Pharmacodynamic Responses of Low Dose New P2Y12 Inhibitor in Korean

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2. PD of Low vs High LD of Prasugrel *in CAD Patients*
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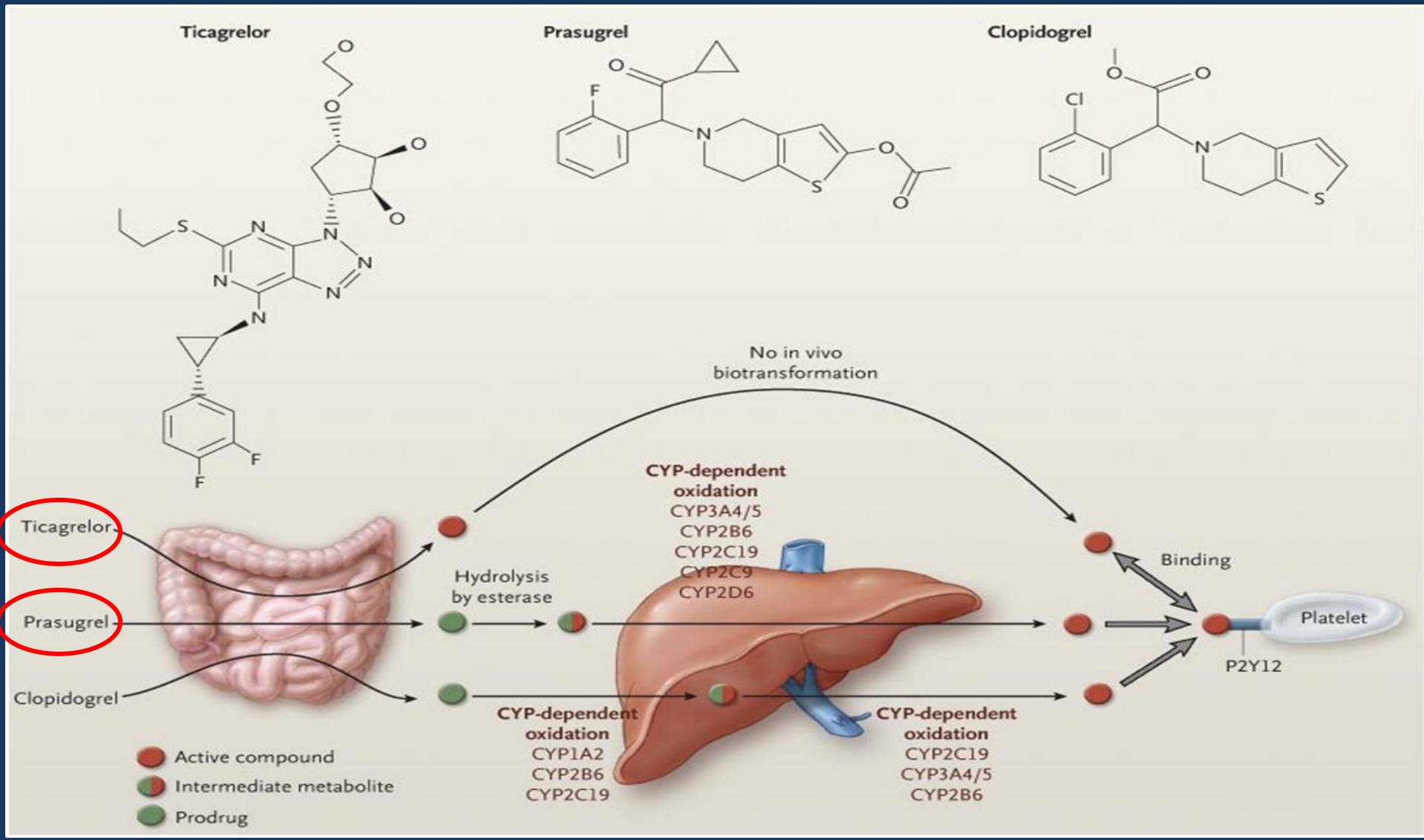
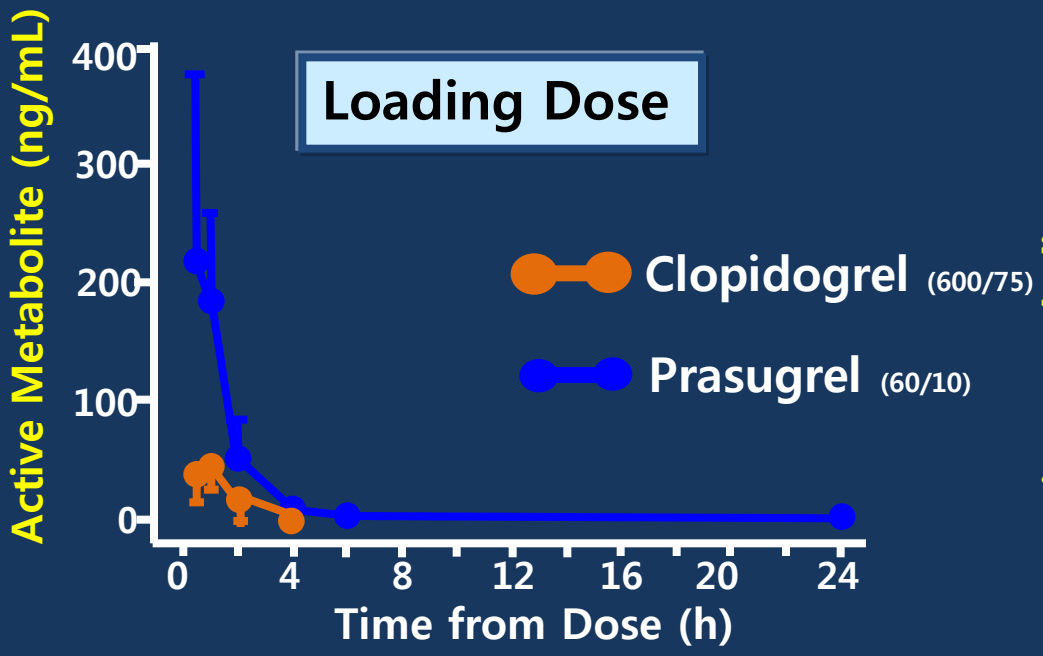
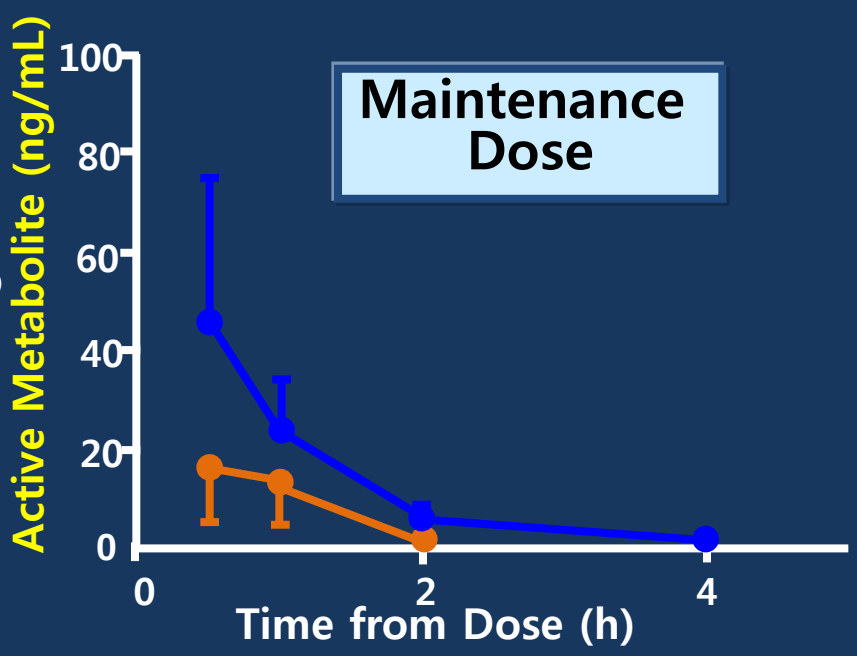
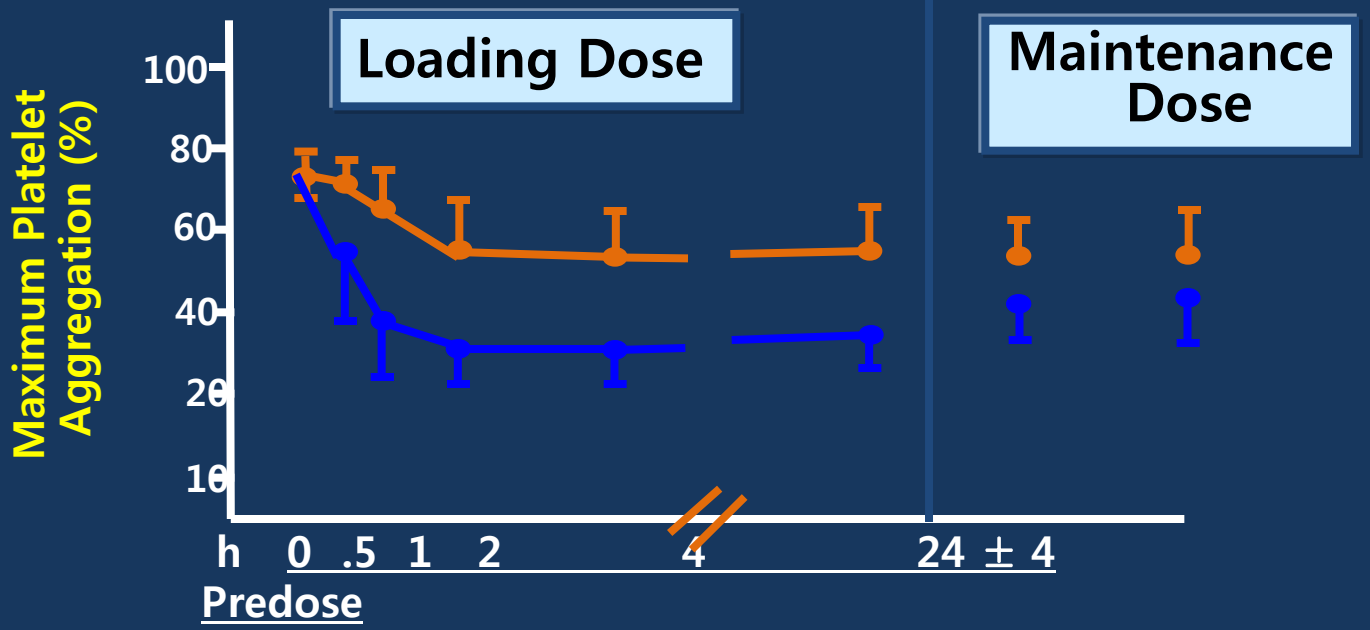
5. Low Dose (Single dose) of Ticagrelor Loading and Maintenance *in Healthy Volunteer*
6. Standard Dose of Prasugrel and Ticagrelor Loading *in STEMI Patients*


Ticagrelor
Prasugrel
Clopidogrel
No in vivo biotransformation
CYP-dependent oxidation
CYP3A4/5
CYP2B6
CYP2C19
CYP2C9
CYP2D6
Ticagrelor
Prasugrel
Clopidogrel
Hydrolysis by esterase
Binding
Platelet
P2Y12
CYP-dependent oxidation
CYP1A2
CYP2B6
CYP2C19
CYP-dependent oxidation
CYP2C19
CYP3A4/5
CYP2B6
Active compound
Intermediate metabolite
Prodrug

Clopidogrel vs. Prasugrel: Pharmacokinetics and Pharmacodynamics



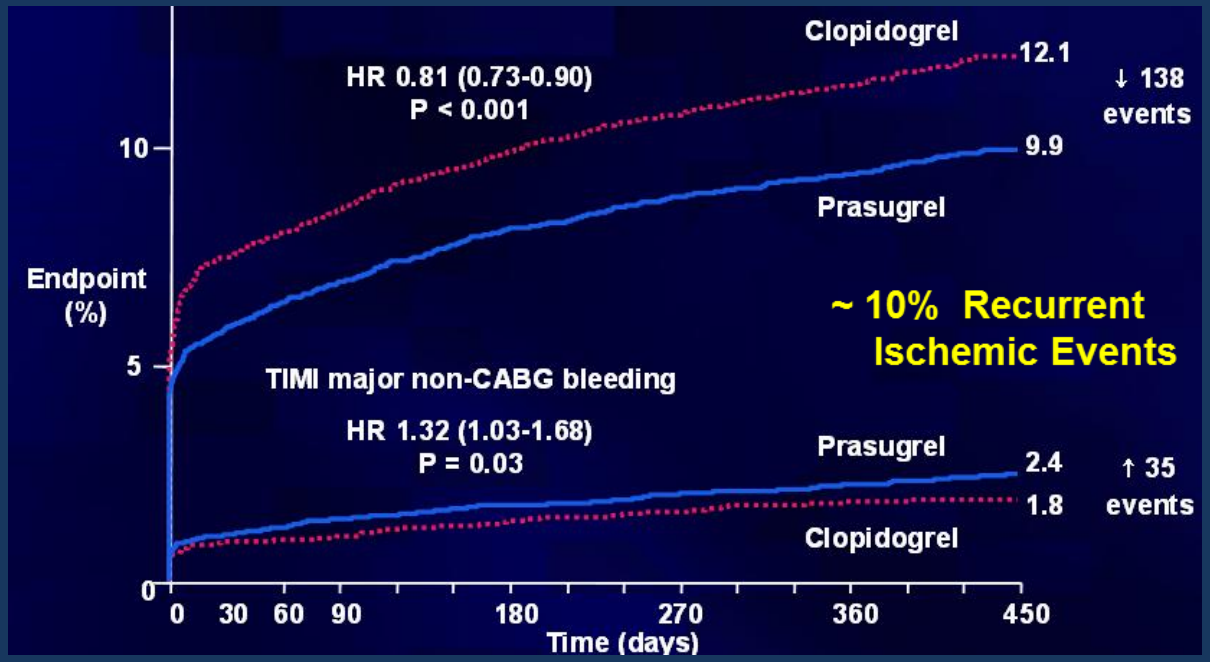




Wallentin L et al. *Eur Heart J* 2008;29:21-30

TRITON-TIMI 38 Study

Prasugrel vs. Clopidogrel

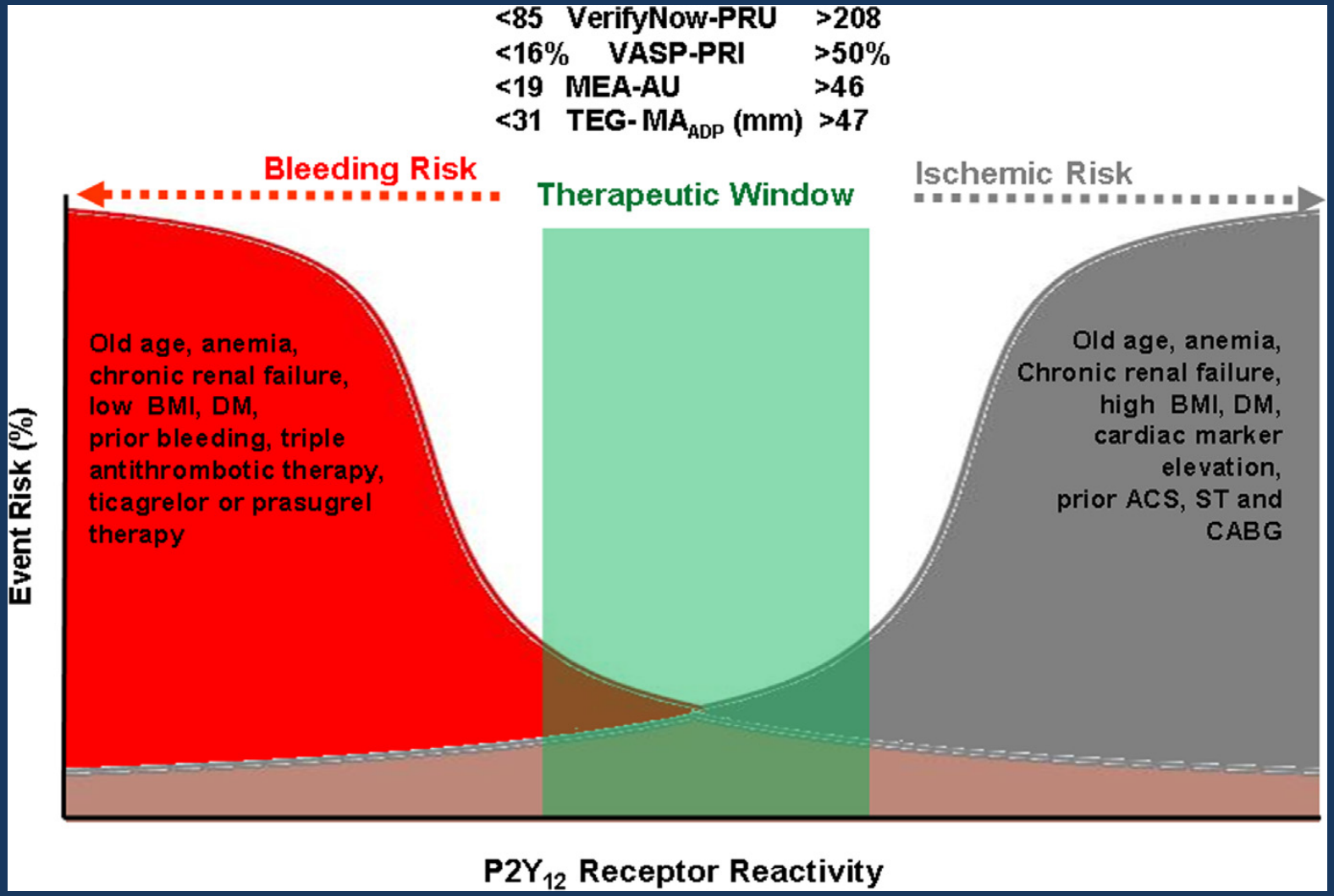


TIMI Bleeding

	Prasugrel	Clopidogrel	p-value
Non-CABG	2.4%	1.8%	0.03
Major or Minor	4.0%	3.0%	<0.001
CABG-related	13.4%	3.2%	<0.001

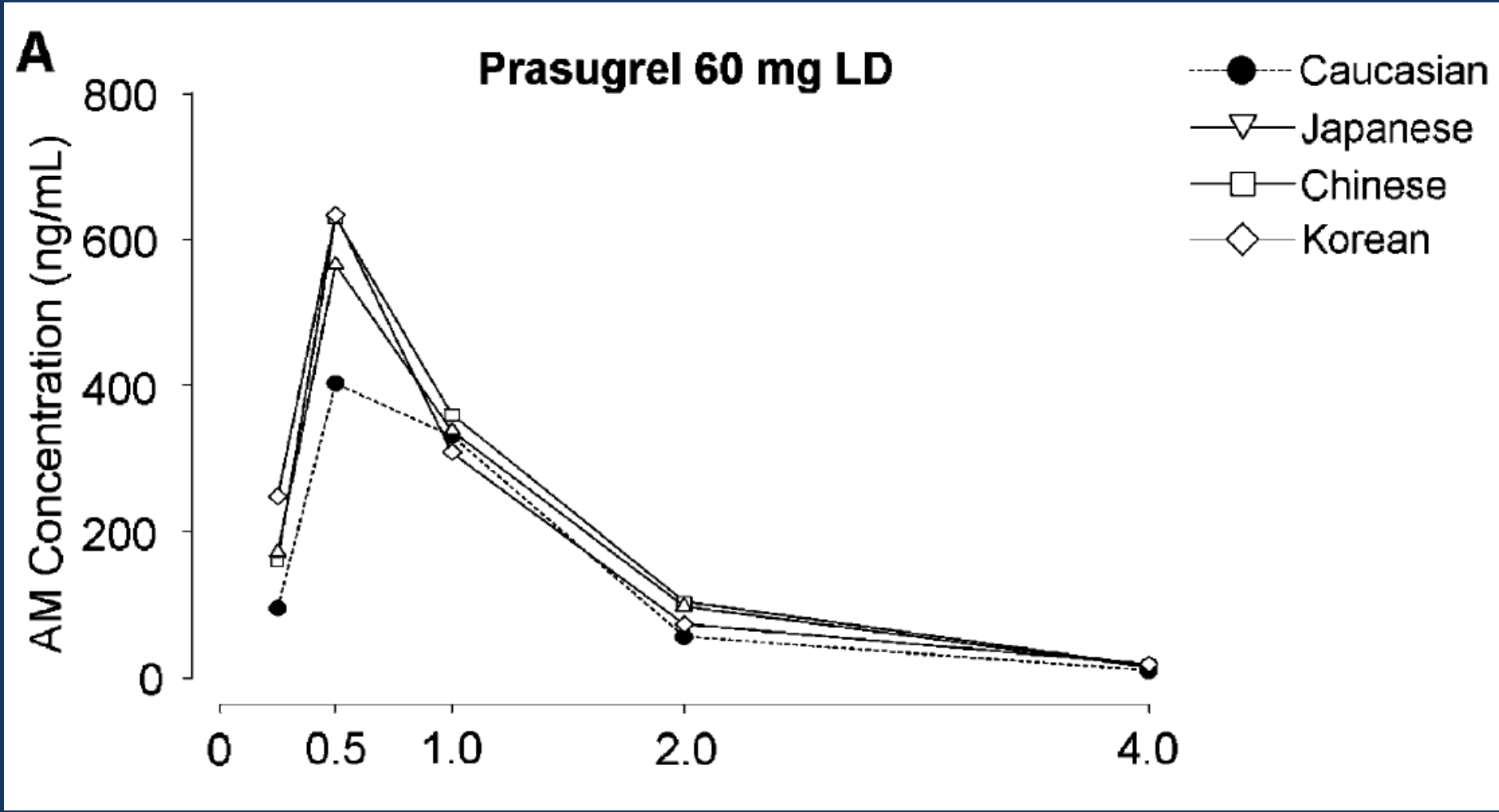
Wiviott SD et al. *N Engl J Med* 2007;357:2001-15

Consensus on the Definition of HPR and LPR



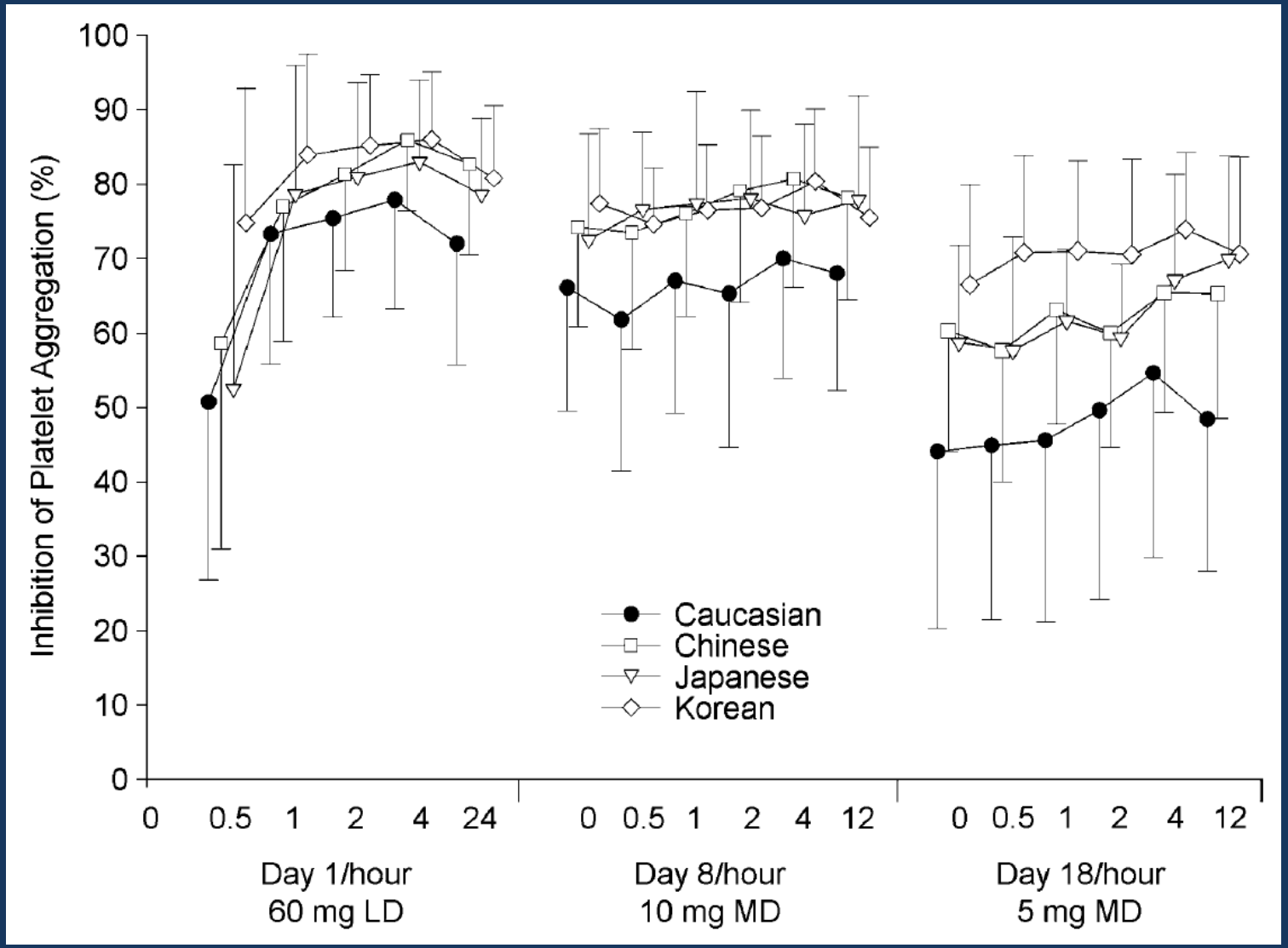
Tantry US et al, J Am Coll Cardiol. 2013 ; 62: 2261-2273.

Ethnic Difference of Prasugrel Loading



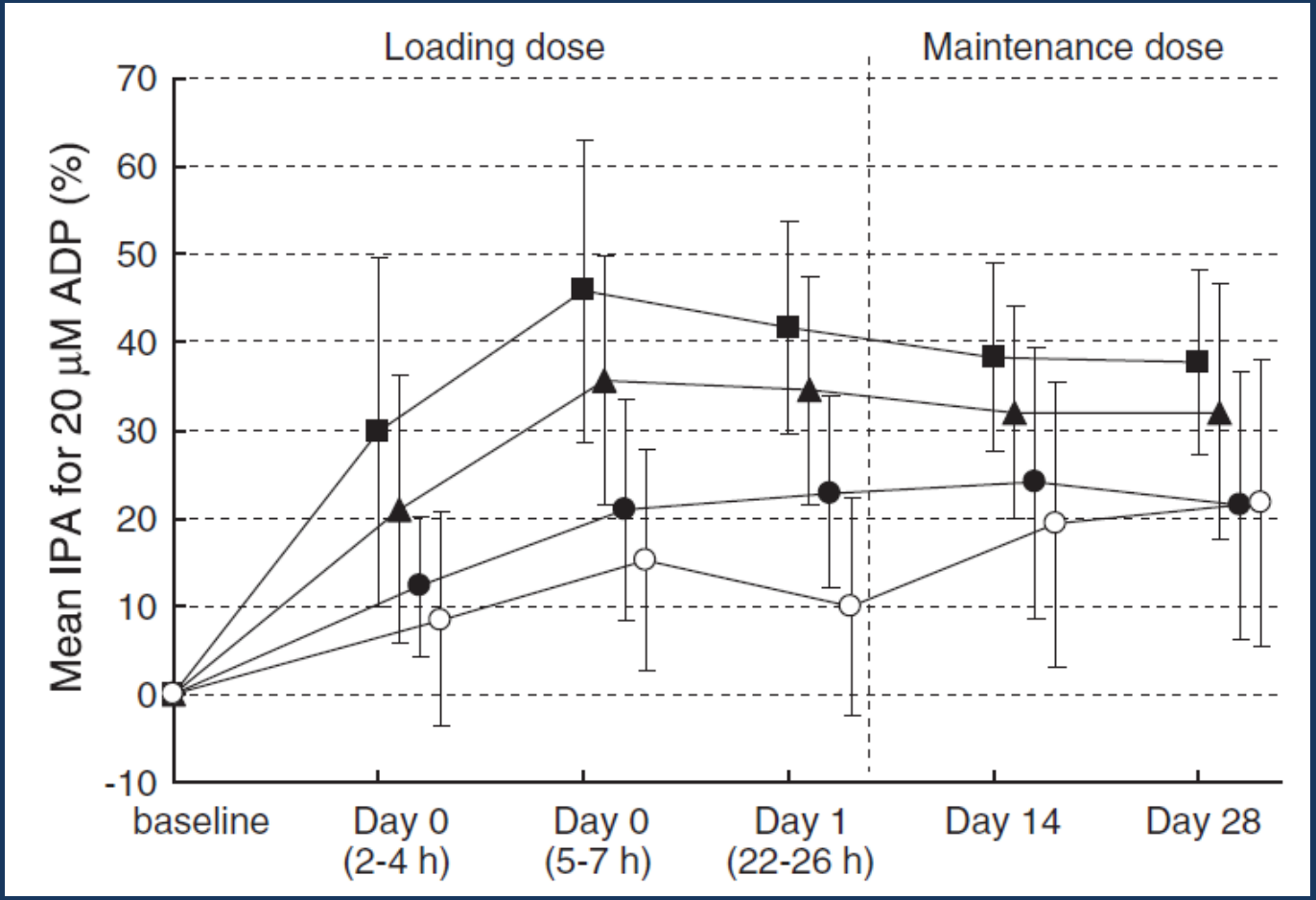
David S. Small et al. Eur J Clin Pharmacol, 2010: 66:127–135

Ethnic Difference of Prasugrel Loading and Maintenance Dose



David S. Small et al. Eur J Clin Pharmacol, 2010: 66:127–135

Low Dose Prasugrel and Clopidogrel mg in Japanese



- Prasugrel 20/5
- Prasugrel 15/3.75
- Prasugrel 10/2.5
- Clopidogrel 300/75

H. Yokoi et al. Thrombosis Research 129, 2012: 623–628

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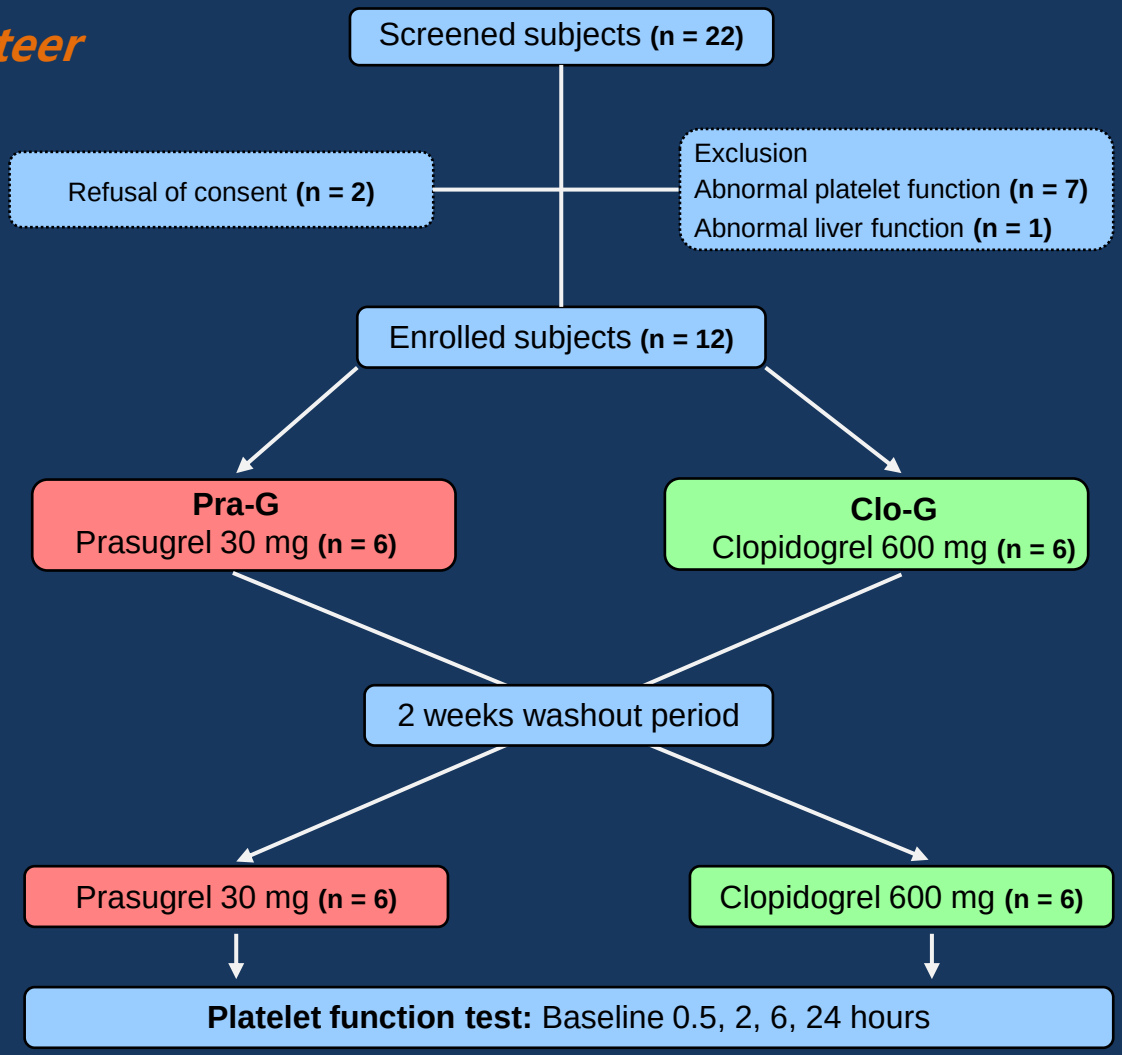
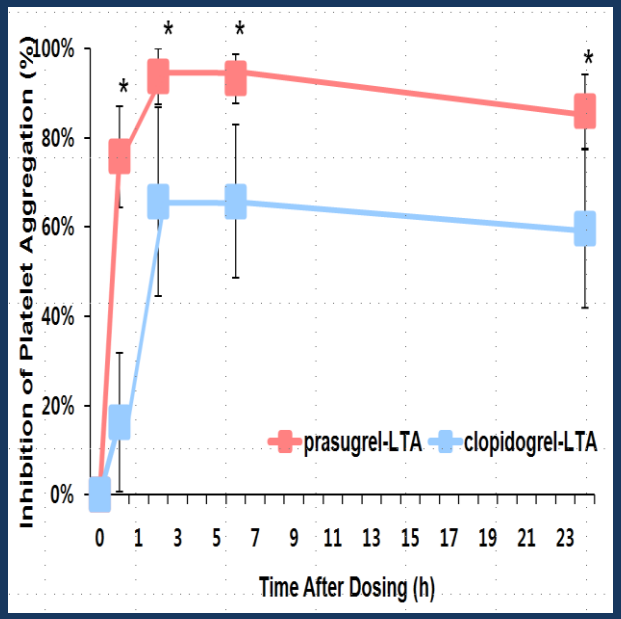
Clopidogrel 600mg vs Prasugrel 30mg

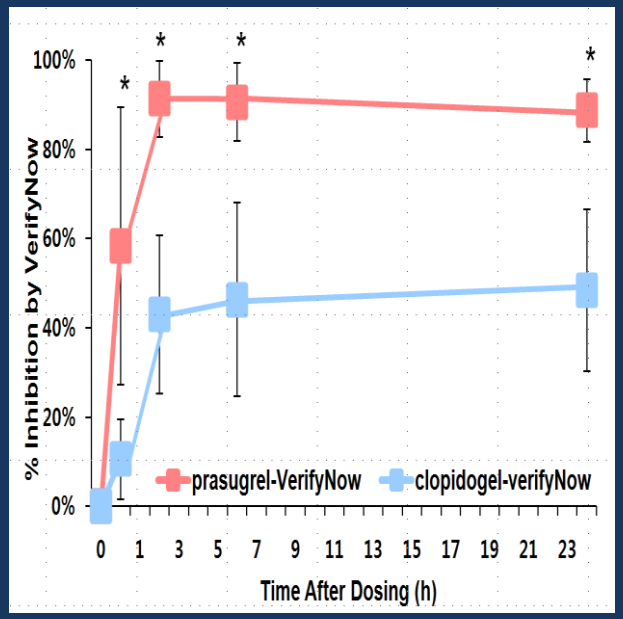
Healthy Volunteer

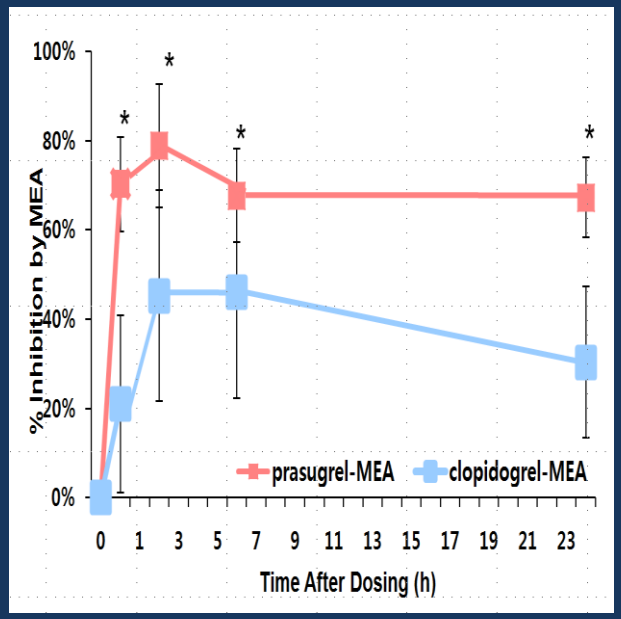


Kim MH, et al, Circulation Journal, 2013

Clopidogrel 600mg vs Prasugrel 30mg Loading in Heathy Voluteer







Kim MH, et al, Circulation Journal, 2013

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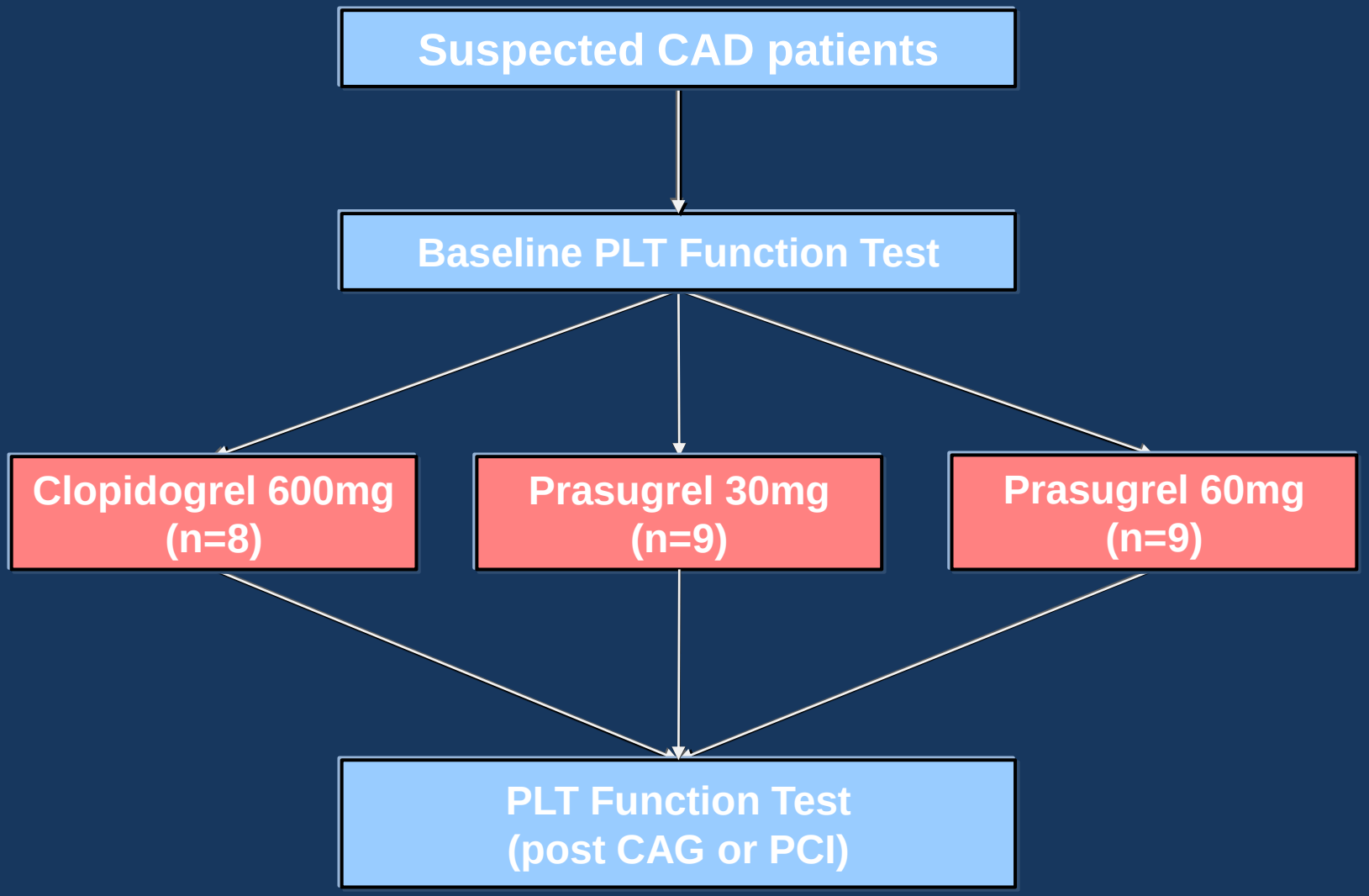
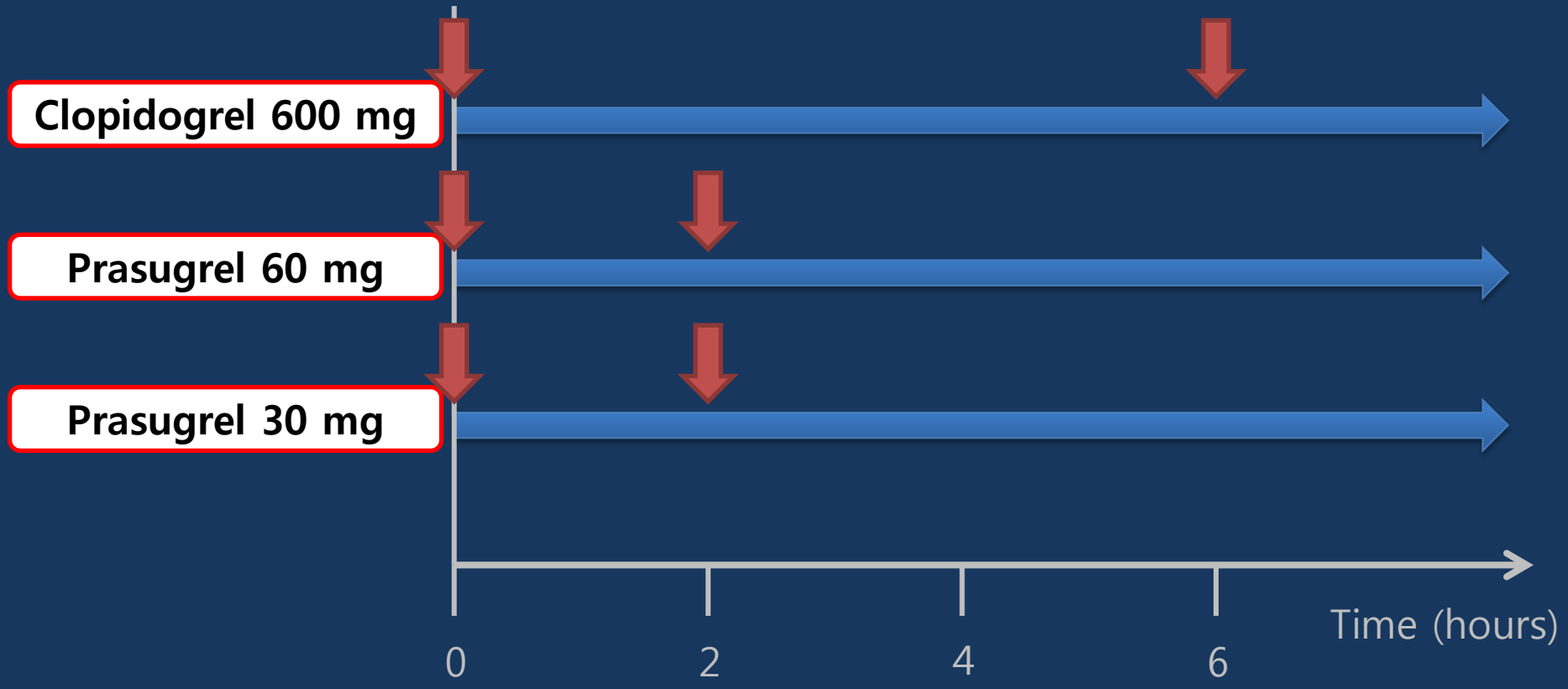


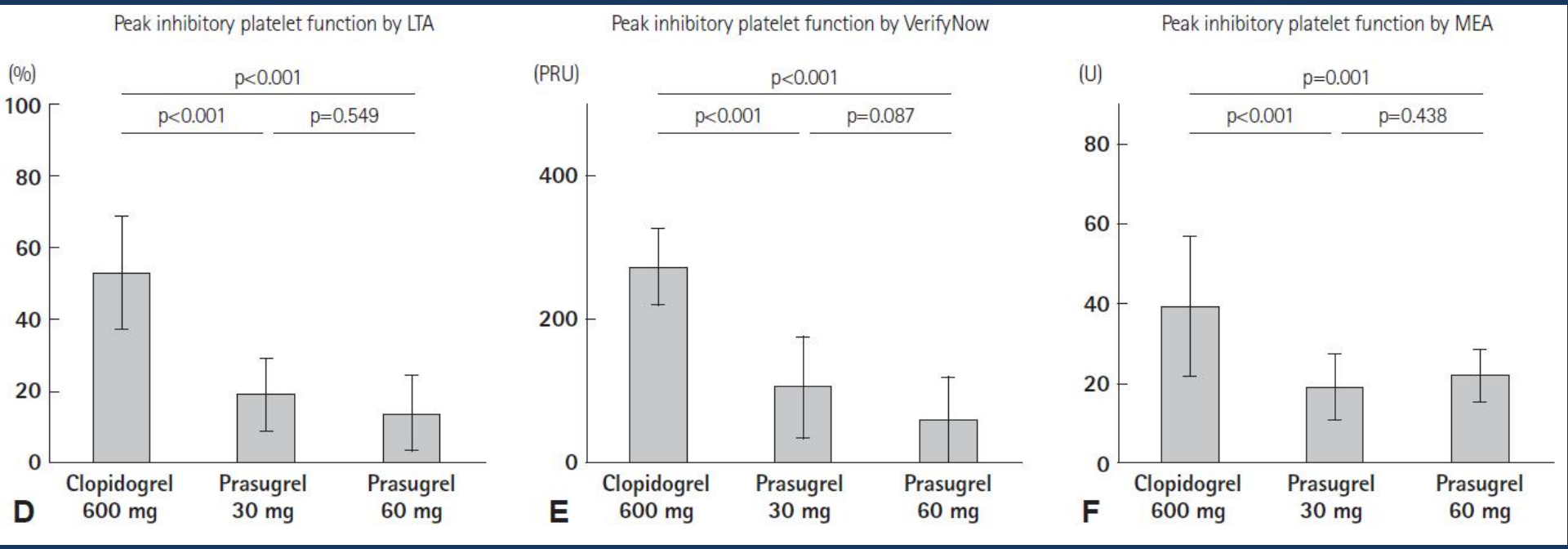
* **Platelet Function Measurement**
; light transmission aggregometry, VerifyNow, multiple electrode aggregometry

Methods – Time of Platelet Function Measurement



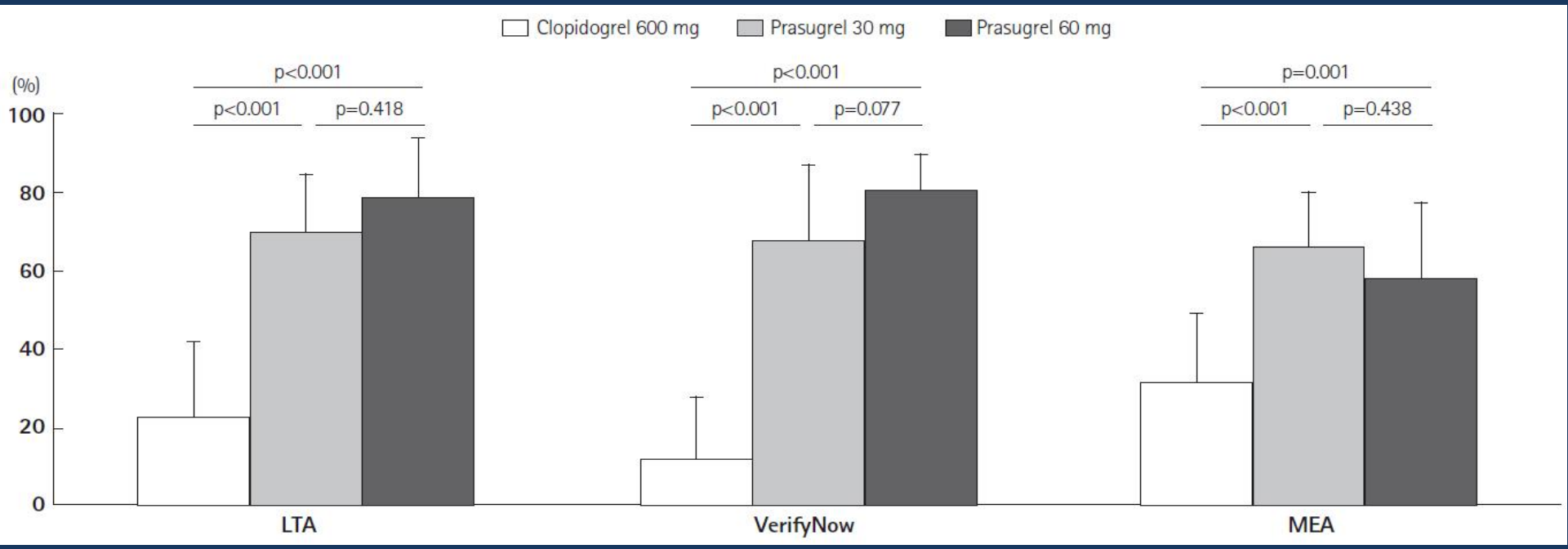
Results

Mean Platelet Activity ±SD at Peak by LTA, VerifyNow and MEA



Lee DH et al. Korean Circ J. 2014 ;44:386-393

Percent Inhibition of Platelet



Lee DH et al. Korean Circ J. 2014 ;44:386-393

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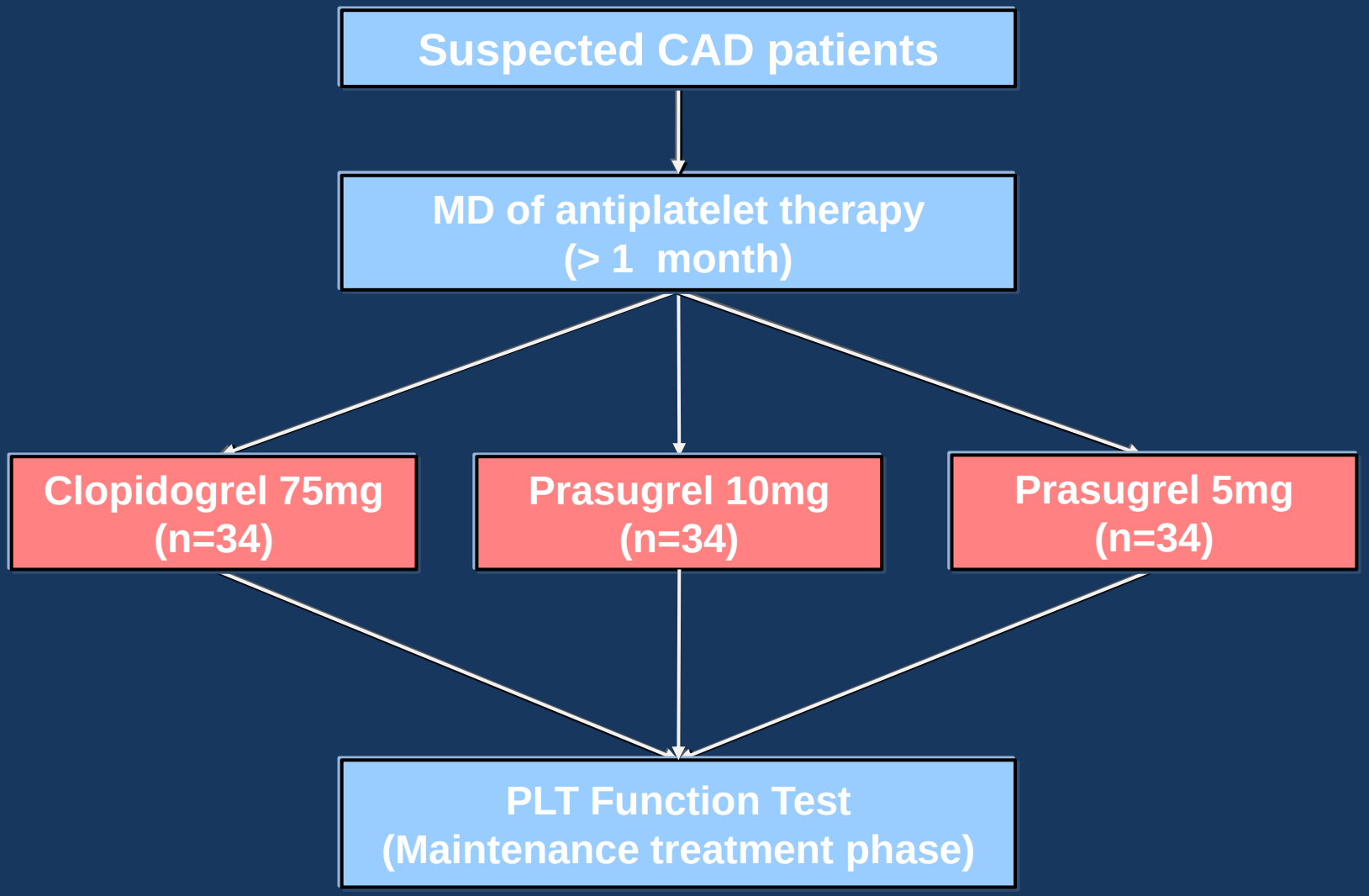
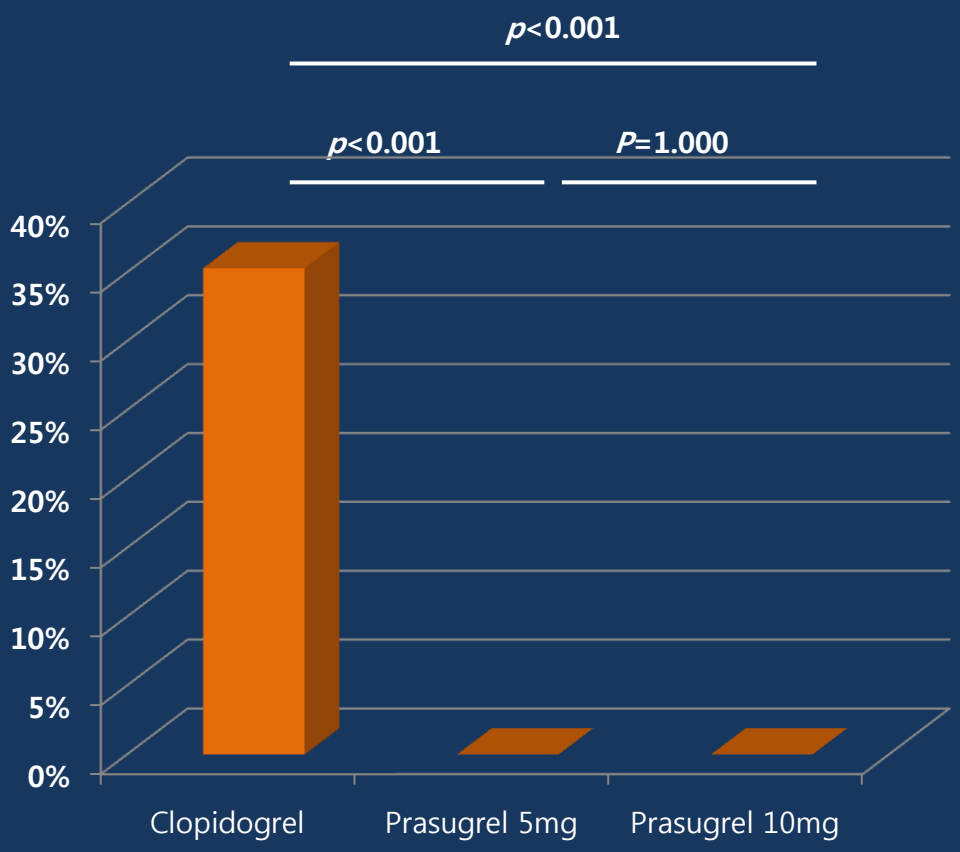
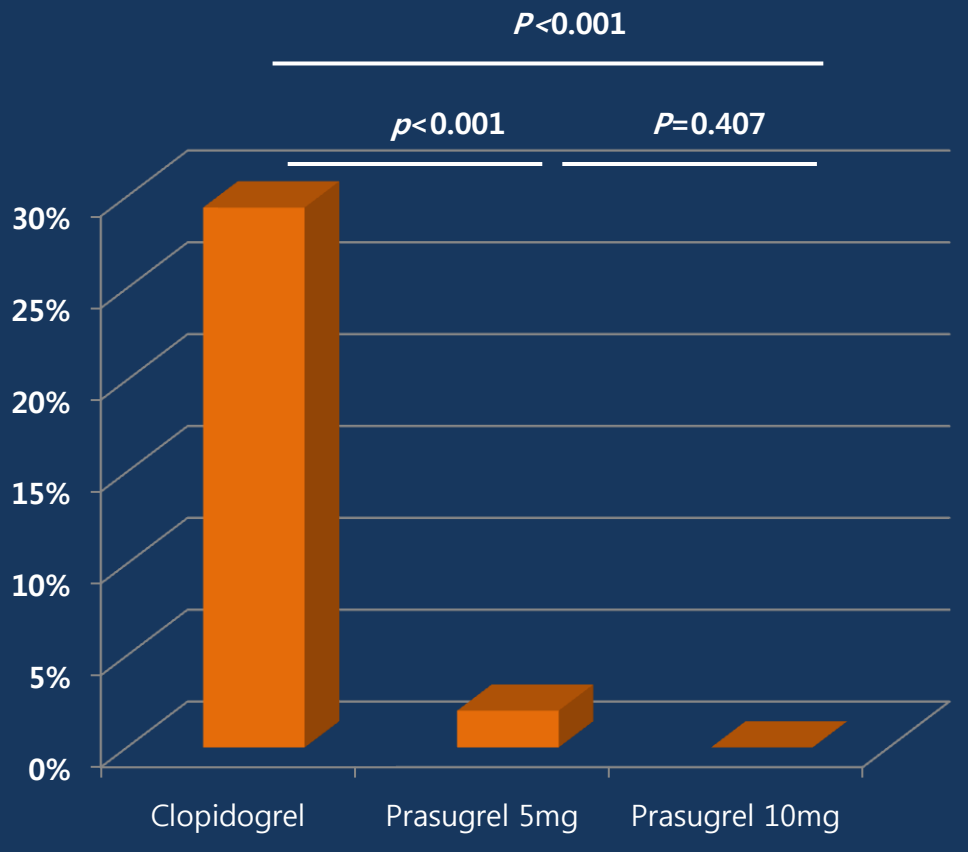


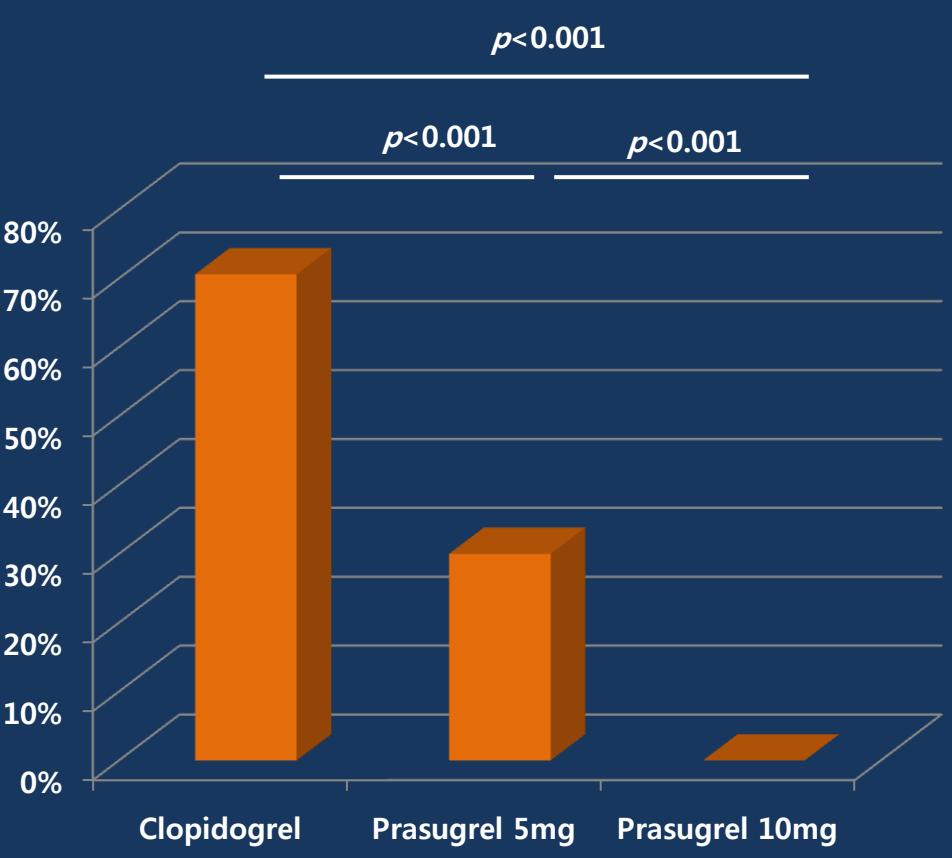
Platelet Function Measurement;
light transmission aggregometry, VerifyNow,
multiple electrode aggregometry.

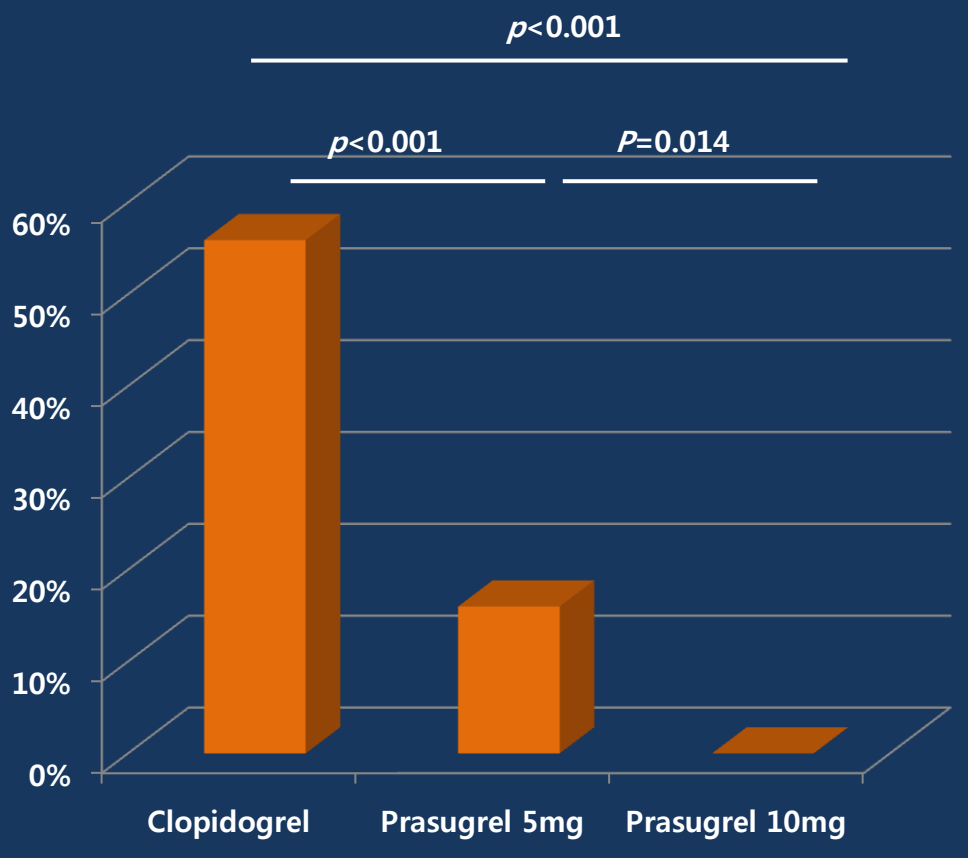
HPR by LTA(55) and MEA(46.8)



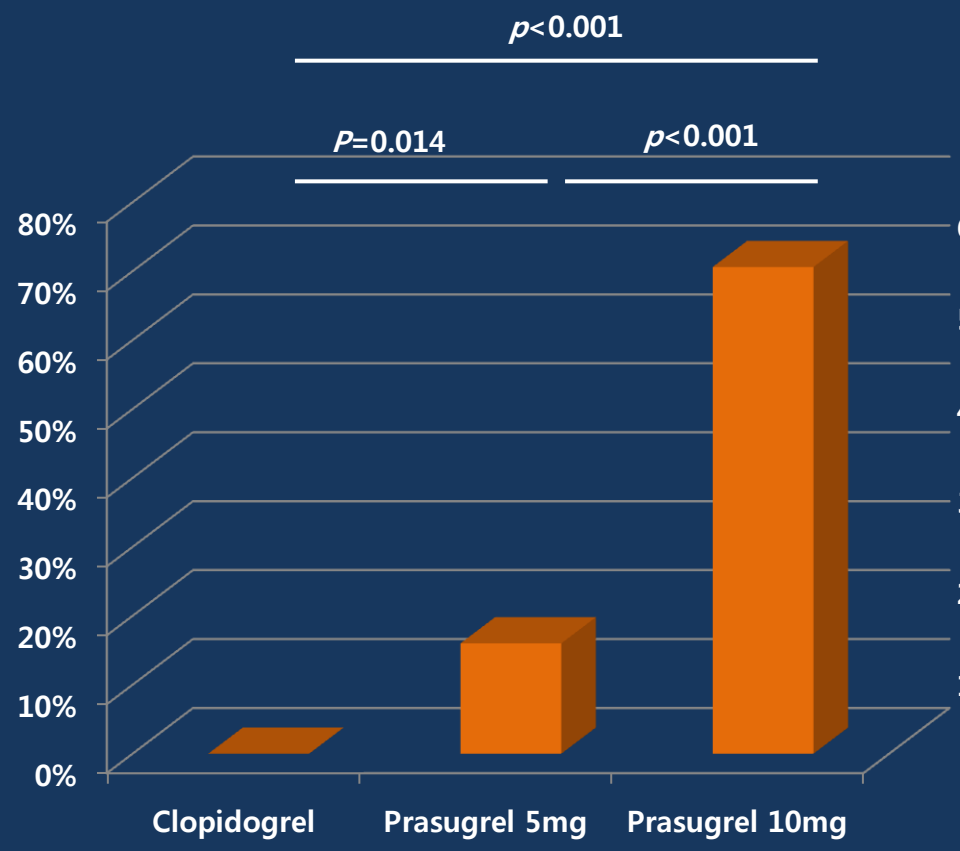


HPR by VerifyNow(208 and 240)

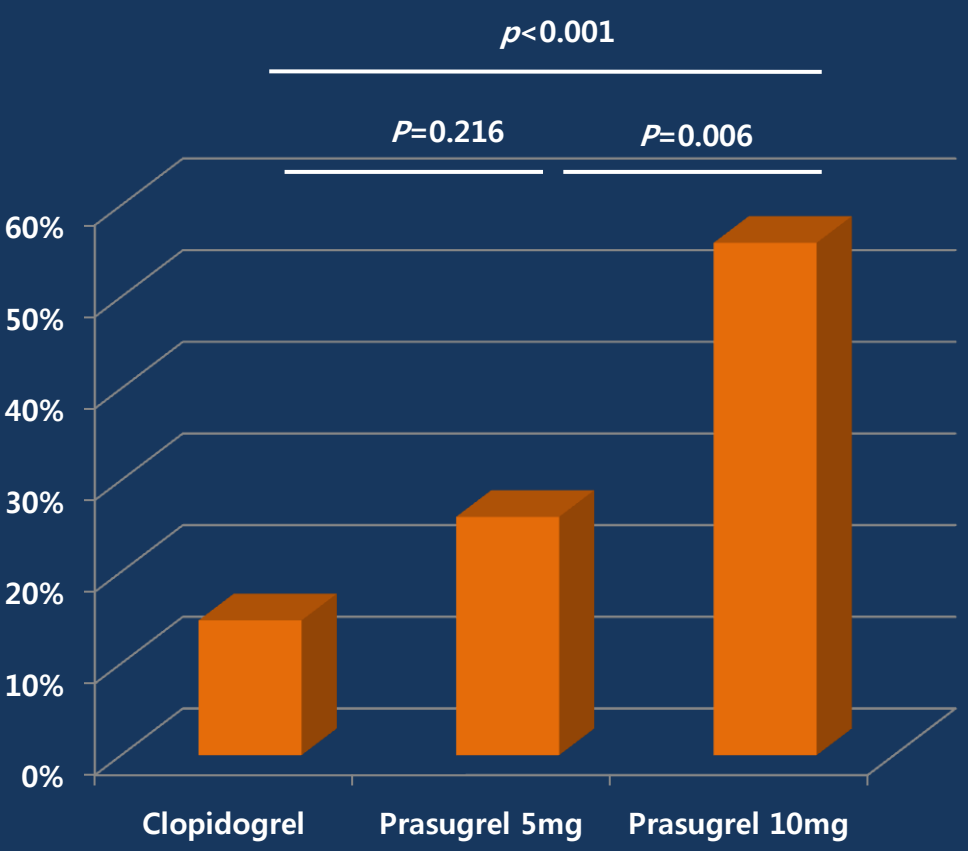




LPR by VerifyNow(85) and MEA(19)

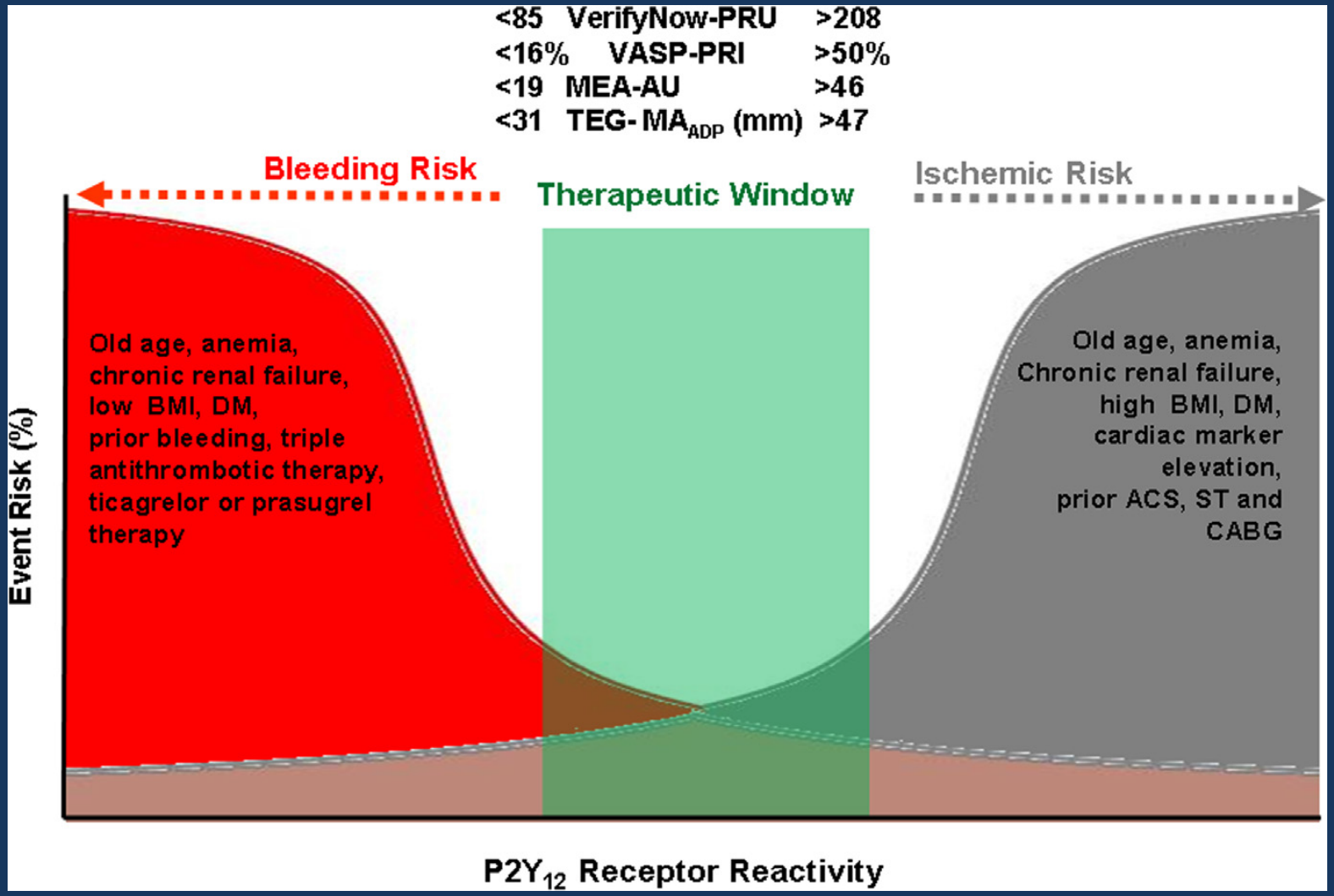


VerifyNow



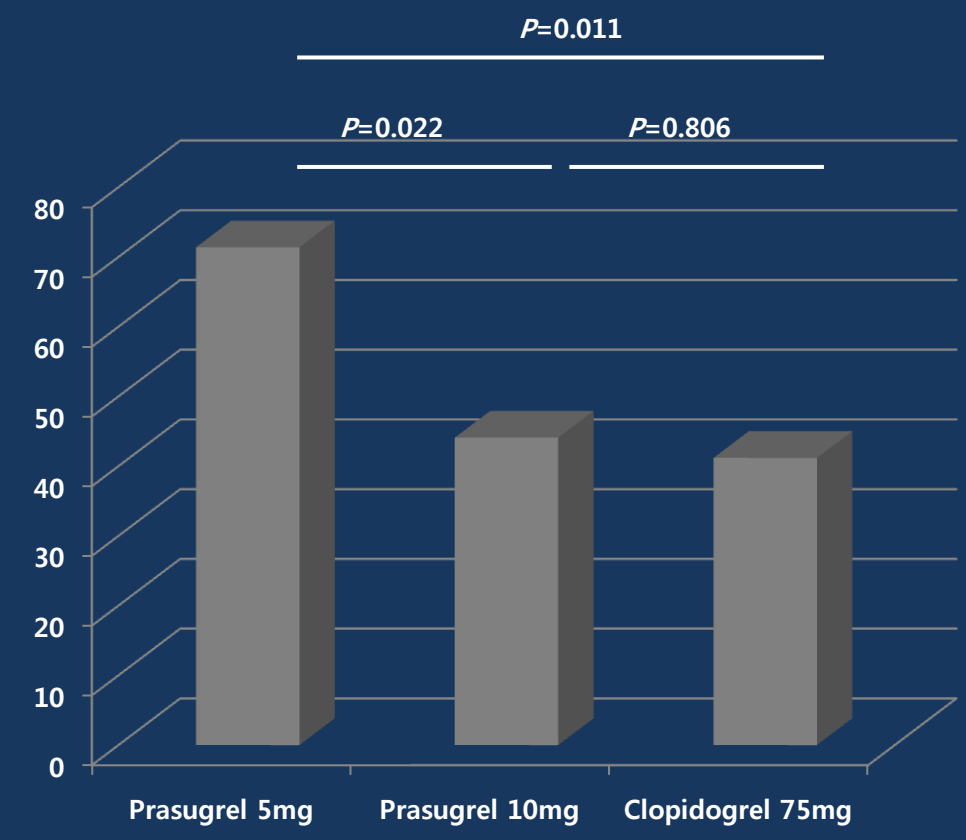
MEA

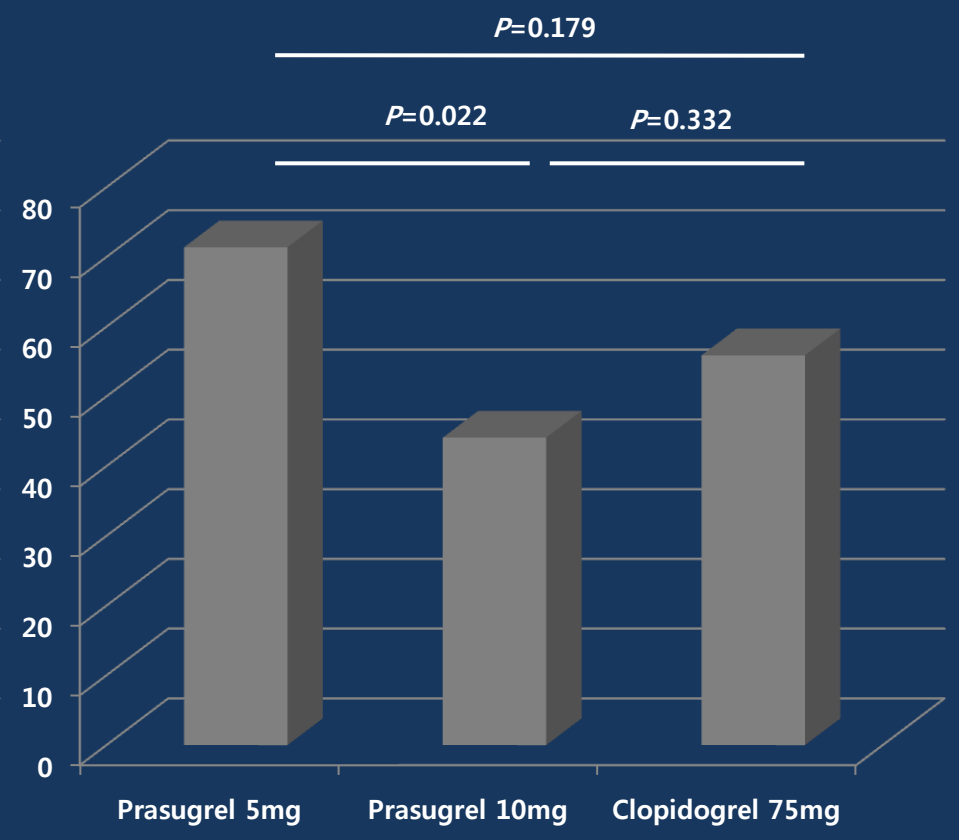
Consensus on the Definition of HPR and LPR



Tantry US et al, J Am Coll Cardiol. 2013 ; 62: 2261-2273.

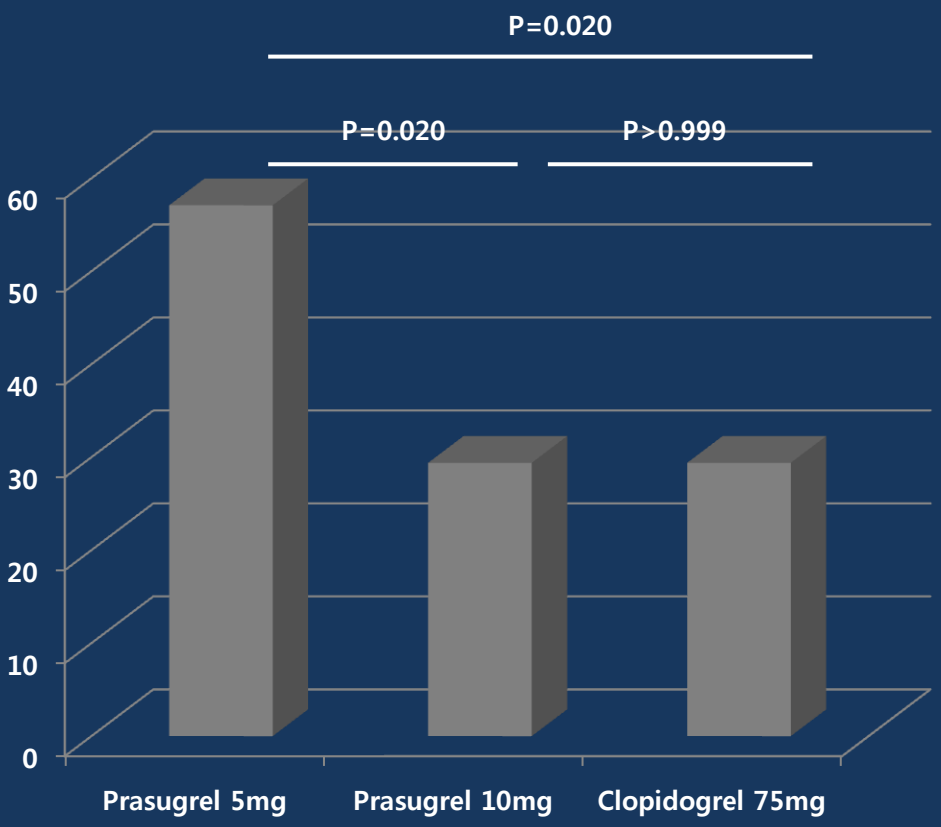
Optimal Platelet Reactivity

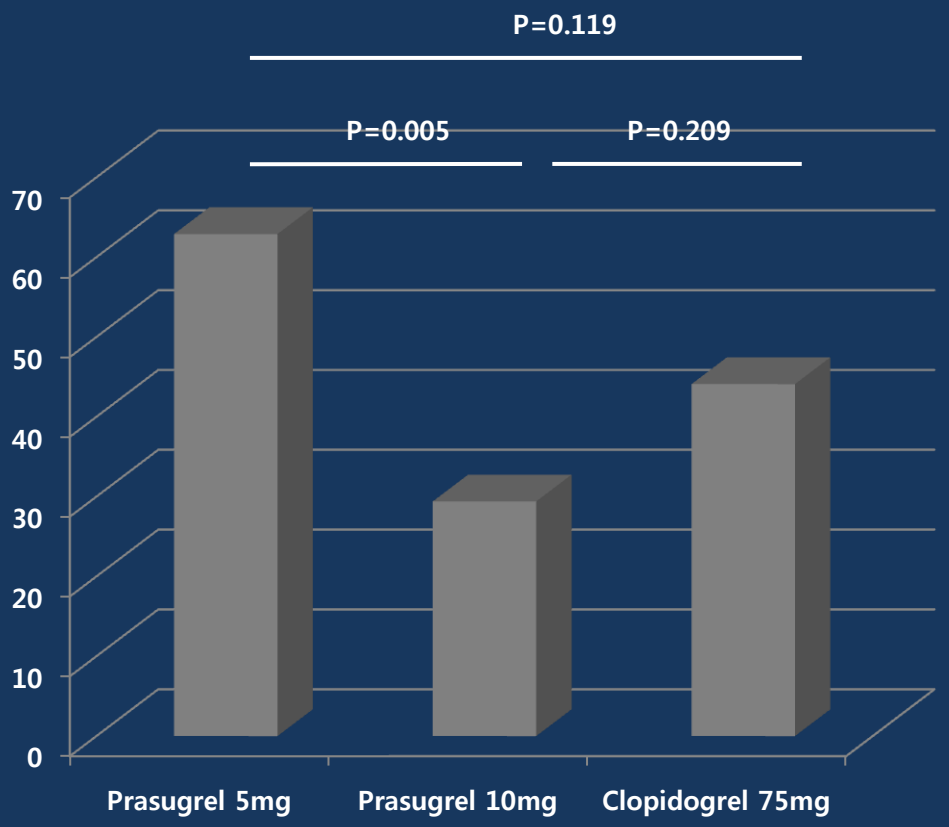




MEA (19-46.8) and LTA (12-55)

Optimal Platelet Reactivity





VerifyNow (85 vs. 208 or 235)

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6. Standard Dose of Prasugrel and Ticagrelor Loading *in STEMI Patients*

Lee et al. Trials 2013, 14:62
http://www.trialsjournal.com/content/14/1/62

TRIALS

STUDY PROTOCOL Open Access

Comparison of prasugrel and clopidogrel reloading on high platelet reactivity in clopidogrel-loaded patients undergoing percutaneous coronary intervention (PRAISE-HPR): a study protocol for a prospective randomized controlled clinical trial

Dong-Hyun Lee[1], Moo Hyun Kim[1,2*], Tae-Ho Park[1], Jong Sung Park[1], Kyungil Park[1], Jeong-Min Seo[1] and Michael S Lee[3]

PRAISE-HPR Study
NCT01609647

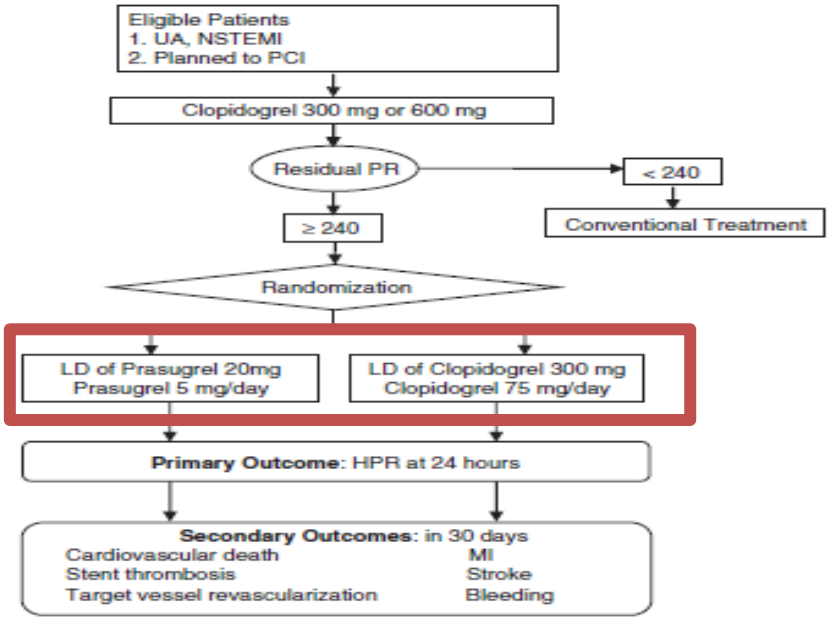
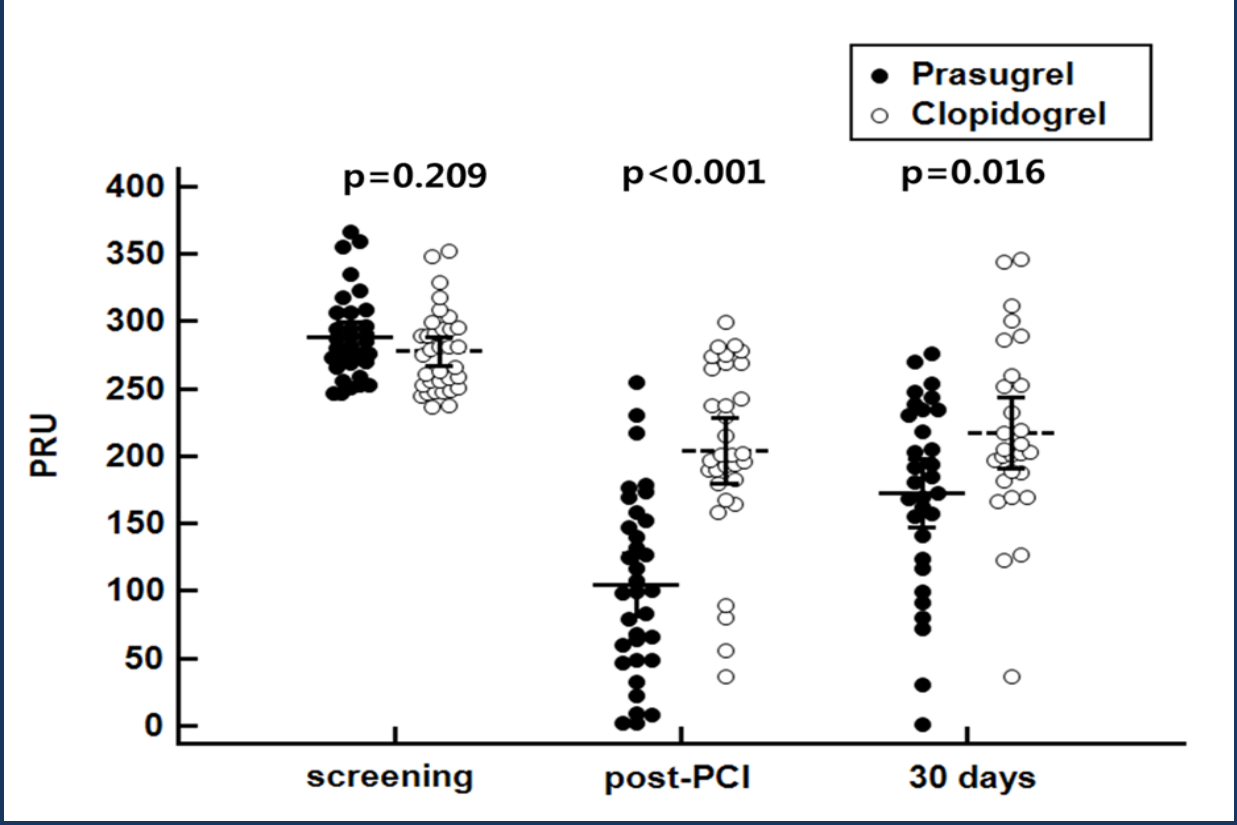
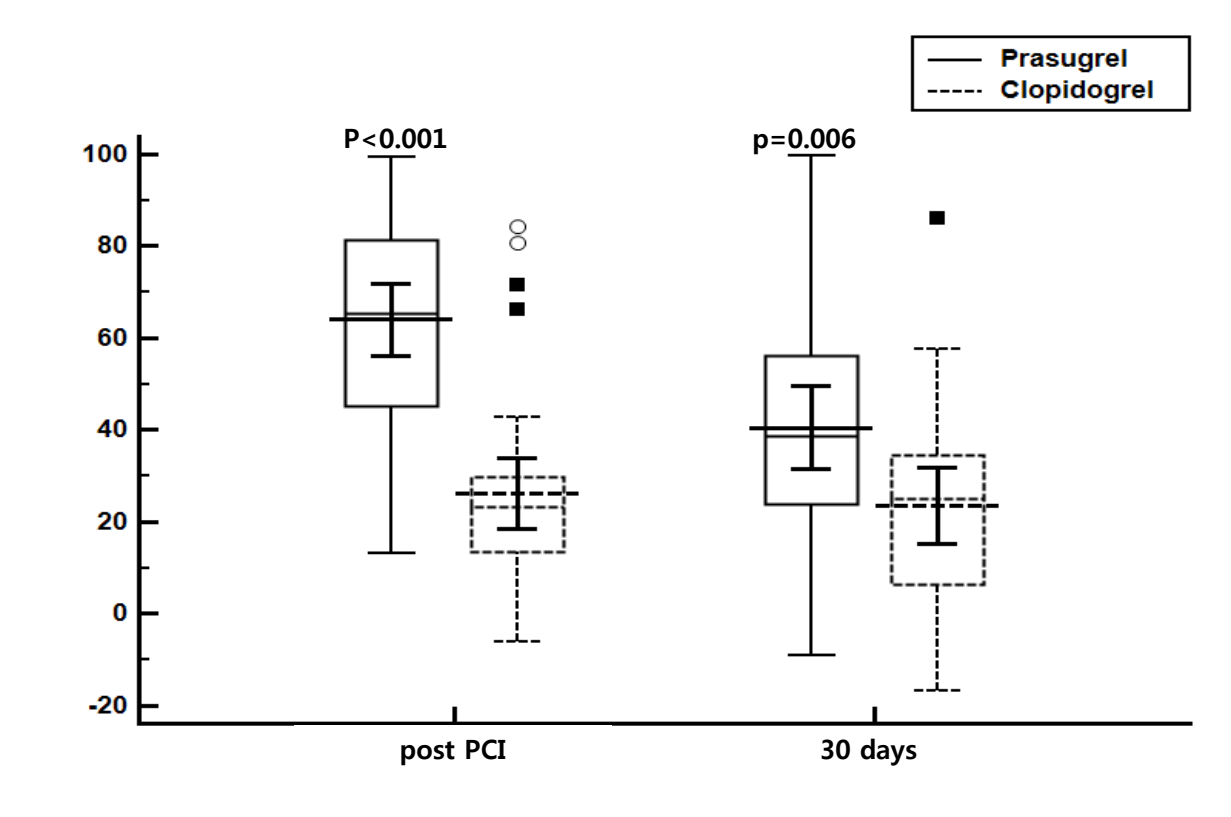


Figure 1 Overall study design. ACS, acute coronary syndrome; UA, unstable angina; NSTEMI, myocardial infarction without ST-segment elevation; PCI, percutaneous coronary intervention; PR, platelet reactivity; MI, myocardial infarction.

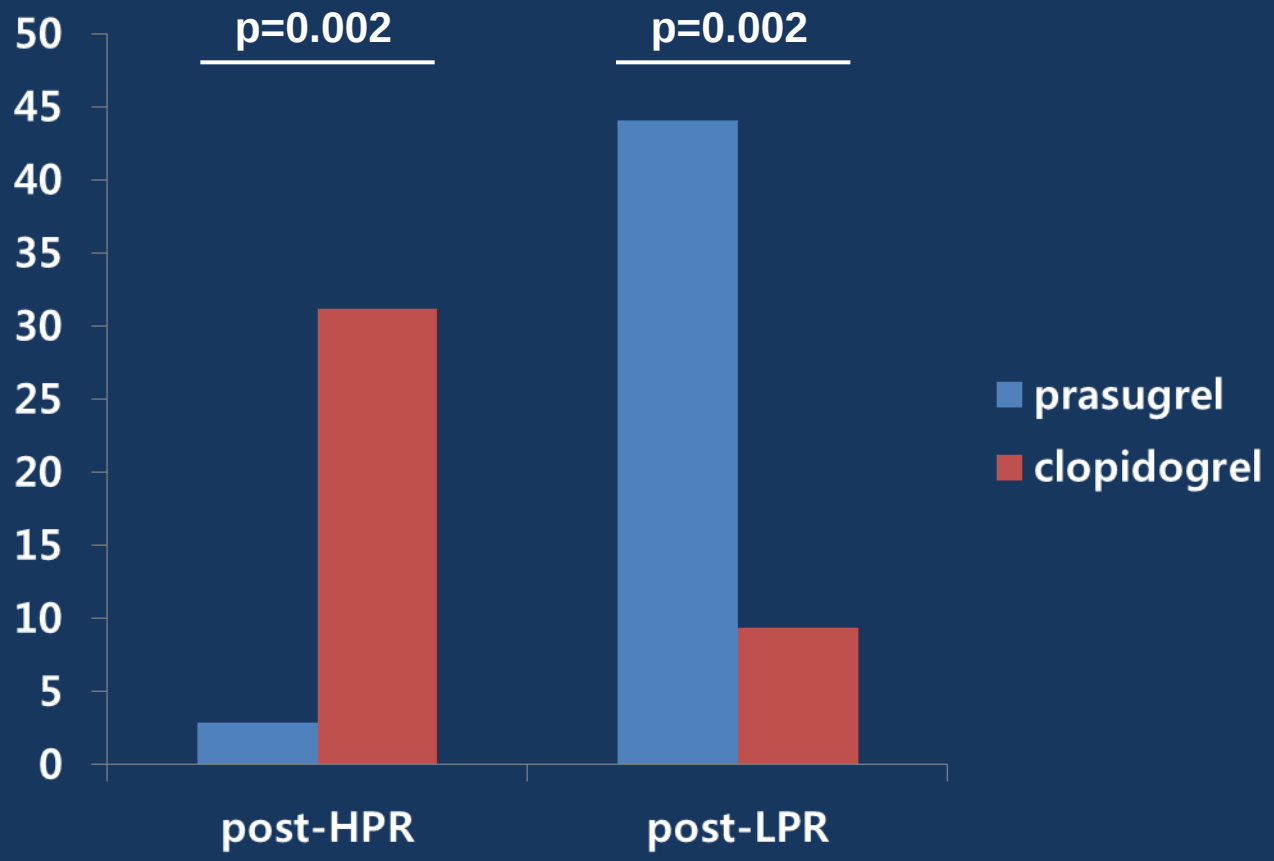
Mean Platelet Activity ±SD by VerifyNow at screening, post-PCI and 30 days



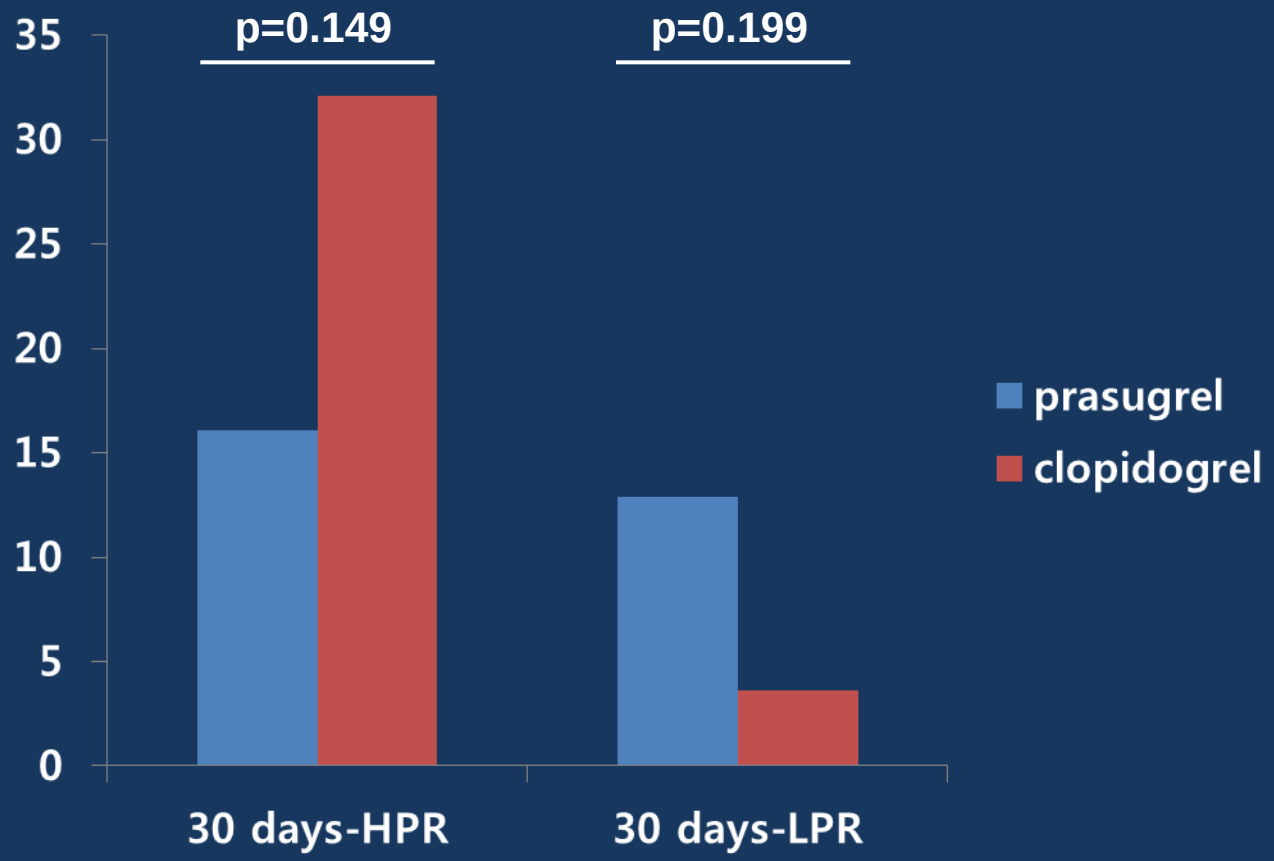
% Change in platelet reactivity during study course by VerifyNow



Primary Endpoint: The percentage of HPR and LPR at post-PCI



The percentage of HPR and LPR at 30 days



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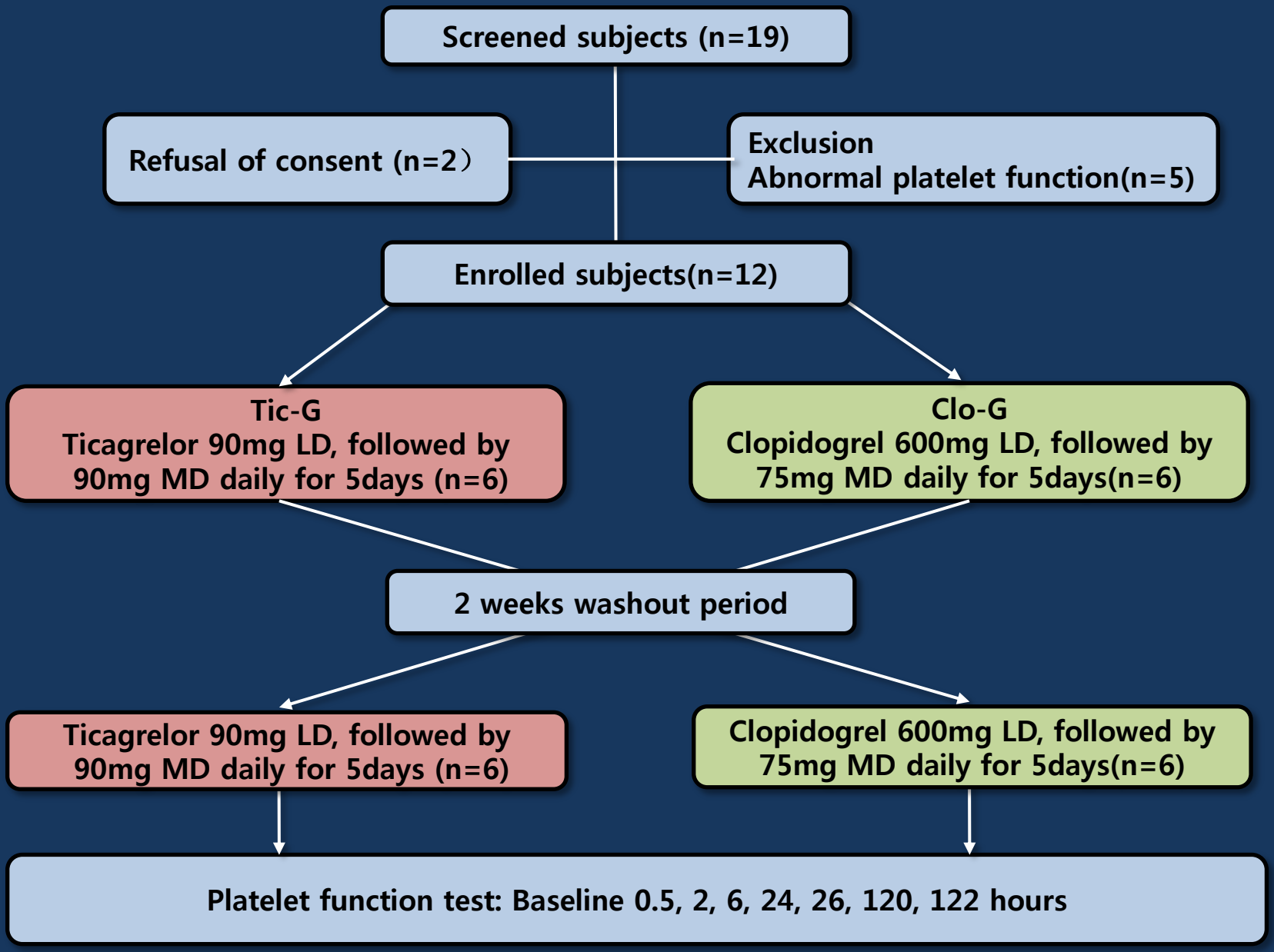
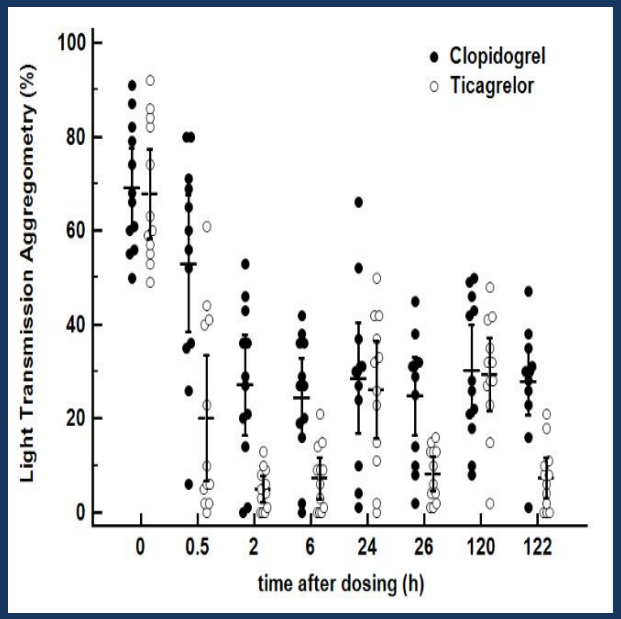
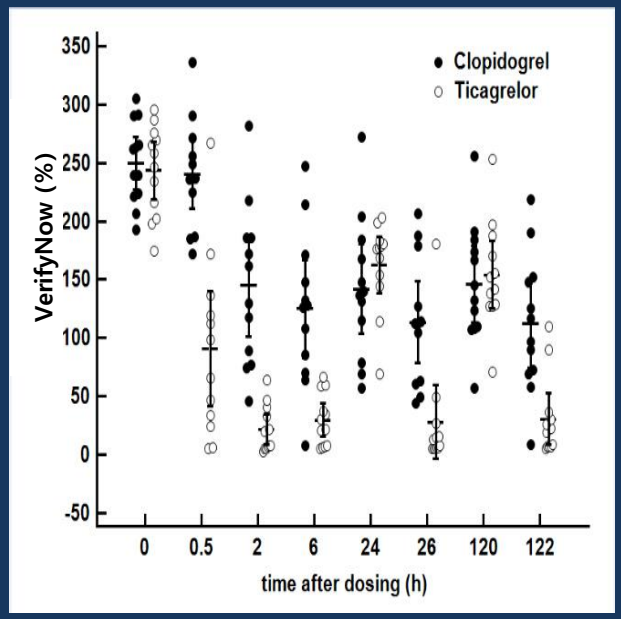
Study design overview



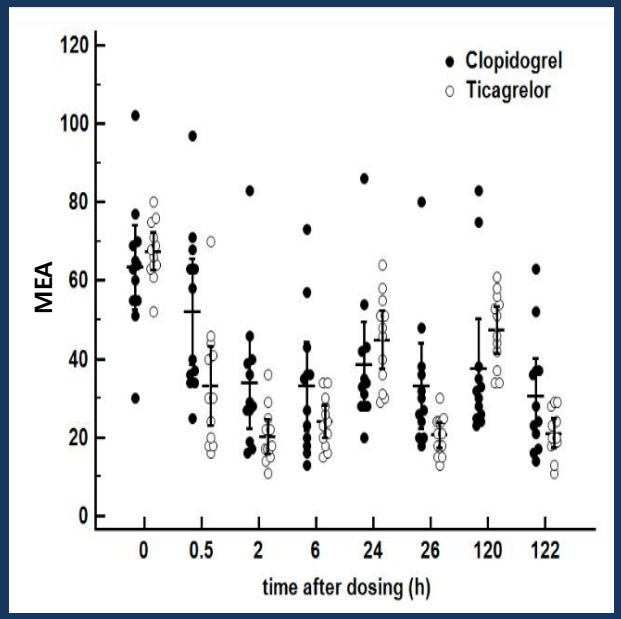
Lose Dose (Single Daily Dose) of Ticagrelor



LTA



VerifyNow

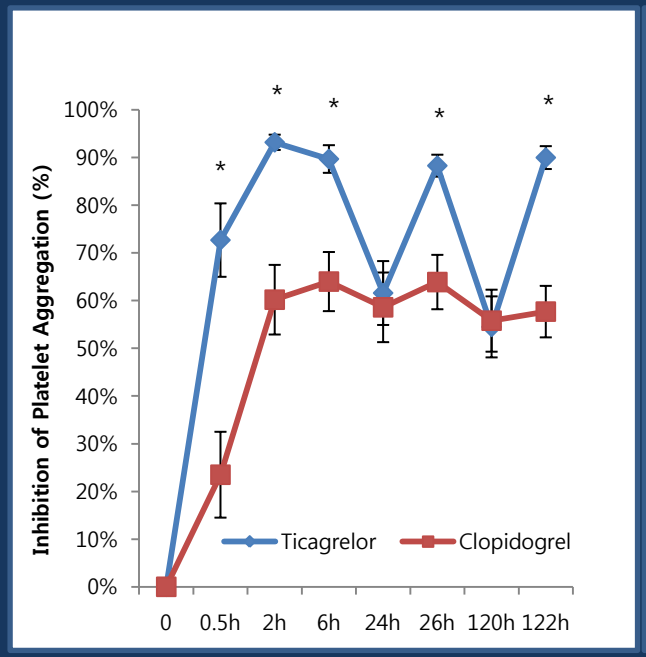


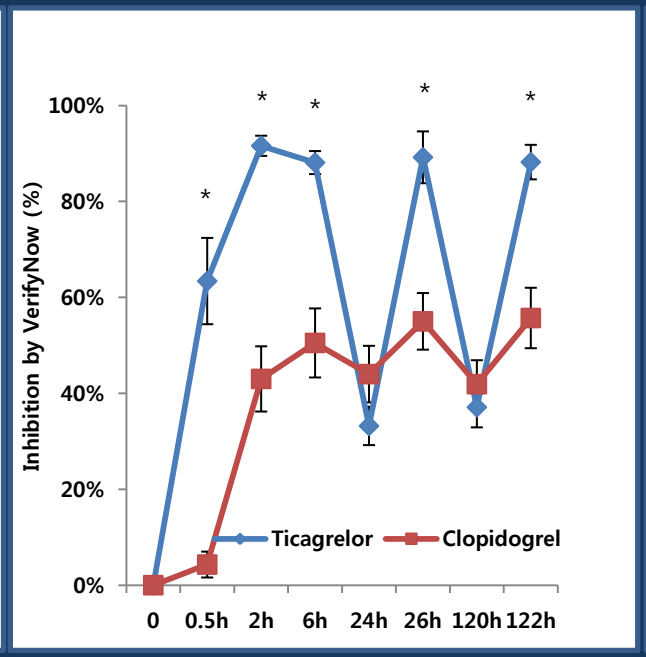
MEA

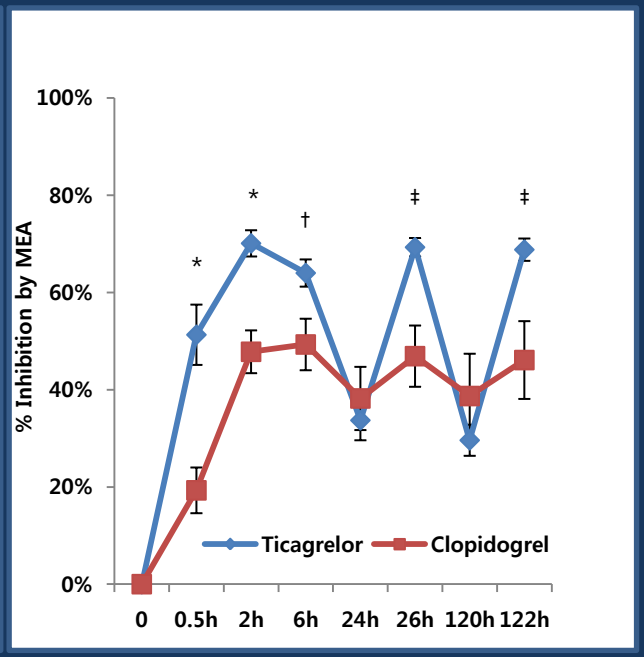
The individual platelet function test values at variable time points

Guo LZ et al, Platelets. 2014; 2:1-7.

Lose Dose (Single Daily Dose) of Ticagrelor





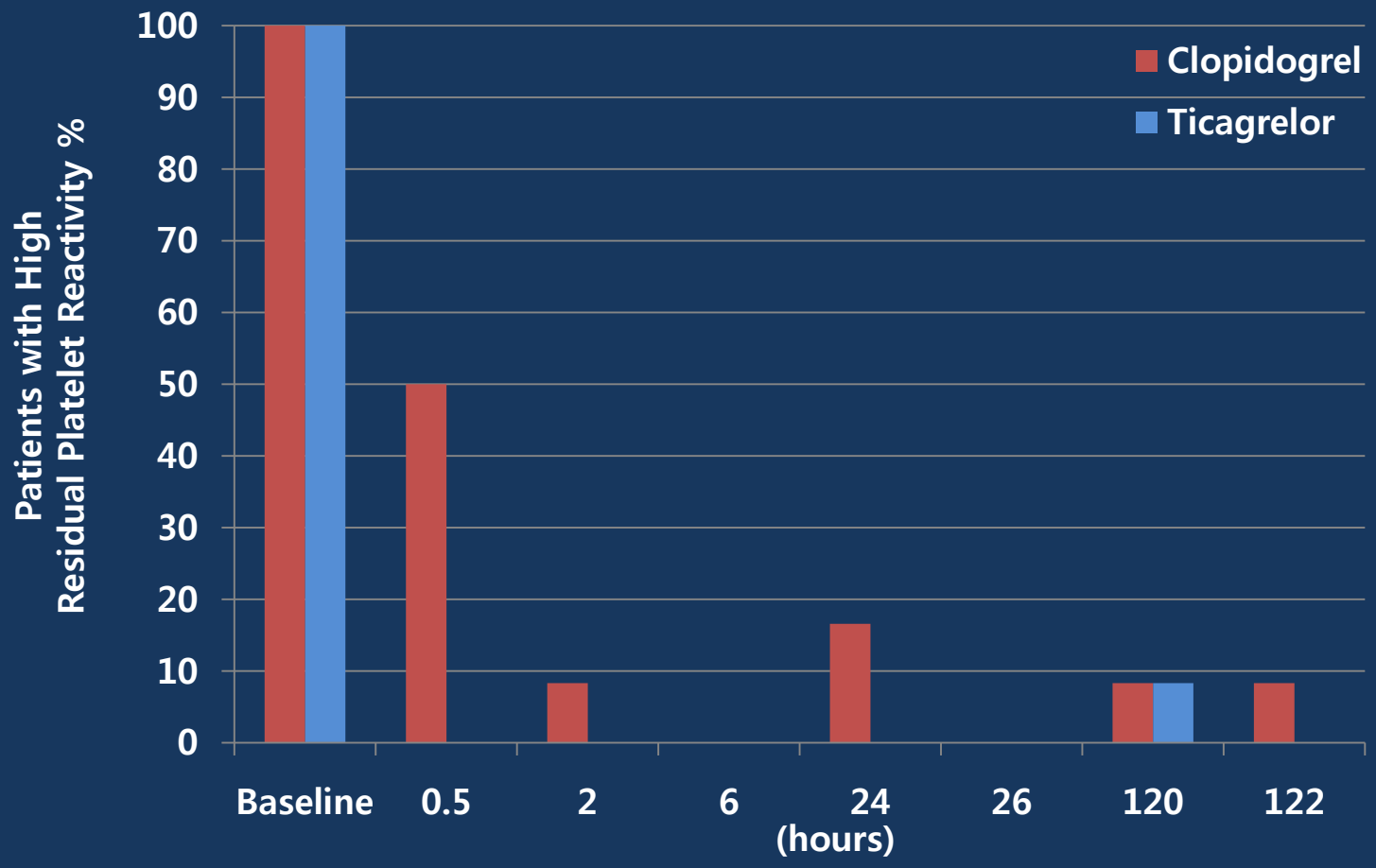


LTA **VerifyNow** **MEA**

Mean inhibition of platelet aggregation after LD and MD of ticagrelor or clopidogrel

Guo LZ et al, Platelets. 2014; 2:1-7.

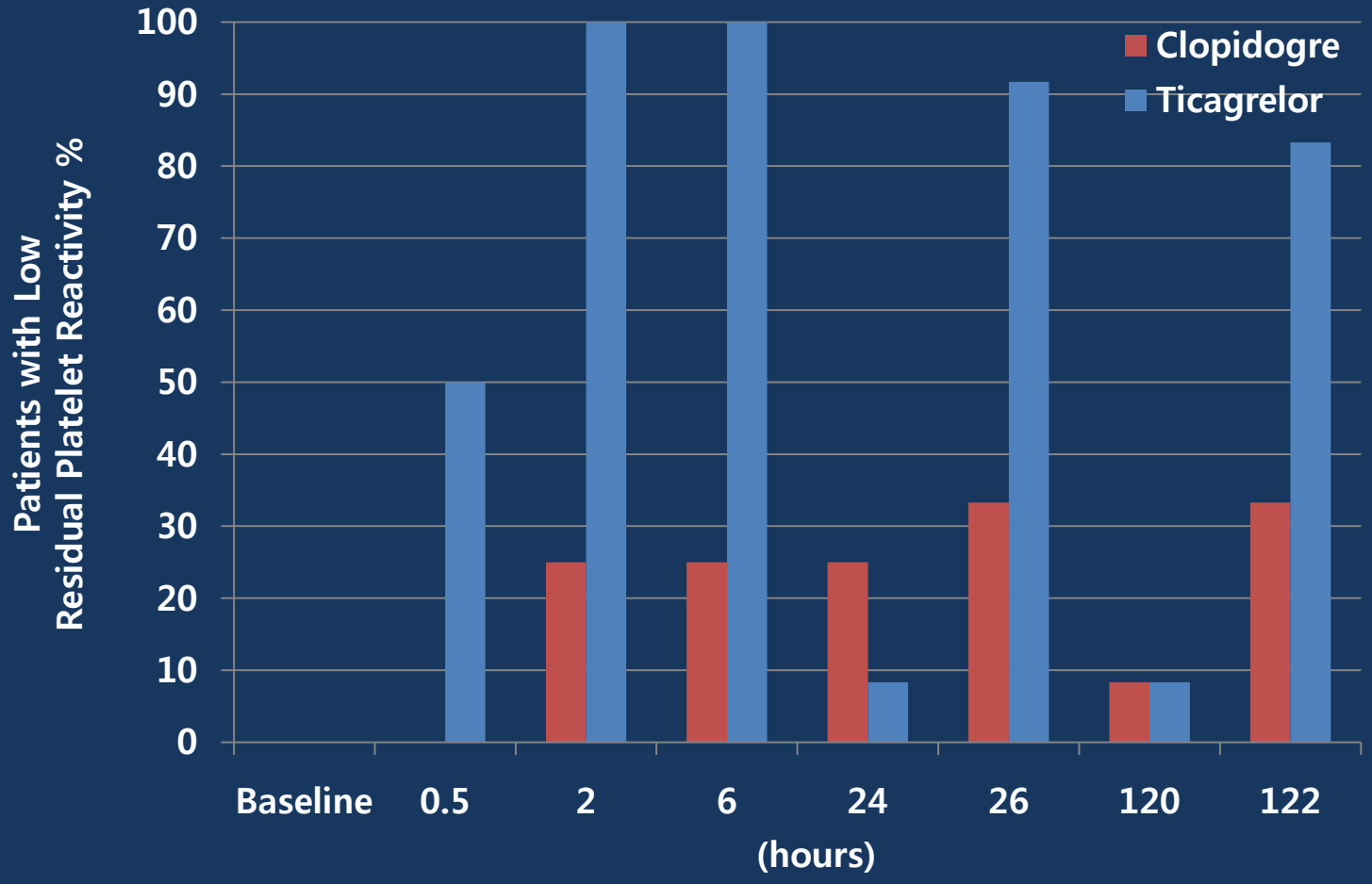
Lose Dose (Single Daily Dose) of Ticagrelor



The percentage of HPR at different time points in the ticagrelor and clopidogrel groups

Guo LZ et al, Platelets. 2014; 2:1-7.

Lose Dose (Single Daily Dose) of Ticagrelor



The percentage of LPR at different time points in the ticagrelor and clopidogrel groups

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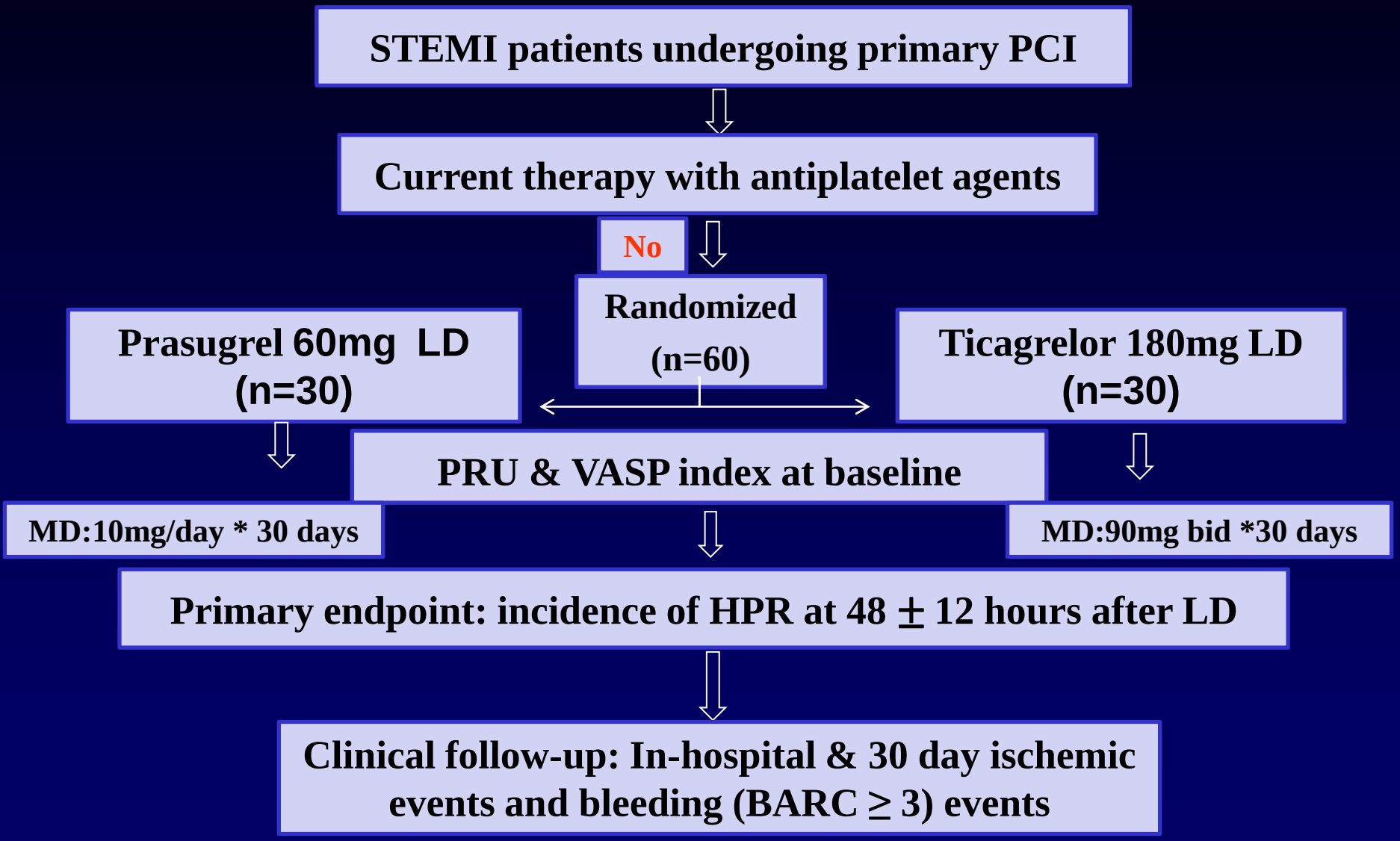
Comparison of Prasugrel and Ticagrelor Antiplatelet Effects in Korean Patients Presenting with ST-segment Elevation Myocardial Infarction - PANTASTIC Trial

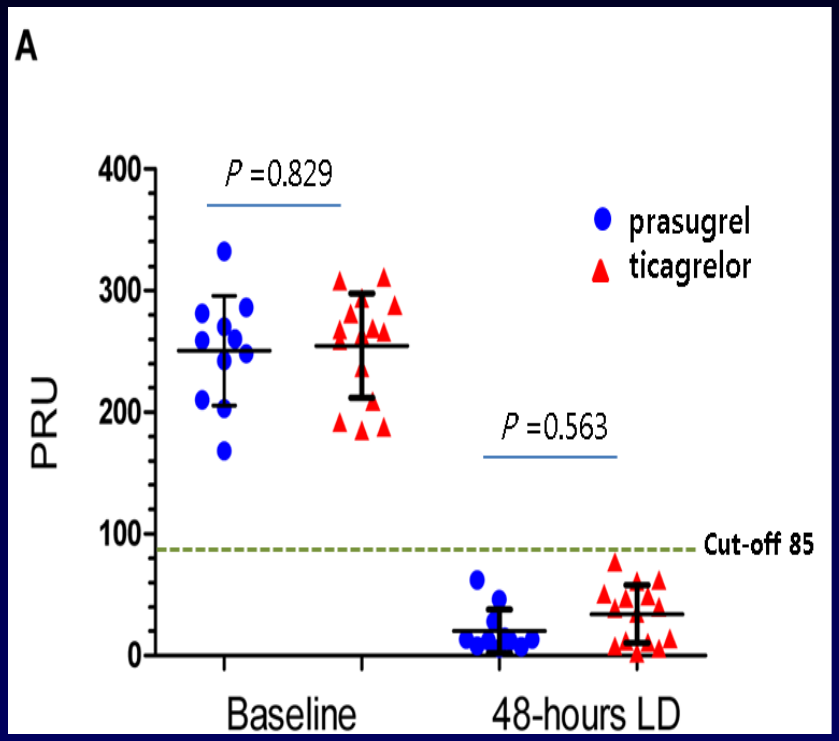
Cai De Jin, Moo Hyun Kim, Long Zhe Guo, Young-Rak Cho,
Kyungil Park, Jong-Sung Park, Tea-Ho Park, Young-Dae Kim

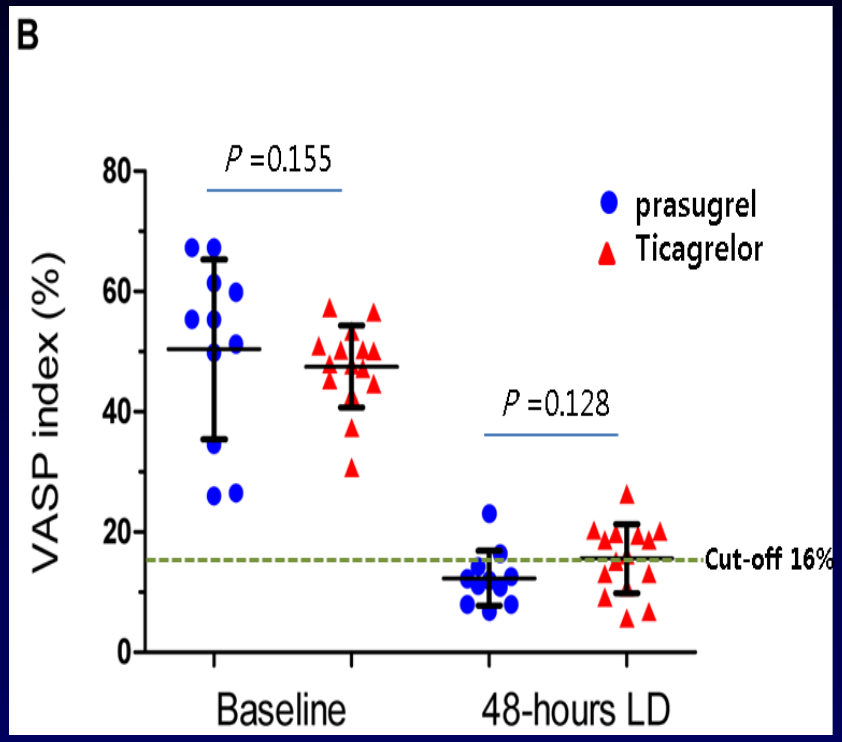
Department of Cardiology
Regional Clinical Trial Center
College of Medicine, Dong-A University

Study Flow Chart



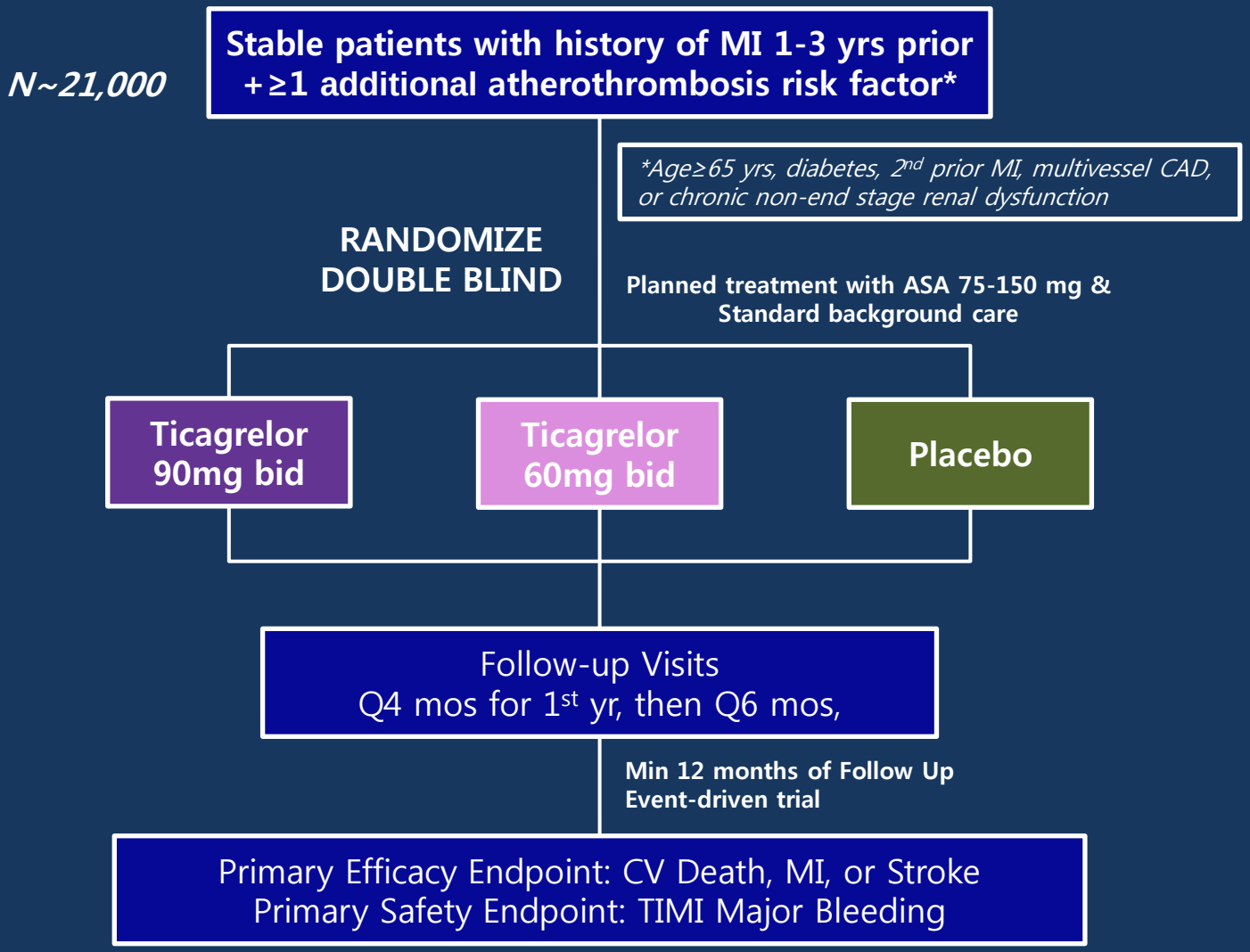
Results (4) Platelet Function Test





Platelet reactivity values assessed by VerifyNow (a) and VASP (b) at baseline and 48 hours after loading dose.

Trial Schema



Study Schema for PEGASUS-TIMI 54. CAD, Coronary artery disease; MI, myocardial infarction.

Summary

Our study suggests that compared to the high dose of prasugrel and ticagrelor, the pharmacodynamics effect of low loading and maintenance dose may be a better option in East-Asian CAD patients.


Thank You