TCTAP 2024. Optimizing care pathways for Cardiovascular health. 20분

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Navigating Acute Coronary Syndrome: Effective De-escalation Strategies

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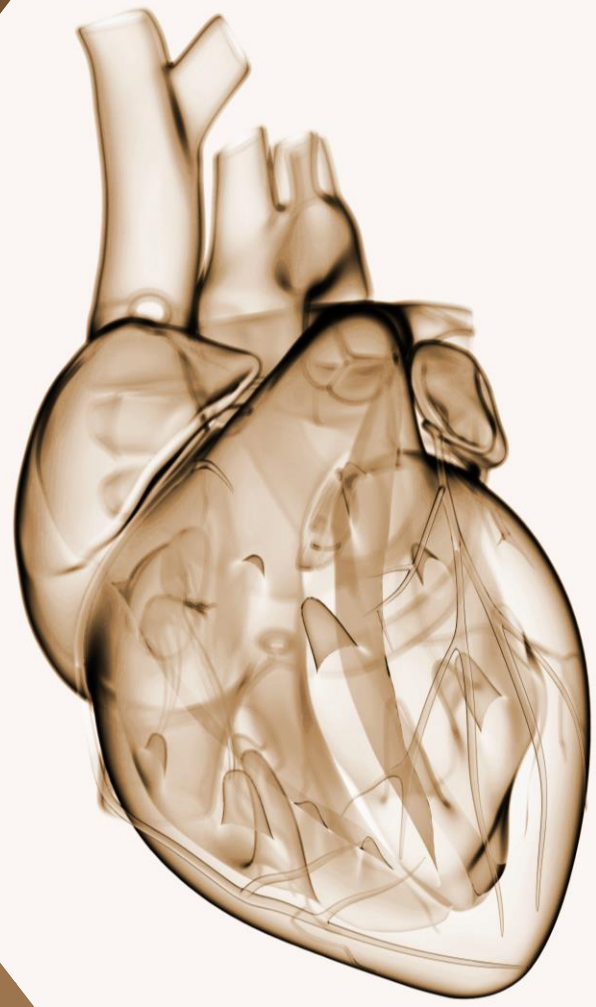


Just as referred to….

Transformative impact changed the world

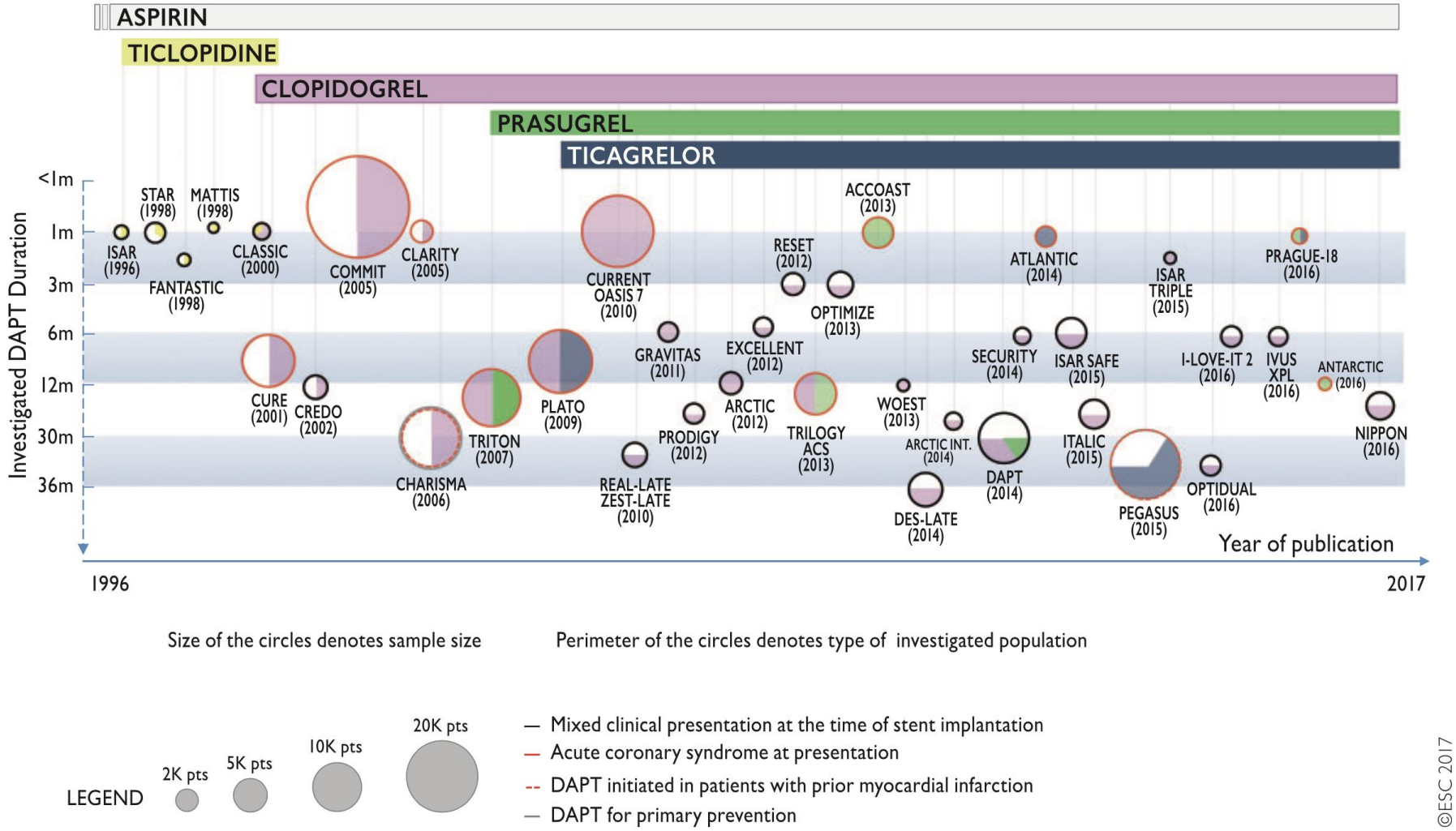
2010

Steve Jobs

1998

Jean-Pierre Maffrand

J.-P. Maffrand / C. R. Chimie 15 (2012) 737–743



*Eur Heart J 2018;*39: 213-60

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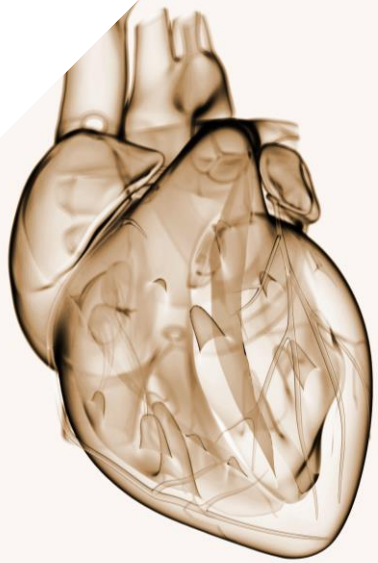

Antiplatelet agents:

$P2Y_{12}$ receptor antagonists: clopidogrel, prasugrel, ticagrelor

	Clopidogrel	Prasugrel	Ticagrelor
Activation	**Prodrug**	Prodrug	Active drug
Bioavailability	**50%**	>79%	36%
Metabolism	**Hepatic** (2 steps)	Hepatic (1 step)	Hepatic (CYP3A4)
Half-life	**6 hrs***	7 hrs (2-15)	7 hrs
Excretion	**Urine** (50%), **Feces** (46%)	Urine (68%), Feces (27%)	Biliary
Onset of effect	**2-4 hrs**	30 min	30 min
Duration of effect	**3-10 days**	5-10 days	3-4 days
Withdrawal before surgery	**5 days**	7 days	5 days
Administration	**75 mg** (QD)	10 mg (QD)	90 mg (BID)
Action	**Irreversible binding**	Irreversible binding	Reversible binding

*Approximately 6hrs.
※ 위 표는 indirect comparison으로 자세한 정보는 각 문헌 및 각 제품의 허가사항을 확인하시기 바랍니다.
BID, twice a day; **QD**, once daily.

References 1. Christian WH, et al. Eur Heart J. 2011;32:2999-3054. **2.** Jeong YH, et al. Expert Opin Pharmacother 2012;13:1771-1796. **3.** Plavix, Brilinta, Effient FDA label available at https://www.accessdata.fda.gov/scripts/cder/daf/ > as of Dec. 2021

Clopidogrel

- **Clopidogrel is a "classic" $P2Y_{12}$ receptor inhibitor that has withstood the test of time[1]**

- **Landmark studies have proven its efficacy in a broad population of patients with ACS, CVA or PAD[2]**
  - Medical management of **ACS**
  - **Alternative to aspirin** as single therapy in aspirin intolerant patients
  - For secondary prevention of **stroke**
  - To prevent **CVA** in patients with Atrial fibrillation in warfarin intolerant patients (ACTIVE-A)

ACS, acute coronary syndrome; **CVA,** cerebrovascular accident; **PAD,** peripheral arterial disease; **PCI,** percutaneous coronary interventions

References 1. Li C, et al. Eur J Clin Pharmacol. 2022;78(12):1949-1958. **2.** Beavers CJ, Naqvi IA. Clopidogrel. [Updated 2023 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470539/

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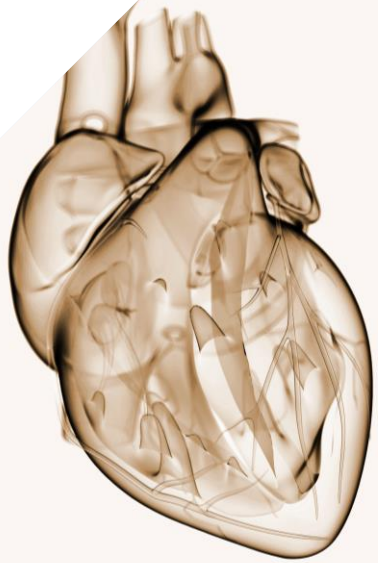


East Asian Paradox

East Asian patients showed a higher level of platelet reactivity than white patients

PRU: Westerners (208-235) and East Asians (253-275)

Study	Cohort	EP	Cutoff
ACCEL-LOADING-ACS (Randomized)	NSTE-ACS (n=218); emergent PCI	1-mo MACE	**PRU ≥289**
Zhang *et al*. (Registry)	NSTE-ACS (n=228); emergent PCI	1-mo MACE	**PRU >272**
Ko *et al*. (Registry)	All comer (n=222); PCI	1-mo MACE	**PRU ≥ 274**
CILON-T (Randomized)	All comer (n=960); DES implantation	6-mo MACE	**PRU ≥ 252.5**
PRASFIT-ACS (Randomized)	ACS (n=660); PCI (99.1%)	6-mo MACE	**PRU >262**
Ahn *et al*. (Registry)	All comer (n=1,226); stenting	12-mo MACE	**Non-AMI: no cutoff** **AMI-PRU ≥272**
CROSS-VERIFY (Registry)	All comer (n=809); elective PCI	12-mo MACE	**PRU ≥275**

AMI, acute myocardial infarction; **DES**, drug-eluting stent; **MACE**, major adverse cardiovascular event; **NSTE-ACS**, non ST-elevation acute coronary syndrome; **PCI**, percutaneous coronary intervention; **PRU,** Platelet Reactivity Unit

References 1. Lee K, et al. Int J Cardiol. 2015;190:370-375. **2.** Zhang HZ, et al. Platelets. 2014;25(4):292-9. **3.** Ko YG, et al. Am Heart J. 2011 Feb;161(2):383-390. **4.** Suh JW, et al. J Am Coll Cardiol. 2011;57(3):280-289. **5.** Ahn SG, et *al.* JACC Cardio Interv 2012;5:259. **6.** Park KW, et al. Am J Cardiol. 2011;108:1556-1563.

East Asian Paradox: decoupling of clinical events with the level of platelet reactivity in response to antithrombotic therapy in East Asian patients

During antithrombotic treatment, East Asian patients have shown a lower risk of thromboembolic events and a higher tendency of bleeding.

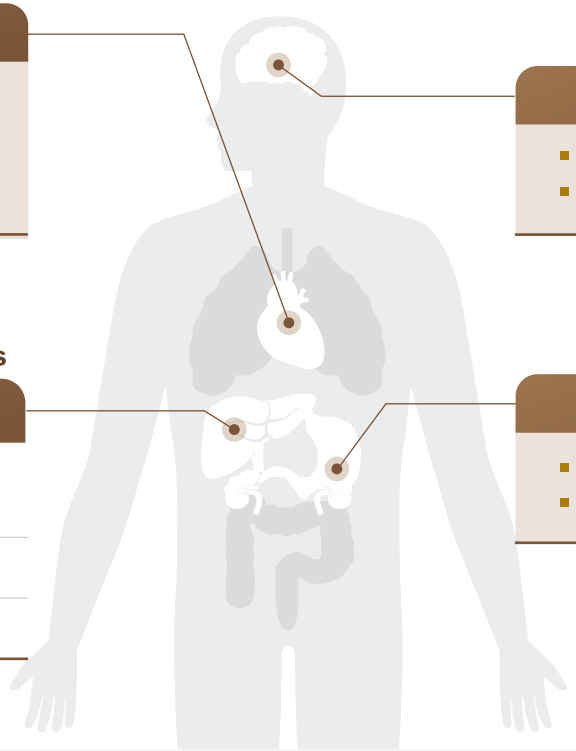
Unique characteristics of East Asian population in terms with ischemic & bleeding tendency

↓ *Ischemic event*

- ↓ CV death, MI
- ↓ Stent thrombosis
- ↓ Inflammation
- ↓ Coagulation activity

↑ *Hemorrhagic stroke*

- ↑ Lacunar infarct
- ↑ Hemorrhagic transformation



Different response to $P2Y_{12}$ receptor inhibitors

	Active metabolite concentration in blood	Mechanism
Clopidogrel	↓↓	↑CYP2C19 Loss of function allele (2*or3*) carriage (~65% of population)
Prasugrel	↑~30%	?
Ticagrelor	↑~40%	?

↑ *GI bleeding*

- ↑ *Helicobacter pylori* infection
- ↑ CYP polymorphism

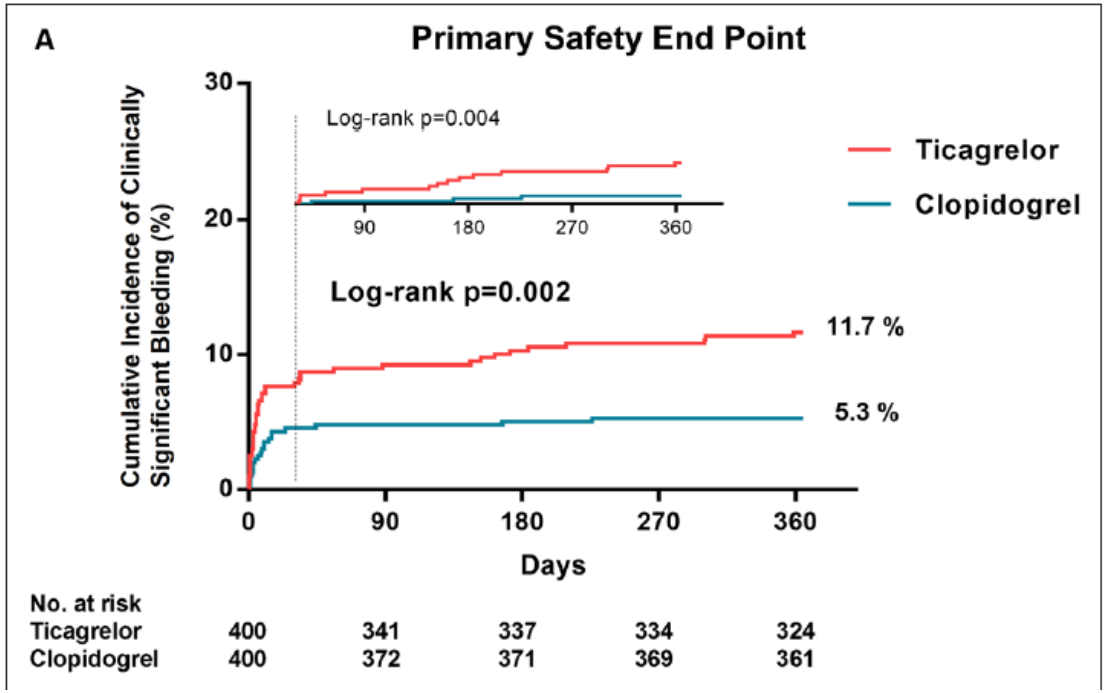
ACS, acute coronary syndrome; **CAD,** coronary artery disease; **DES,** drug-eluting stent; **DAPT,** dual antiplatelet therapy; **GI**, gastrointestinal; **LD,** loading dose; **MI**, myocardial infarction; **PCI,** percutaneous coronary intervention

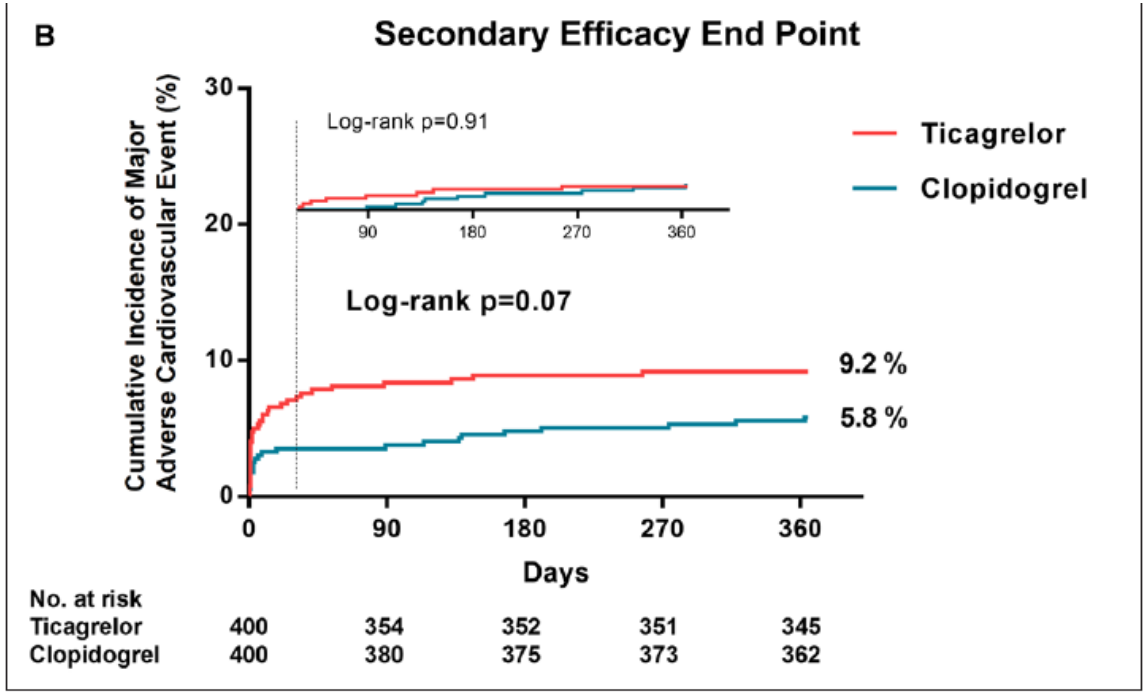
Reference 1. Huo Y, et al. Sci Bull (Beijing). 2019;64(3):166-179.

TICAKOREA

Compared with Clopidogrel, ticagrelor resulted in

significant higher bleeding events and numerically higher ischemic events in East Asian ACS patients





Circulation. 2019;140:00–00. DOI: 10.1161/CIRCULATIONAHA.119.041766

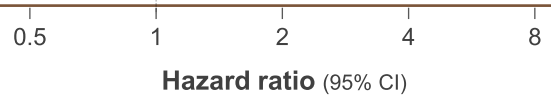
More Bleeding, Higher Mortality:

Impact of bleeding on mortality after PCI

17,034 patients from REPLACE-2, ACUITY and HORIZONS-AMI

Independent Hazard of the Occurrence of Different Types of Major Bleed within 30 Days on Subsequent Mortality within 1 Year

Type of bleed	Hazard Ratio (95% CI)	Deaths	*P* Value
TIMI major bleed	4.89 (3.61 to 6.63)	56	<0.001
Transfusion with TIMI minor bleed	2.73 (1.67 to 4.45)	18	<0.001
Transfusion with no TIMI bleed	2.91 (1.80 to 4.70)	20	<0.001
TIMI minor bleed with no transfusion	1.66 (1.09 to 2.50)	25	0.017
Hematoma ≥5 cm only	1.43 (0.64 to 3.21)	6	0.39



Study design This study represents a patient-level pooled analysis including 17,034 patients undergoing PCI from 3 large, randomized trials of bivalirudin versus heparin plus glycoprotein IIb/IIIa inhibitors, including the REPLACE-2 (Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events), ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy), and HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trials. We developed a risk score to predict noncoronary artery bypass graft (CABG)-related TIMI (Thrombolysis In Myocardial Infarction) major bleeding and evaluated the impact of various types of bleeding on 1-year mortality.

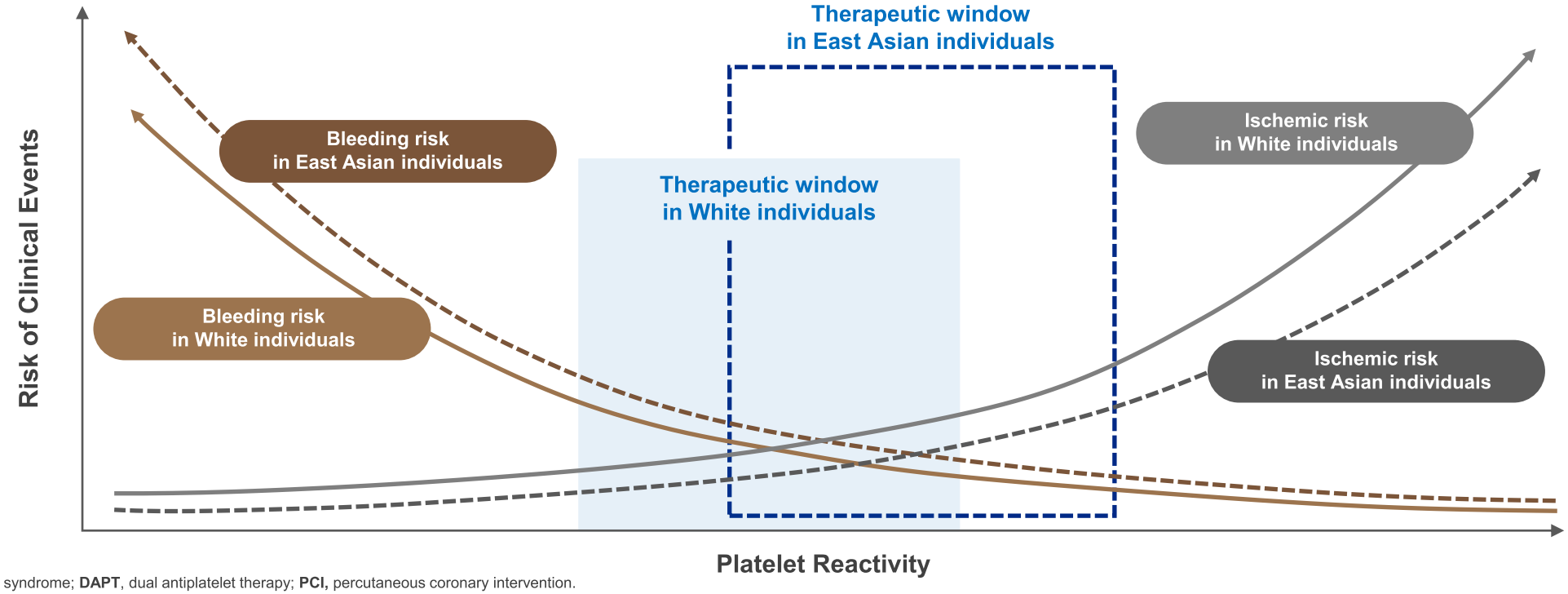
CI, confidence interval; **PCI,** percutaneous coronary intervention; **TIMI,** thrombolysis in myocardial infarction

Reference 1. Mehran R, et al. J Am Coll Cardiol Intv. 2011;4:654-664.

Balancing Ischemic and Bleeding Risks

- The findings suggest that the optimal ‘therapeutic window’ of platelet reactivity might differ between White and East Asian patients.
- The use of clopidogrel and aspirin may be a reasonable first choice of DAPT for, in particular, East Asian patients with ACS or undergoing PCI.

Postulated Differences in the Optimal ‘Therapeutic Window’ of Platelet Reactivity



ACS, acute coronary syndrome; **DAPT**, dual antiplatelet therapy; **PCI,** percutaneous coronary intervention.

Reference 1. Levine GN, et al. Nat Rev Cardio.l 2014;11:597-606.

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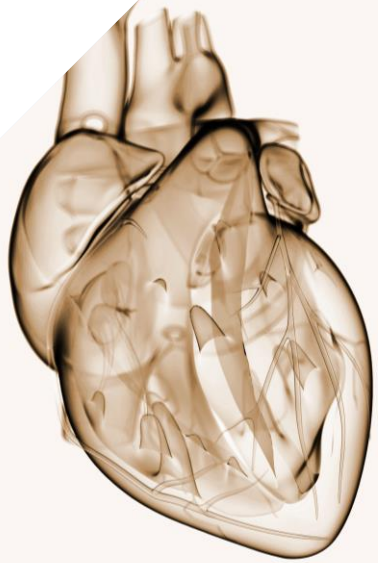
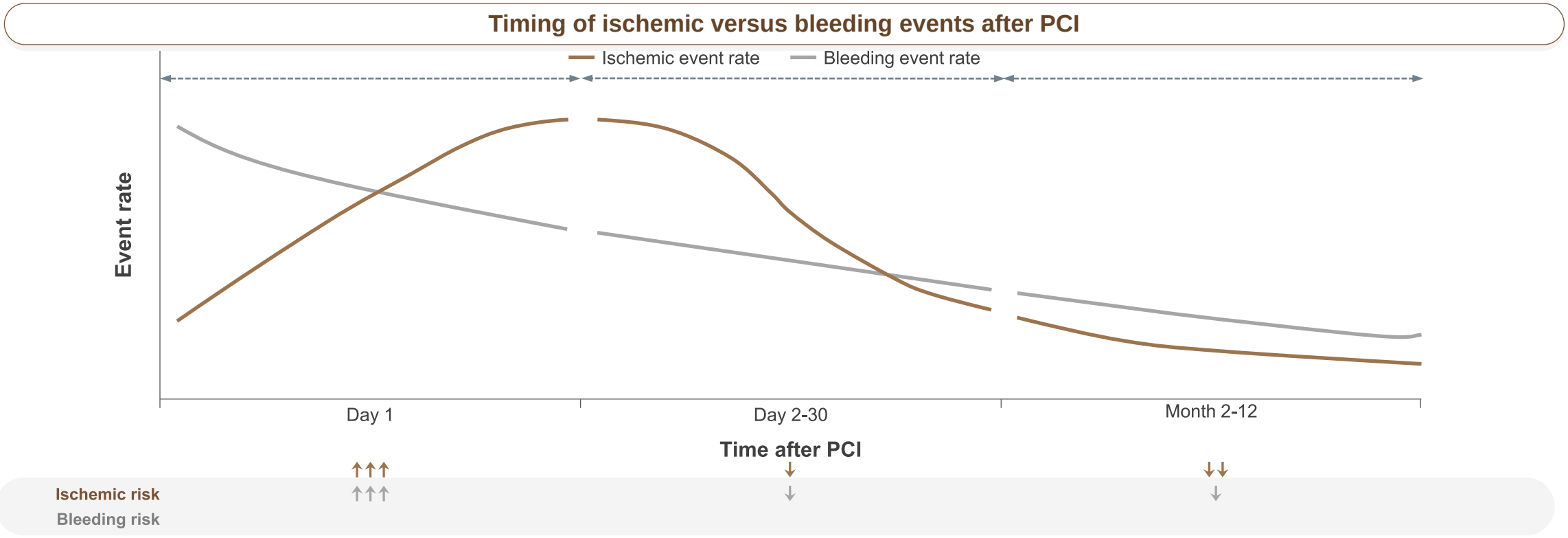


The Rationale for De-escalation Therapy

Timing of ischemic versus bleeding events after PCI

- **While ischemic rates reach a plateau during the first month, bleeding rates steadily decline.**
- **In the second month, ischemic events substantially decrease resulting in an exuberant bleeding risk in the later phase post-PCI.**



Ischemic and bleeding rates after PCI are displayed dependent on time.
PCI, percutaneous coronary intervention.

Reference 1. Kupka d, et al. Korean Circ J. 2018;48(10):863-872.

Strategies for a de-escalation

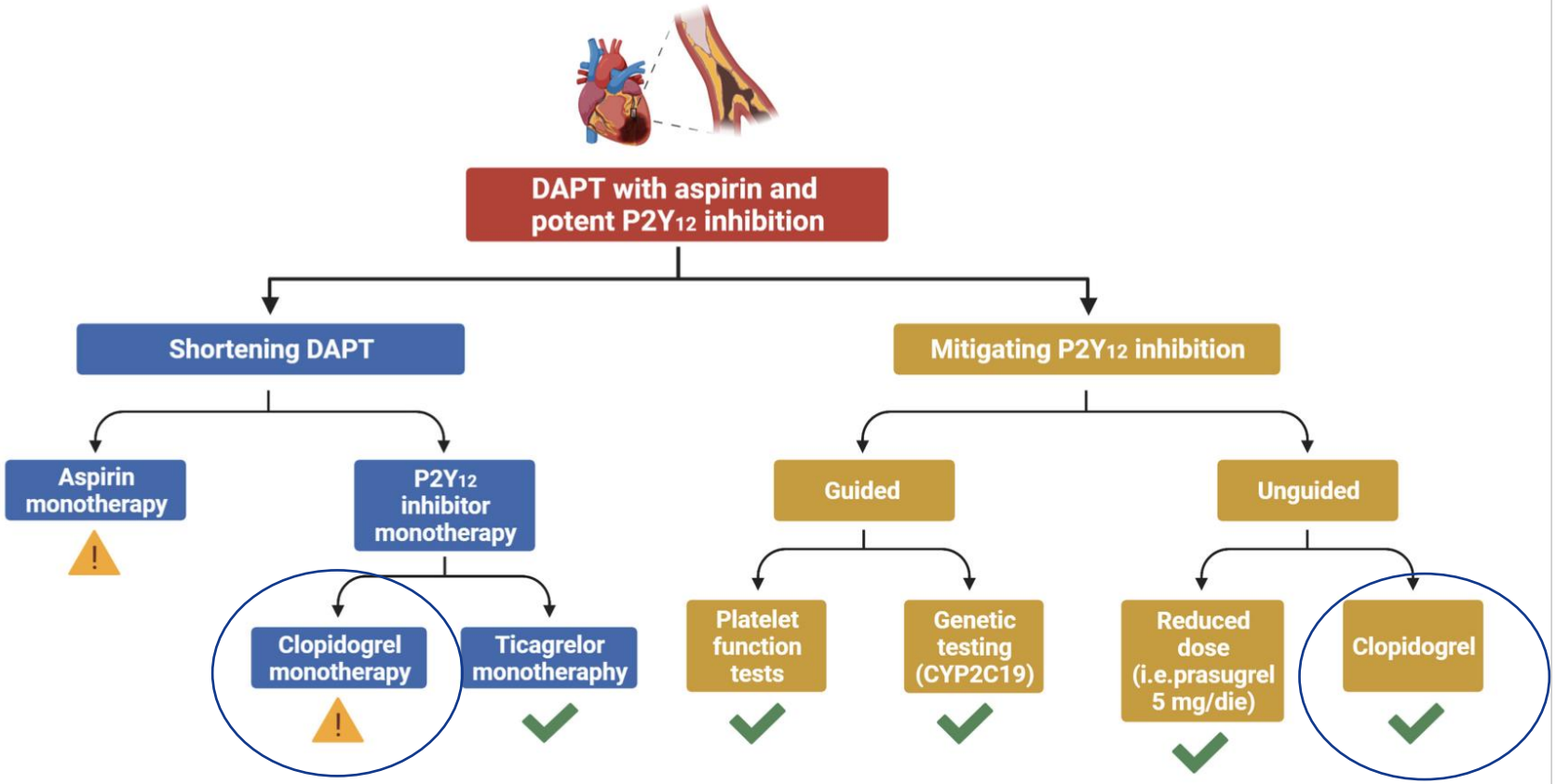


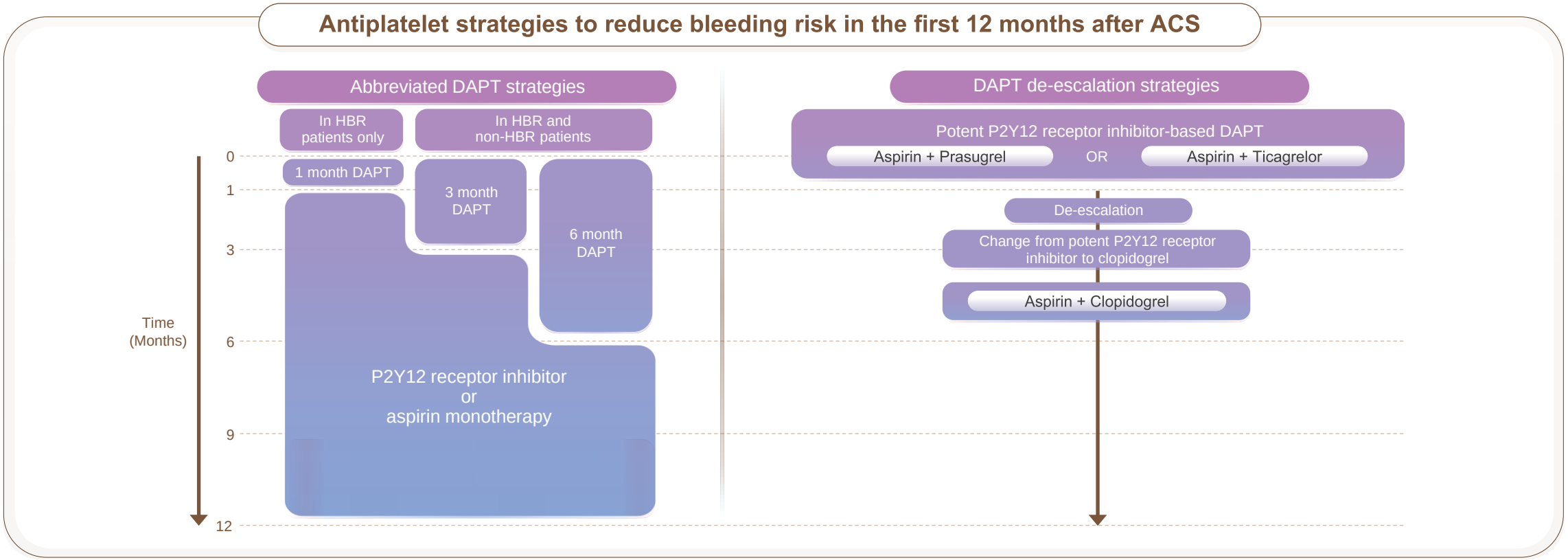
FIGURE 1
Strategies for a de-escalation of antiplatelet therapy among patients with ACS undergoing PCI. Yellow exclamation mark, strategy associated with possible increased ischemic risk. Green check, strategy not associated with any trade-off in ischemic events. ACS, acute coronary syndrome; DAPT, dual antiplatelet therapy; CYP, cytochrome P450.

Front. Cardiovasc. Med. 9:975969. doi: 10.3389/fcvm.2022.975969

ESC Guidelines

Alternative antiplatelet strategies to reduce bleeding risk in the first 12 months after an ACS

Alternatives to the default strategy of 12 months DAPT in patients with ACS include shortening the DAPT duration to 1 or 3-6 months (depending on the balance of bleeding and ischaemic risks) **and de-escalating DAPT from prasugrel/ticagrelor-based DAPT to clopidogrel-based DAPT**



ACS, acute coronary syndrome; **DAPT,** dual antiplatelet therapy; **ESC**, European Society of Cardiology; **HBR,** high bleeding risk.

Reference 1. Byrne RA, et al. Eur Heart J. 2023ug 25:ehad191.

ESC Guidelines

Recommended de-escalation of P2Y12 receptor inhibitor

2018 ESC Guidelines on myocardial revascularization

Recommendations	Class[a]	Level[b]
De-escalation of P2Y12 receptor inhibitor treatment (e.g. with a switch from prasugrel or ticagrelor to clopidogrel) **guided by** platelet function testing may be considered as an alternative DAPT strategy, especially for ACS patients deemed unsuitable for 12-month potent platelet inhibition	IIb	B

2020 ESC Guidelines of NSTE-ACS

Shortening antithrombotic treatment duration		
After stent implantation witn high risk of bleed-ing (e.g. PRECISE-DAPT-DAPT ≥25 or ARC-HBR cri-teria met), discontinuation of P2Y12 receptor inhibitor therapy after 3 months should be considered.[154.226]	IIa	B
After stent implantation in patients undergoing a strategy of DAPT, **stopping aspirin after 3-6 months should be considered**, depending on the balance between the ischaemic and bleeding risk.[208.209.227]	IIa	A
De-escalation of $P2Y_{12}$ receptor inhibitor treatment (e.g. with a switch from prasugrel or ticagrelor to clopidogrel) may be considered as an altenative DAPT strategy, especially for ACS patients deemed unsuitable for potent platelet inhibition. **De-escalation may be done unguided based on clinical judgment** or guided by platelet function testing or CYP2C19 genotyping, depending on patient's risk profile and availability of respective assays.[218.220.221]	IIb	A

Classes of recommendations: I, recommended/indicated; IIa, should be considered; IIb, may be considered; III, not recommendation [a]Class of recommendation; [b]Level of evidence; A, Data derived from multiple randomized clinical trials or meta-analyses; B, Data derived from a single randomized clinical trial or large non-randomized studies; C, Consensus of opinion of the experts and/or small studies, retrospective studies, registries.
ACS, acute coronary syndrome; **DAPT,** dual antiplatelet therapy.

References 1. Neumann FJ, et al. Eur Heart J. 2019;40(2):87-165. **2.** Collet JP, et al. Eur Heart J. 2020;42(14):1289-1367.

ESC Guidelines

Recommended de-escalation of P2Y12 receptor inhibitor treatment

2023 ESC Guidelines for management of ACS

Recommendations for alternative antithrombotic therapy regimens	Class[a]	Level[b]
Shortening/de-escalation of antithrombotic therapy		
In patients who are event-free after 3-6 months of DAPT and who are not high ischaemic risk, single antiplatelet therapy (preferably with a $P2Y_{12}$ receptor inhibitor) should be considered.	IIa	A
P2Y12 receptor inhibitor monotherapy may be considered as an alternative to aspirin monotherapy for long-term treatment.	IIb	A
In HBR patients, aspirin or $P2Y_{12}$ receptor inhibitor monotherapy after 1 month of DAPT may be considered.	IIb	B
De-escalation of antiplatelet therapy in the first 30 days after an ACS event is not recommended.	III	B

[a]Class of recommendation.; [b]Level of evidence.
ACS, acute coronary syndrome; **DAPT**, dual antiplatelet therapy;

Reference 1. Byrne RA, et al. Eur Heart J. 2023 Aug 25:ehad191.

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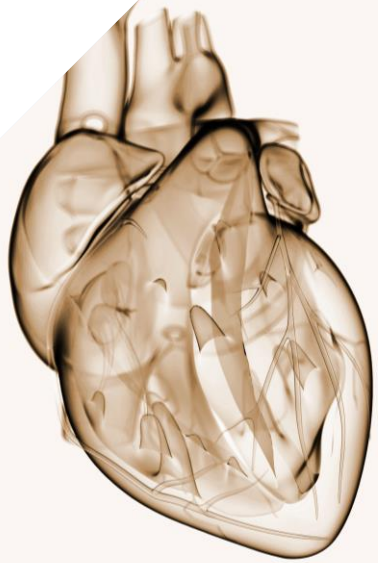
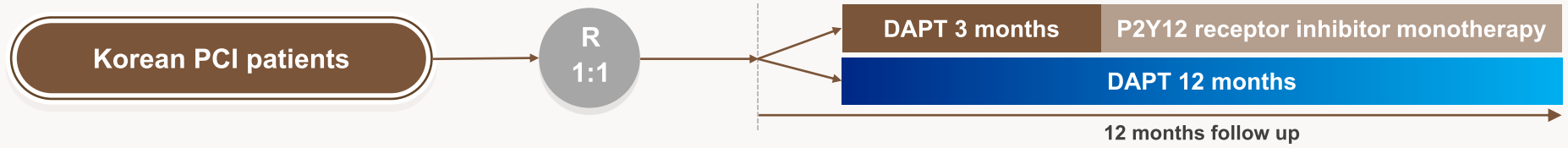


SMART-CHOICE

- An open-label, noninferiority, randomized study that was conducted in 33 hospitals in Korea
- 2,993 patients undergoing PCI with drug-eluting stents.
- Patients were randomly assigned to receive aspirin plus a P2Y12 receptor inhibitor for 3 months and thereafter P2Y12 receptor inhibitor alone (n=1,495) or DAPT for 12 months (n=1,498).



- The primary end point was major adverse cardiac and cerebrovascular events(a composite of all-cause death, myocardial infarction, or stroke) at 12 months after the index procedure.
- Secondary end points included the components of the primary end point and bleeding defined as Bleeding Academic Research Consortium type 2 to 5.
- Adherence to the study protocol was 79.3% of the P2Y12 receptor inhibitor monotherapy group and 95.2% of the DAPT group.

Discharge P2Y12 receptor inhibitor

	P2Y12 receptor inhibitor monotherapy (n=1,495)	DAPT (n=1,498)
P2Y12 receptor inhibitor	1,493/1,495 (99.9)	1,496/1,498 (99.9)
Clopidogrel	1,149/1,495 (76.9)	1,163/1,498 (77.6)
Prasugrel	62/1,495 (4.1)	67/1,498 (4.5)
Ticagrelor	284/1,495 (19.0)	268/1,498 (17.9)

DAPT, dual antiplatelet therapy; **PCI,** percutaneous coronary intervention.

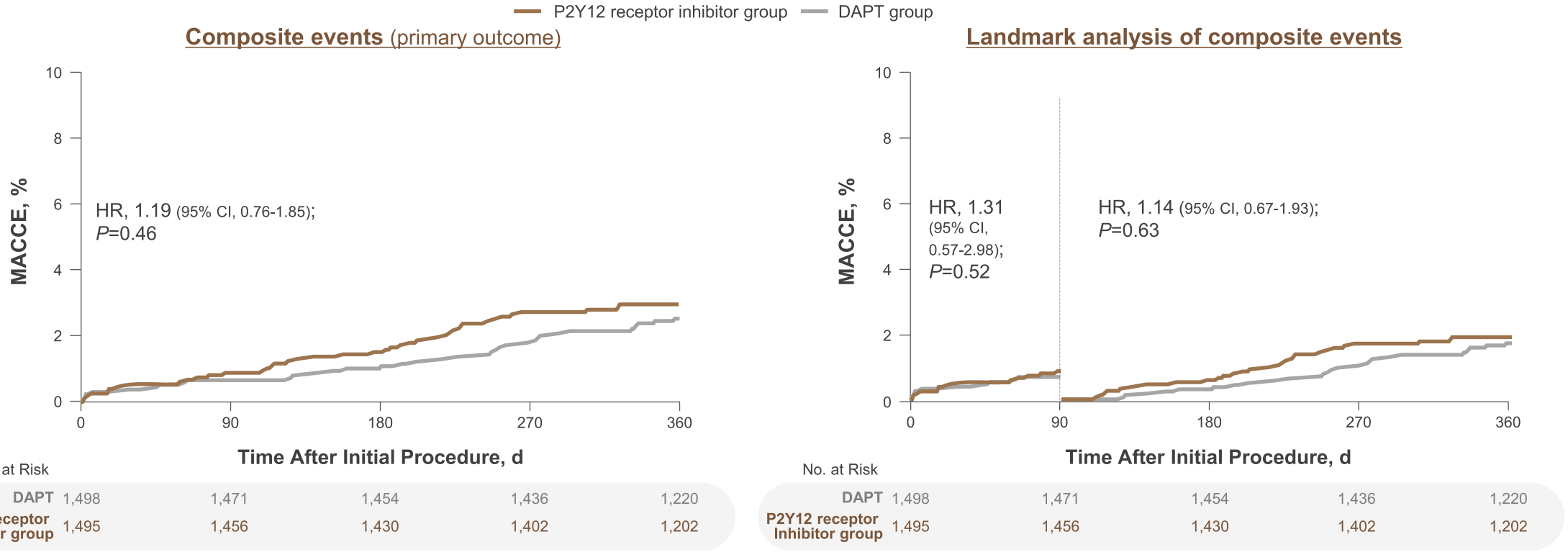
Reference 1. Hahn JY, et al. JAMA. 2019;321(24):2428-2437 and suppl.

SMART-CHOICE

Primary endpoint (A composite of all-cause death, myocardial infarction, or stroke)

At 12 months, MACCE occurred in 42 patients in the P2Y12 receptor inhibitor monotherapy group and in 36 patients in the DAPT group (2.9% and 2.5%; 1-sided 95% CI, -∞%to 1.3%; *P*=0.007 for noninferiority).

Time-to-Event Curves for the Major Adverse Cardiovascular and Cerebrovascular Events and Landmark Analysis at 3 Months



No. at Risk

DAPT	1,498	1,471	1,454	1,436	1,220
P2Y12 receptor Inhibitor group	1,495	1,456	1,430	1,402	1,202

No. at Risk

DAPT	1,498	1,471	1,454	1,436	1,220
P2Y12 receptor Inhibitor group	1,495	1,456	1,430	1,402	1,202

Event rates were based on Kaplan-Meier estimates in time-to-first-event analyses. Hazard ratios are for the patients in the P2Y12 receptor inhibitor monotherapy group.; MACCE was defined as a composite of all-cause death, myocardial infarction, or stroke. Landmark analysis were performed at 3 months (the point after which one group received P2Y12 receptor inhibitor only and the other received DAPT).
CI, confidence interval; **DAPT,** dual antiplatelet therapy; **HR,** hazard ratio; **MACCE,** major adverse cardiac and cerebrovascular events.

Reference 1. Hahn JY, et al. JAMA. 2019;321(24):2428-2437.

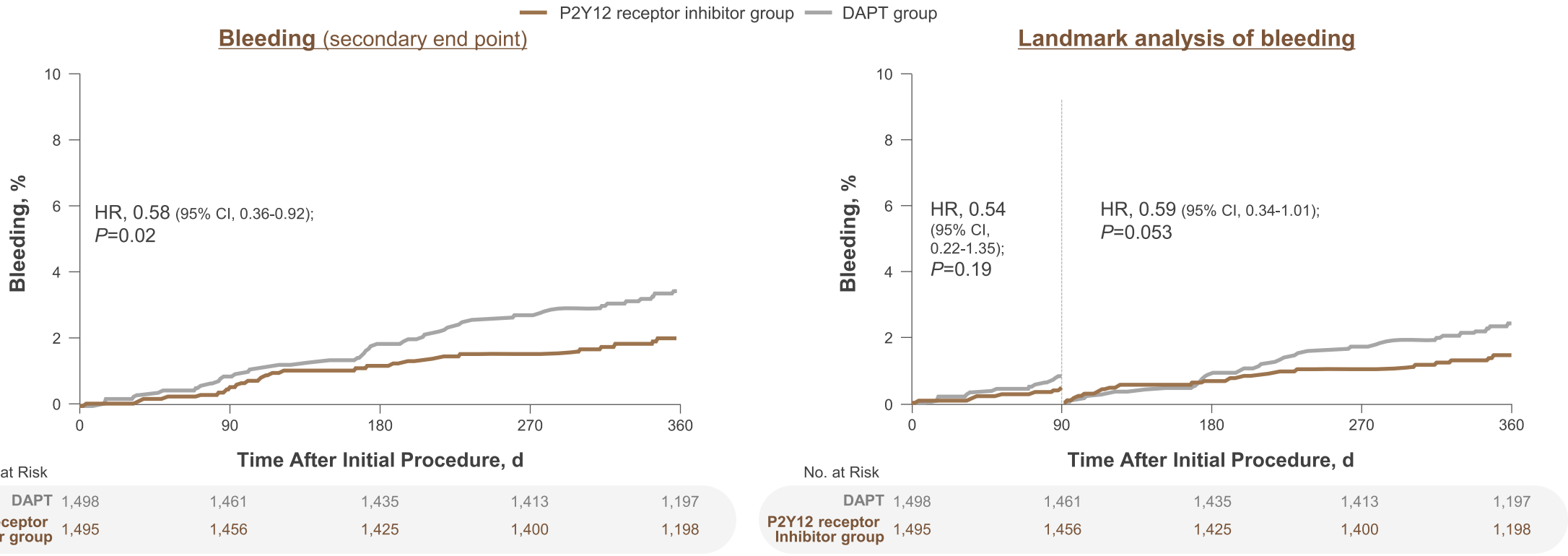
Plavix Clopidogrel 75mg Take Protection Further. Today.

SMART-CHOICE

Secondary end point

The rate of bleeding was significantly lower in the P2Y12 receptor inhibitor monotherapy group than in the DAPT group (2.0% and 3.4%; HR, 0.58; 95%CI, 0.36-0.92; *P*=0.02)**.**

Time-to-Event Curves for the Bleeding and Landmark Analysis at 3 Months



Event rates were based on Kaplan-Meier estimates in time-to-first-event analyses. Hazard ratios are for the patients in the $P2Y_{12}$ inhibitor monotherapy group. Landmark analysis were performed at 3 months (the point after which one group received P2Y12 receptor inhibitor only and the other received DAPT.

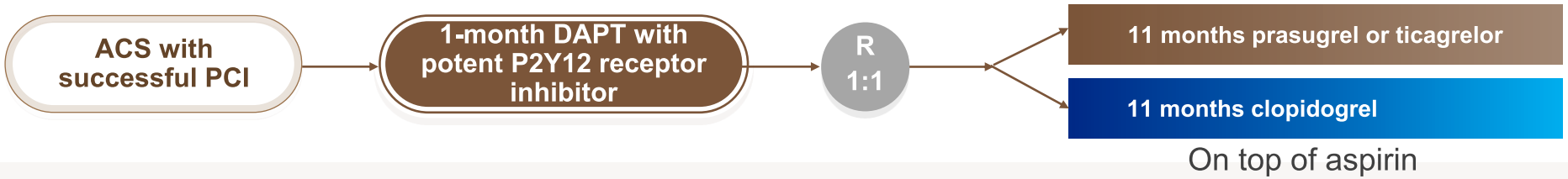
CI, confidence interval; **DAPT,** dual antiplatelet therapy; **HR,** hazard ratio

Reference 1. Hahn JY, et al. JAMA. 2019;321(24):2428-2437.

TOPIC

- An open-label, monocentric, and randomized trial. From March 2014 to April 2016, French patients admitted with ACS requiring coronary intervention, on aspirin and a newer P2Y12 receptor blocker and without adverse event at 1 month, were assigned to switched DAPT or unchanged DAPT.

- **Treatment**
  - **Switched DAPT**: switch to aspirin and clopidogrel (de-escalation)
  - **Unchanged DAPT**: continuation of their drug regimen



- The primary outcome was a composite of cardiovascular death, urgent revascularization, stroke and bleeding as defined by the Bleeding Academic Research Consortium (BARC) classification ≥2 at 1 year post ACS

ACS, acute coronary syndrome, **DAPT,** dual antiplatelet therapy, **PFT**, platelet function testing; **TOPIC**, timing of optimal platelet inhibition after acute coronary syndrome; **TROPICAL-ACS**, Testing Responsiveness to Platelet Inhibition on Chronic Antiplatelet Treatment for Acute Coronary Syndrome.

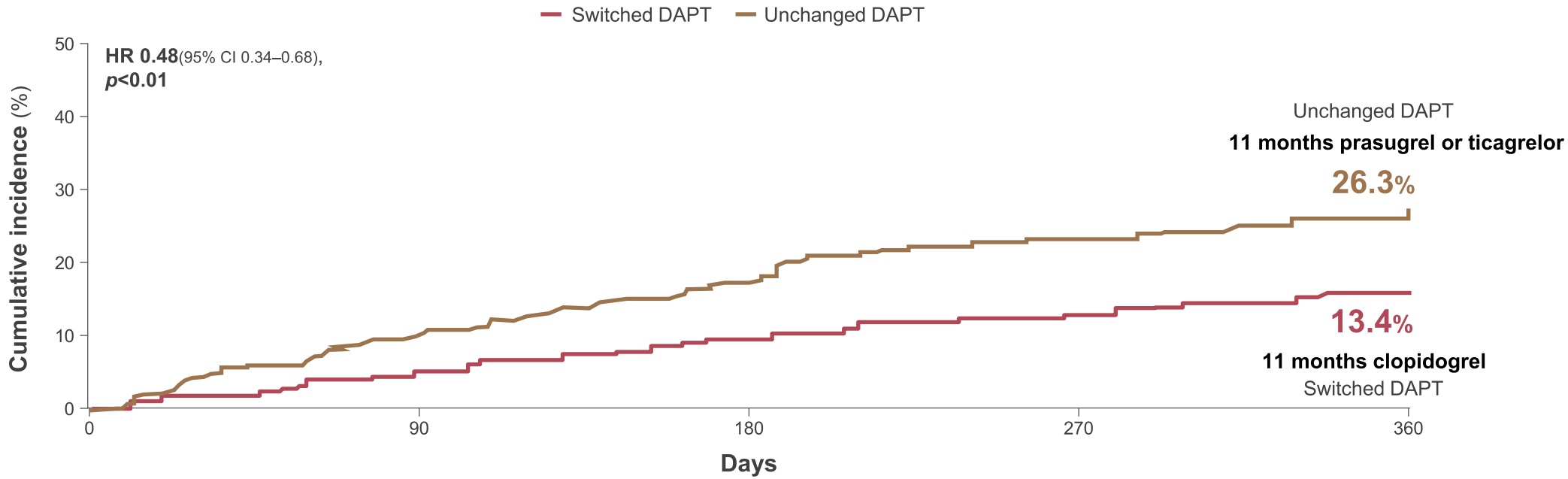
Reference 1. Kupka d, et al. Korean Circ J. 2018;48(10):863-872.

TOPIC :

Better prognosis with switched DAPT

During the 1 year follow-up, the rate of primary endpoint (net clinical benefit) **occurred in 43** (13.4%) **patients in the switched DAPT group and in 85** (26.3%) **patients in the unchanged DAPT group** (HR 95% CI 0.48 (0.34-0.68), *P*<0.01).

Incidence of the primary endpoint (net clinical benefit) **at 1 year**



No. at Risk

Switched DAPT	322	309	295	284	273
Unchanged DAPT	323	289	266	246	233

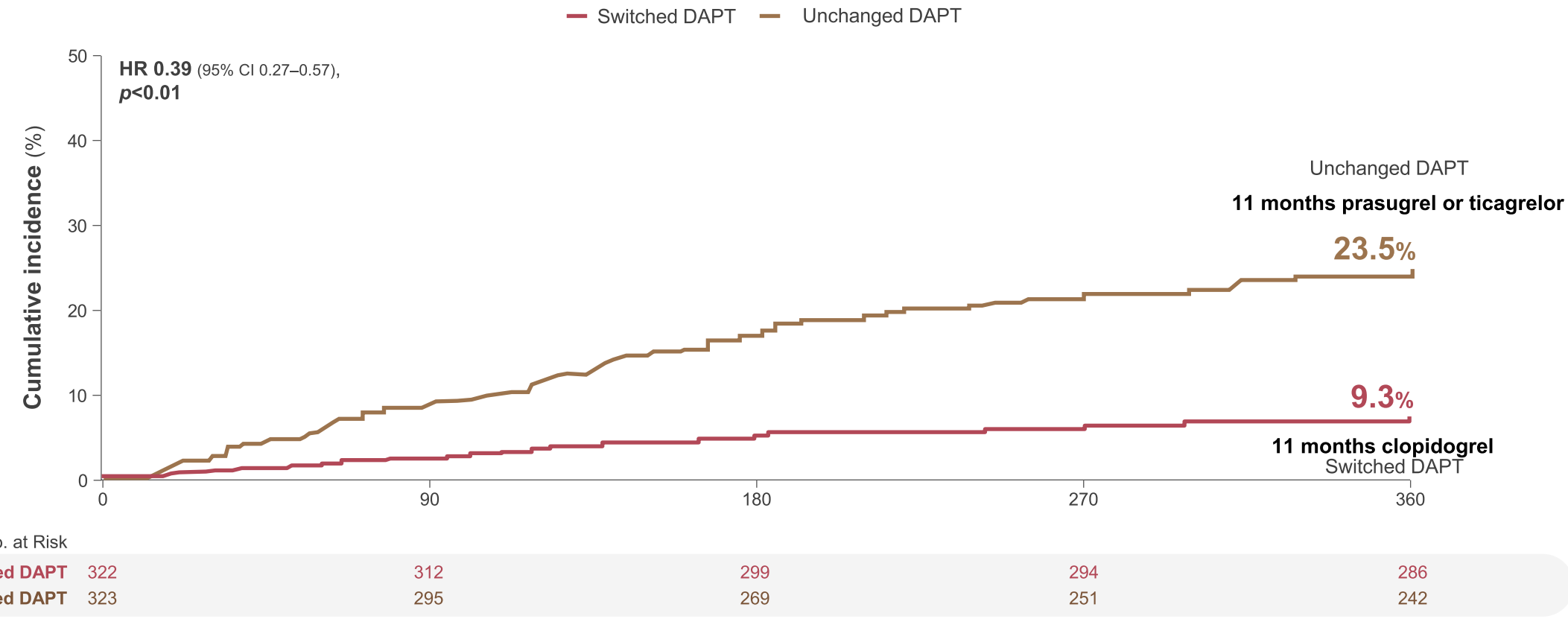
CI, confidence interval; **DAPT,** dual antiplatelet therapy; **HR,** Hazard ratio.

Reference 1. Cuisset T, et al. Eur Heart J. 2017;38(41):3070-3078.

TOPIC:

Higher Rate of all BARC bleeding with Unchanged DAPT

Bleeding events defined as all BARC occurred in 30 (9.3%) **patients in the switched DAPT group and in 76** (23.5%) **in the unchanged DAPT group** (HR 95% CI 0.39 (0.27-0.57), *P*<0.01)



No. at Risk

Switched DAPT	322	312	299	294	286
Unchanged DAPT	323	295	269	251	242

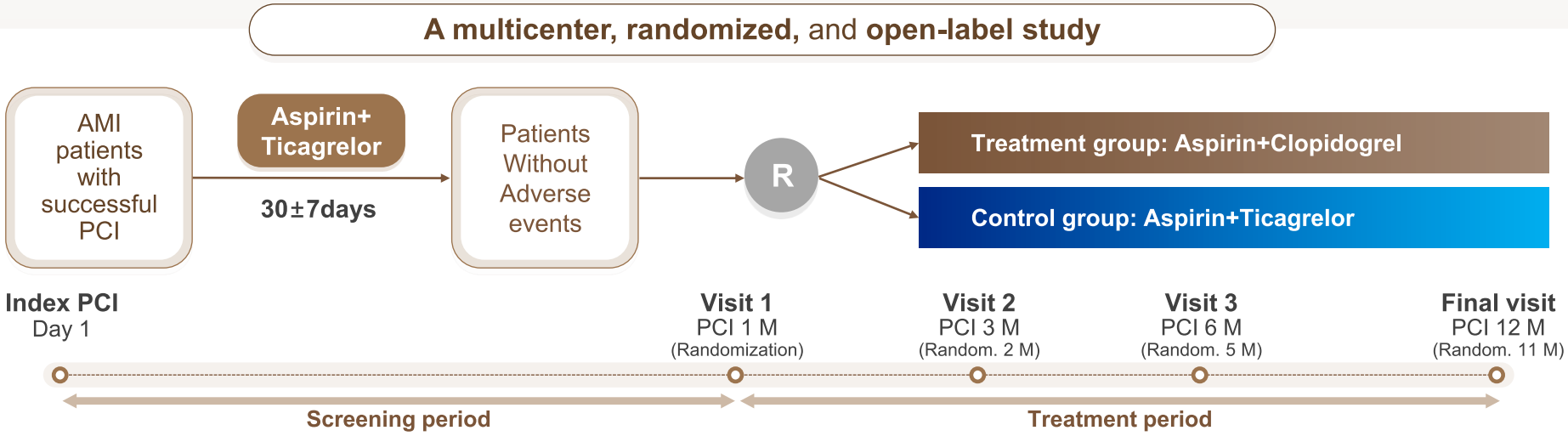
BARC, Bleeding Academic Research Consortium; **CI,** confidence interval; **DAPT**, dual antiplatelet therapy; **HR,** Hazard ratio.

Reference 1. Cuisset T, et al. Eur Heart J. 2017;38(41):3070-3078.

TALOS-AMI

Switching potent P2Y12 receptor inhibitor to Clopidogrel at the 1st-month post PCI

- **A multicenter, randomized, and open-label study conducted in South Korea**
- **N=2,697, AMI patients receiving ticagrelor+ASA and without major events in the first month after index PCI were randomized to the de-escalation group** (clopidogrel + aspirin, N=1,349) **or active control group** (continuing ticagrelor + ASA, N=1,348). **Patients were followed up until 12 months after PCI.**
- **In TALOS-AMI trial, a uniform, unguided de-escalation** (no platelet function testing, non-genotype-guided) **was performed. After the final dose of ticagrelor, clopidogrel 75 mg was given without loading dose.**



ASA, acetyl salicylic acid; **PCI,** percutaneous coronary intervention; **TALOS-AMI,** The Ticagrelor versus Clopidogrel in Stabilized Patients with acute myocardial infarction

Reference 1. Kim, CJ, et al. Lancet. 2021;398(10308):1305-1316.

TALOS-AMI

Outcomes

Primary endpoint: Net adverse clinical events

- A composite of cardiovascular death, myocardial infarction, stroke, and bleeding type 2, 3, or 5 according to the BARC criteria, from 1 to 12 months after an index PCI

Main secondary endpoints:

- A composite of BARC bleeding type 2, 3 or 5 (safety)
- A composite of CV death, MI or ischemic stroke
- A composite of cardiovascular death, myocardial infarction ,stroke, and BARC bleeding type 3 or 5

Other secondary endpoints:

- Individual components of the primary and main secondary endpoints
- All-cause death
- Ischaemia-driven revascularization
- Stent thrombosis

BARC, Bleeding Academic Research Consortium; **CV,** cardiovascular; **MI,** myocardial infarction; **PCI,** percutaneous coronary intervention; **TALOS-AMI**, The Ticagrelor versus Clopidogrel in Stabilized Patients with acute myocardial infarction

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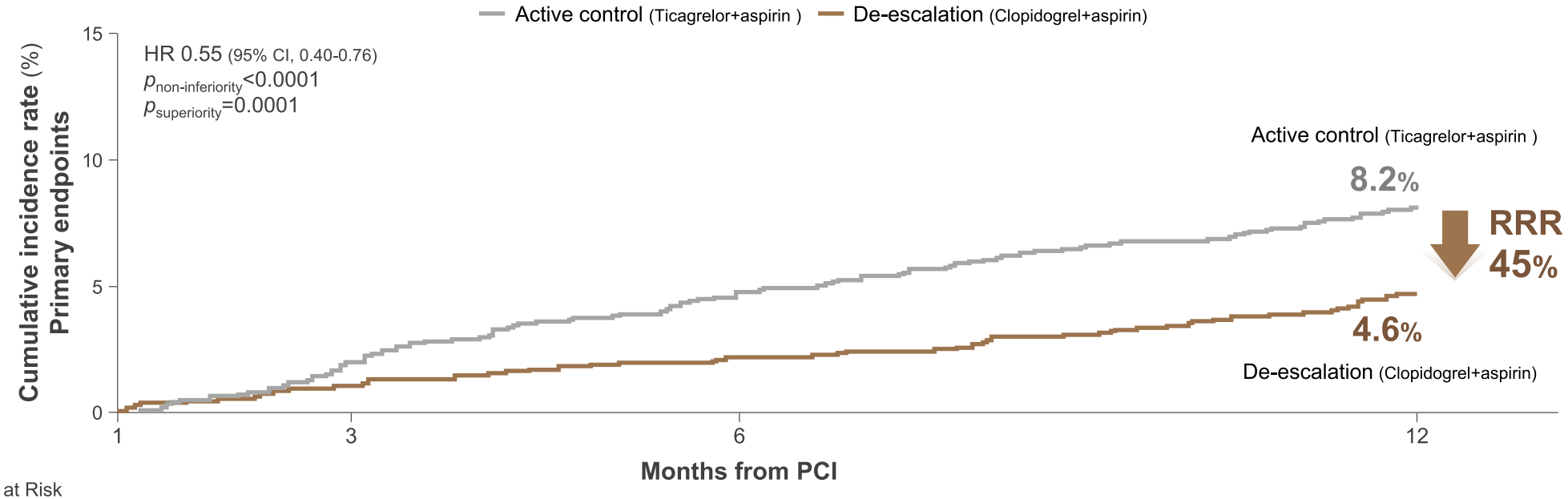
TALOS-AMI

Primary endpoint: Net adverse clinical events

- **Demographic, clinical, and procedural data were similar between the two groups.**
- **At 12 months, the primary endpoints occurred in 59** (4.6%) **in the de-escalation group and 104** (8.2%) **patients in the active control group** ($p_{non\text{-}inferiority}$<0.001; HR 0.55 [95% CI 0.40-0.76], $p_{superiority}$=0.0001)**.**

Estimates for the primary endpoint (A composite of CV death, MI, stroke, and BARC bleeding type 2,3, or 5 from 1 to 12 months after PCI)



No. at Risk

Active control	1,348	1,273	1,191	1,099
De-escalation	1,349	1,291	1,247	1,172

BARC, Bleeding Academic Research Consortium; **CV,** cardiovascular; **HR,** hazard ratio; **MI,** myocardial infarction; **PCI,** percutaneous coronary intervention; **RRR,** relative risk reduction; **TALOS-AMI,** The Ticagrelor versus Clopidogrel in Stabilized Patients with acute myocardial infarction

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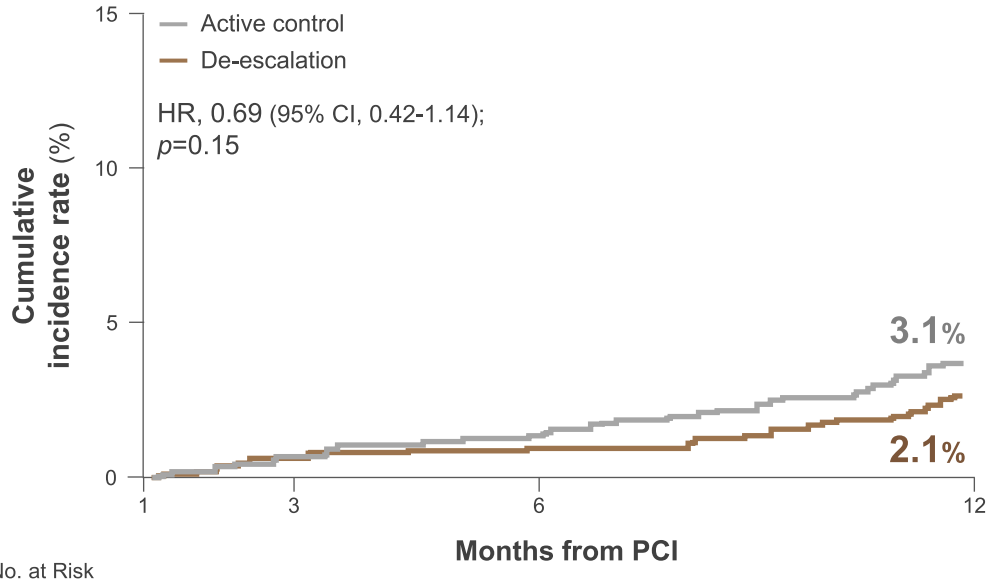
TALOS-AMI

Main secondary endpoints

- **There was no significant difference in the composite of cardiovascular death, myocardial infarction, and stroke between the de-escalation and active control groups** (27 [2.1%] vs 38 [3.1%]; HR 0.69, 95% CI 0.42-1.14, *p*=0.15).
- **A composite of BARC bleeding type 2, 3, or 5 occurred significantly less frequently in the de-escalation group than in the active control group** (38 [3.0%] vs 71 [5.6%]; HR 0.52, 95% CI 0.35-0.77, *p*=0.0012)

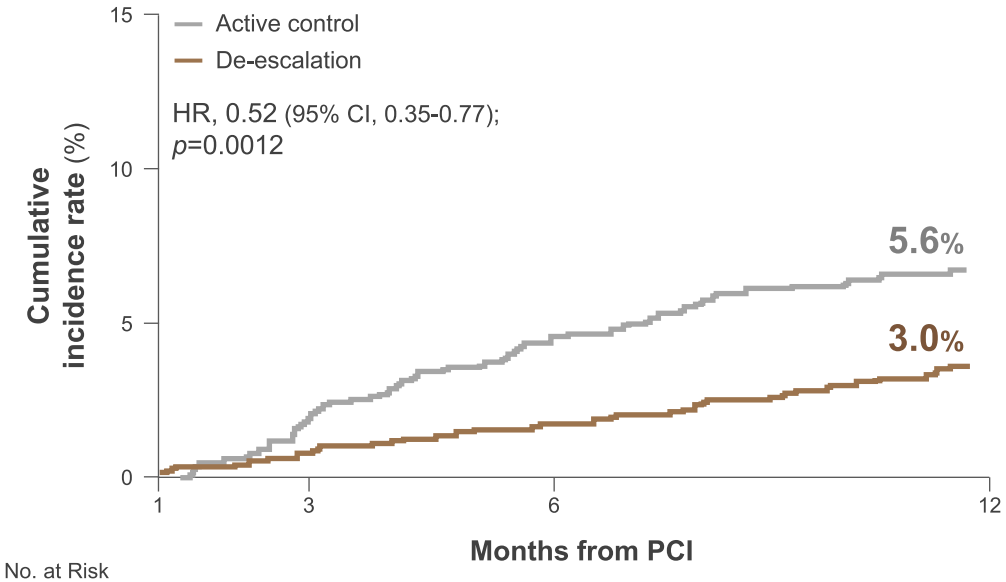
Composite of cardiovascular death, MI, stroke



No. at Risk

Active control	1,348	1,288	1,226	1,147
De-escalation	1,349	1,299	1,264	1,201

Composite of BARC bleeding (type 2,3, or 5)



No. at Risk

Active control	1,348	1,276	1,197	1,120
De-escalation	1,349	1,293	1,251	1,180

BARC, Bleeding Academic Research Consortium; **CI**, confidential interval; **HR,** hazard ratio; **MI,** myocardial infarction; **PCI,** percutaneous coronary intervention; **TALOS-AMI,** The Ticagrelor versus Clopidogrel in Stabilized Patients with acute myocardial infarction

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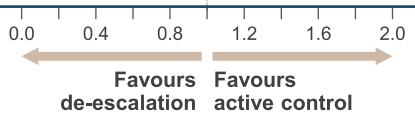
TALOS-AMI

Primary endpoint: Net adverse clinical events

The HRs for the primary endpoint favoring de-escalation were consistent across the prespecified subgroups

Subgroup analysis of the primary endpoint (In prespecified subgroups of the present study population)

		De-escalation group	Active control group	Hazard ratio (95% CI)	$P_{interaction}$
Clinical presentation	STEMI	4.1% (30/734)	8.0% (58/721)	0.50 (0.32-0.78)	0.53
	NSTEMI	4.7% (29/615)	7.3% (46/627)	0.62 (0.39-0.98)	
Sex	Male	4.7% (53/1132)	7.8% (87/1111)	0.58 (0.41-0.82)	0.43
	Female	2.8% (6/217)	7.2% (17/237)	0.39 (0.16, 0.98)	
Age (years)	≥75	6.4% (10/157)	11.6% (19/164)	0.55 (0.26, 1.18)	0.98
	<75	4.1% (49/1192)	7.2% (85/1184)	0.56 (0.39, 0.79)	
Diabetes	Yes	4.1% (15/362)	7.9% (29/369)	0.51 (0.27, 0.95)	0.78
	No	4.5% (44/987)	7.7% (75/978)	0.57 (0.39, 0.82)	
LVEF	≥40%	4.1% (50/1222)	7.3% (89/1211)	0.54 (0.38, 0.76)	0.79
	<40%	7.8% (8/103)	16.1% (15/93)	0.48 (0.20, 1.12)	
eGFR	≥60	4.0% (47/1161)	6.9% (82/1180)	0.57 (0.40, 0.81)	0.64
	<60	6.3% (10/160)	13.1% (19/145)	0.47 (0.22, 1.00)	
Stent length	<40	4.3% (48/1120)	7.5% (86/1144)	0.55 (0.39, 0.79)	0.97
	≥40	5.0% (11/221)	8.7% (17/196)	0.57 (0.27, 1.21)	
Multivessel treatment	Single vessel	4.0% (39/978)	7.5% (72/965)	0.52 (0.35, 0.76)	0.57
	Multivessel	5.4% (20/371)	8.4% (32/383)	0.64 (0.36, 1.11)	



CI, confidential interval; **eGFR**, estimated glomerular filtration; **LVEF**, left ventricular ejection fraction; **NSTEMI**, non-STEMI; **STEMI**, ST elevation myocardial infarction; **TALOS-AMI,** The Ticagrelor versus Clopidogrel in Stabilized Patients with acute myocardial infarction

Reference 1. Kim, CJ, et al. Lancet. 2021;398(10308):1305-1316.

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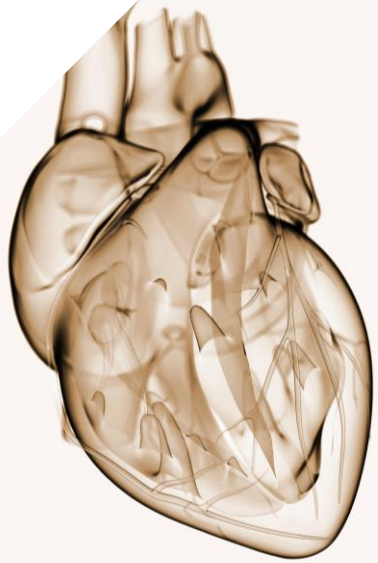

Summary

- **Unique Characteristics of East Asian:** Asian patients have different risk profiles for both thrombogenicity and bleeding compared with Caucasian patients[1]
- **De-escalation strategy:** Safety concerns associated with switching between antiplatelet agents, has prompted the use of clopidogrel for patients with ACS especially after PCI as a de-escalation strategy[2]
- The de-escalation strategy to clopidogrel had a **net clinical benefit with a significant decrease in bleeding risk and no increase in ischemic risk especially in East Asian patients with ACS or undergoing PCI.**[3]

Always **balance the risk of thrombosis and bleeding and choose the most appropriate therapy** for our patients

ACS, acute coronary syndrome; **CCS,** chronic coronary syndrome; **DAPT,** dual antiplatelet therapy; **PCI,** percutaneous coronary intervention

References 1. Huo Y, et al. Sci Bull (Beijing). 2019;64(3):166-179. **2.** Han YL. Chin Med J (Engl). 2019;132(2):197-210. **3.** Kim CJ, et al. Lancet. 2021;398(10308):1305-1316.