

# Potent Platelet Inhibition in Korean AMI Patients

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# The Korean Society of Cardiology

## COI Disclosure

*Name of First Author: Yongwhi Park*

The authors have no financial conflicts of interest to disclose concerning the presentation

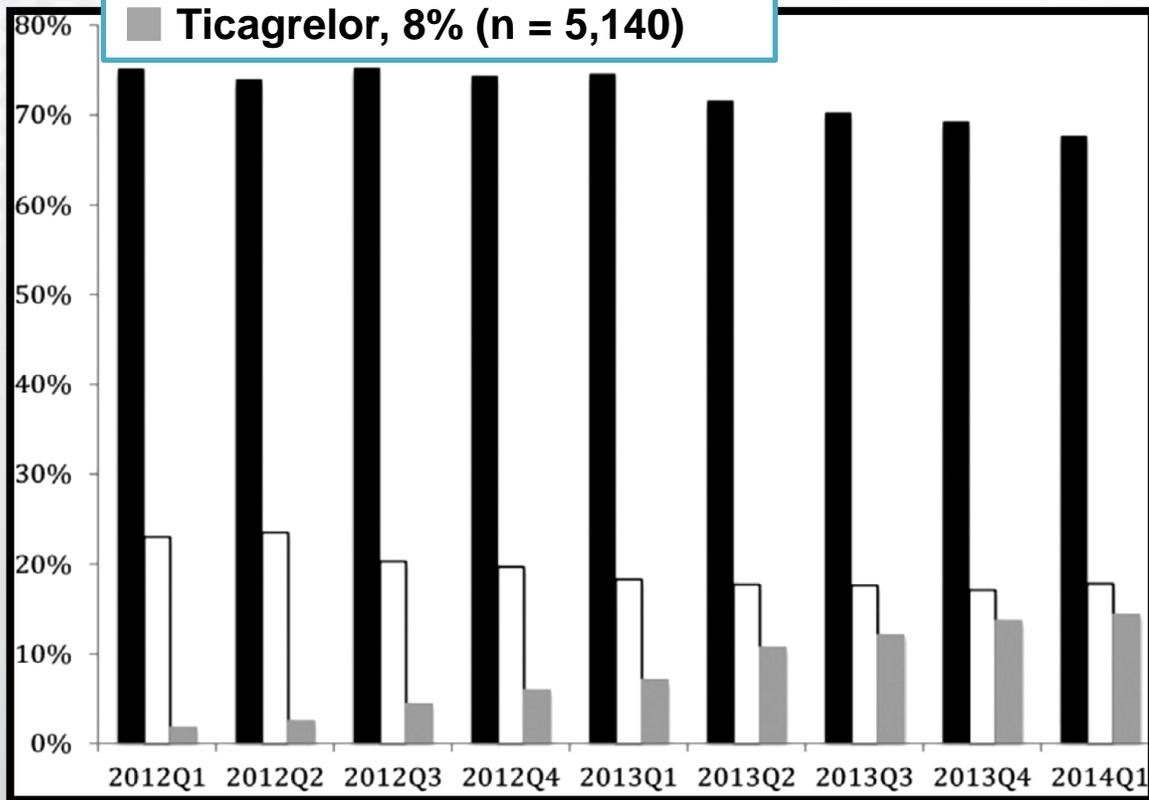


2017 Annual Spring Scientific Conference of the KSC  
in conjunction with KHRS, KSIC, KSE, and KSoLA

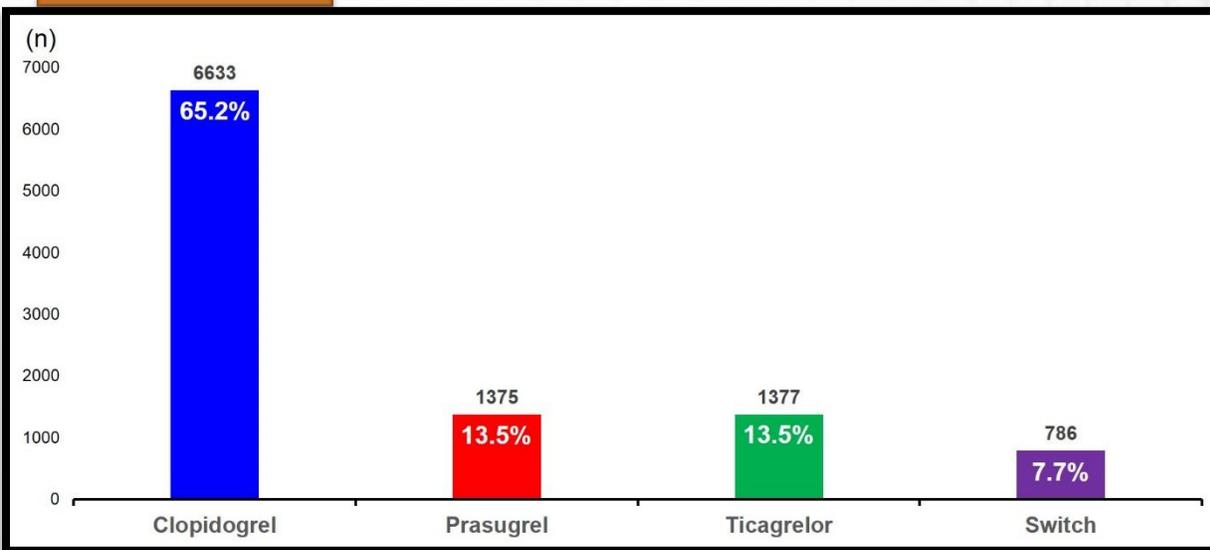
# P2Y<sub>12</sub> inhibitors in real clinical practices

In the U.S.

- Clopidogrel, 72% (n = 46,864)
- Prasugrel, 20% (n = 12,596)
- Ticagrelor, 8% (n = 5,140)



In Korea

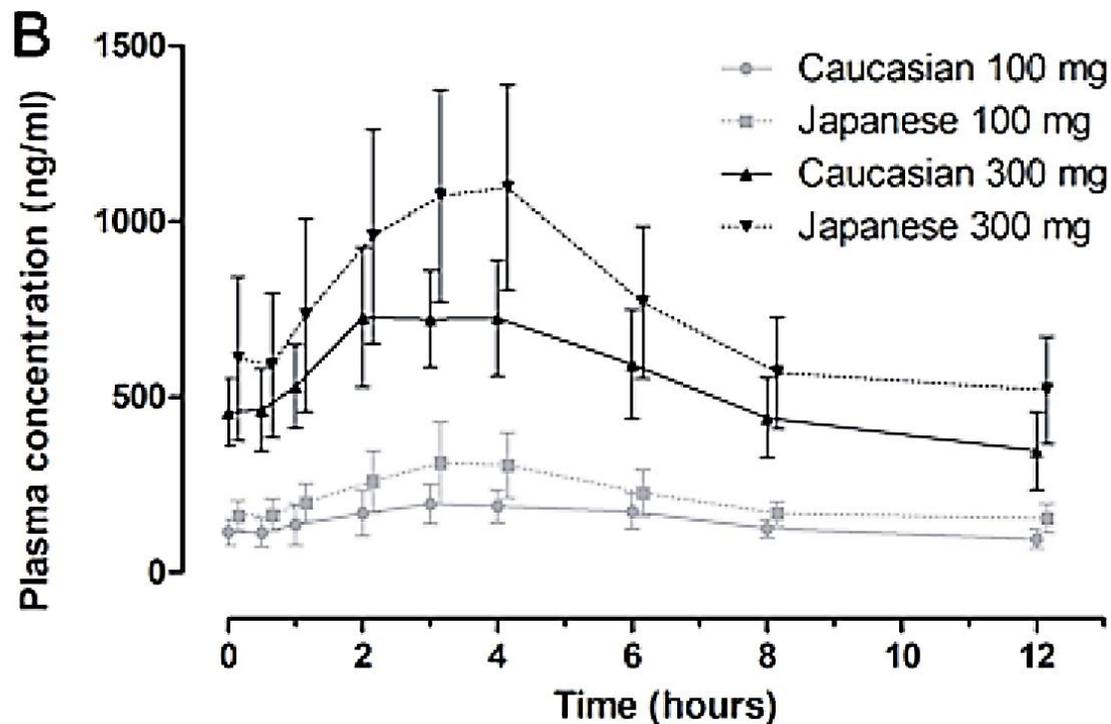


# Treatment Paradox of Potent P2Y<sub>12</sub> inhibitors in “Real Clinical Practice”

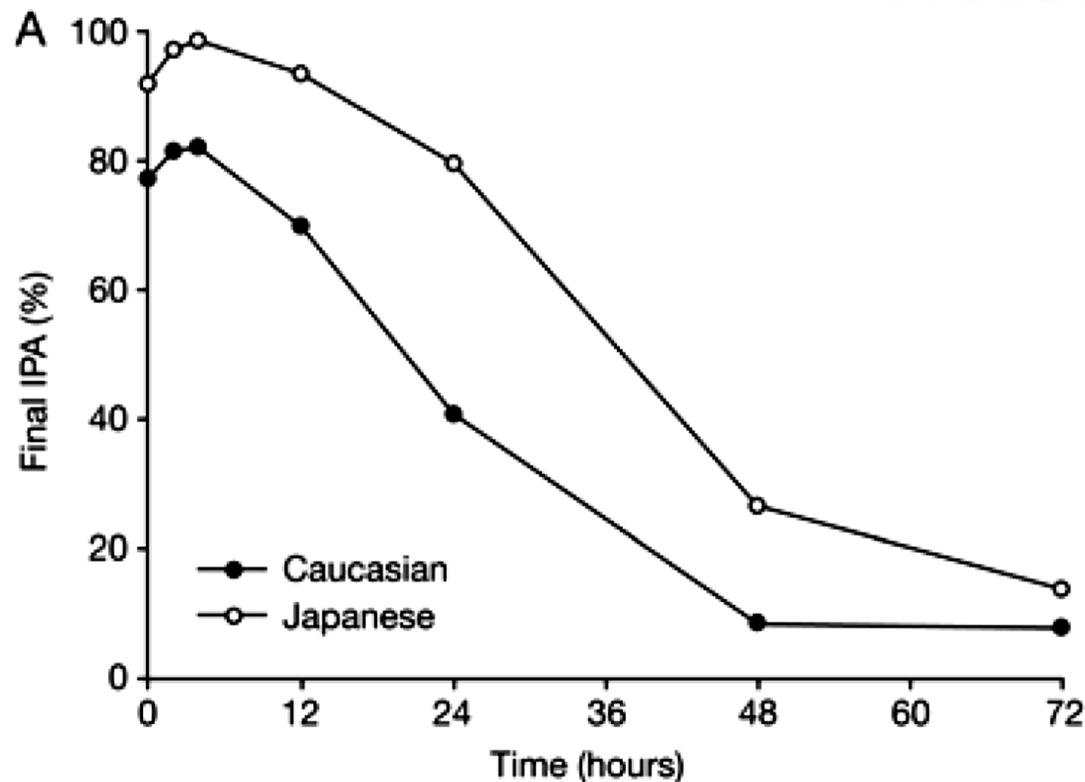
	Ticagrelor (n = 6633)	Clopidogrel (n = 6633)	p-Value
Age, years	62.30 ± 12.06	64.80 ± 12.61	<0.001
Age ≥ 75 years (%)	259 (18.8)	1718 (25.9)	<0.001
Body weight, kg	66.35 ± 11.92	64.51 ± 11.79	<0.001
Body weight < 60 kg (%)	382 (27.7)	2133 (32.2)	0.001
Male gender (%)	4791 (77.7)	4791 (72.2)	<0.001
Hypertension (%)	3477 (46.1)	3477 (52.4)	<0.001
Diabetes (%)	1955 (29.5)	1955 (29.5)	<0.001
Dyslipidemia (%)	773 (11.7)	773 (11.7)	0.675
Current smoker (%)	2505 (37.8)	2505 (37.8)	0.002
Family history of CAD (%)	442 (6.7)	442 (6.7)	0.385
Previous history of MI (%)	493 (7.4)	493 (7.4)	0.005
Previous history of CVA (%)	507 (7.6)	507 (7.6)	<0.001
Killip class (%)			<0.001
I	5158 (77.8)	5158 (77.8)	
II to IV	1475 (22.2)	1475 (22.2)	

In a real-world practice, there was an **underutilization** of potent P2Y<sub>12</sub> inhibitors which was more **pronounced** in **higher-risk subsets**.

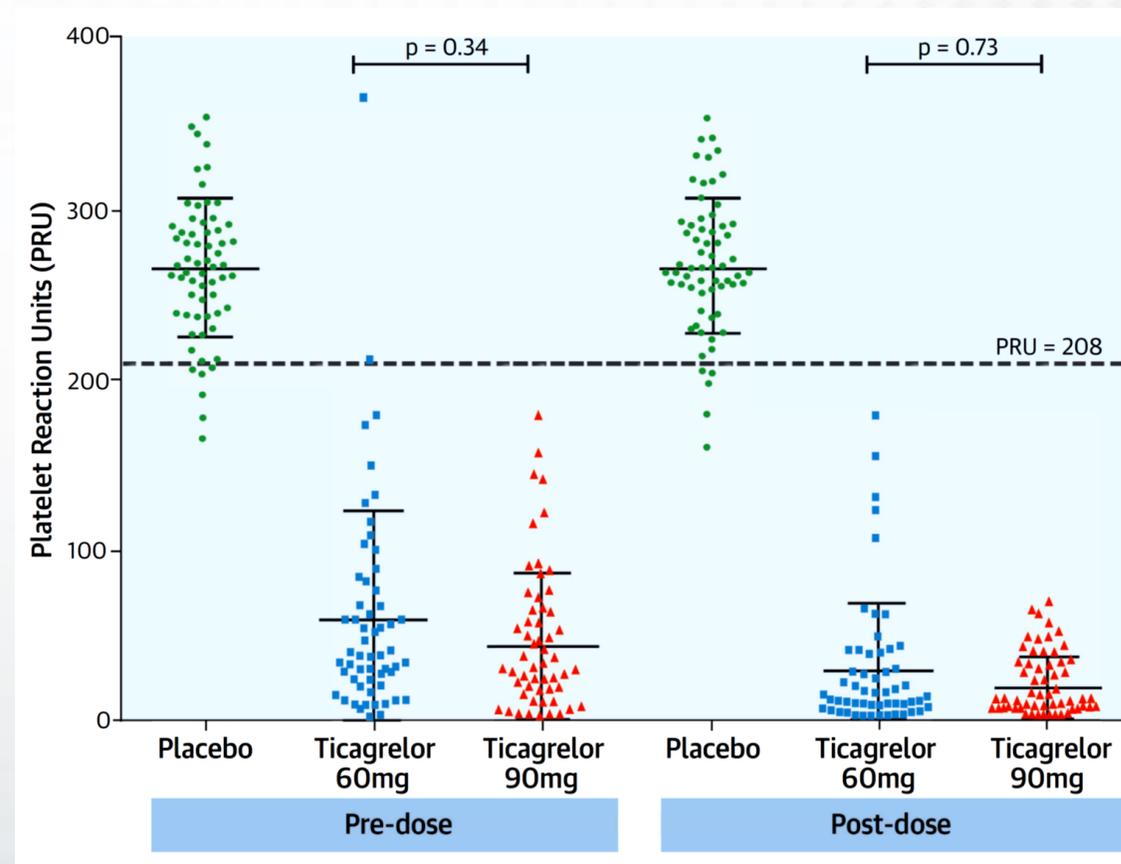
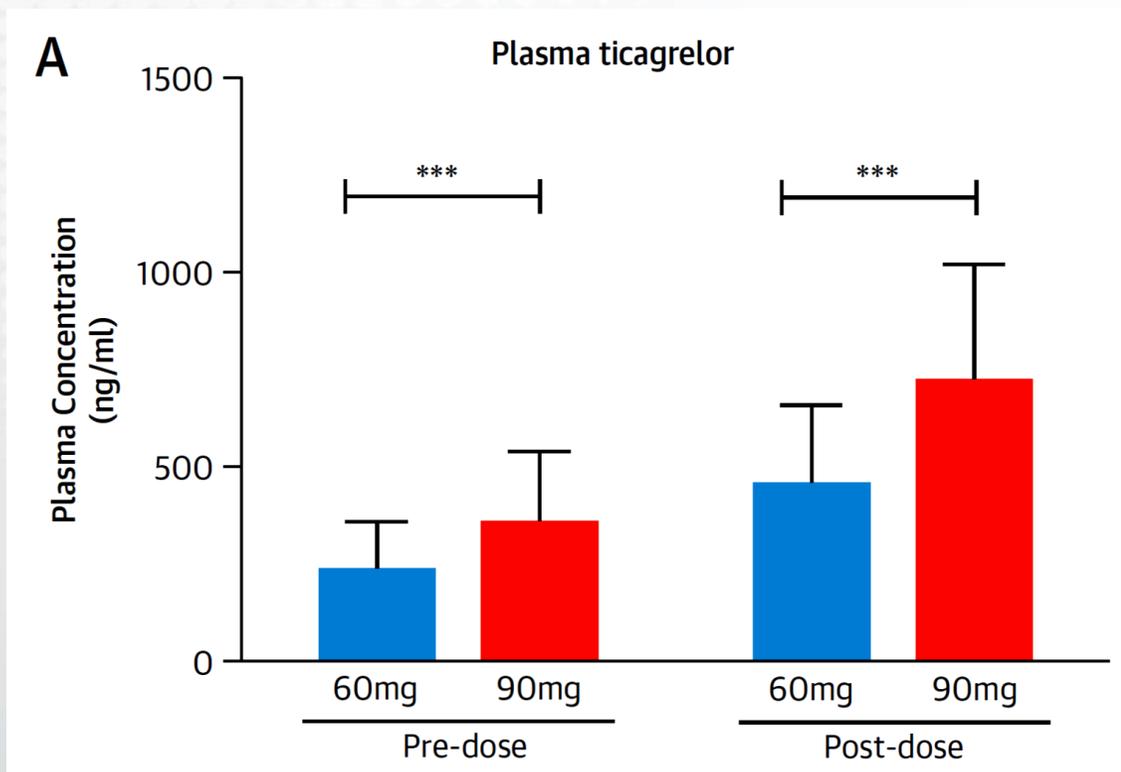
# Ethnic Differences of Ticagrelor



**33% ~ 48%** higher plasma concentration in Japanese compared with Caucasian.  
After adjusting body weight, **20%** of difference still persists.

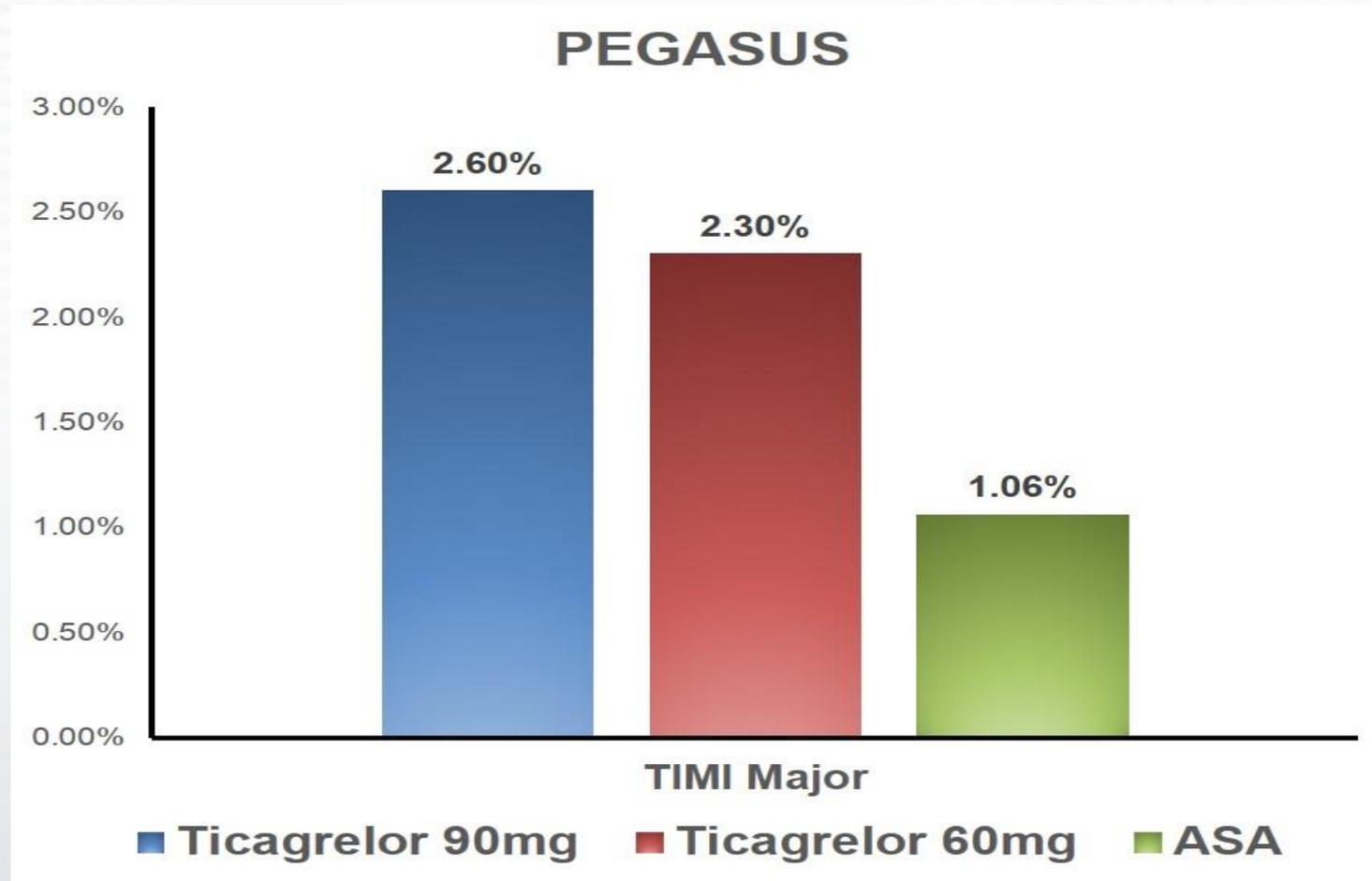


# Ticagrelor 90mg vs. 60mg in PEGASUS



**Ticagrelor 60mg bid achieved similar PD efficacy despite lower plasma concentration vs. Ticagrelor 90mg bid.**

# Bleeding Risks Associated With P2Y<sub>12</sub> Inhibitors



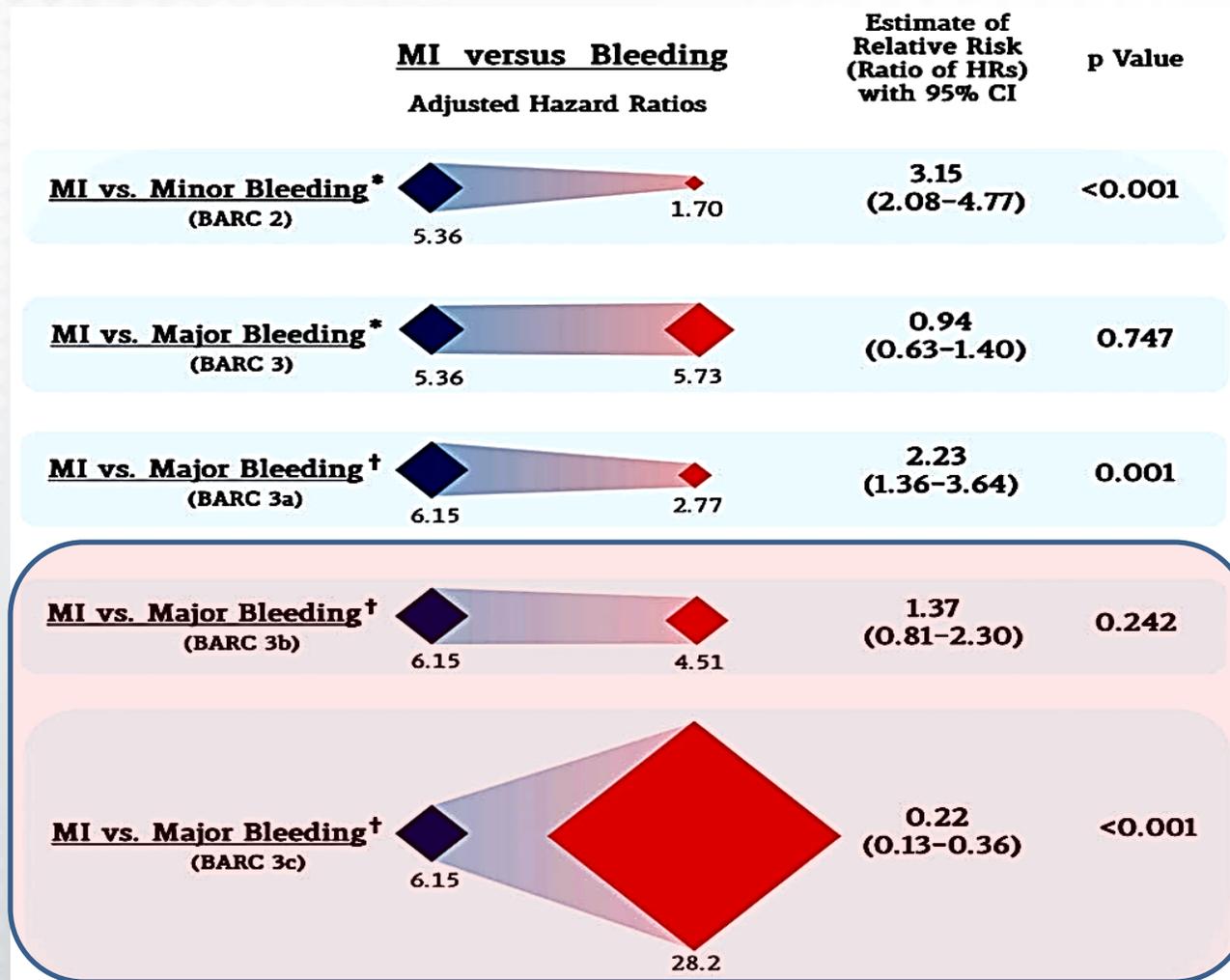
**Higher Platelet Inhibition = Higher Bleeding Risks**

# Factors related to ischemic/bleeding risks

Increased ischemic/ST risks	Increased Bleeding risk
<b>Increased ischemic risk</b>	<b>History of prior bleeding</b>
<div style="border: 1px solid #d62728; padding: 2px; display: inline-block; margin-bottom: 5px;">Advanced age</div> ACS Multiple prior MIs Extensive CAD <div style="border: 1px solid #d62728; padding: 2px; display: inline-block; margin-bottom: 5px;">DM</div> <div style="border: 1px solid #d62728; padding: 2px; display: inline-block; margin-bottom: 5px;">CKD</div>	OAC Female <div style="border: 1px solid #d62728; padding: 2px; display: inline-block; margin-bottom: 5px;">Advanced age</div> Low body weight <div style="border: 1px solid #d62728; padding: 2px; display: inline-block; margin-bottom: 5px;">CKD</div> <div style="border: 1px solid #d62728; padding: 2px; display: inline-block; margin-bottom: 5px;">DM</div>
<b>Increased risk of ST</b>	Anemia
ACS <div style="border: 1px solid #d62728; padding: 2px; display: inline-block; margin-bottom: 5px;">DM</div> LVEF <40% 1G DES Stent under-sizing/under-deployment Small stent diameter Greater stent length Bifurcation stent ISR	Chronic steroid or NSAIDs

**High ischemic risk = High bleeding risk**

# Impact of MI vs. Bleeding on mortality



**MI**

**= BARC 3b**

**= TIMI Major**

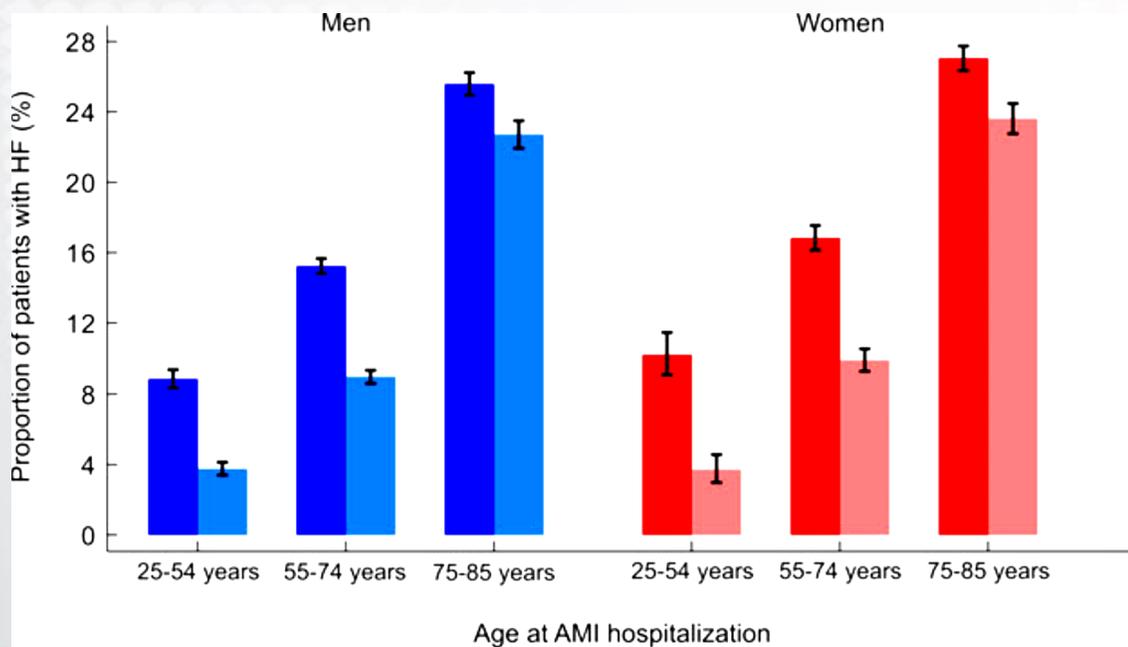
**= GUSTO severe**

**= PLATO Major**

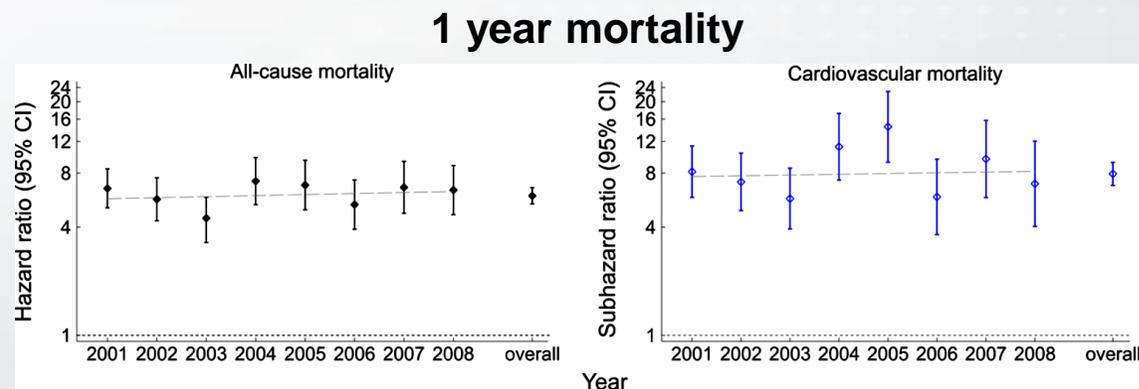
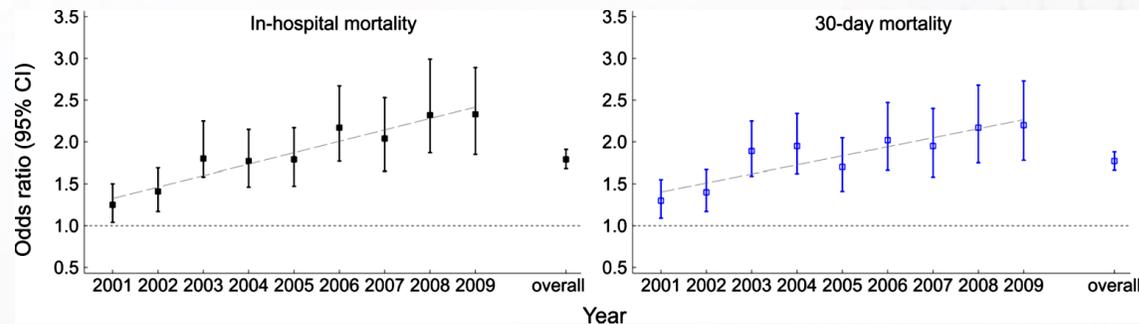
# Temporal Trends in the Incidence and In-Hospital Mortality of AMI in Western and Asian Countries

Country	Period	Gender	Incidence	In-hospital Mortality	Reference
USA	1987 – 2008	Male (White)	-4.3%/year	-3.5%/year	Circulation 2012;125:1848-57
		Female (White)	-3.8%/year	-3.0%/year	
USA	1999 – 2008	Overall	274 → 208*	10.5% → 7.8%	N Engl J Med 2010;362:2155-65
Denmark	1984 – 2008	Male	410 → 213*	31.4% → 14.8*	BMJ 2012;344: e356
		Female	209 → 131*		
Six EU countries	1985 – 2010	Male	-4.0%/year	-6.0%/year	Heart 2015; 101:1413-21
		Female	-4.2%/year	-6.3%/year	
Taiwan	1999 - 2008	Male	41.8 → 62.5*	20% → 8%	J Am Heart Assoc 2014;3: e001066
		Female	13.5 → 26.0*		
Japan	1979 – 2008	Male	18.7 → 46.4*	21.4% → 6.3%	Circ J 2010;74: 93-100
		Female	4.2 → 9.6*	19.4% → 12.2%	
Japan	2005 – 2014	Male	61.3 → 68.1*	4.4% → 6.1%	Circ J 2017;81:520-8
		Female	17.7 → 12.2*	9.1% → 9.9%	
Korea	1997 – 2007	Male	60.4 → 92.2*	13.4% → 9.7%	Korean Circ J 2009;39:467-76
		Female	40.7 → 63.7*	15.2% → 12.4%	
Korea	2006 - 2010	Male	60.1 → 40.9*		J Korean Med Sci 2013;28:16-27
		Female	3.16 → 17.6*		

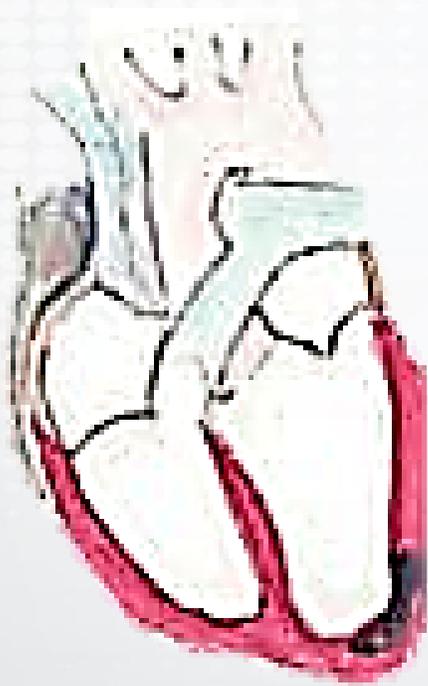
# CHF After AMI: a Lost Battle



In-hospital (fully colored bars) and Post-AMI discharge (light-colored bars) heart failure



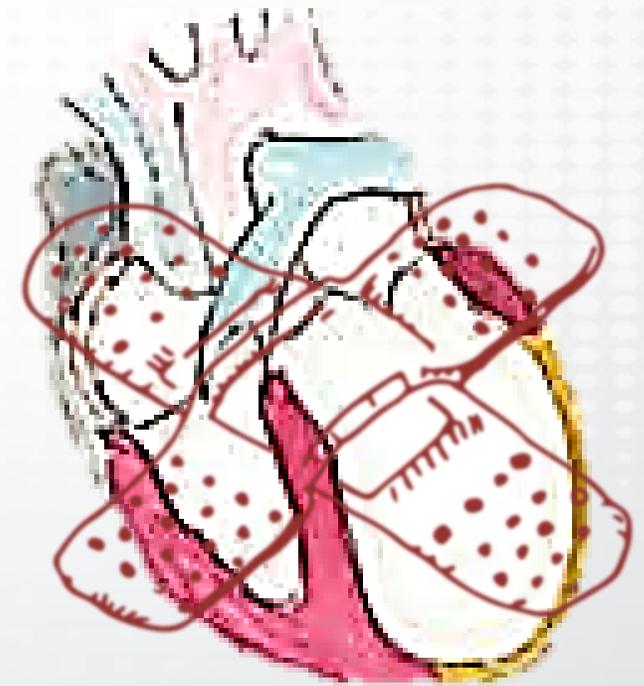
# How to Prevent CHF after AMI



Infarction

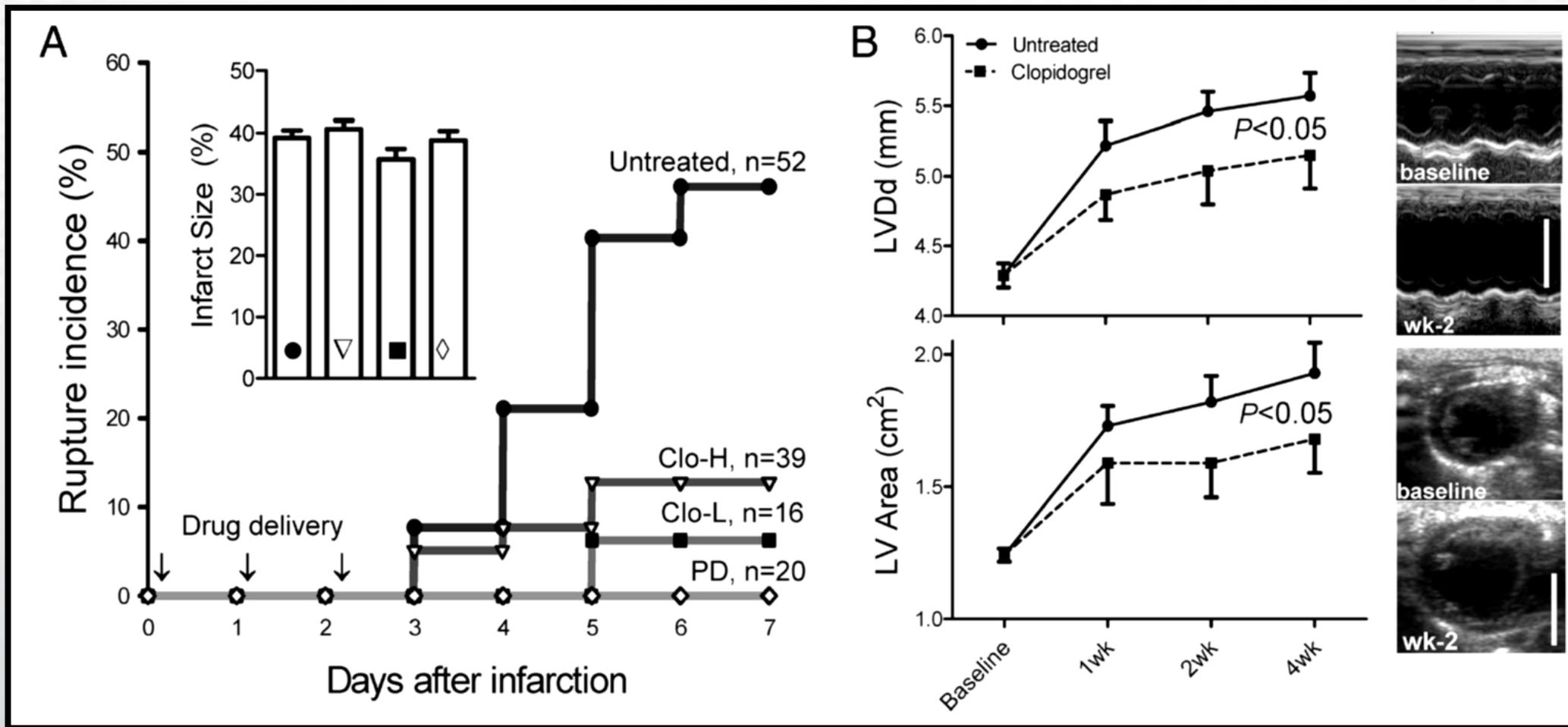


Wound Healing



Infarct Expansion &  
Pathologic remodeling

# Platelet Inhibition and LV Remodeling



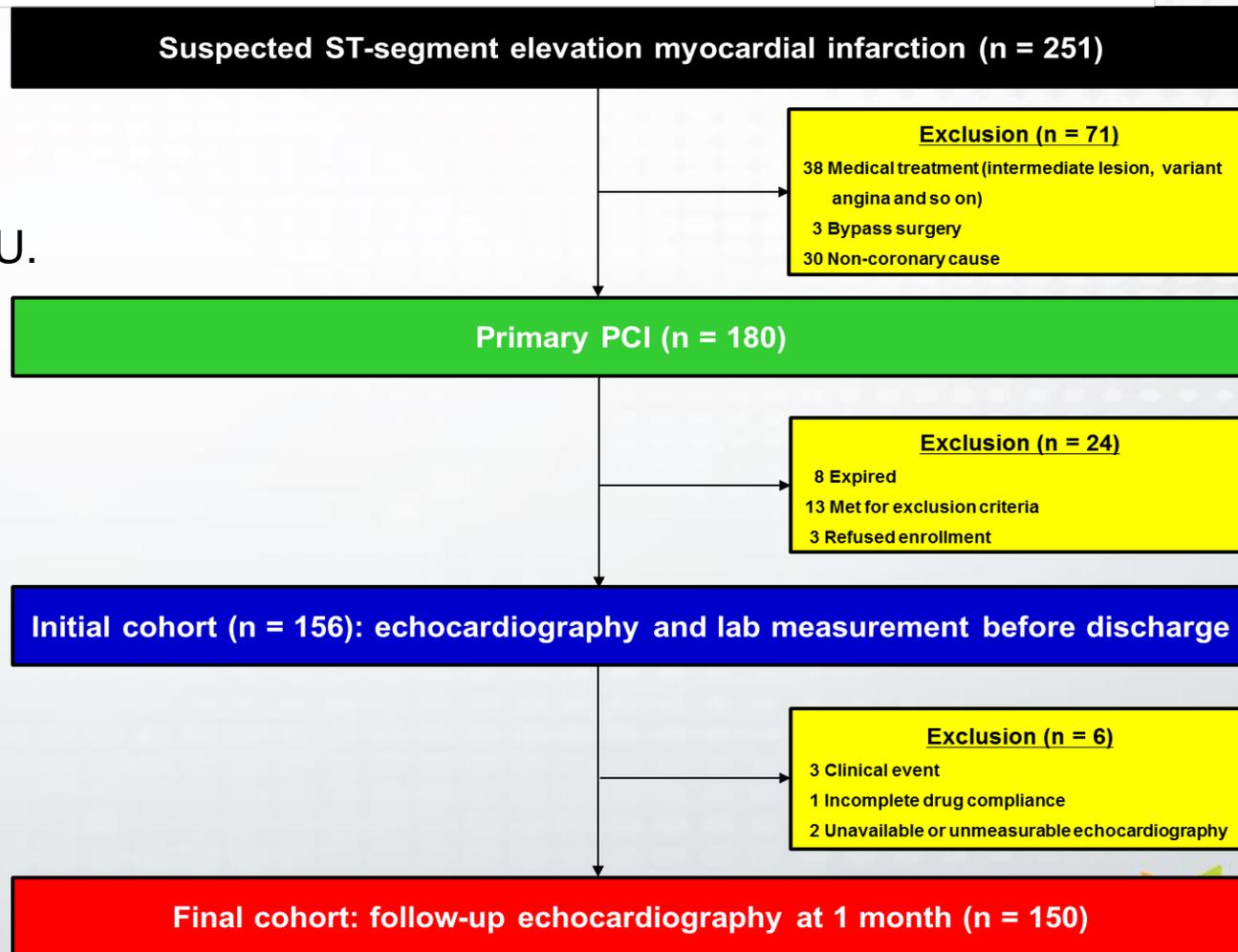
# Novel role of platelet reactivity in adverse left ventricular remodelling after ST-segment elevation myocardial infarction: The REMODELING Trial

## Primary Endpoint:

- ✓ the prevalence of LVR in relation to quartile distribution of platelet reactivity measured by PRU.

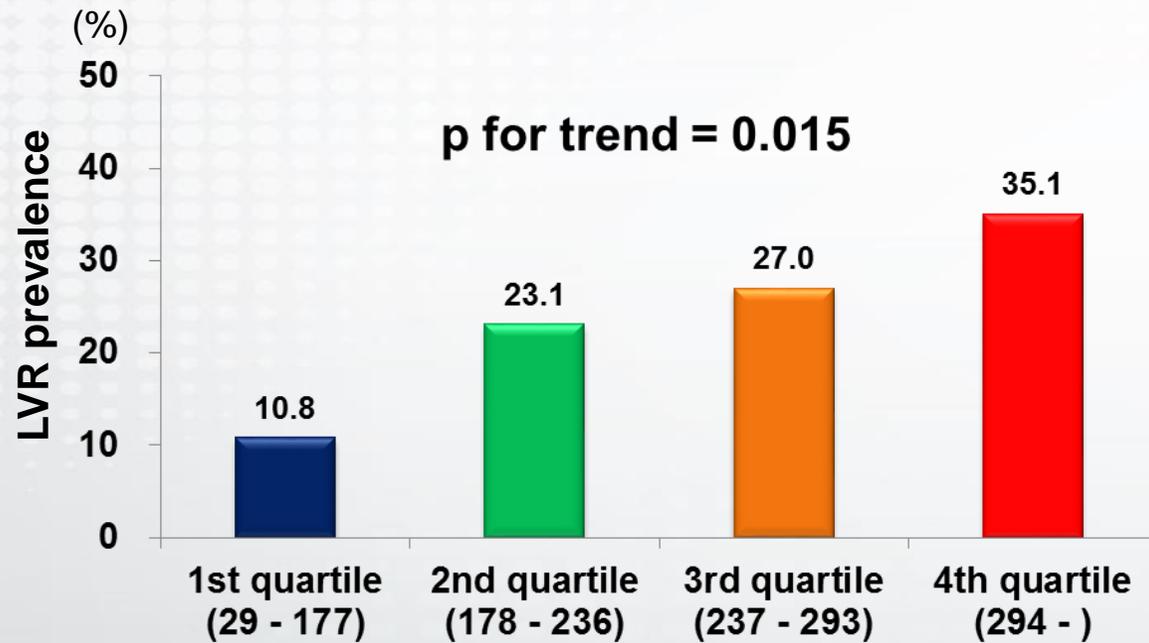
## Secondary Endpoints:

- 1) the correlation between prevalence of LVR and inflammatory marker indicated by hs-CRP;
- 2) the determinants of adverse LVR; and
- 3) performance of different models associated with LVR.



# Prevalence of LV Remodeling

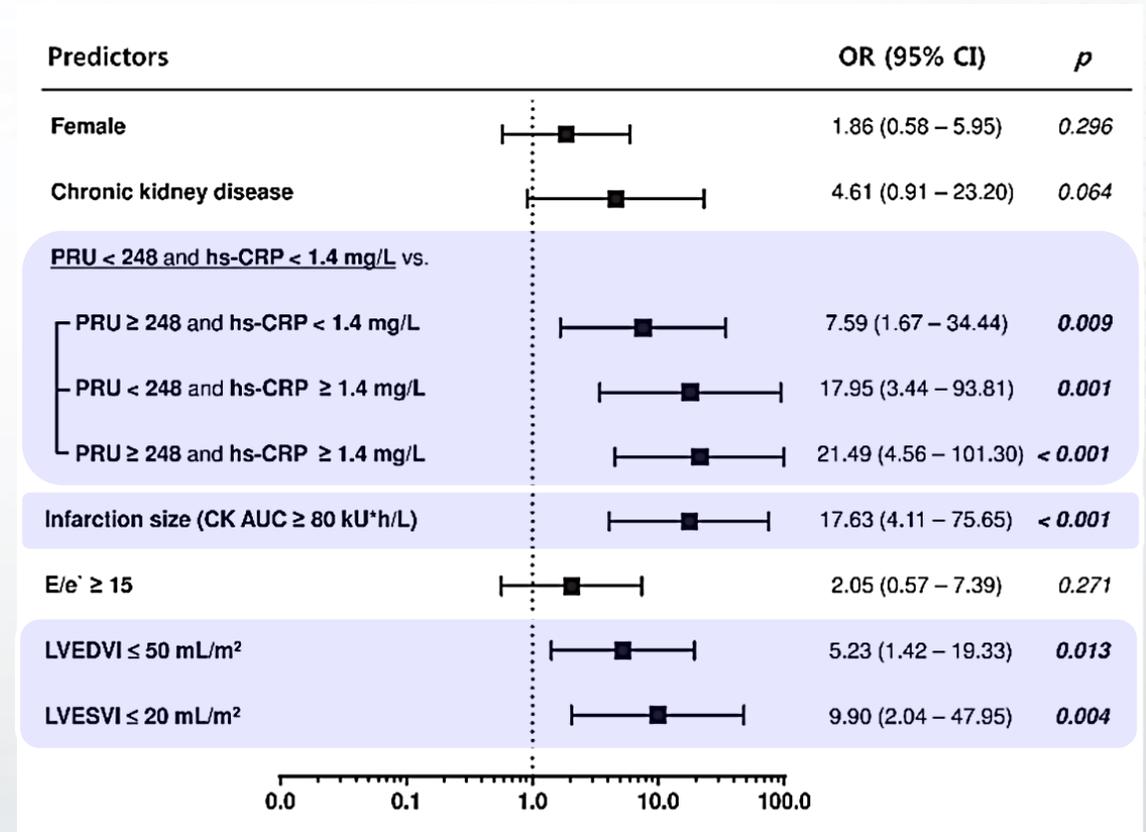
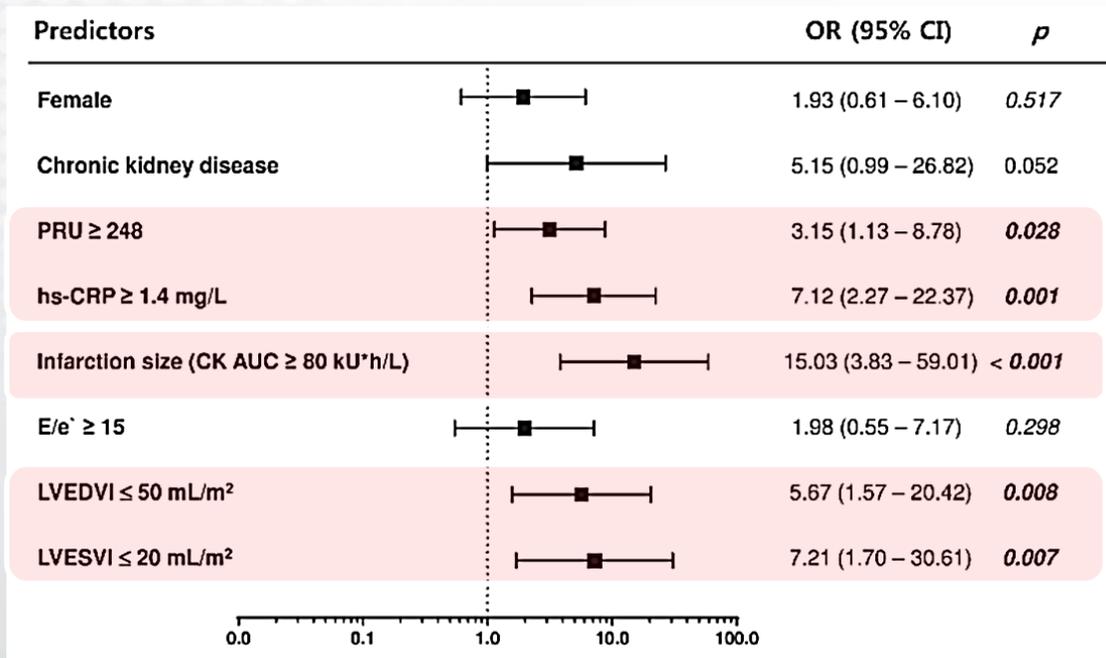
## A. PRU criteria



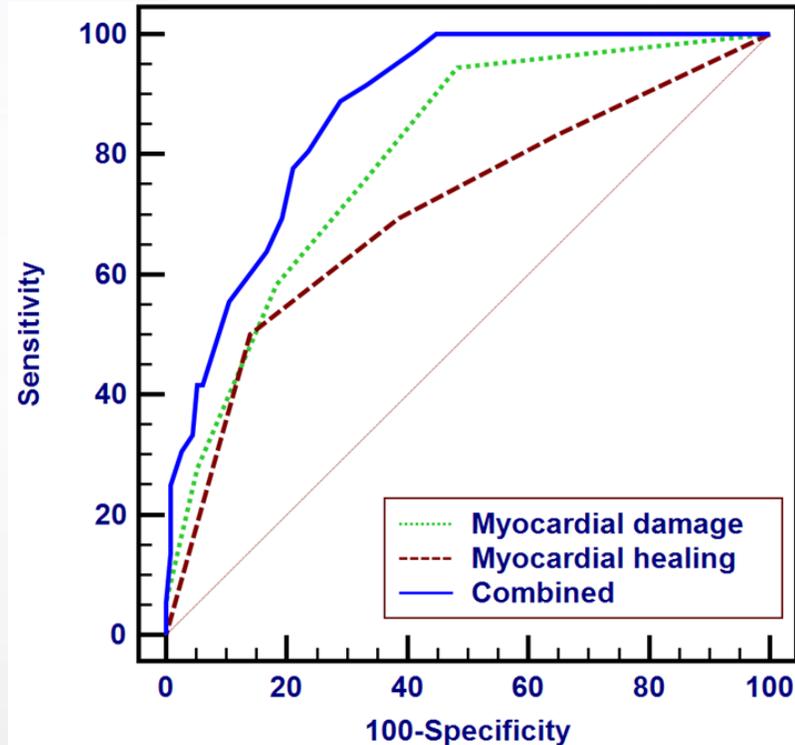
## B. hs-CRP criteria



# Predictors of LV Remodeling



# Myocardial Damage vs. Healing



	AUC	95% CI	p Value
<b>Myocardial-damage model</b> (LVEDVI $\leq$ 50 mL/m <sup>2</sup> , LVESVI $\leq$ 20 mL/m <sup>2</sup> , CK AUC $\geq$ 80 kU*h/L)	0.796	0.723 – 0.857	Reference value
<b>Myocardial-healing model</b> (PRU $\geq$ 248, hs-CRP $\geq$ 1.4 mg/L)	0.704	0.625 – 0.776	0.213*
<b>Combined model</b> (Myocardial-damage model + myocardial-healing model)	0.874	0.810 – 0.922	<b>0.015*/0.002<sup>†</sup></b>

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Trial record **1 of 1** for: HEALING-AMI

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## Ticagrelor Versus Clopidogrel in Left Ventricular Remodeling After ST-segment Elevation Myocardial Infarction (HEALING-AMI)

**This study is currently recruiting participants.** (see [Contacts and Locations](#))

*Verified November 2016 by Gyeongsang National University Hospital*

### Sponsor:

Gyeongsang National University Hospital

### Collaborators:

Chinese PLA General Hospital  
Chungnam National University Hospital  
Pusan National University Yangsan Hospital  
National University Heart Centre, Singapore  
Ulsan University Hospital  
Kyungpook National University  
Samsung Changwon Hospital  
Kyunghee University Medical Center  
Chungbuk National University Hospital  
Chonnam National University Hospital  
Seoul National University Bundang Hospital

### Information provided by (Responsible Party):

Yongwhi Park, Gyeongsang National University Hospital

### ClinicalTrials.gov Identifier:

NCT02224534

First received: August 20, 2014

Last updated: November 14, 2016

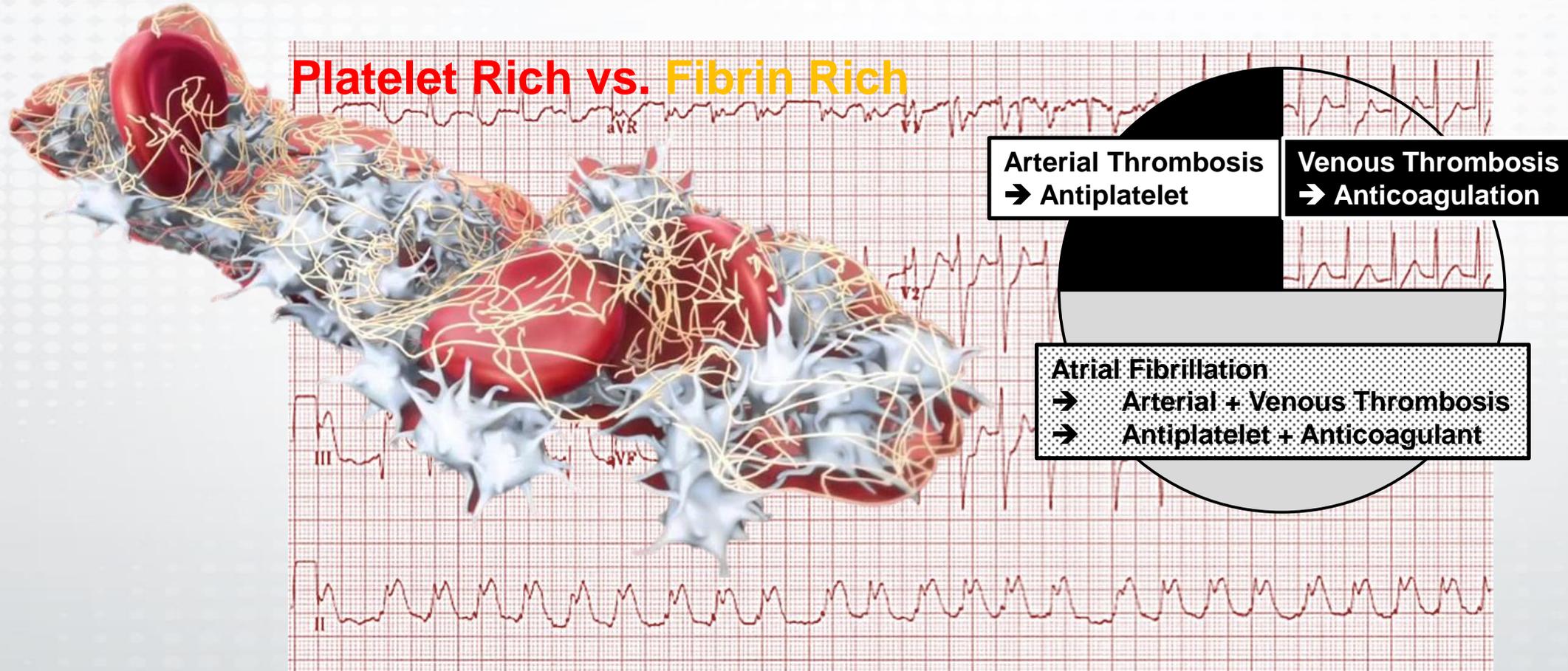
Last verified: November 2016

[History of Changes](#)

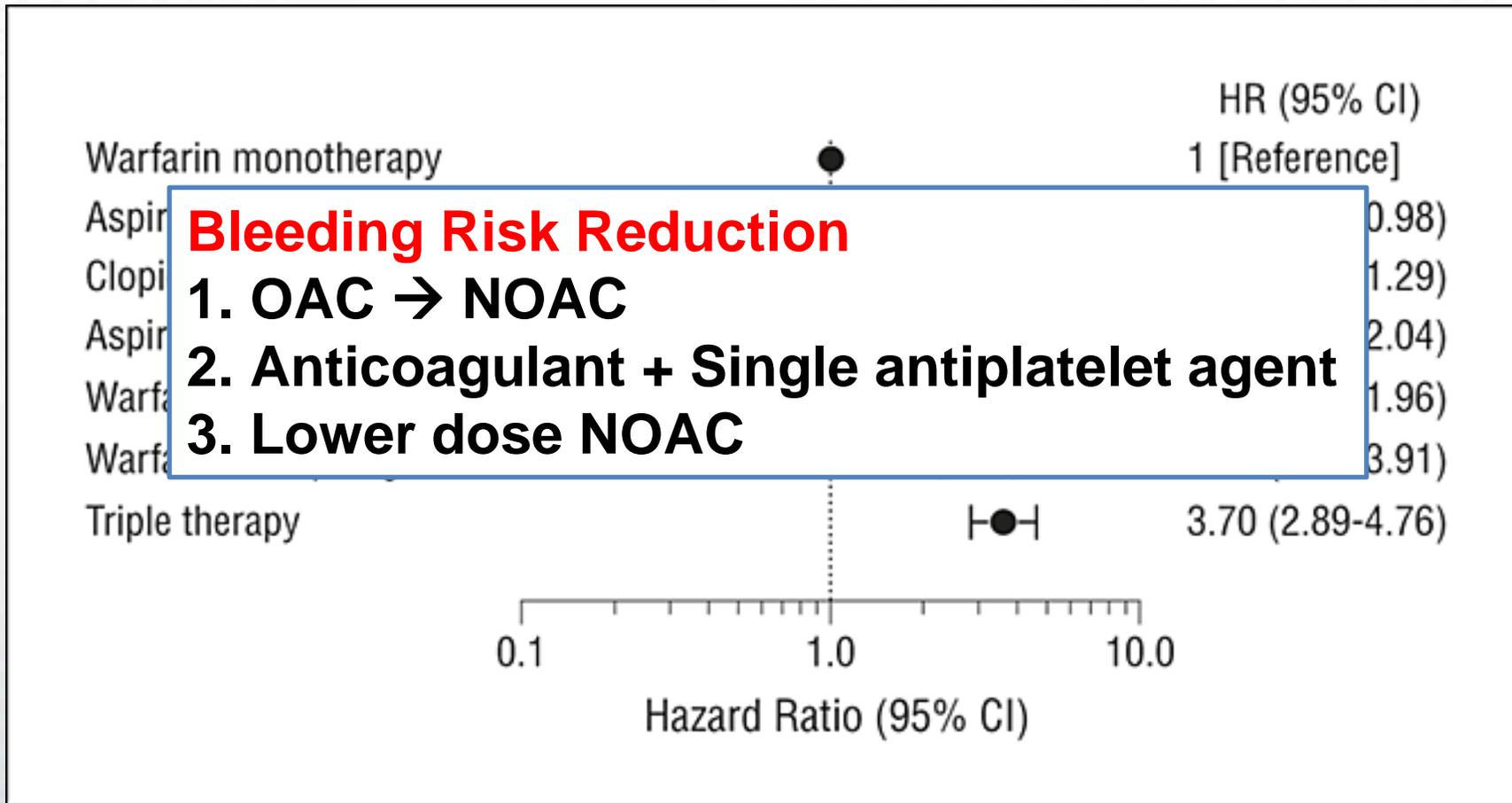
# Summary of the REMODELING study

- Enhanced levels of platelet activation and inflammation determined the incidence of adverse LV expansion after STEMI.
- Combining the measurements of these risk factors increased risk stratification of LVR.
- The role of intensified antiplatelet therapy in wound healing of infarcted myocardium is under investigation in the HEALING-AMI trial.

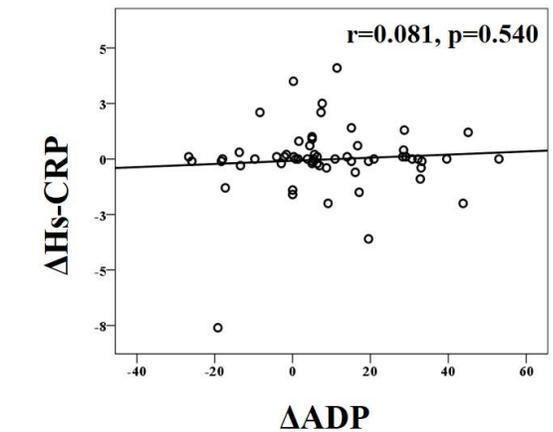
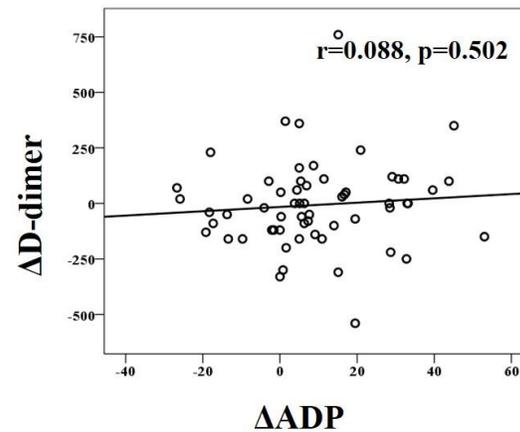
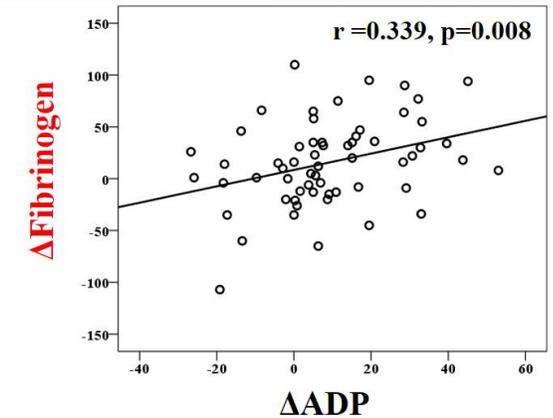
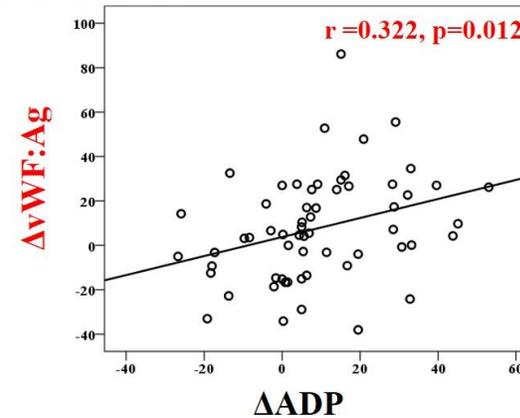
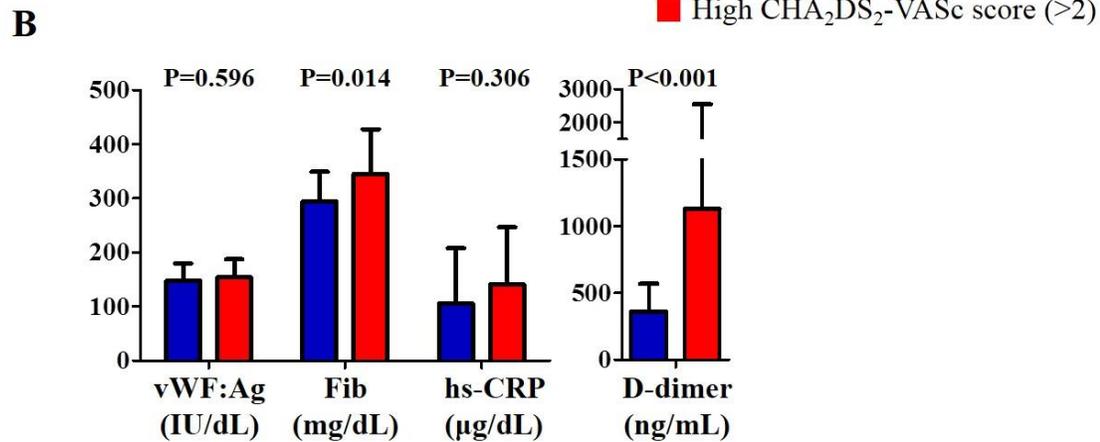
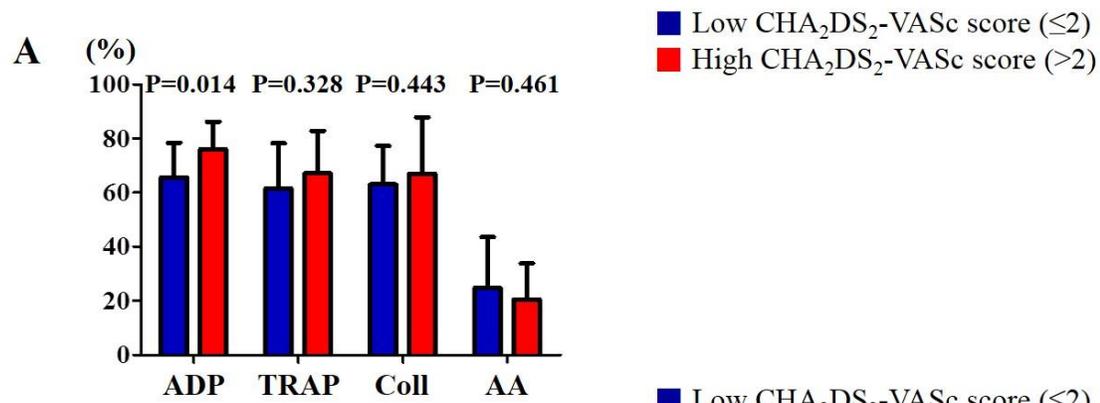
# PCI in Patients at Hypercoagulable Condition



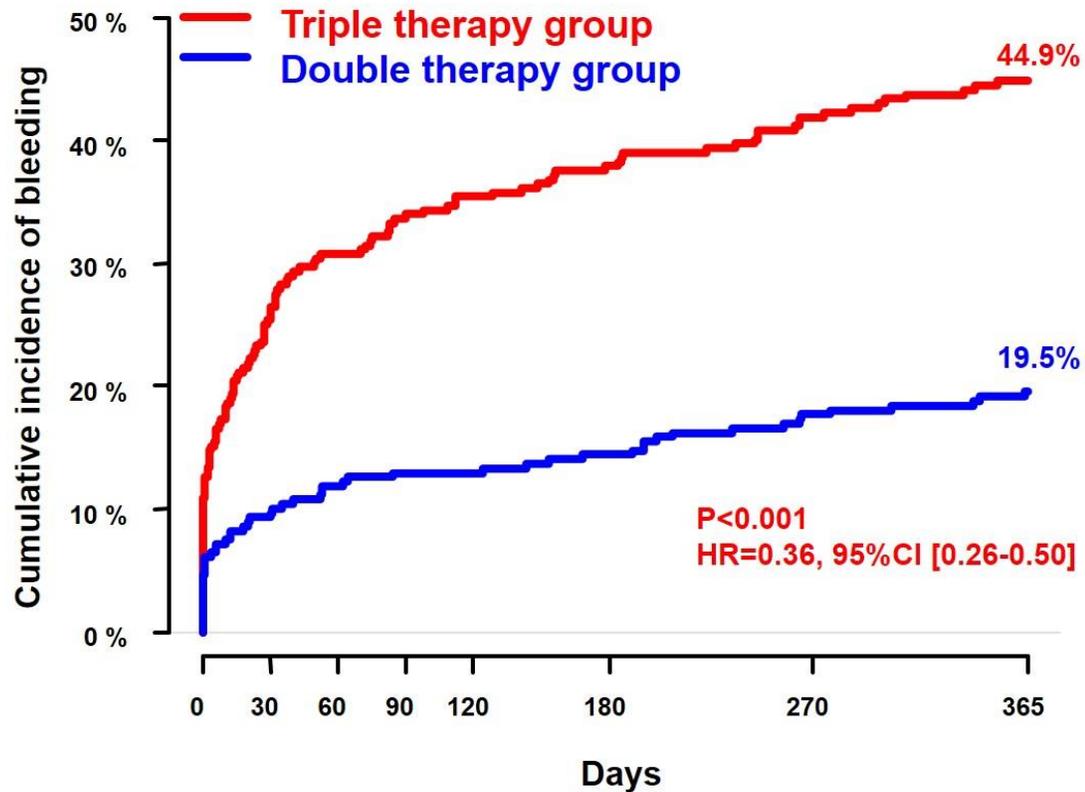
# Risk of Bleeding With Single, Dual, or Triple Therapy



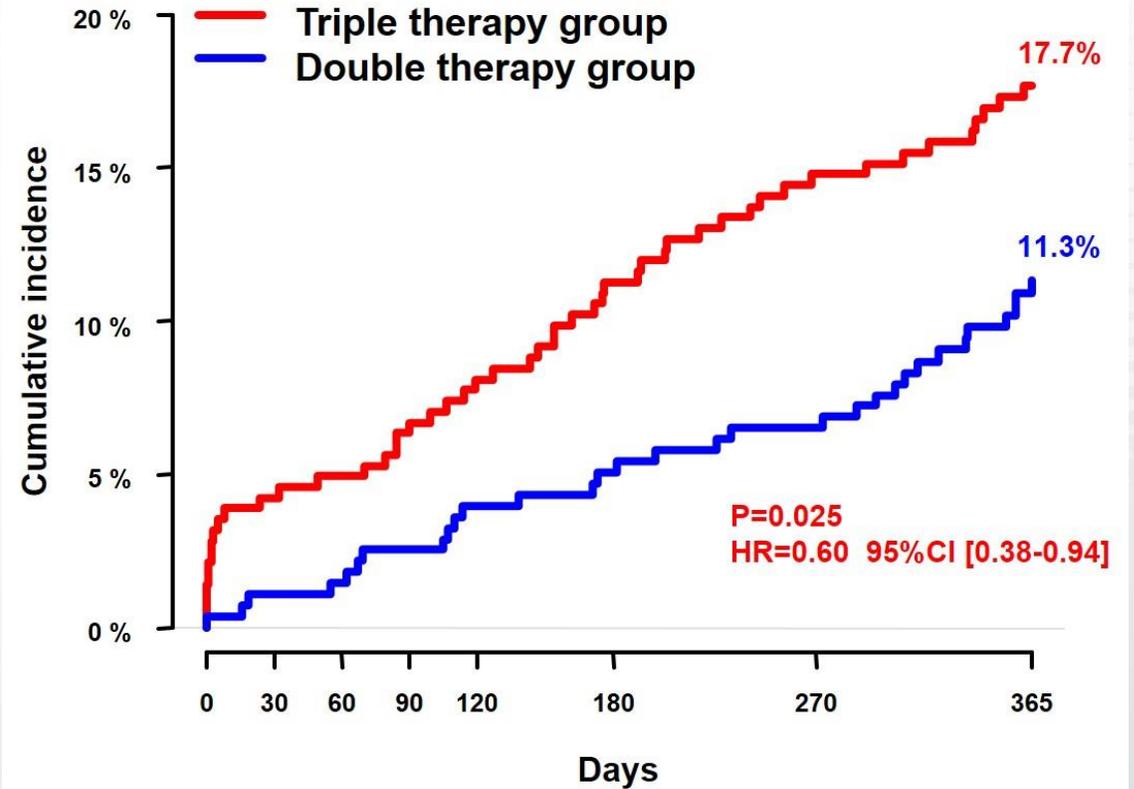
# Cross-talk Between Platelet Activation and Coagulation in AF



# Omission of ASA: WOEST

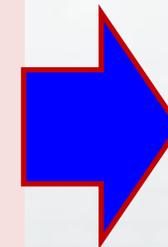
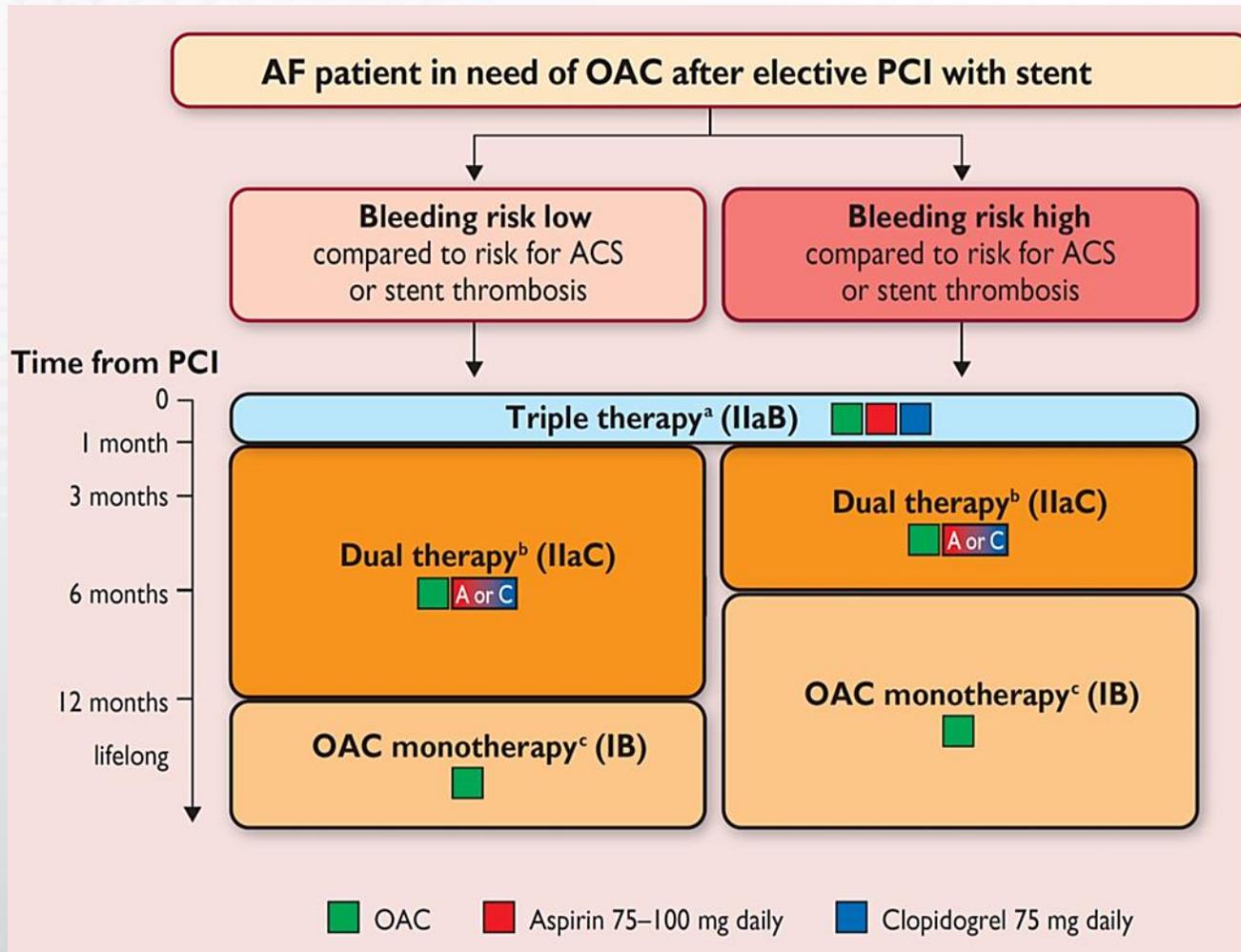


n at risk:	284	210	194	186	181	173	159	140
	279	253	244	241	241	236	226	208



n at risk:	284	272	270	266	261	252	242	223
	279	276	273	270	266	263	258	234

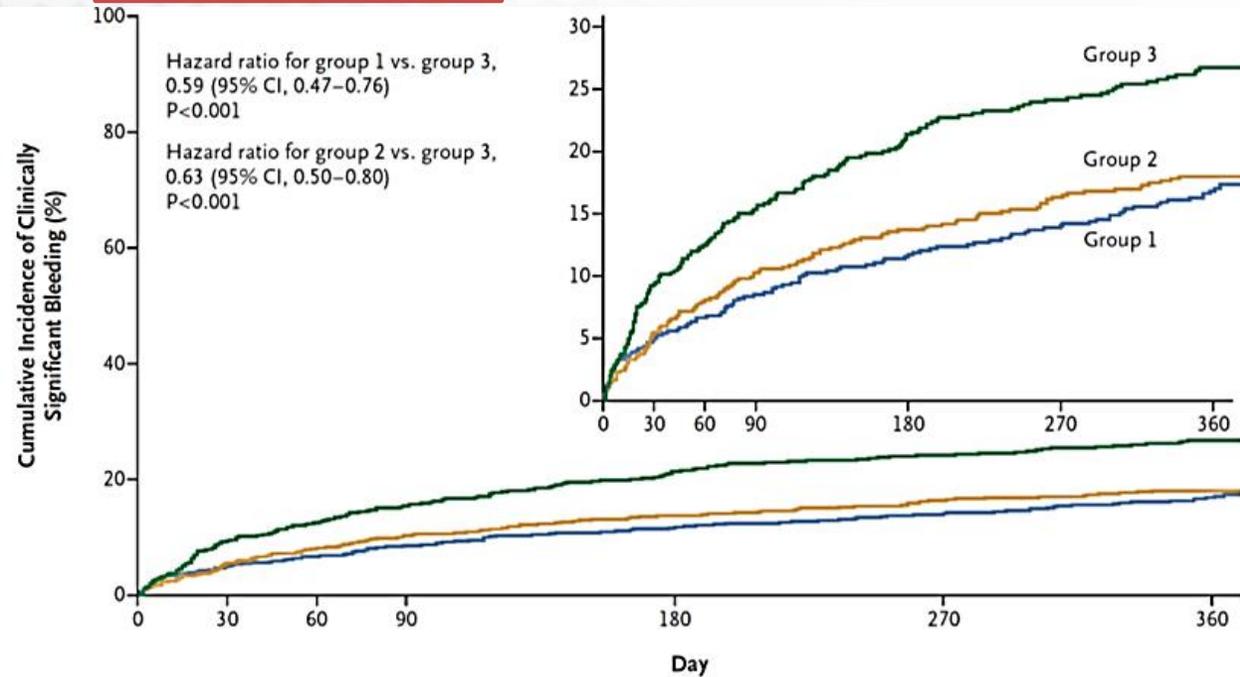
# Antithrombotic Therapy in MI Patients



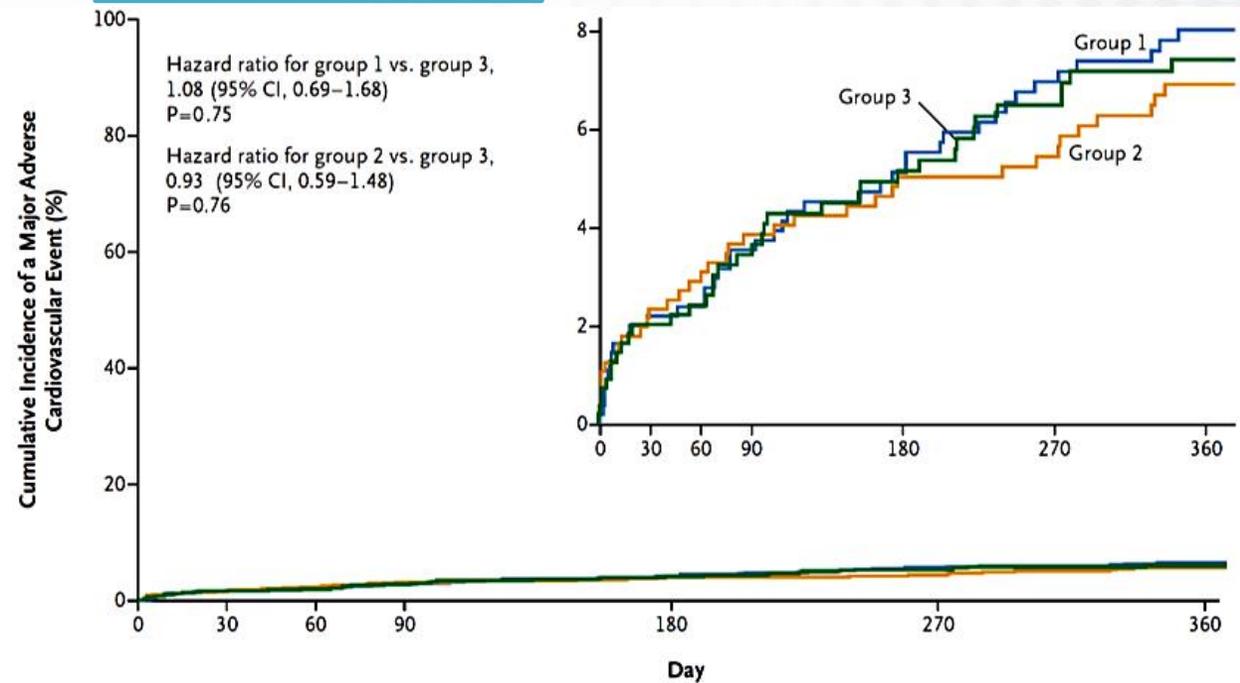
Ischemic Risk?

# PIONEER AF-PCI

## Safety Endpoint



## Efficacy Endpoint

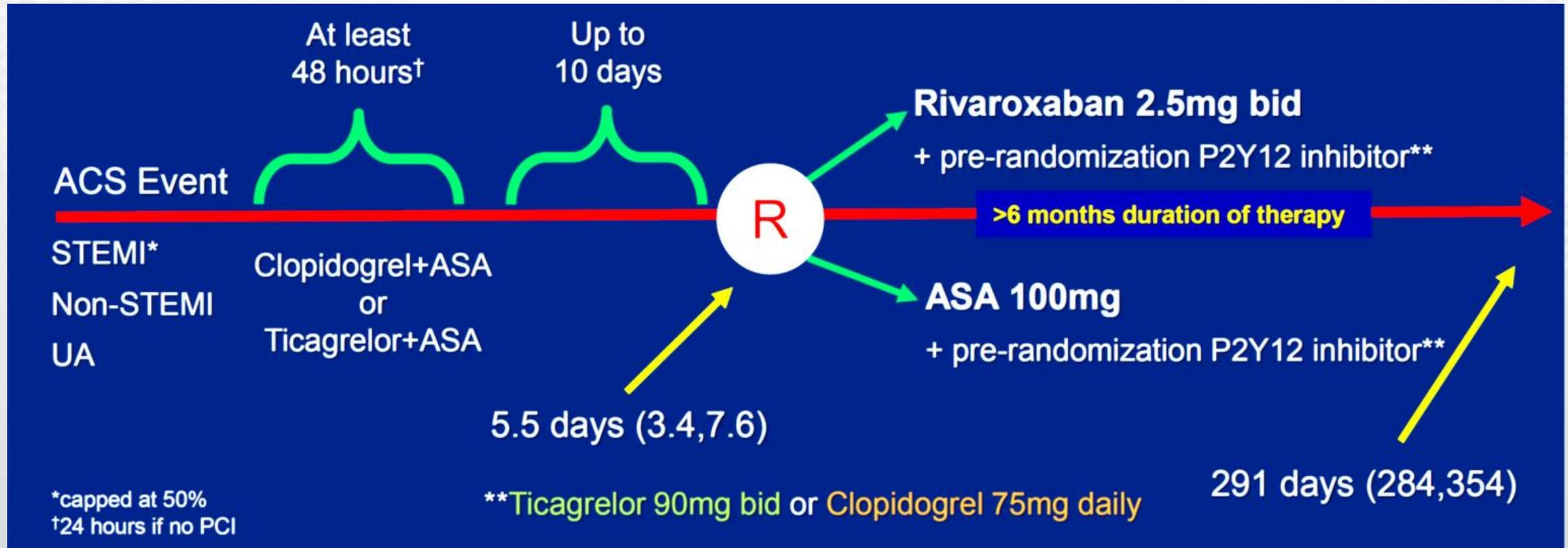


**Group 1: Rivaroxaban 15 (10)mg qd + Clopidogrel/Ticagrelor/Prasugrel for 12 months**

**Group 2: Rivaroxaban 2.5 mg bid + DAPT for 1, 6, or 12 months → Rivaroxaban 15 (10) mg qd + ASA for the remain**

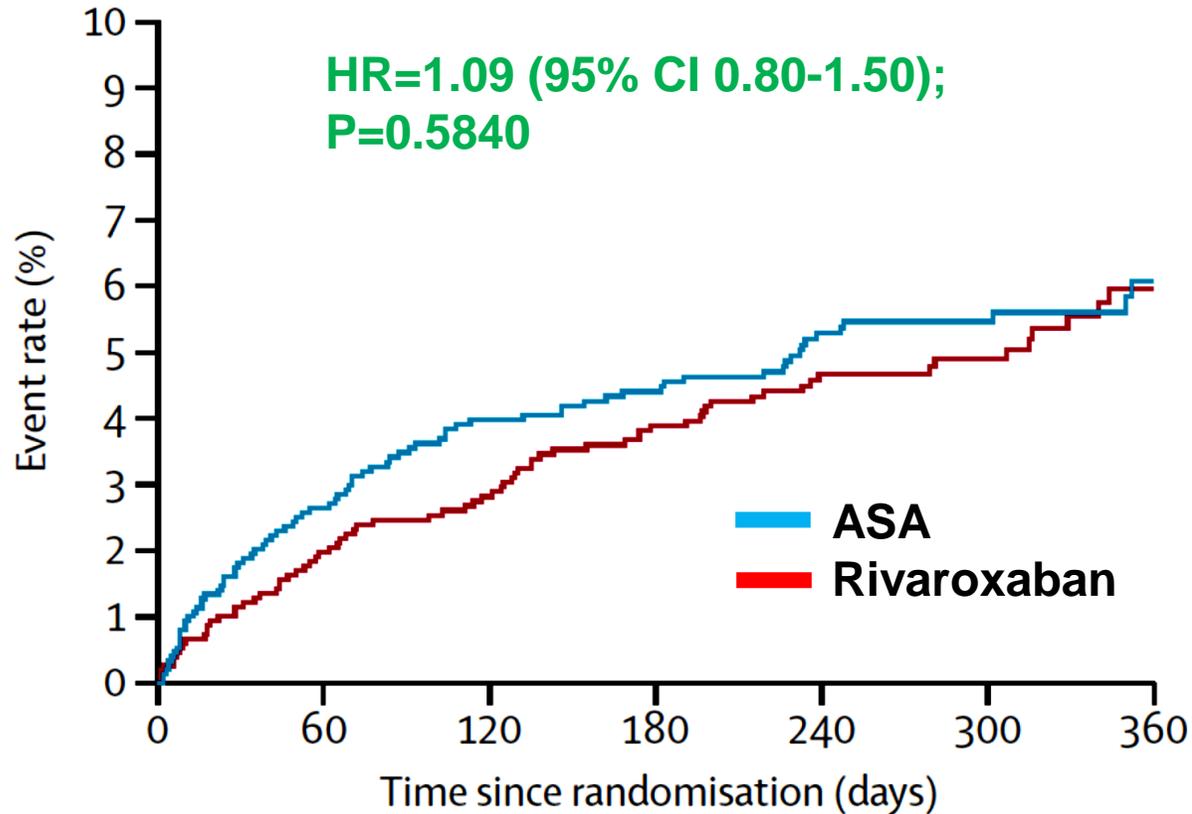
**Group 3: OAC + DAPT for 1, 6, 12 months → OAC + ASA for the remain**

# GEMINI-ACS-1

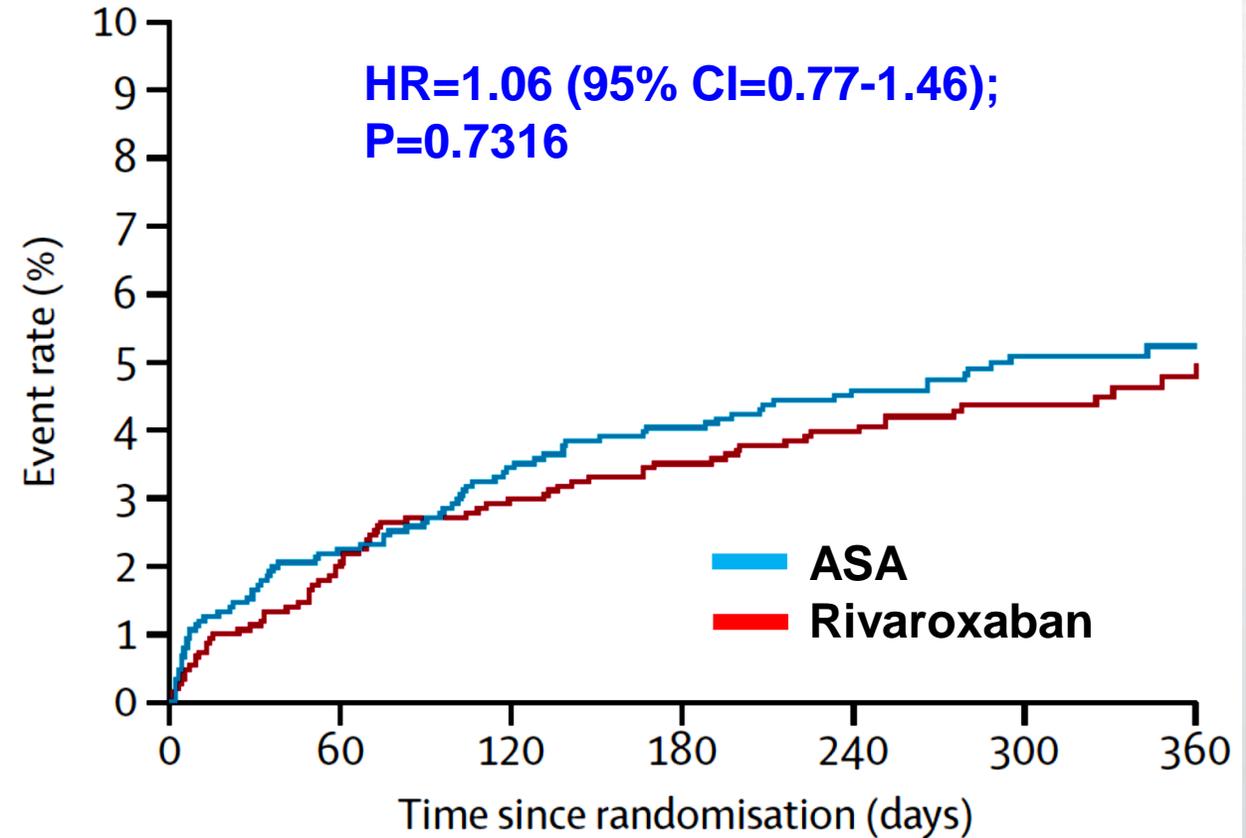


# GEMINI-ACS-1

## Safety Endpoint

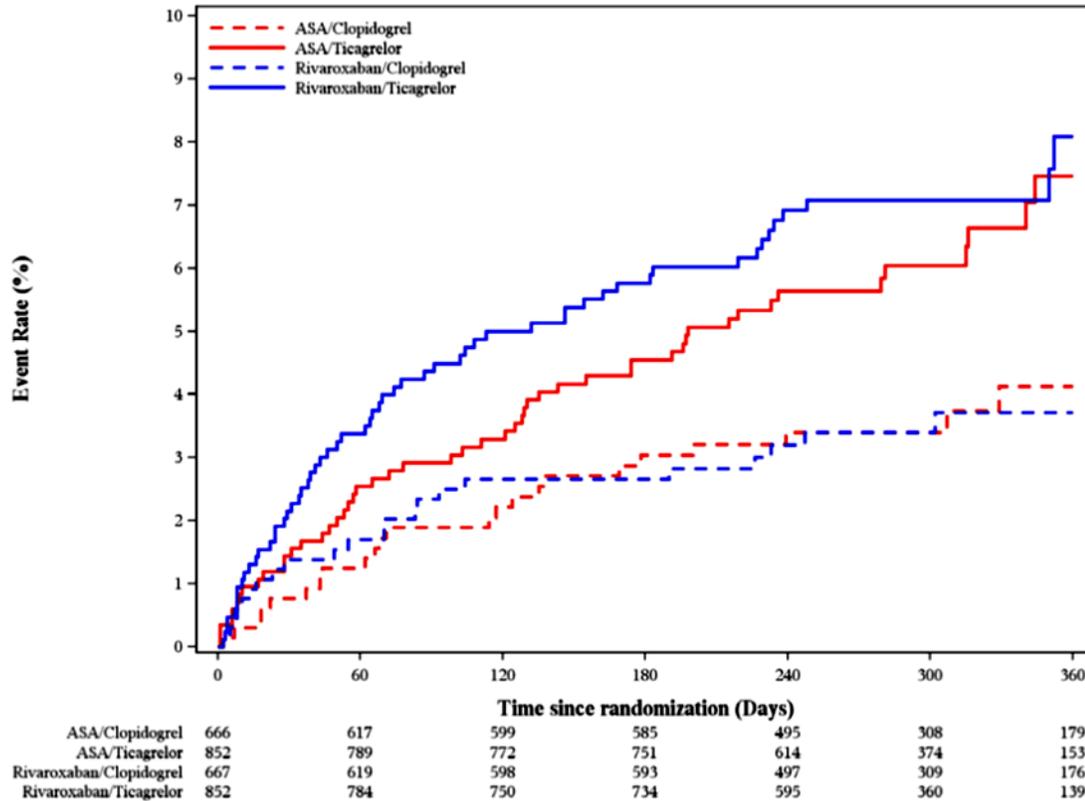


## Efficacy Endpoint



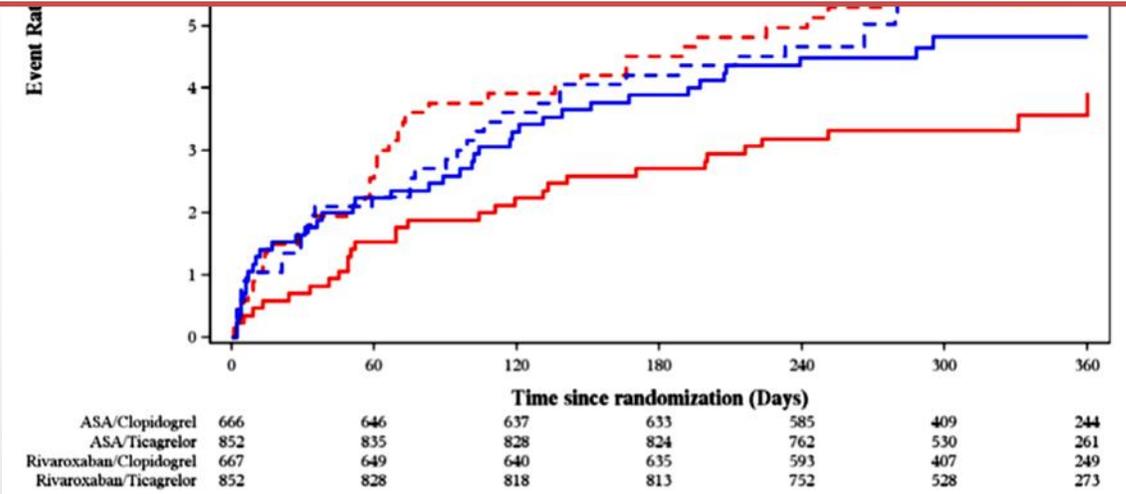
# GEMINI-ACS-1: Analysis by P2Y<sub>12</sub> Strata

## Safety Endpoint



## Efficacy Endpoint

**Ticagrelor + ASA = 3.9%;**  
**Ticagrelor + Rivaroxaban = 4.7%;**  
**Clopidogrel + Rivaroxaban = 5.4%;** and  
**Clopidogrel + ASA = 5.9%**

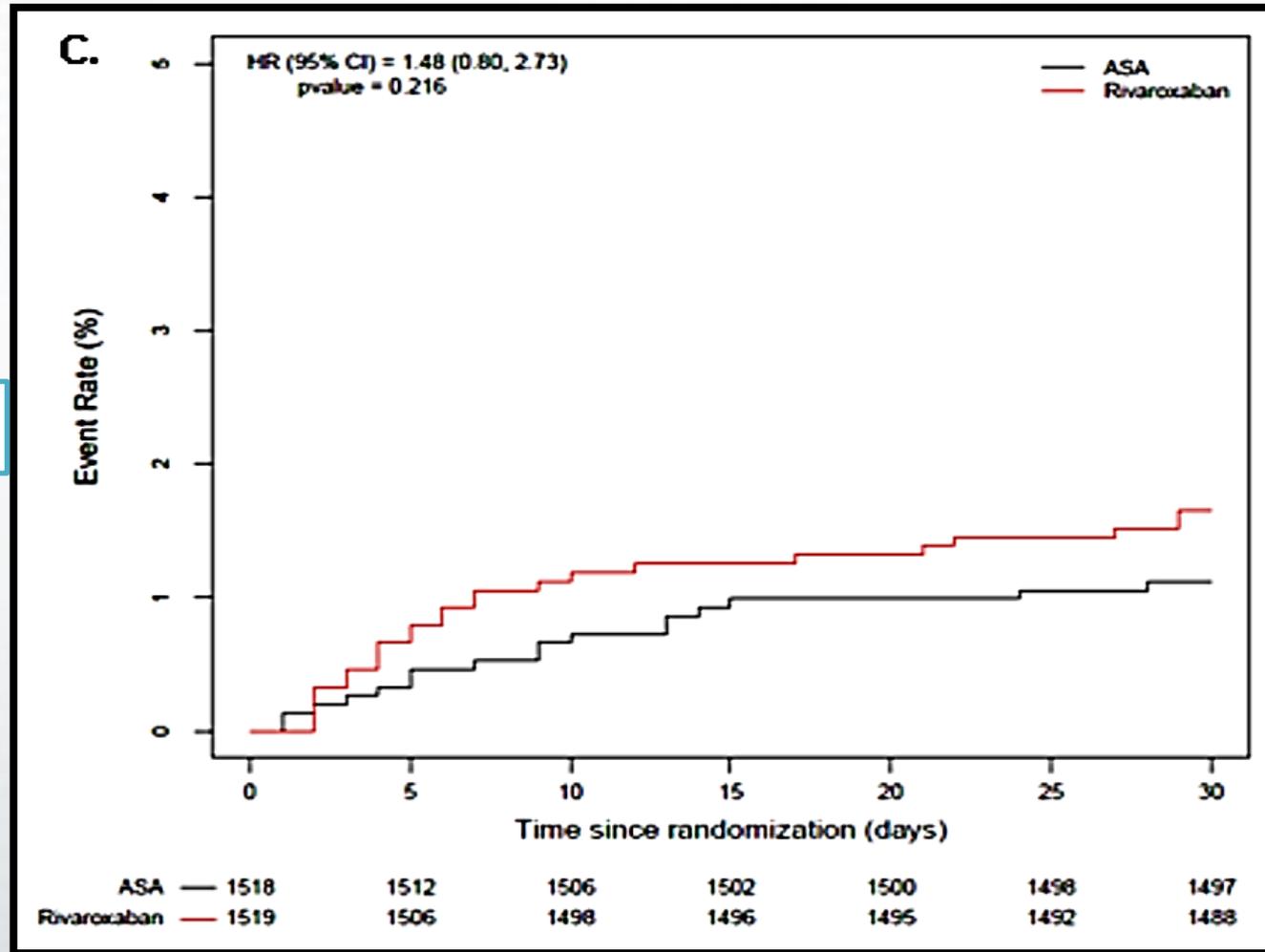


- - - ASA/Clopidogrel  
— ASA/Ticagrelor

- - - Rivaroxaban/Clopidogrel  
— Rivaroxaban/Ticagrelor

# GEMINI-ACS-1: 30-day Landmark Analysis

Efficacy Endpoint



# Summary

1. Potent platelet inhibitors are underutilized in Korean MI patients.
2. This may be mainly due to the fear of the inherent bleeding risk by potent platelet inhibition.
3. Korean MI patients have a similar in-hospital mortality with Western patients, which underlines more wide acceptance of potent P2Y<sub>12</sub> inhibitors.
4. Enhanced platelet inhibition may prevent the development of heart failure after MI.
5. Low dose rivaroxaban with a P2Y<sub>12</sub> inhibitor may be a possible option for MI patients at hypercoagulable state.
6. Potent platelet inhibition definitely reduced a ischemic risk and increased a bleeding risk in MI patients.

# Conclusion

- Historical clopidogrel based DAPT may be a decent antiplatelet agent, but high proportion of Korean MI patients need a better antiplatelet care.



감사합니다