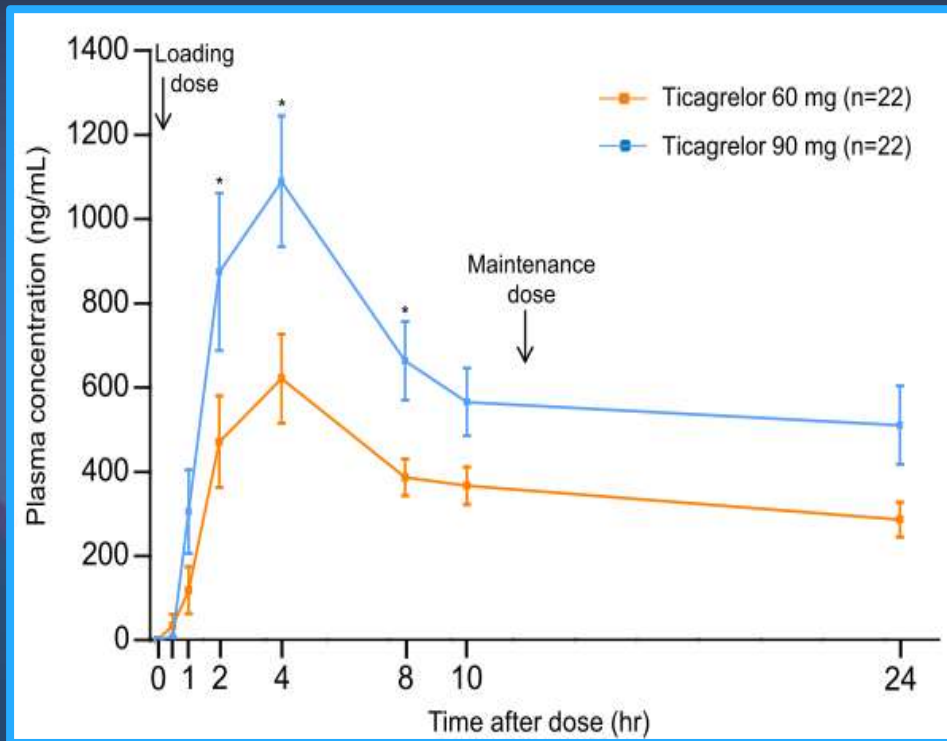
PRU and % Inhibition



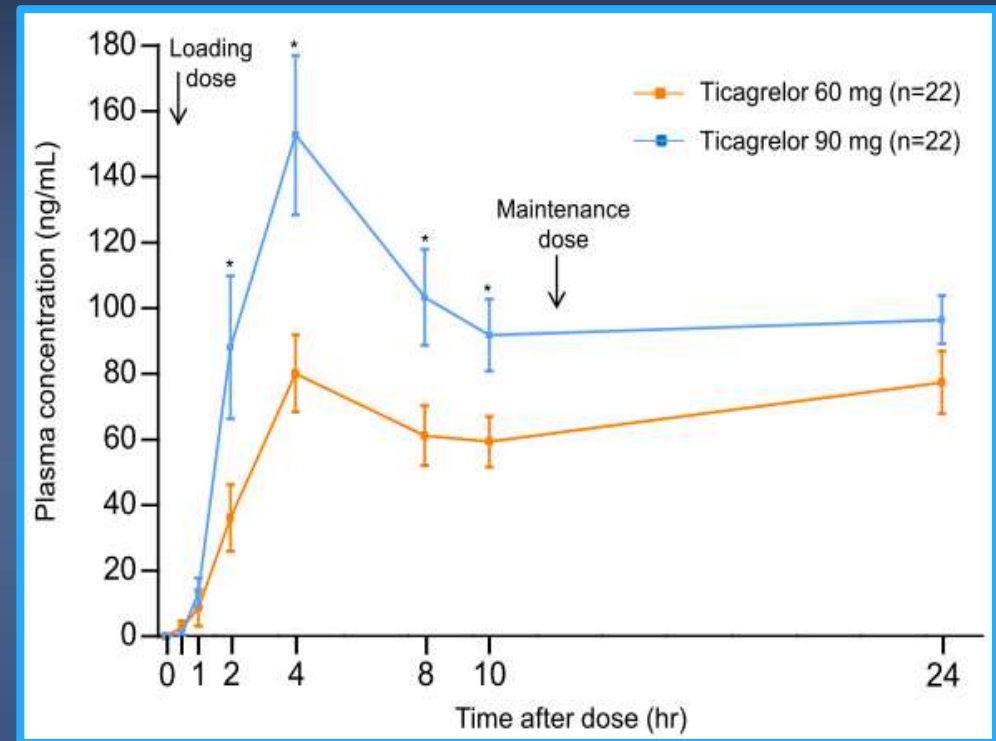
JACC 2018. April 10: 1594-9

Pharmacokinetics

Mean plasma concentrations
of ticagrelor

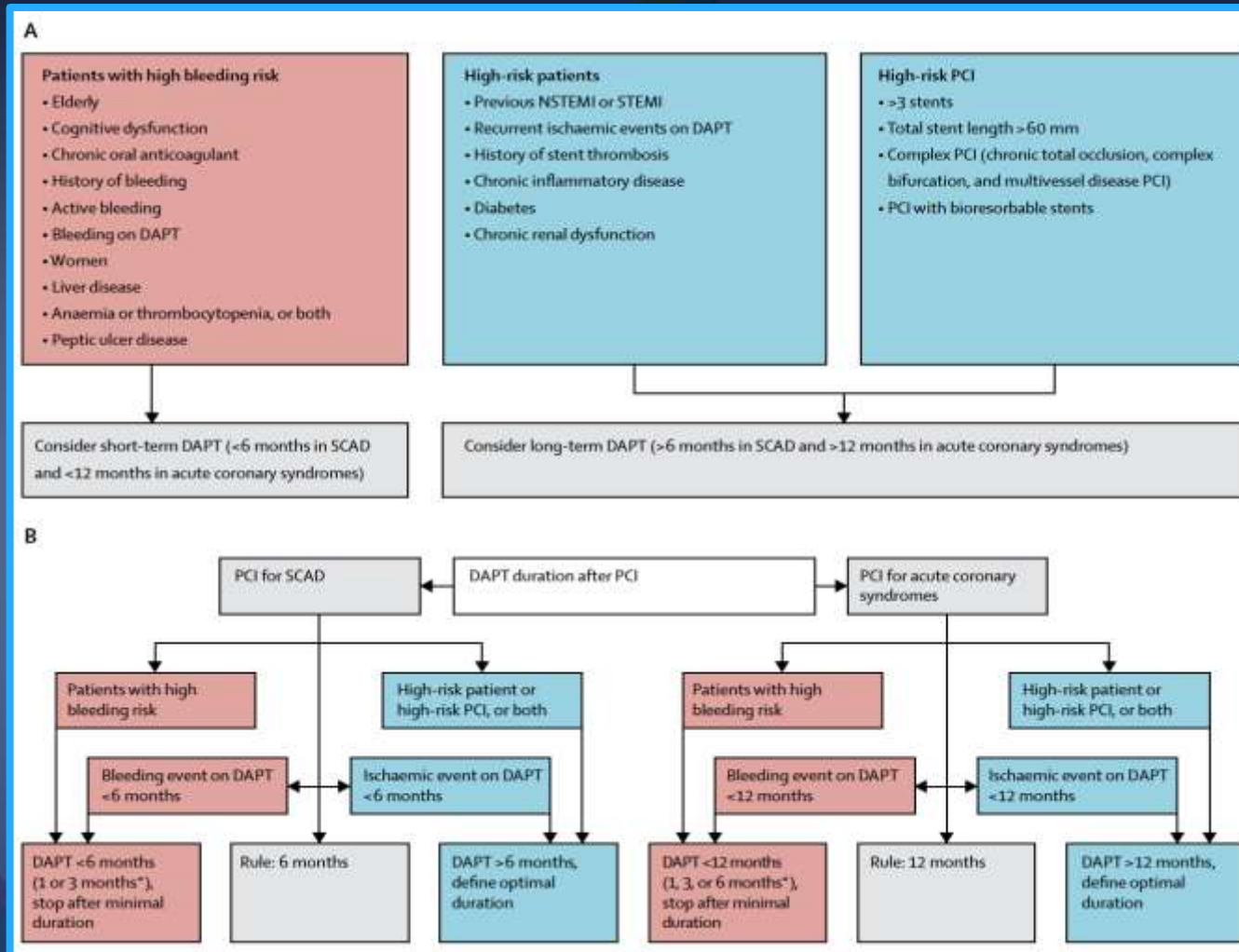


Mean plasma concentrations
of AR-C124910XX



Complex High-Risk Patients

Still Unmet Need for Optimal Antithrombotic Therapy



Complex High-Risk Patients: Many Studies Regarding Duration of DAPT

High-risk features of stent-driven recurrent ischaemic events



- Prior stent thrombosis on adequate antiplatelet therapy.
- Stenting of the last remaining patent coronary artery.
- Diffuse multivessel disease especially in diabetic patients.
- Chronic kidney disease (i.e. creatinine clearance <60 mL/min).
- At least three stents implanted.
- At least three lesions treated.
- Bifurcation with two stents implanted.
- Total stent length >60 mm.
- Treatment of a chronic total occlusion.

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)

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Prolonged (i.e. >12 months^c) DAPT duration should be considered in patients with prior stent thrombosis, especially in the absence of correctable causes (e.g. lack of adherence or correctable mechanical stent-related issues).

IIa

C

Prolonged (i.e. >12 months) DAPT duration may be considered in CAD patients with LEAD.^{140,246}

IIb

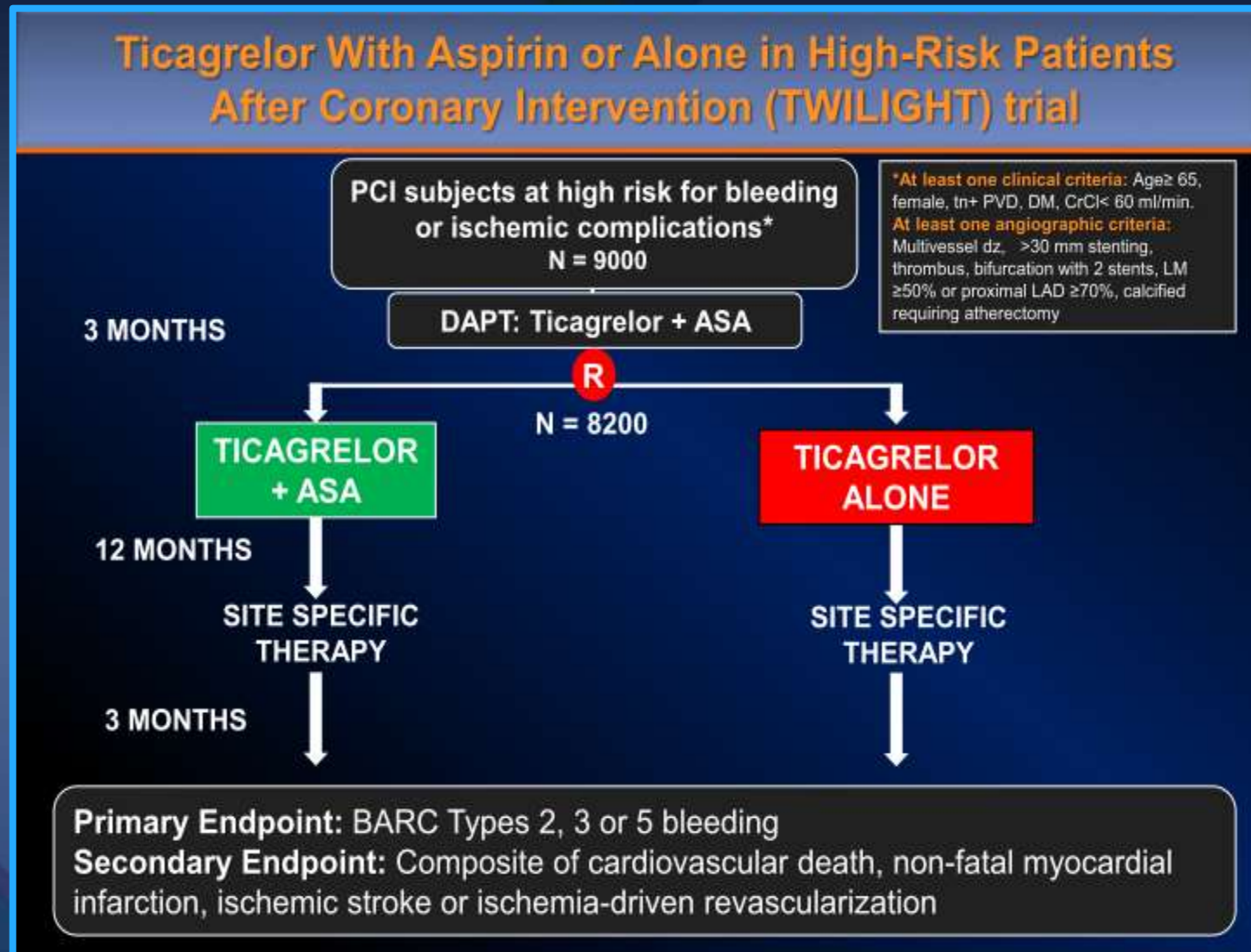
B

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

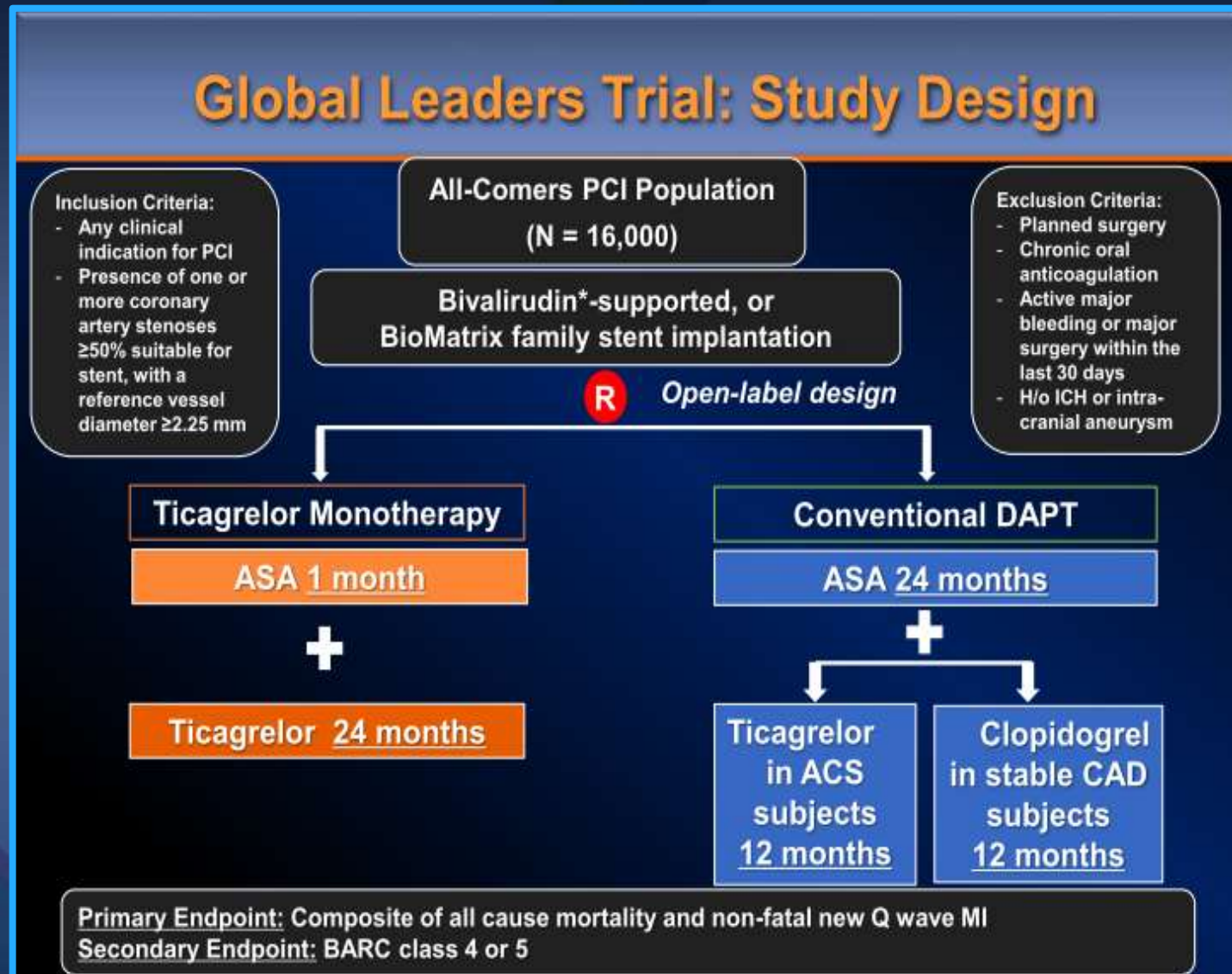
IIb

B

Complex High-Risk Patients : Other Combination and Intensity for DAPT

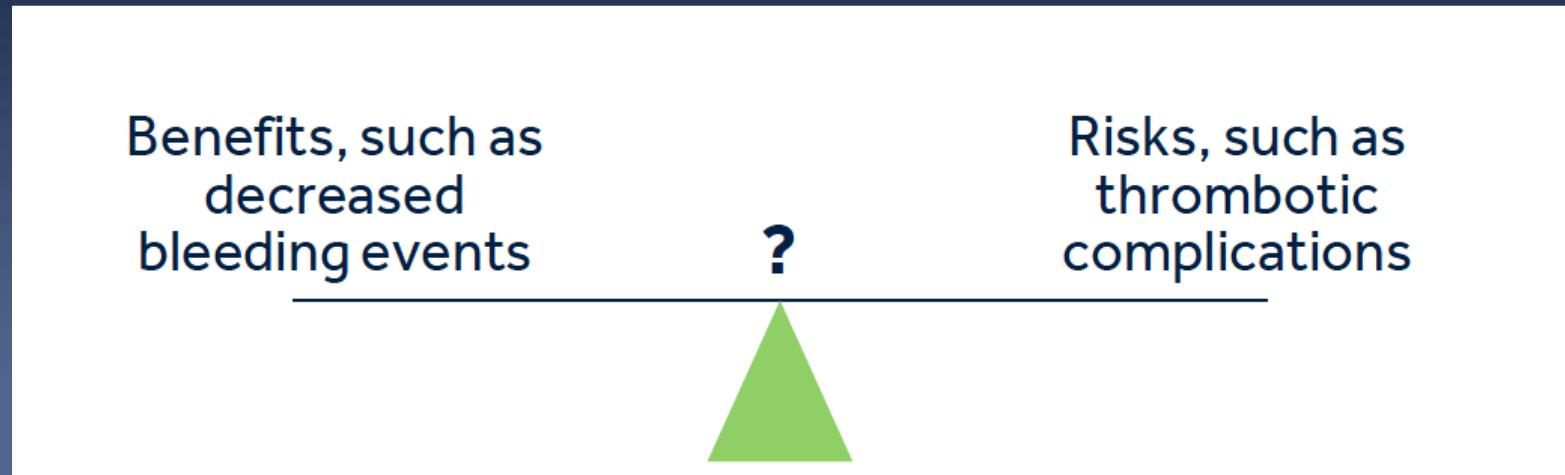


Complex High-Risk Patients : Other Combination and Intensity for DAPT



“East-Asian Paradox”

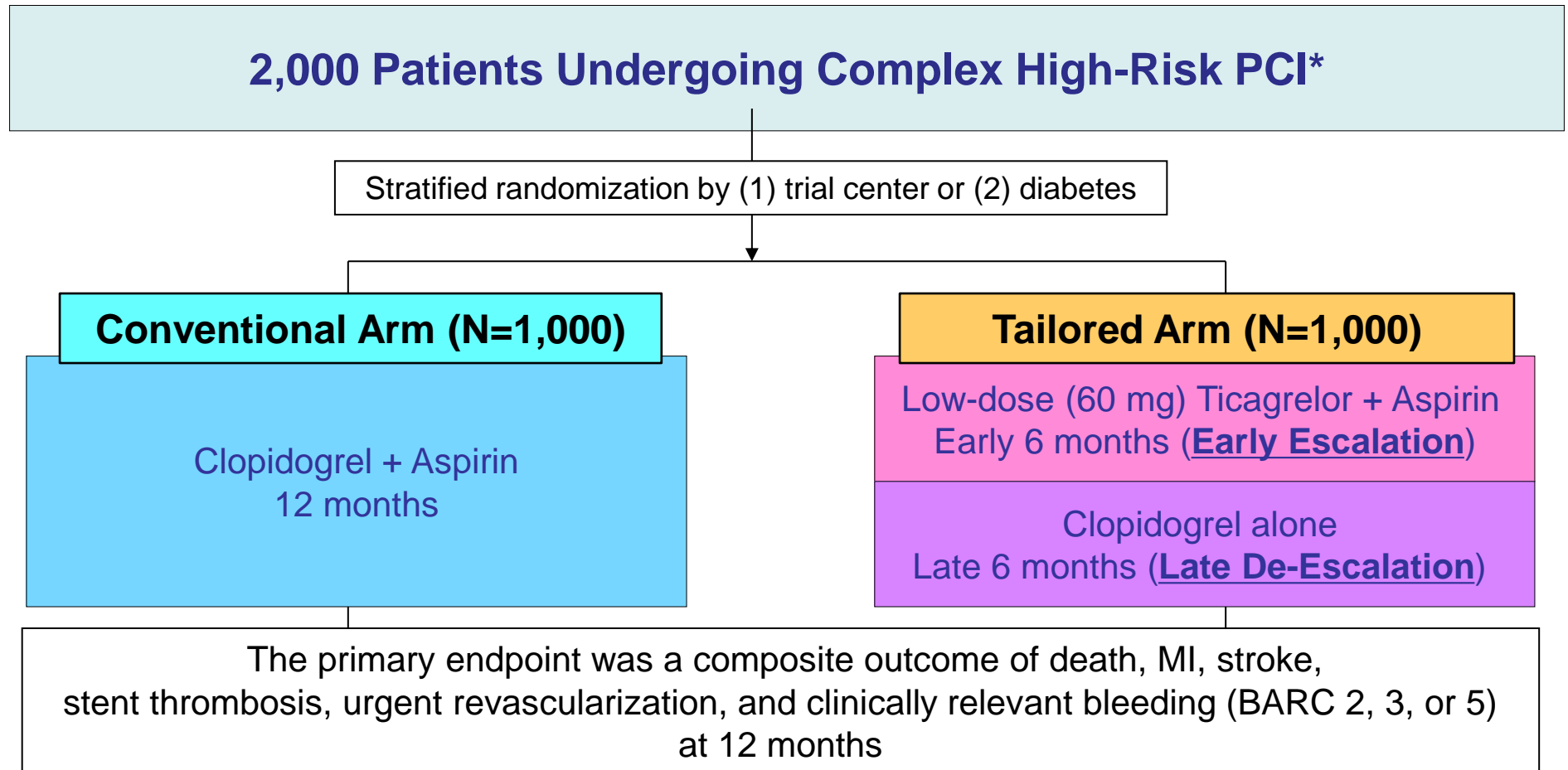
How To Do ?



***Different Dosing and Strategy Is
Required for East-Asian Population !!!***

TAIlored versus COnventional AntithRombotic StratEgy
IntenDed for Complex High-Risk PCI

TAILORED-CHIP Trial



*Complex High-Risk PCI

: Left main PCI, chronic total occlusion, bifurcation with 2 stents implanted, severe calcification, diffuse long lesion (lesion length $\geq 30\text{mm}$), multivessel PCI (≥ 2 vessels stented), ≥ 3 stents implanted, ≥ 3 lesions treated, total stent length $>60\text{mm}$, diabetes, CKD (Cr-clearance $<60\text{ml/min}$) or severe LV dysfunction (EF $<40\%$).

Definition of High-Risk PCI in the TAILORED-CHIP Trial

- Left main PCI,
- Chronic total occlusion,
- Bifurcation with 2 stents implanted,
- Severe coronary calcification,
- Diffuse long lesion (lesion length \geq at least 30 mm)
- Multivessel disease PCI (\geq 2 vessels stented),
- \geq 3 stents implanted (at least 3 stents implanted),
- \geq 3 lesions treated (at least three lesions treated),
- Total stent length >60 mm
- Chronic kidney disease (creatinine clearance <60 mL/min)
- Diabetes
- Severe LV dysfunction (EF $<40\%$)

P2Y12 Dose Adjustment for East-Asian ACS Patients

How To Do ?

- The “East Asian paradox” describes a phenomenon of differential ischemic and bleeding response to antithrombotic therapies.
- Despite a higher level of platelet reactivity to antithrombotic therapy, East Asian patients have a higher risk of bleeding events, but a similar or even lower risk of ischemic events as compared with White patients.

P2Y12 Dose Adjustment for East-Asian ACS Patients

How To Do ?

- Further studies are required to assess the efficacy and safety of potent P2Y12 inhibitors (ticagrelor or prasugrel) for ACS or PCI among East Asian patients.
- The **TAILORED-CHIP** trial will evaluate the potential impact of tailored antithrombotic therapy with a stage-adapted strategy (potent platelet inhibition with low-dose ticagrelor in the early phase and de-escalation to clopidogrel in the late phase) for East Asian patients undergoing complex, high-risk PCI.