

# Potent P2Y12 Inhibitors for East-Asian Patients: Insights from the TWILIGHT in Western vs. Asian Population

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# Disclosures

Affiliation/Financial Relationship	Company
<b>Consultant/Advisory/Speaking Engagements</b>	Boston Scientific, Cine-Med Research, Janssen, Medscape/WebMD
<b>Research Funding to Institution</b>	Abbott, Abiomed, Applied Therapeutics, AstraZeneca, Bayer, Beth Israel Deaconess, BMS, CERC, Chiesi, Concept Medical, CSL Behring, DSI, Medtronic, Novartis, OrbusNeich, Zoll.
<b>Advisory Board, paid to the institution</b>	Abbott Laboratories, Abiomed (spouse), Bayer (spouse), Beth Israel Deaconess, BMS, CardiaWave, Chiesi, Concept Medical, DSI, Duke University, Idorsia Pharmaceuticals, Medtronic, Novartis, Regeneron (no fee), Spectranetics/Philips/Volcano Corp
<b>Equity, &lt;1%</b>	Applied Therapeutics, Claret Medical, ControlRad (spouse), Elixir Medical, STEL
<b>Associate Editor</b>	ACC, AMA

# East-Asian Paradox

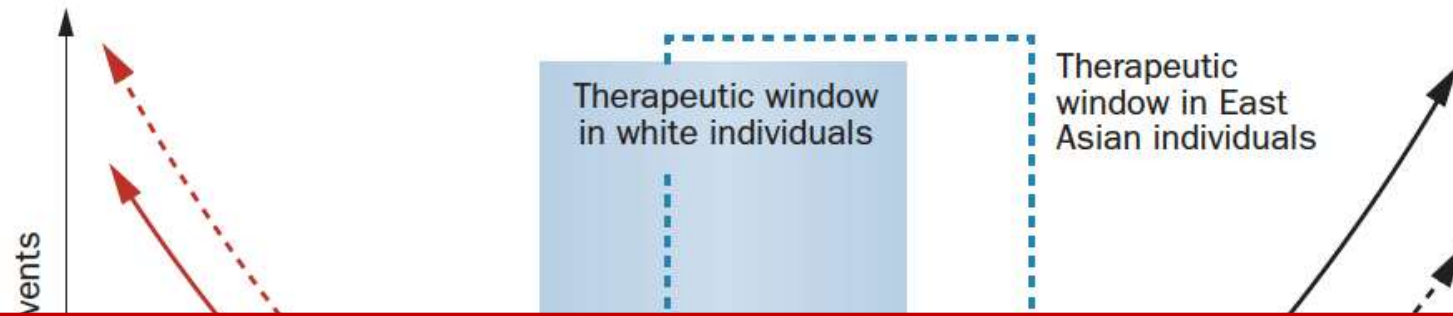
EXPERT CONSENSUS DOCUMENT

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

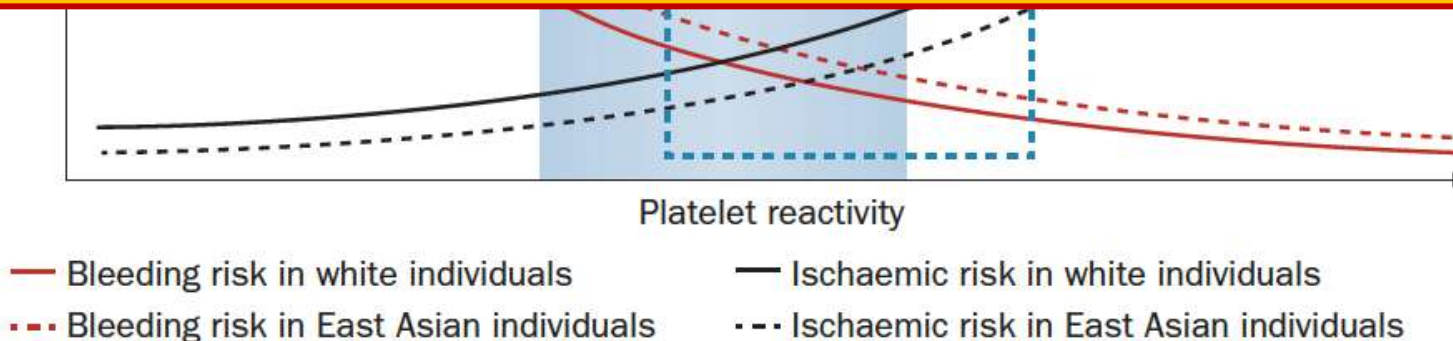
*Glenn N. Levine, Young-Hoon Jeong, Shinya Goto, Jeffrey L. Anderson, Yong Huo, Jessica L. Mega, Kathryn Taubert and Sidney C. Smith Jr*

**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 P2Y<sub>12</sub> 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.

# “East-Asian Paradox”



*Which Antiplatelet Regimen Is Optimal for East-Asian Patients?*



**Figure 2** | Postulated differences in the optimal ‘therapeutic window’ of platelet reactivity between white and East Asian populations.

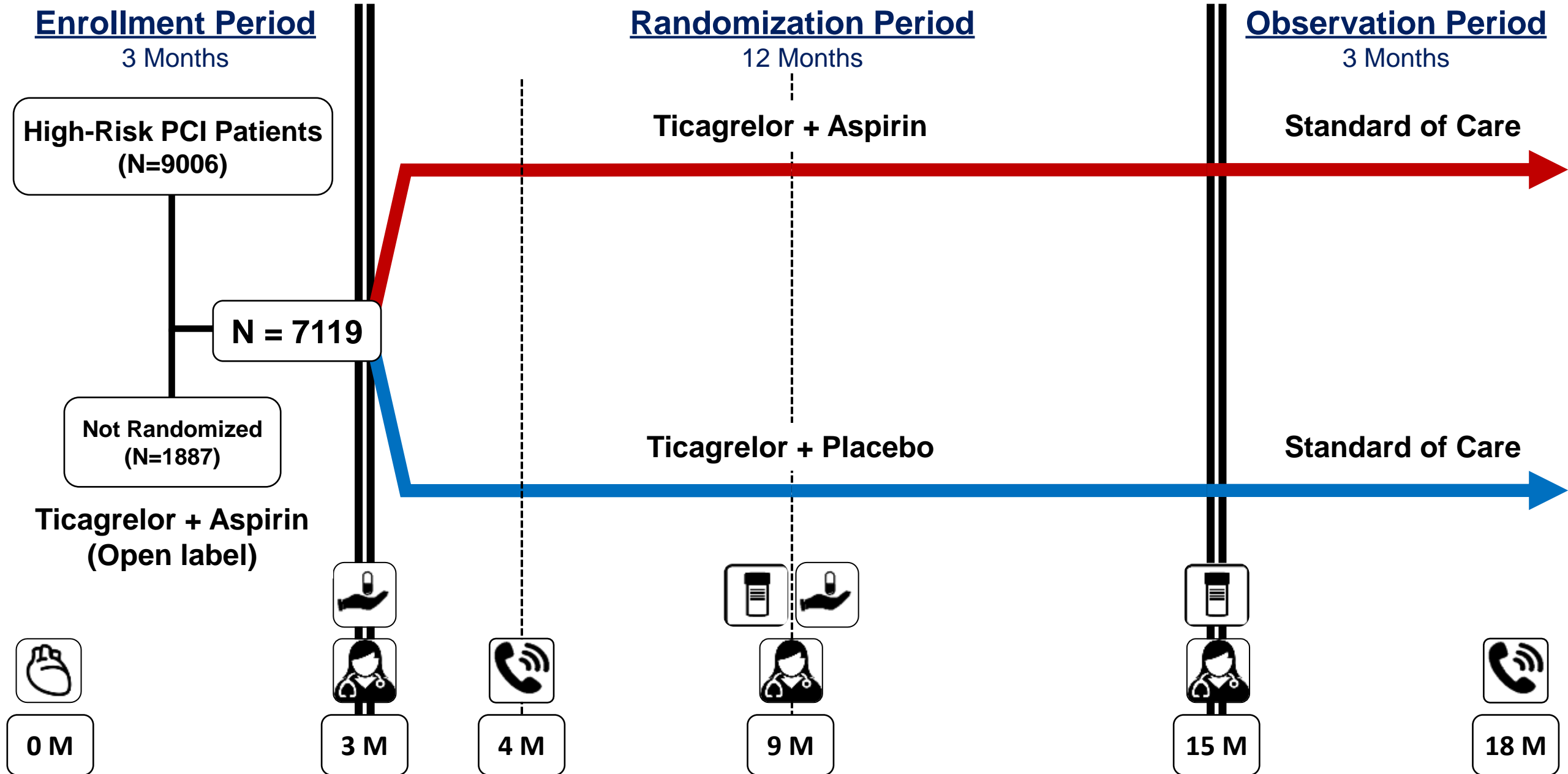
# Antiplatelet Therapy in Asian Patients After PCI

- P2Y<sub>12</sub> inhibitor monotherapy following a short course of DAPT has recently emerged as a new strategy that minimizes bleeding and maximizes antithrombotic effects.
- The risk/benefit calculus for short DAPT durations or aspirin-free strategies after PCI may also vary by race.
- However, there are limited data evaluating P2Y12 inhibitor monotherapy with ticagrelor in high-risk East-Asian PCI population.

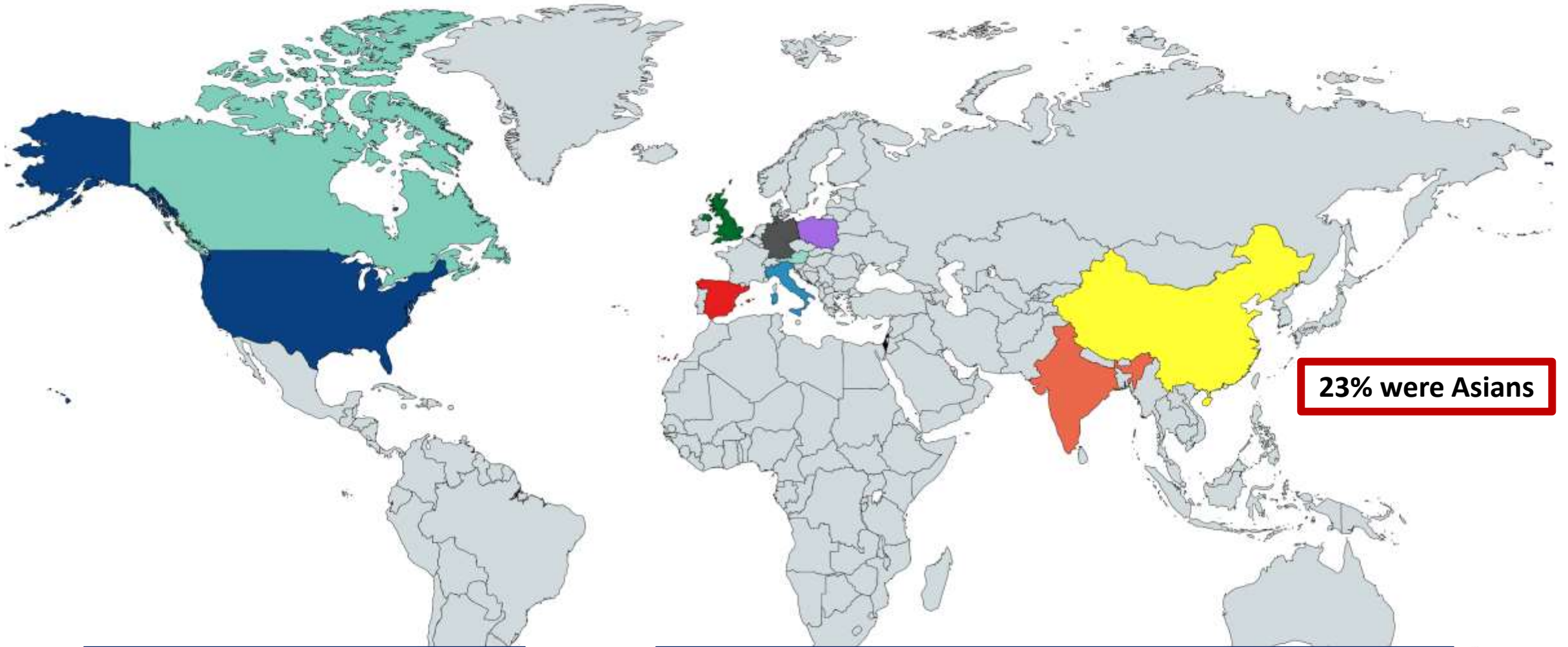


# Ticagrelor **W**ith **A**splrin or **A**Lone **I**n **H**i**G**H-Risk Patients After Coronary **I**n**T**ervention

# Study Design



# TWILIGHT Population



23% were Asians

Total Enrolled 9006

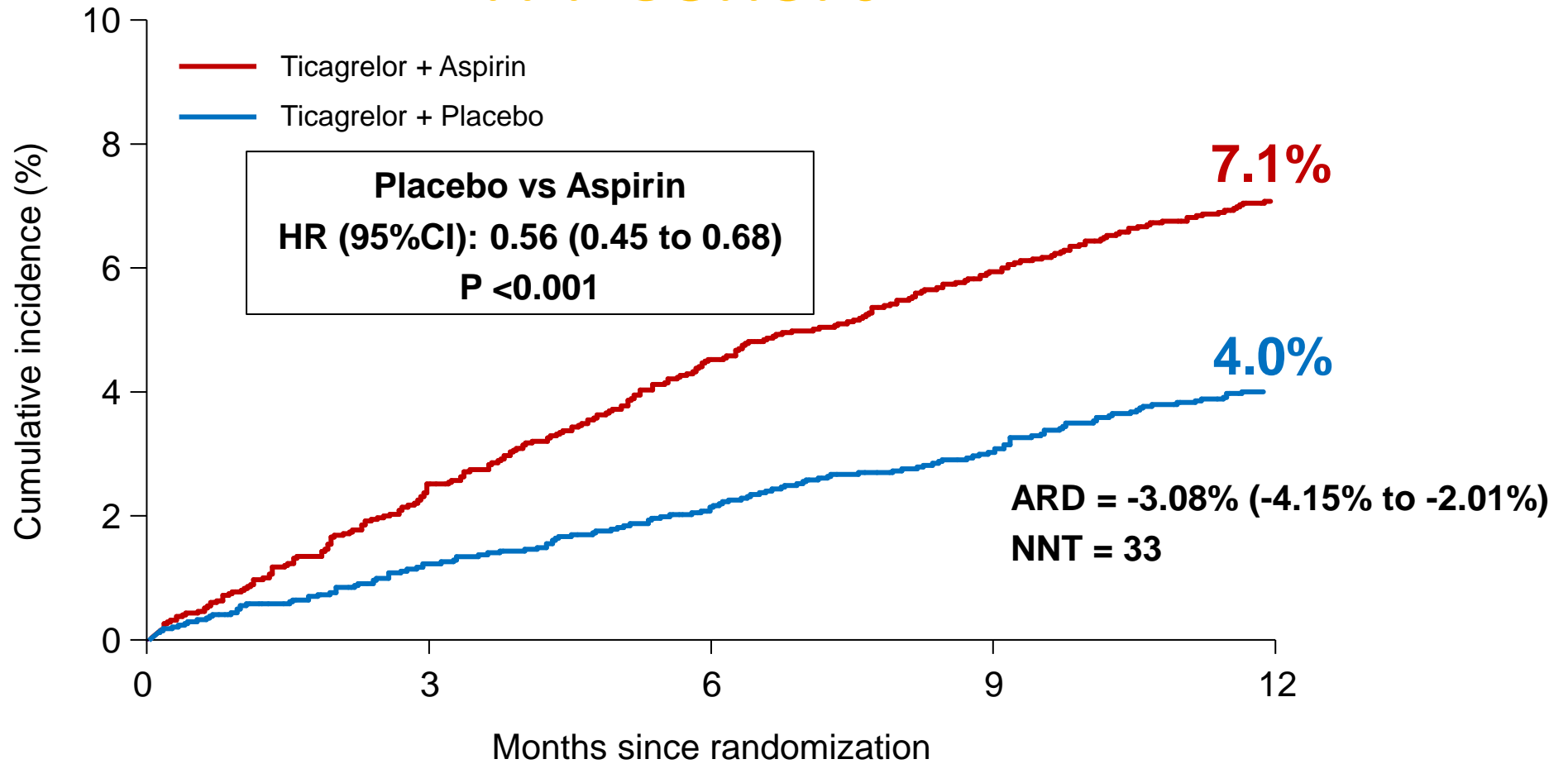
Total Randomized 7119

187 sites across 11 countries in North America, Europe and Asia



# Primary Endpoint: BARC 2, 3, or 5 Bleeding

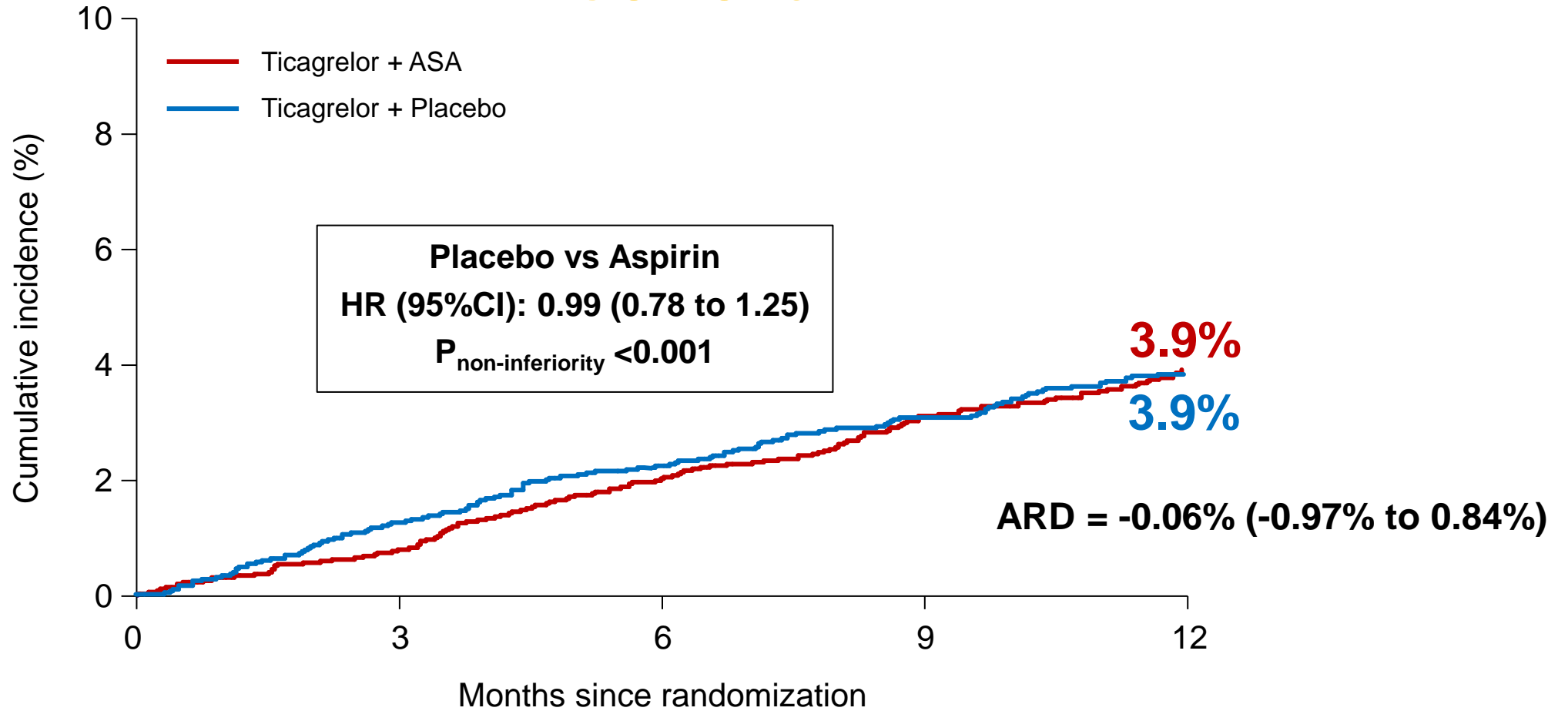
## ITT Cohort



No. at risk						
Ticagrelor + Aspirin	3564	3454	3357	3277	3213	
Ticagrelor + Placebo	3555	3474	3424	3366	3321	

# Key Secondary Endpoint: Death, MI, or Stroke

## PP Cohort



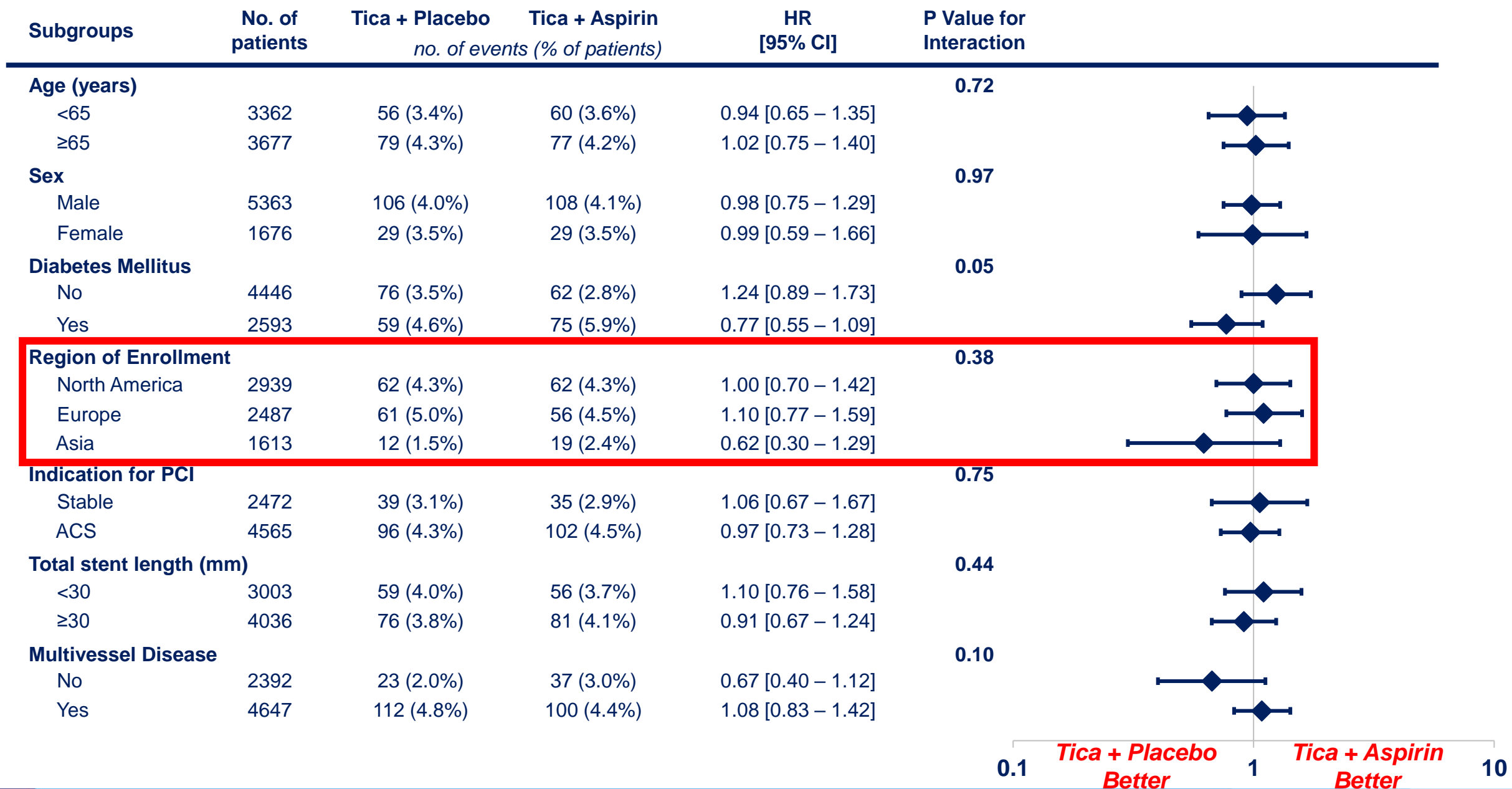
	0	3	6	9	12
<b>No. at risk</b>					
Ticagrelor + Aspirin	3515	3466	3415	3361	3320
Ticagrelor + Placebo	3524	3457	3412	3365	3330

# Subgroup Analysis for Primary Bleeding Endpoint

Subgroups	No. of patients	Tica + Placebo <i>no. of events (% of patients)</i>	Tica + Aspirin <i>(% of patients)</i>	HR [95% CI]	P Value for Interaction	
<b>Age (years)</b>					<b>0.67</b>	
<65	3400	59 (3.5%)	100 (6.0%)	0.59 [0.42 – 0.81]		
≥65	3719	82 (4.5%)	150 (8.2%)	0.54 [0.41 – 0.70]		
<b>Sex</b>					<b>0.89</b>	
Male	5421	99 (3.7%)	178 (6.7%)	0.55 [0.43 – 0.70]		
Female	1698	42 (5.0%)	72 (8.6%)	0.57 [0.39 – 0.83]		
<b>Diabetes Mellitus</b>					<b>0.23</b>	
No	4499	83 (3.8%)	164 (7.3%)	0.50 [0.39 – 0.66]		
Yes	2620	58 (4.5%)	86 (6.6%)	0.65 [0.47 – 0.91]		
<b>Region of Enrollment</b>					<b>0.16</b>	
North America	2972	83 (5.7%)	126 (8.7%)	0.65 [0.49 – 0.85]		
Europe	2509	32 (2.6%)	79 (6.3%)	0.40 [0.27 – 0.61]		
Asia	1638	26 (3.2%)	45 (5.5%)	0.57 [0.35 – 0.92]		
<b>Indication for PCI</b>					<b>0.03</b>	
Stable	2503	60 (4.8%)	75 (6.2%)	0.76 [0.54 – 1.06]		
ACS	4614	81 (3.6%)	175 (7.6%)	0.47 [0.36 – 0.61]		
<b>Total stent length (mm)</b>					<b>0.06</b>	
<30	3036	64 (4.4%)	93 (6.1%)	0.70 [0.51 – 0.97]		
≥30	4082	77 (3.8%)	157 (7.9%)	0.47 [0.36 – 0.62]		
<b>Multivessel Disease</b>					<b>0.74</b>	
No	2422	47 (4.1%)	94 (7.6%)	0.53 [0.37 – 0.75]		
Yes	4697	94 (4.0%)	156 (6.9%)	0.57 [0.44 – 0.74]		

0.1 **Tica + Placebo Better** 1 **Tica + Aspirin Better** 10

# Subgroup Analysis for Key Secondary Ischemic Endpoint



# STOPDAPT-2

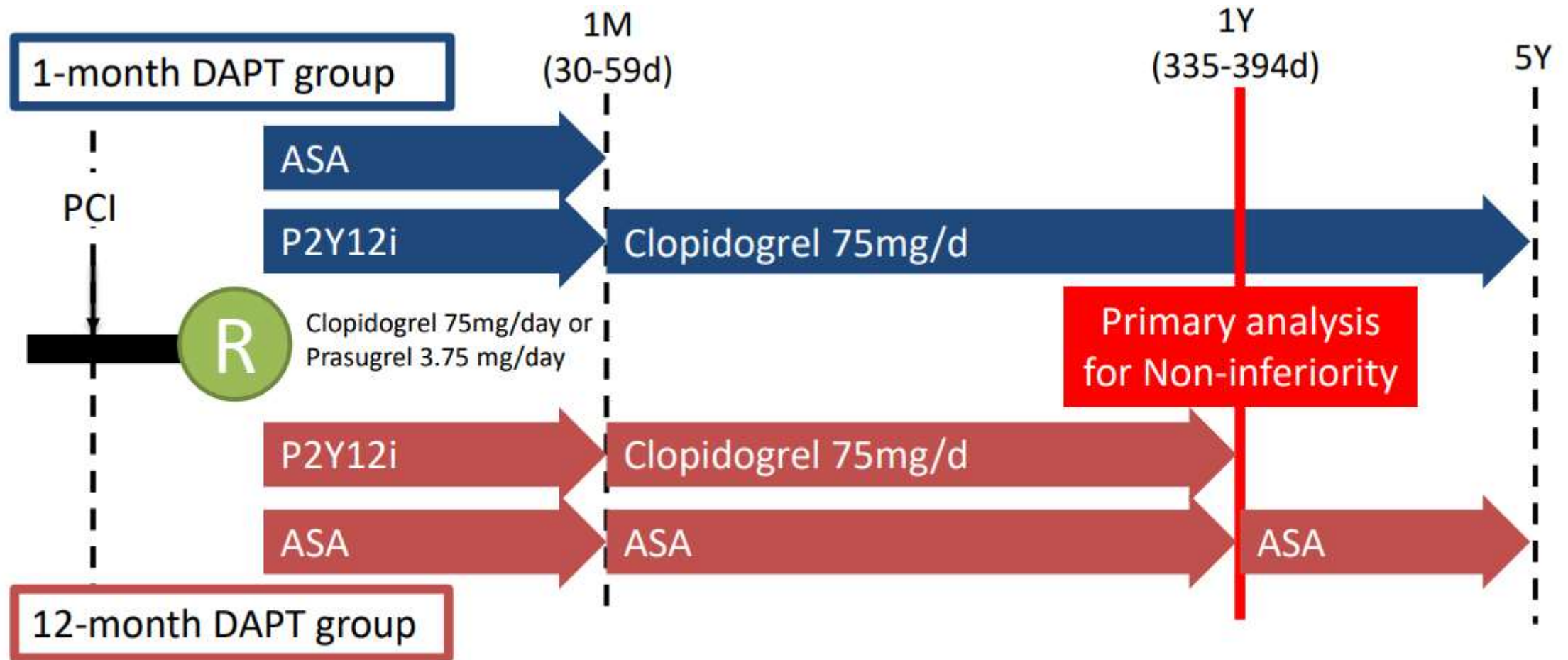
Research

JAMA | **Original Investigation**

**Effect of 1-Month Dual Antiplatelet Therapy Followed by Clopidogrel vs 12-Month Dual Antiplatelet Therapy on Cardiovascular and Bleeding Events in Patients Receiving PCI**  
The STOPDAPT-2 Randomized Clinical Trial

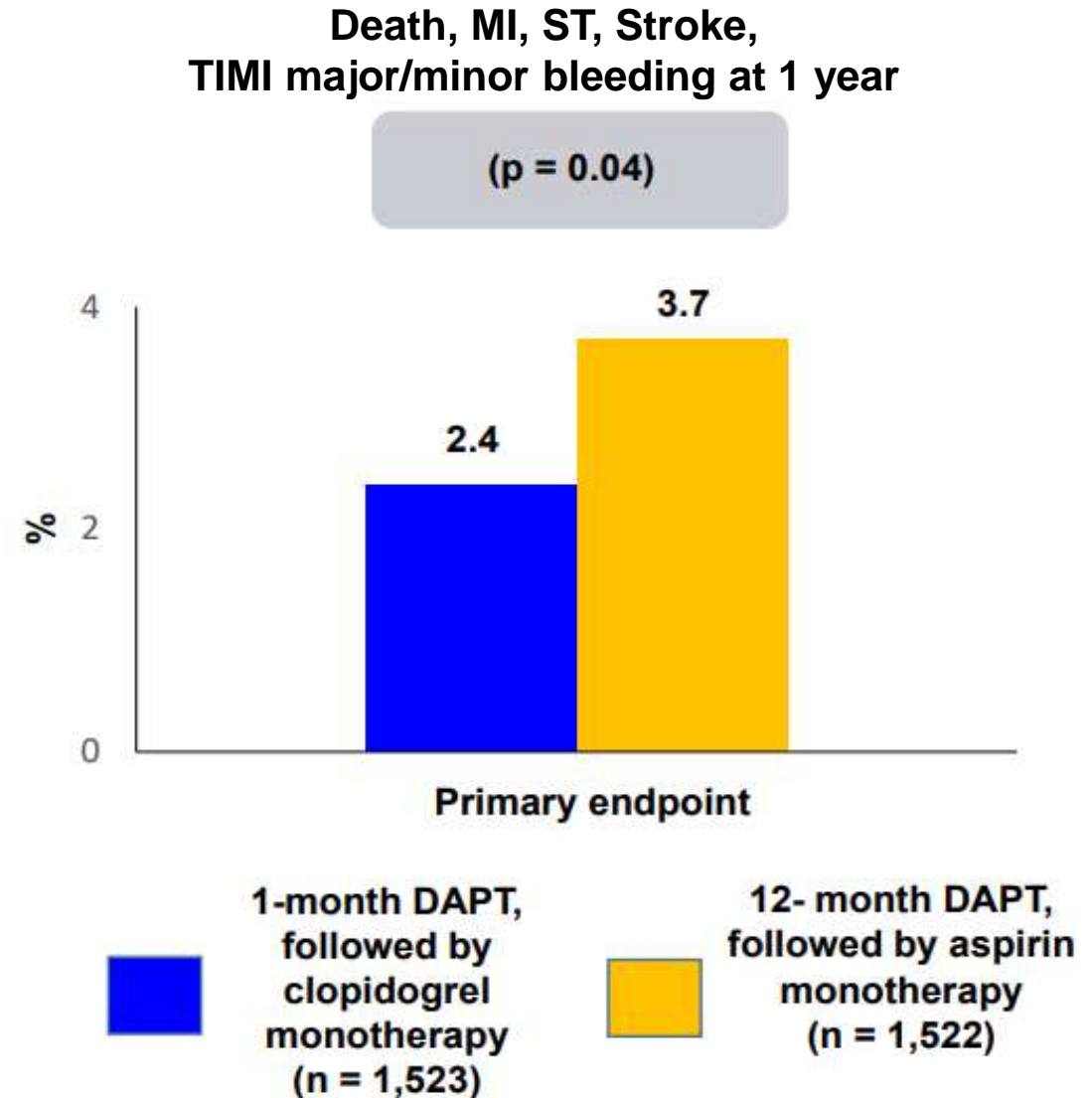
**Conducted in 90 hospitals in Japan and included 3045 patients undergoing PCI.**

# One Vs. 12-Month DAPT with Clopidogrel after DES: STOPDAPT-2 Trial



# STOP DAPT-2 Trial: Conclusions

- 1-month DAPT followed by clopidogrel monotherapy was **superior** to 12-month DAPT followed by aspirin monotherapy at preventing **net adverse clinical events**.
- 1-month DAPT was **non-inferior** to 12-month DAPT at preventing major adverse **ischemic events**.



Research

JAMA | **Original Investigation**

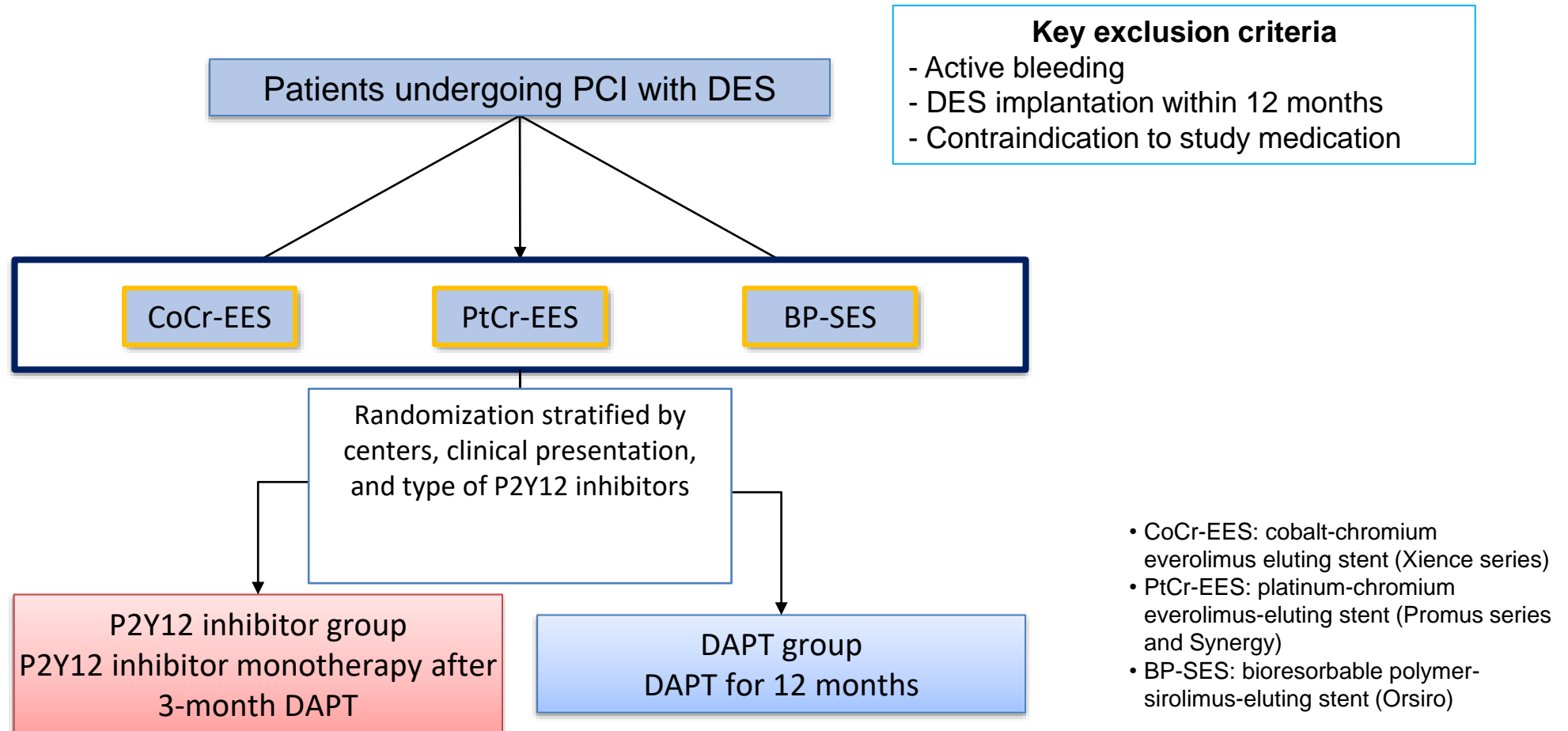
# Effect of P2Y12 Inhibitor Monotherapy vs Dual Antiplatelet Therapy on Cardiovascular Events in Patients Undergoing Percutaneous Coronary Intervention The SMART-CHOICE Randomized Clinical Trial

**Conducted in 33 hospitals in Korea and included 2993 patients undergoing PCI with drug-eluting stents.**



# P2Y12-Inhibitor Monotherapy After PCI: SMART-CHOICE Trial

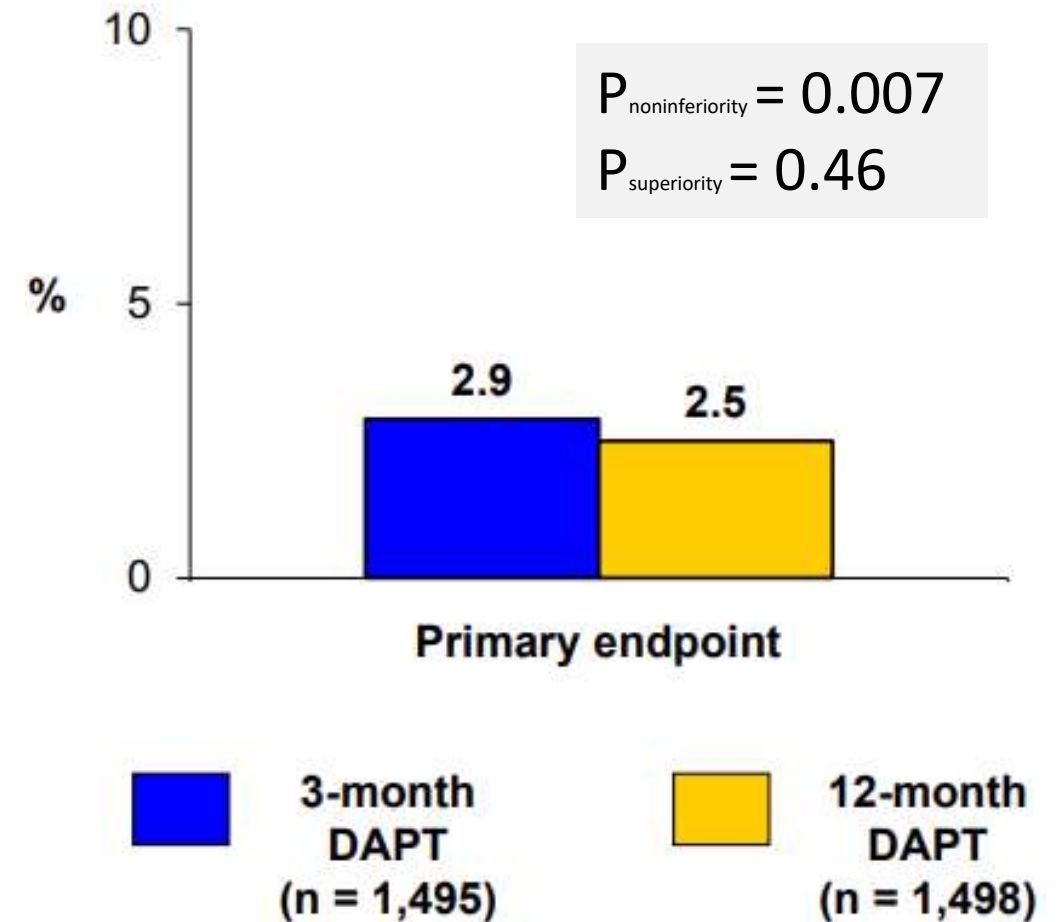
A prospective, multicenter, randomized, open-label, noninferiority trial



# SMART-CHOICE Trial: Conclusions

- 3-month DAPT followed by P2Y<sub>12</sub> inhibitor monotherapy is **non-inferior** to 12-month DAPT in terms of MACCE.
- Bleeding (BARC 2-5) was **lower** with short DAPT: 2.0% vs. 3.4%,  $p = 0.02$

MACCE (death, MI, stroke) at 12 months



Research

JAMA | **Original Investigation**

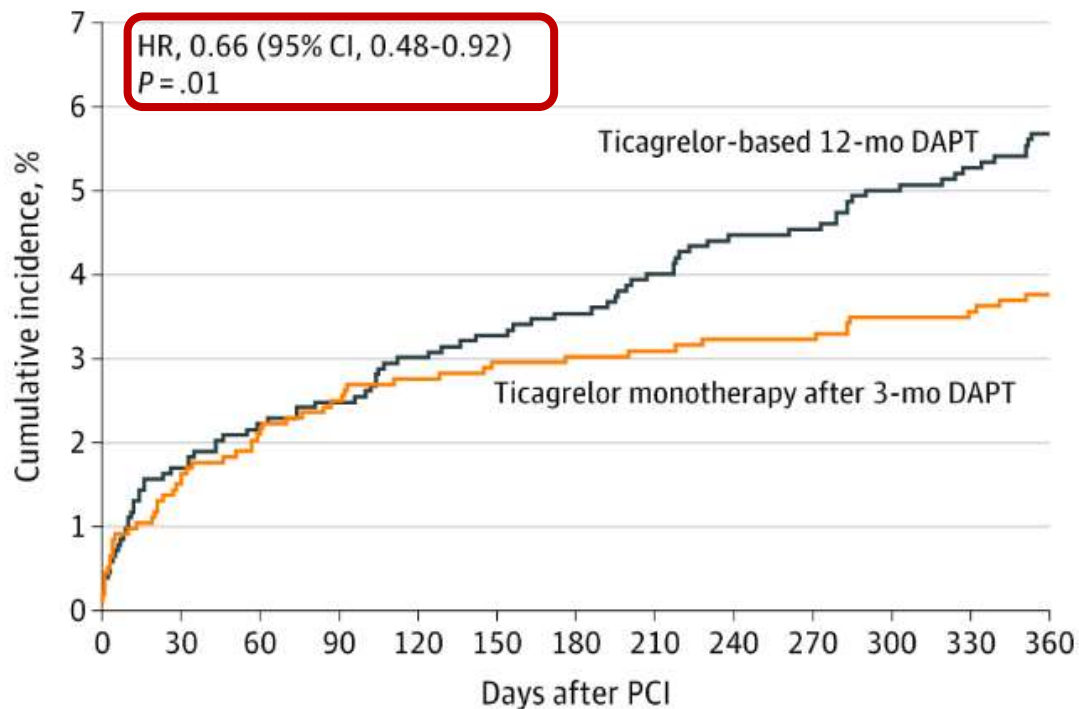
# Effect of Ticagrelor Monotherapy vs Ticagrelor With Aspirin on Major Bleeding and Cardiovascular Events in Patients With Acute Coronary Syndrome

## The TICO Randomized Clinical Trial

**Conducted in 38 hospitals in South Korea and included 3056 patients undergoing PCI with drug-eluting stents.**

# TICO Trial

**A** Primary outcome of the net adverse clinical event



Outcomes	No. of patients with event (% cumulative incidence) <sup>a</sup>		Absolute difference, % (95% CI)	Hazard ratio (95% CI)	P value <sup>b</sup>
	Ticagrelor monotherapy after 3-mo DAPT (n = 1527)	Ticagrelor-based 12-mo DAPT (n = 1529)			
Major adverse cardiac and cerebrovascular event <sup>d</sup>	35 (2.3)	51 (3.4)	-1.05 (-2.23 to 0.13)	0.69 (0.45 to 1.06)	.09
TIMI					
Major bleeding	25 (1.7)	45 (3.0)	-1.33 (-2.40 to -0.27)	0.56 (0.34 to 0.91)	.02
Major or minor bleeding	53 (3.6)	83 (5.5)	-2.06 (-3.52 to -0.60)	0.64 (0.45 to 0.90)	.01

Mainly driven by a reduction in bleeding!

Among patients with ACS treated with DES, ticagrelor monotherapy after 3 months of DAPT, compared with ticagrelor-based 12-month DAPT, resulted in **a modest but statistically significant reduction** in a composite outcome of major bleeding and CV events at 1 year.

# The Essentials to Remember

- East-Asian patients display higher risks for bleeding following PCI as compared to non-East-Asians.
- P2Y<sub>12</sub> receptor inhibitor monotherapy following a short course of DAPT significantly reduced clinically relevant bleeding without increasing ischemic events.
- P2Y<sub>12</sub> receptor inhibitor monotherapy provides a novel antiplatelet strategy that yields an overall clinical benefit in high-risk East-Asian patients undergoing PCI.

# THANK YOU



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