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Pharmacodynamic Effect of Lower Maintenance Dose of Prasugrel in Patients with Dual Antiplatelet Treatment

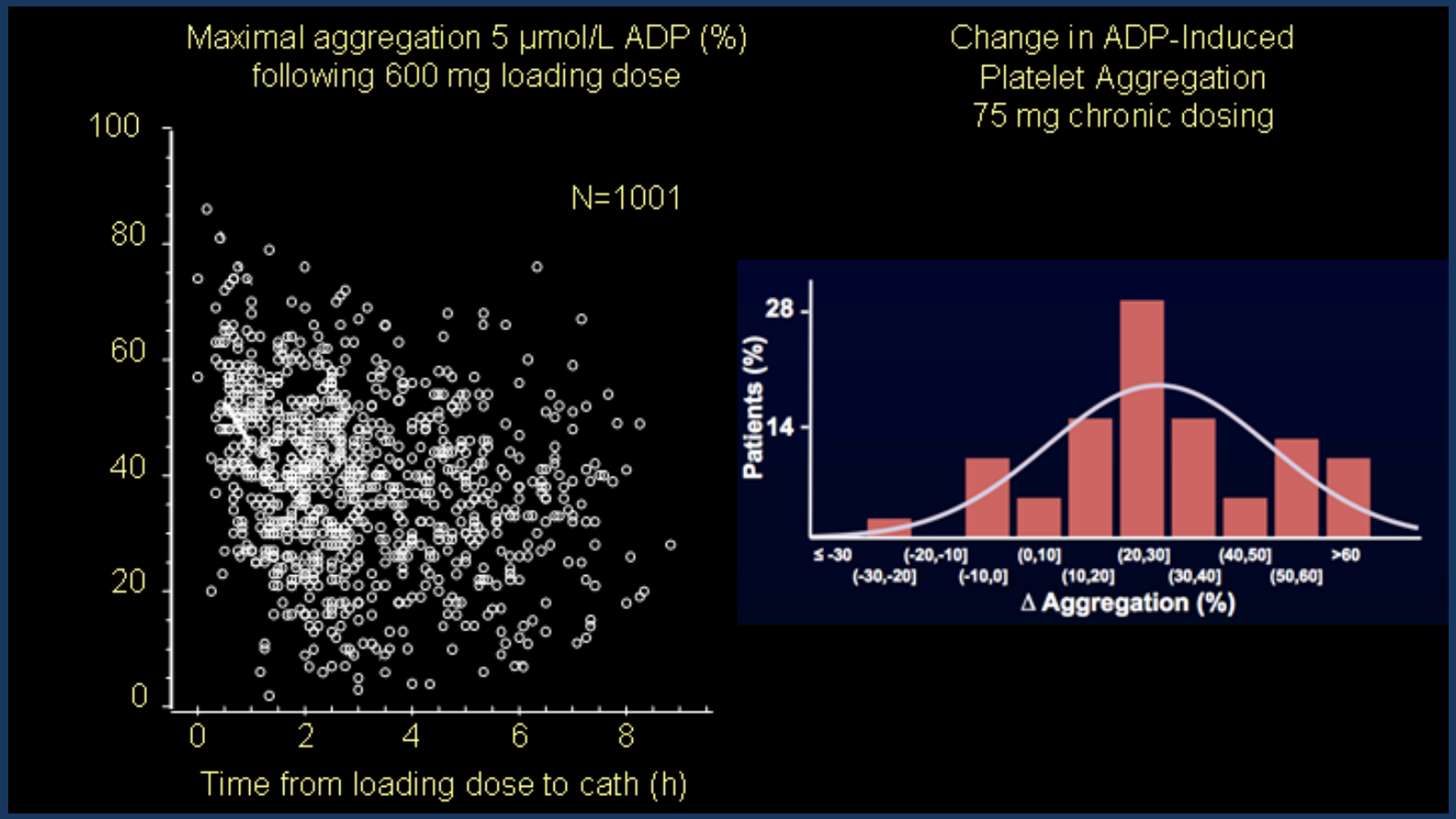
Jae Hyuk Choi[1], Moo Hyun Kim[1,2], Dong Hyun Lee[1], Long Zhe Guo[2], Tae-Ho Park[1], Jong Sung Park[1], Kyungil Park[1], Jeong-Min Seo[1], So Jeong Yi[2]

[1]Department of Cardiology, Dong-A University Hospital, Busan, South Korea

[2]Clinical Trial Center, Dong-A University Hospital, Busan, South Korea

BACKGROUND

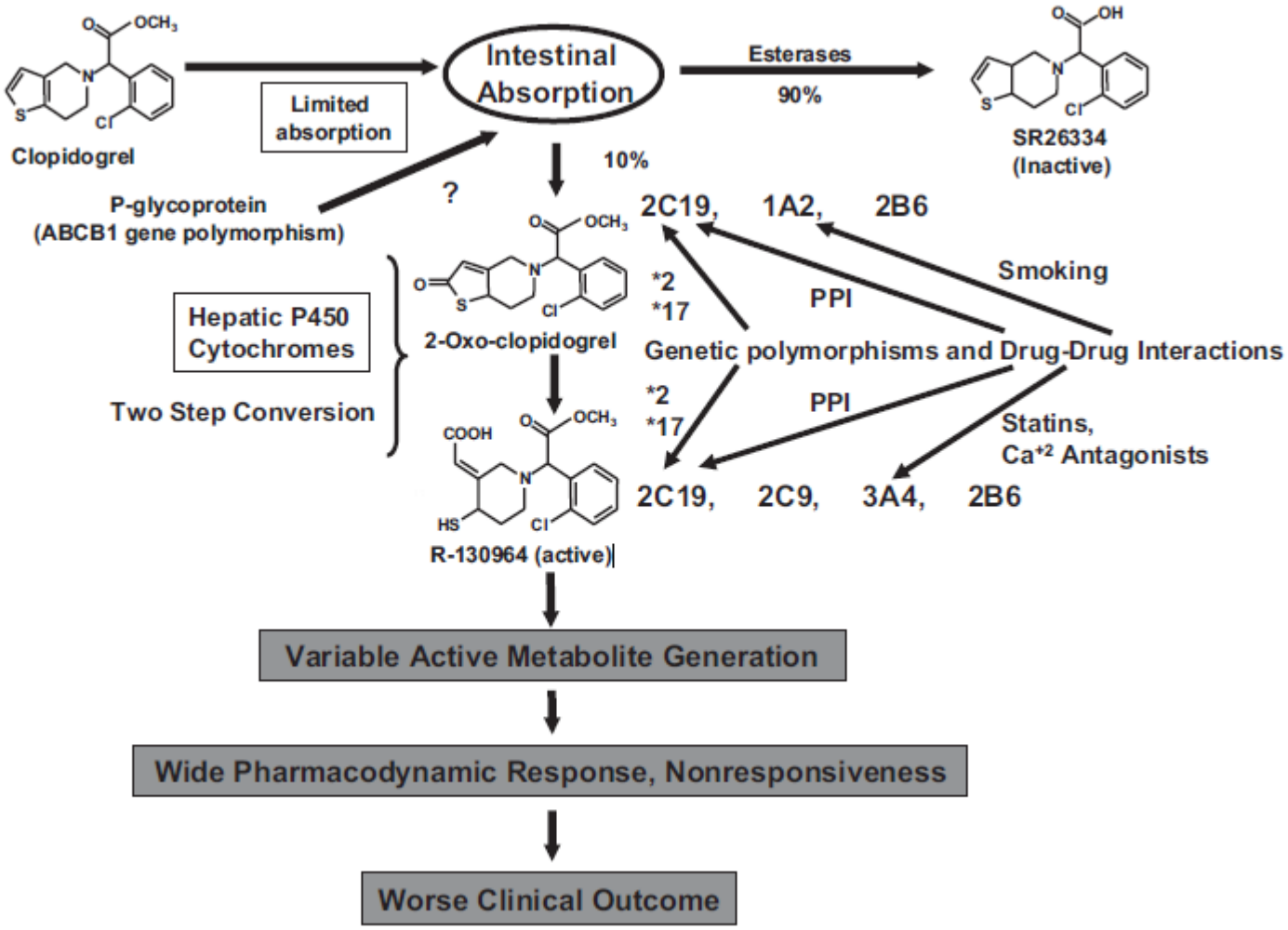
Clopidogrel Response Variability



Hochholzer et al. *Circulation* 2005

Gurbel P et al, *Circulation* 2003

Clopidogrel Response Variability

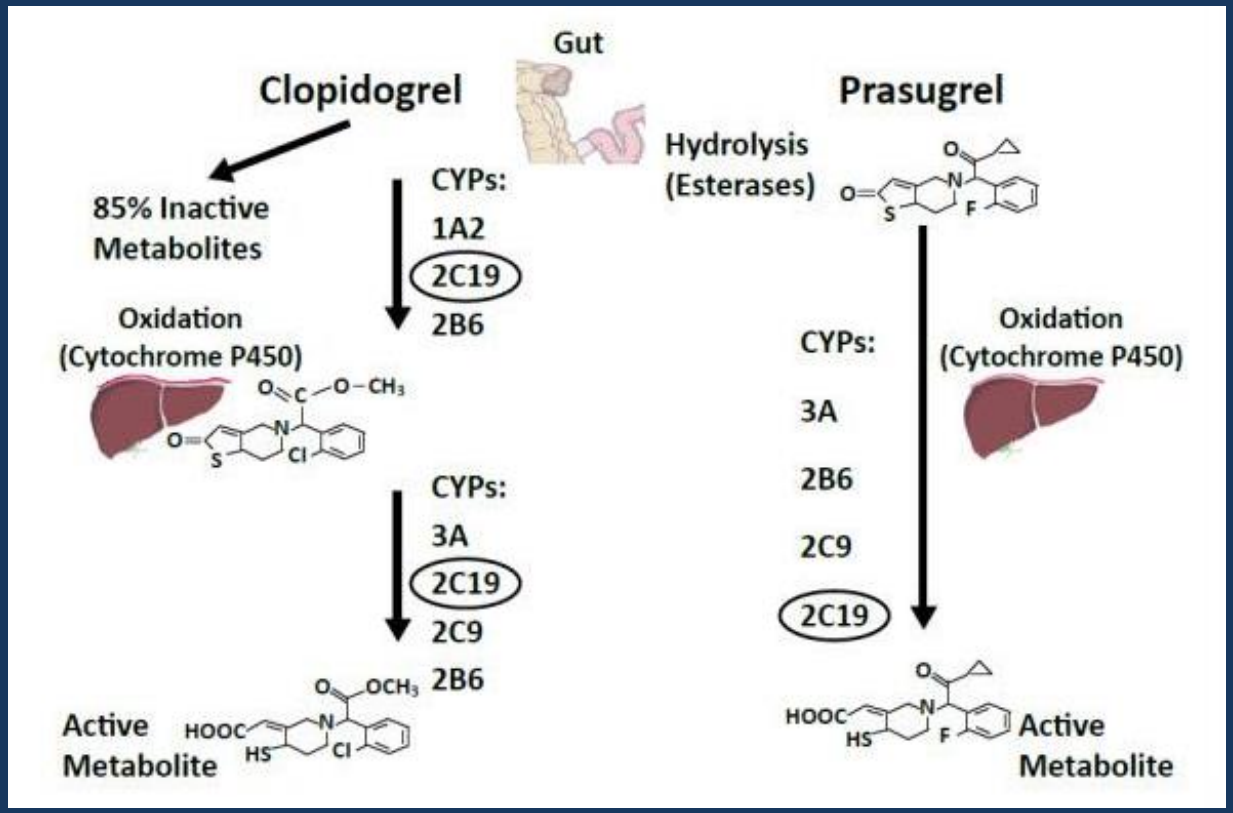


Bonello et al. JACC Vol. 56, No. 12, 2010

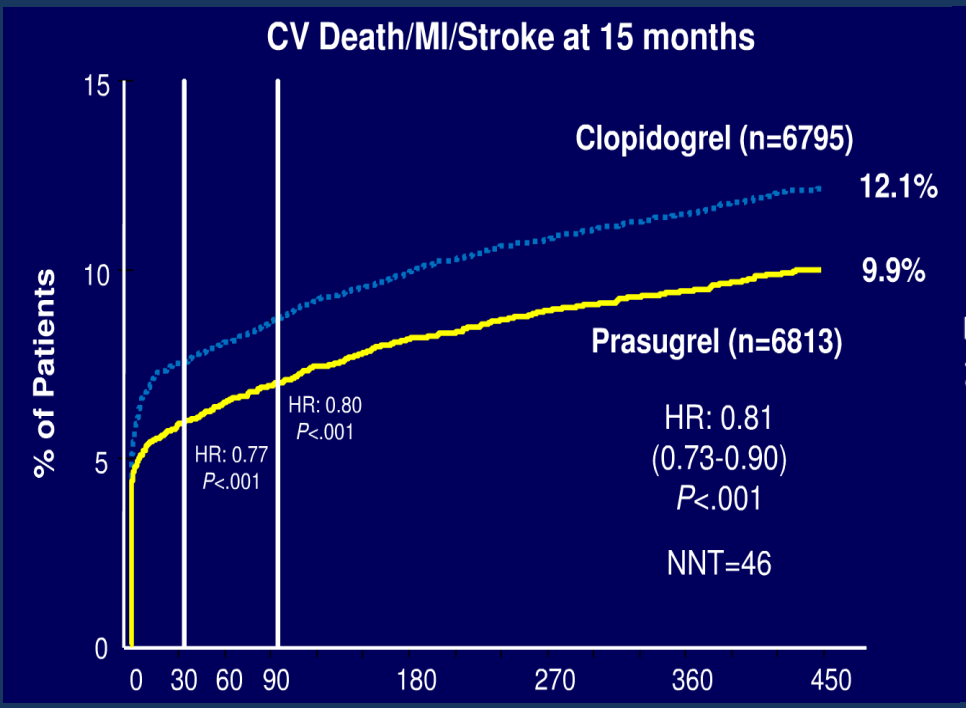
Prasugrel

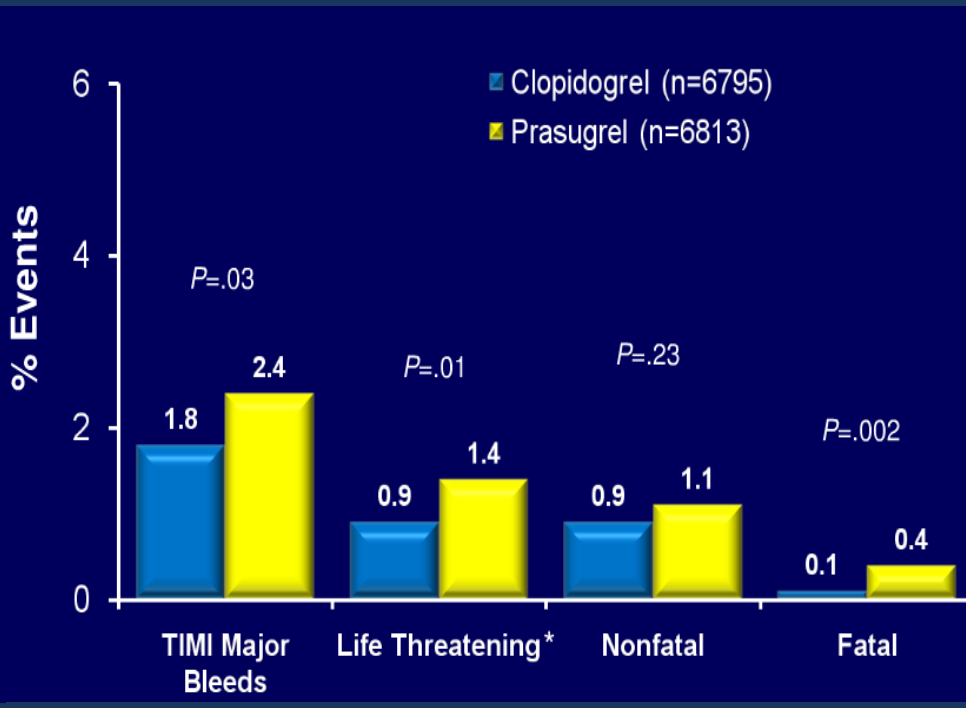
Prasugrel is new, more rapid

Potent anti -P2Y12 receptor antagonist



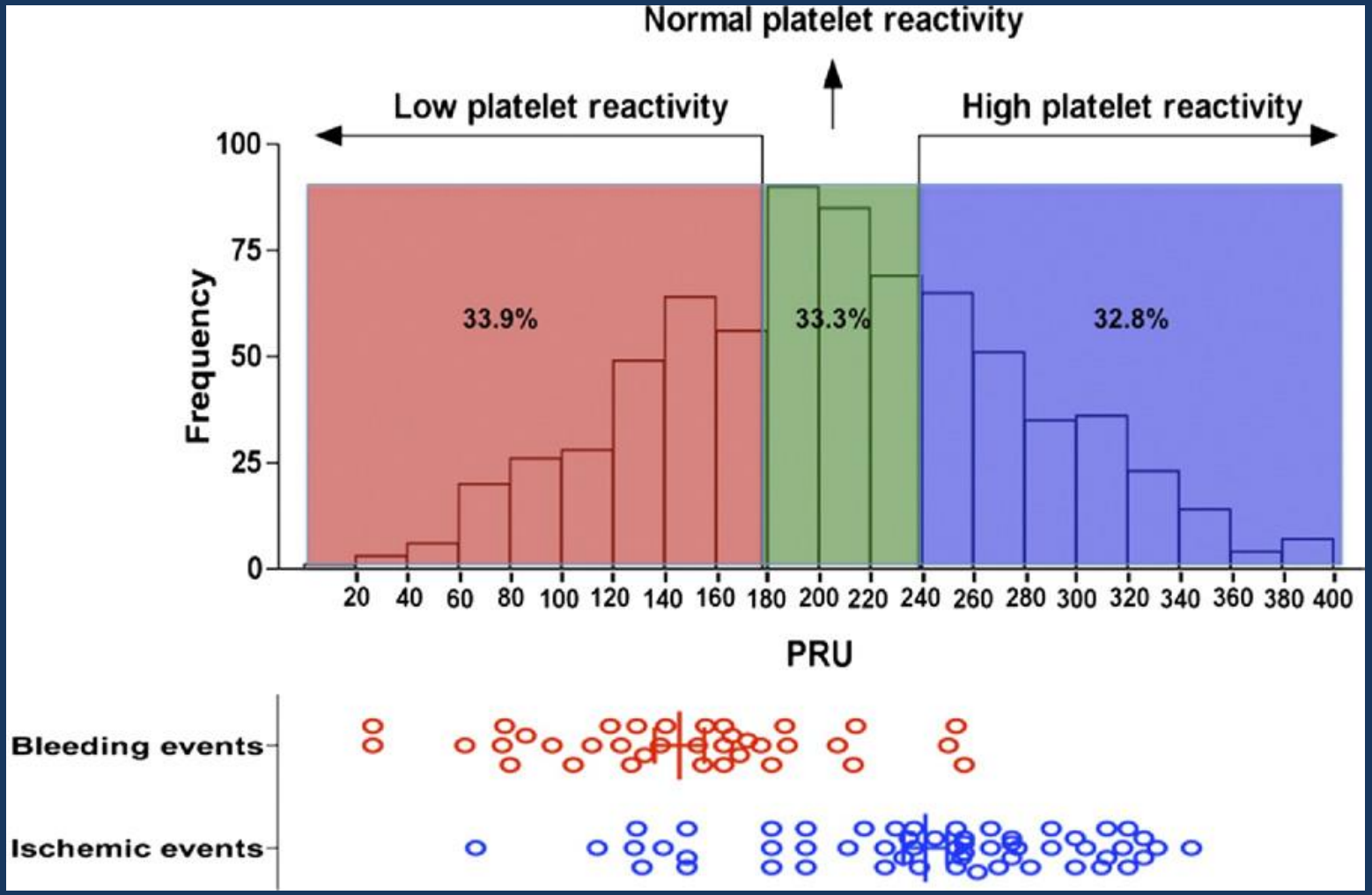
TRITON –TIMI 38 Trial - Bleeding ↑





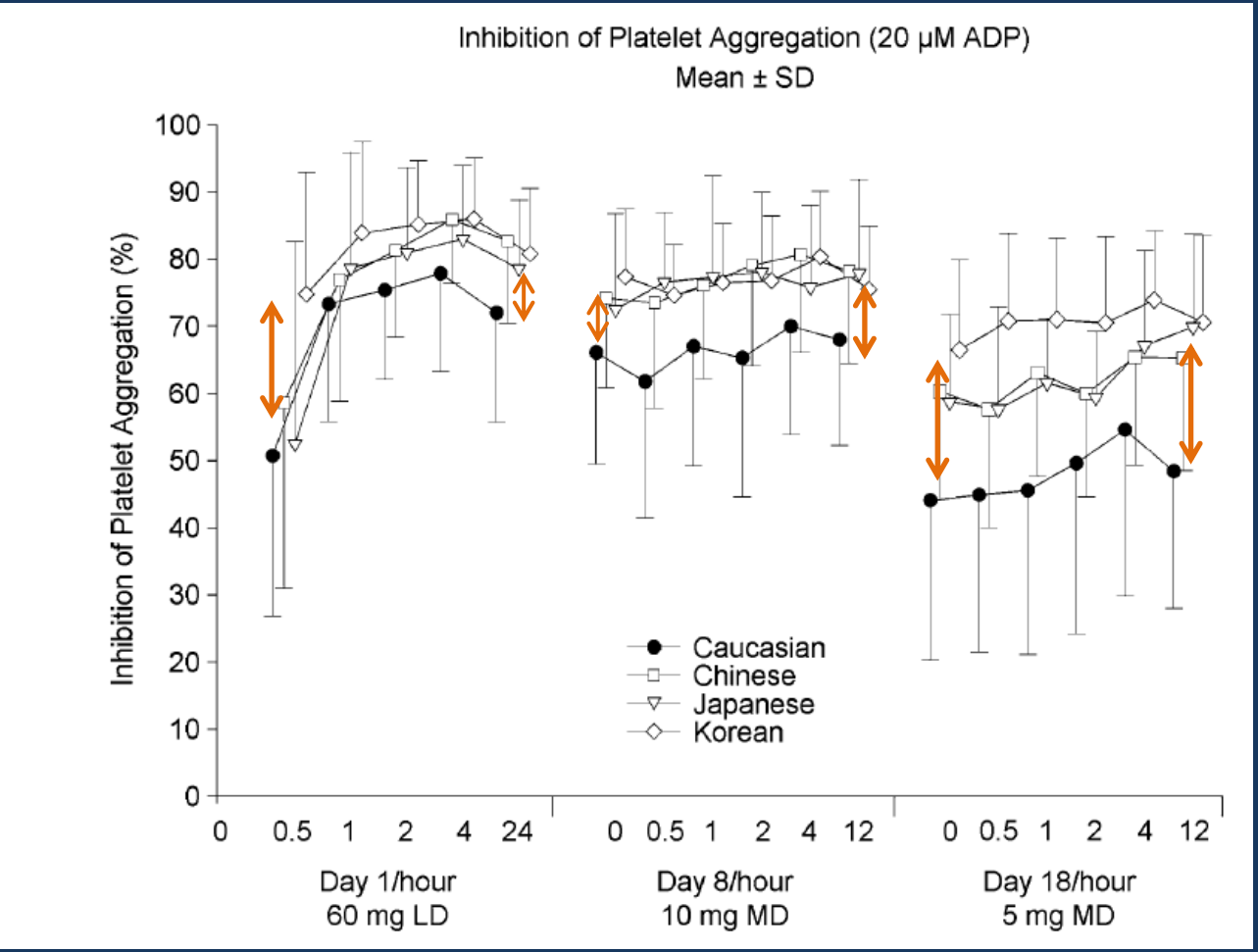
Wiviott SD, et al. N Engl J Med. 2007;357

Significance of HPR and LPR



Mangiacapra et al.
JACC:CARDIOVASCULARINTERVENTIONS,VOL.5,NO.3,2012

Ethnic Differences in Prasugrel Response



DS Small et al Eur J Clin Pharmacol (2010) 66:127–135

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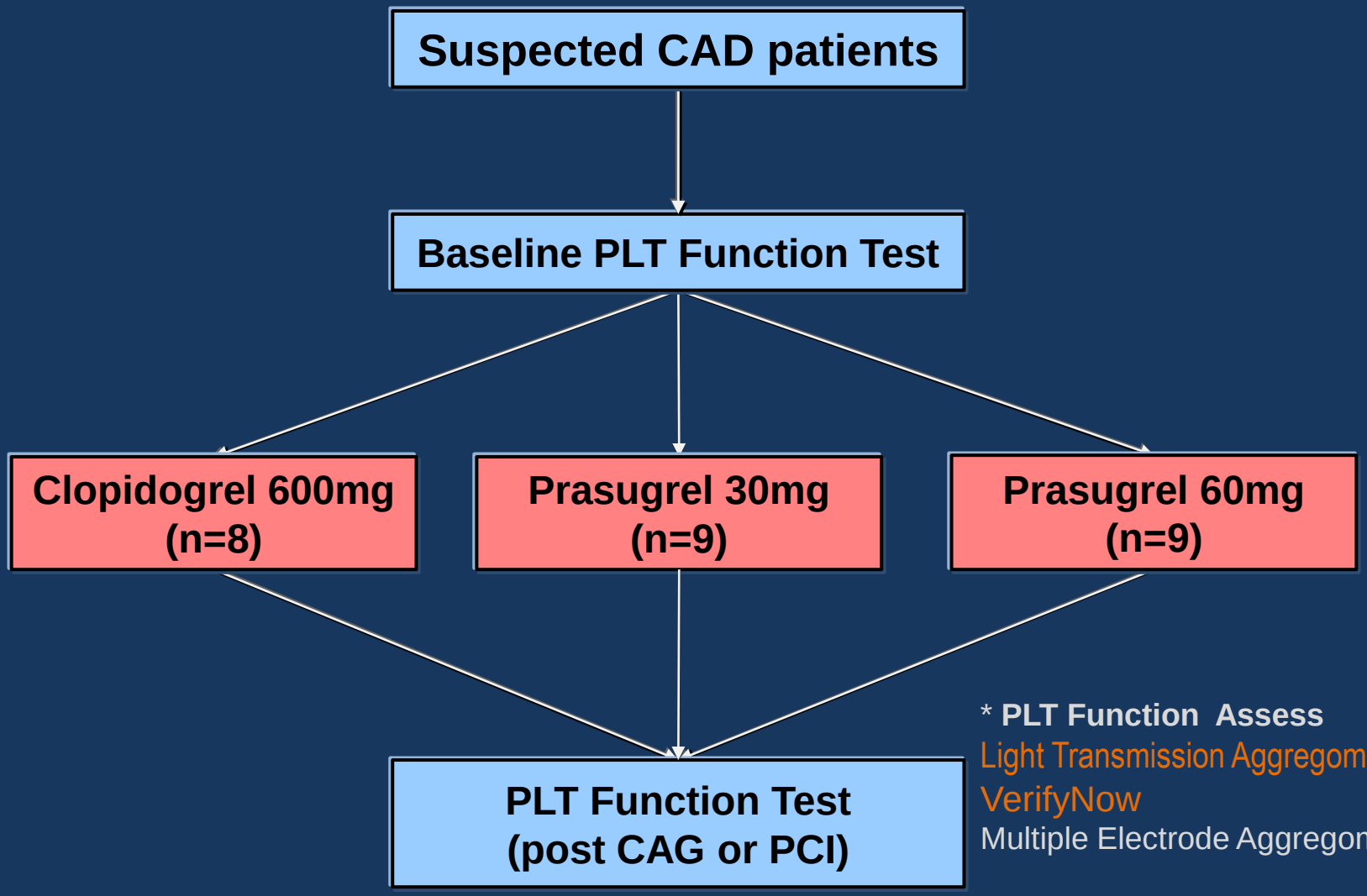
Effect of Lower LD of Prasugrel



* **PLT Function Assess**
Light Transmission Aggregometry
VerifyNow
Multiple Electrode Aggregometry

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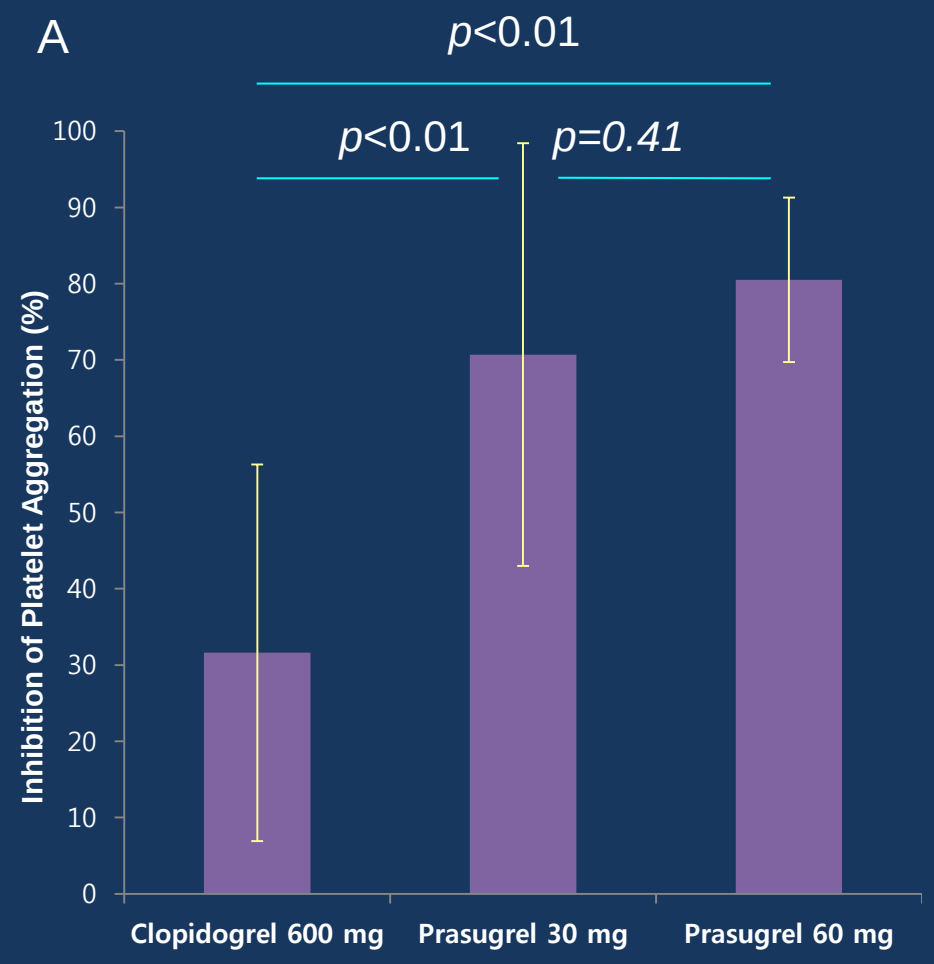
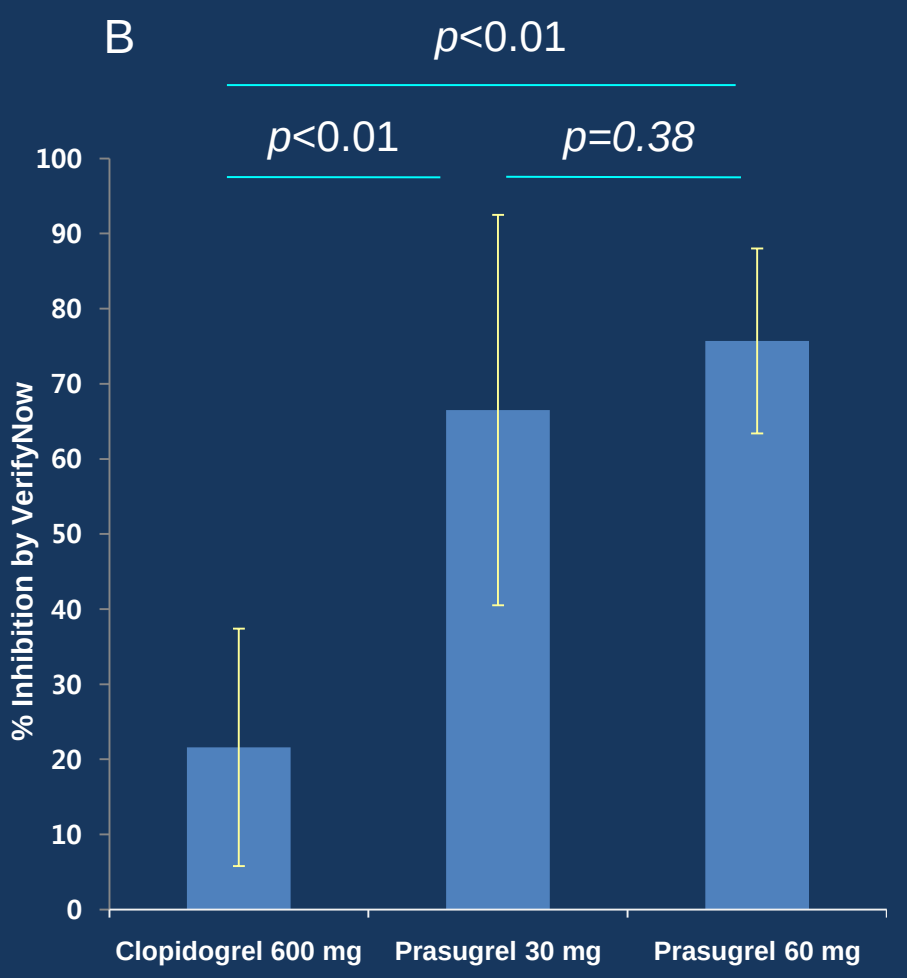
Effect of Lower LD of Prasugrel



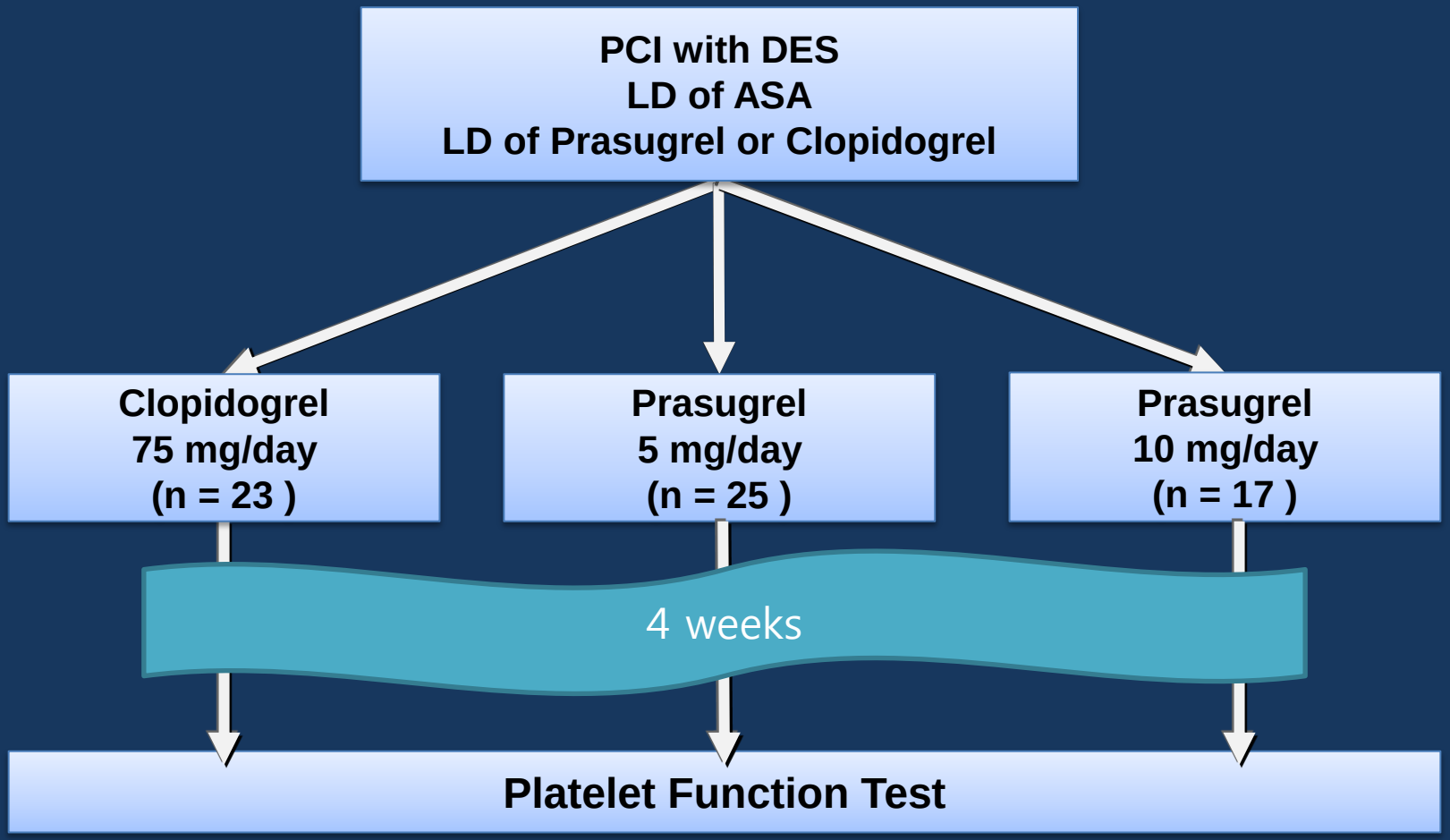


Aim of Study

Evaluate the pharmacodynamic effect of lower maintenance dose (MD) of prasugrel

METHODS

Prospective, Open label Study



Platelet Function Assessment

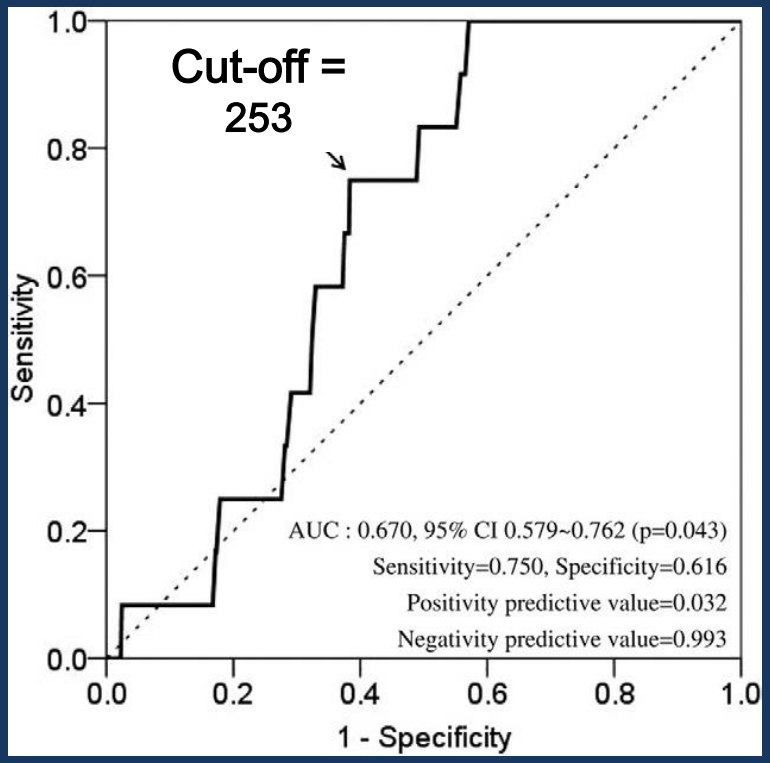
- At 4 weeks (Aspirin + Clopidogrel or Prasugrel)

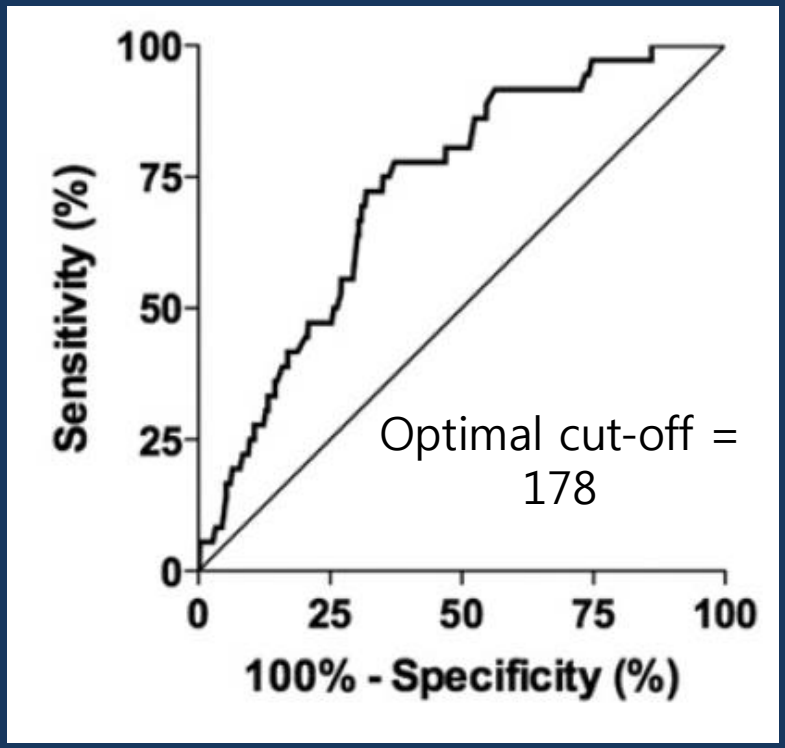
- VerifyNow (P2Y12 reaction unit, PRU)

Study End Point

High platelet reactivity (HPR) - PRU ≥253 or PRU ≥242

Lower platelet reactivity (LPR) - PRU ≤ 178 or PRU ≤ 100





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Suh et al. JACC Vol. 57, No. 3, 2011

RESULTS

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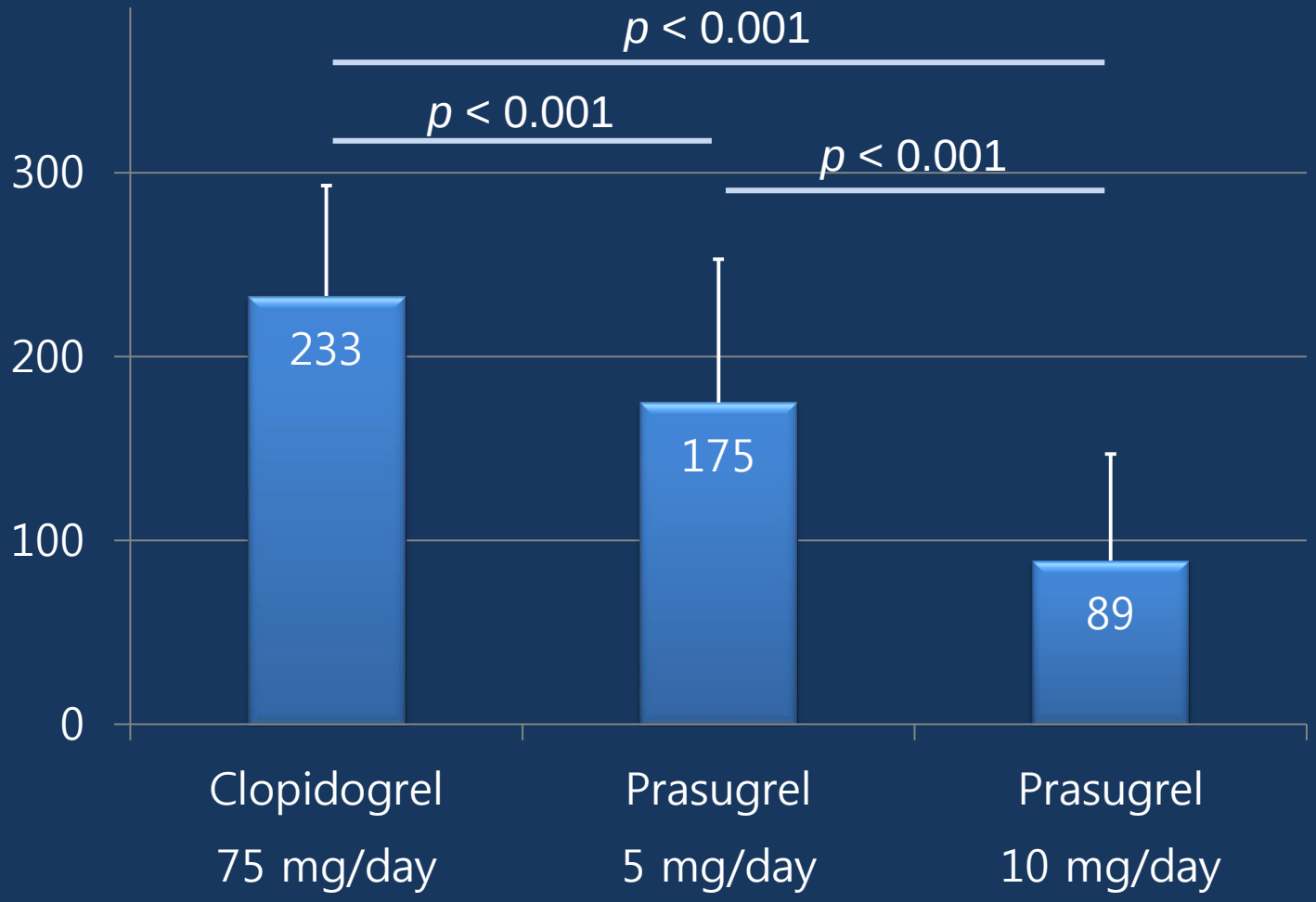
Baseline Characteristics

	Overall (n=65)	Clopidogrel 75 mg/day (n = 23)	Prasugrel 5 mg/day (n = 25)	Prasugrel 10 mg/day (n = 17)	*P*
Male	47 (72%)	17 (74%)	18 (72%)	12 (71%)	0.972
Age (years)	63 ± 11	64 ± 7	65 ± 12	60 ± 12	0.353
DM	20 (31%)	8 (35%)	6 (24%)	6 (35%)	0.660
HTN	24 (37%)	8 (35%)	11 (44%)	5 (29%)	0.650
Smoker	18 (28%)	7 (30%)	6 (24%)	5 (29%)	0.883
LDL (mg/dL)	104 ± 39	99 ± 36	96 ± 33	125 ± 45	0.059
CCB	18 (28%)	7 (30%)	9 (36%)	2 (12%)	0.206
BB	48 (74%)	18 (78%)	18 (72%)	12 (71%)	0.824
Nitrates	25 (39%)	11 (48%)	10 (40%)	4 (24%)	0.310
CYP2C19 LOF	39 (60%)	16 (73%)	15 (65%)	8 (80%)	0.794

PRU of Study Groups



Incidence of HPR & LPR

	Cut-off	Clopidogrel 75 mg/day	Prasugrel 5 mg/day	Prasugrel 10 mg/day	P value
HPR	253	11 (48%)	3 (12%)	0 (0%)	< 0.001
HPR	242	11 (48%)	5 (20%)	0 (0%)	0.002
LPR	178	6 (26%)	12 (48%)	16 (94%)	< 0.001
LPR	100	0 (0%)	3 (12%)	12 (70%)	<0.001

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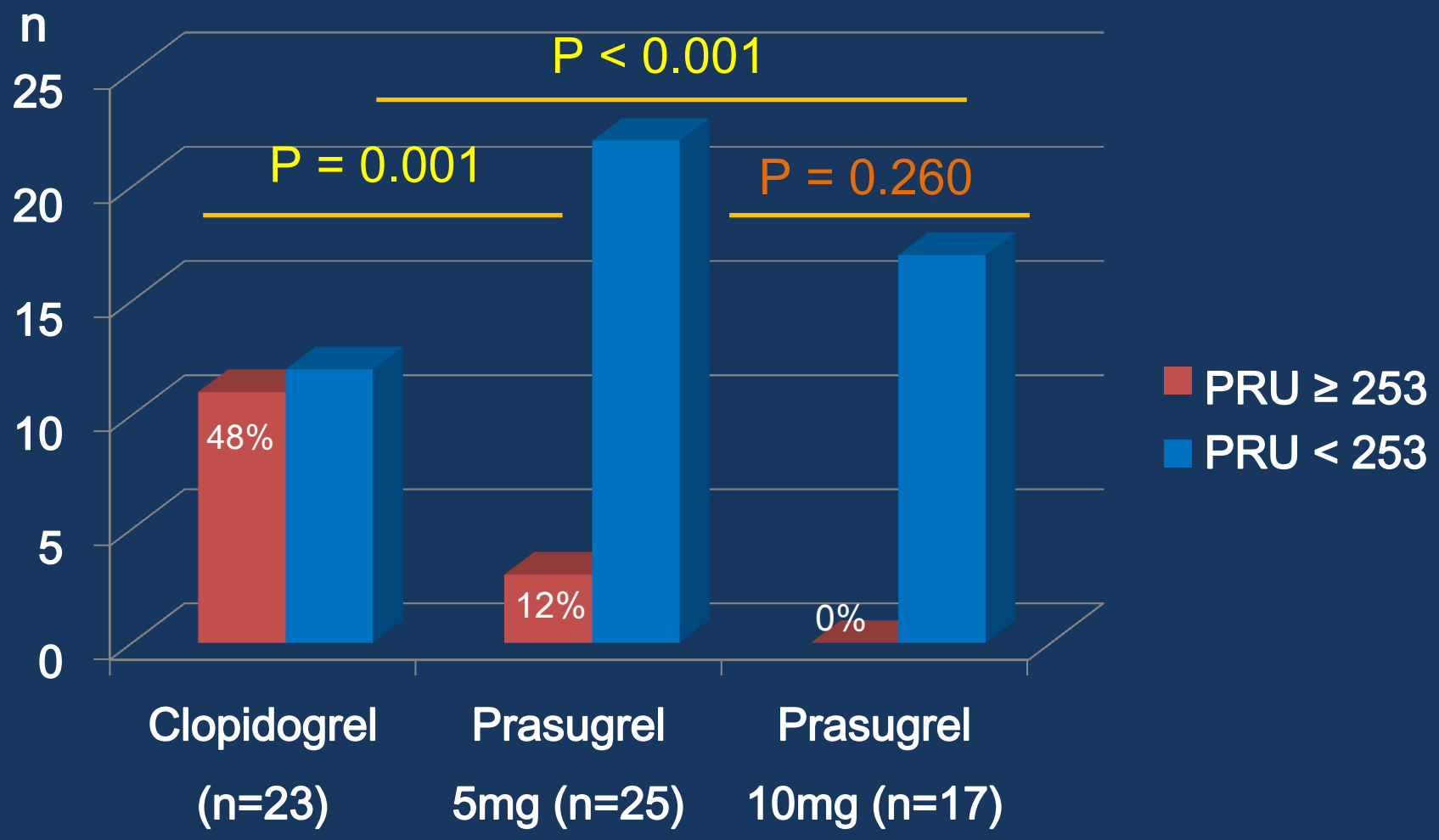
HPR - PRU ≥253



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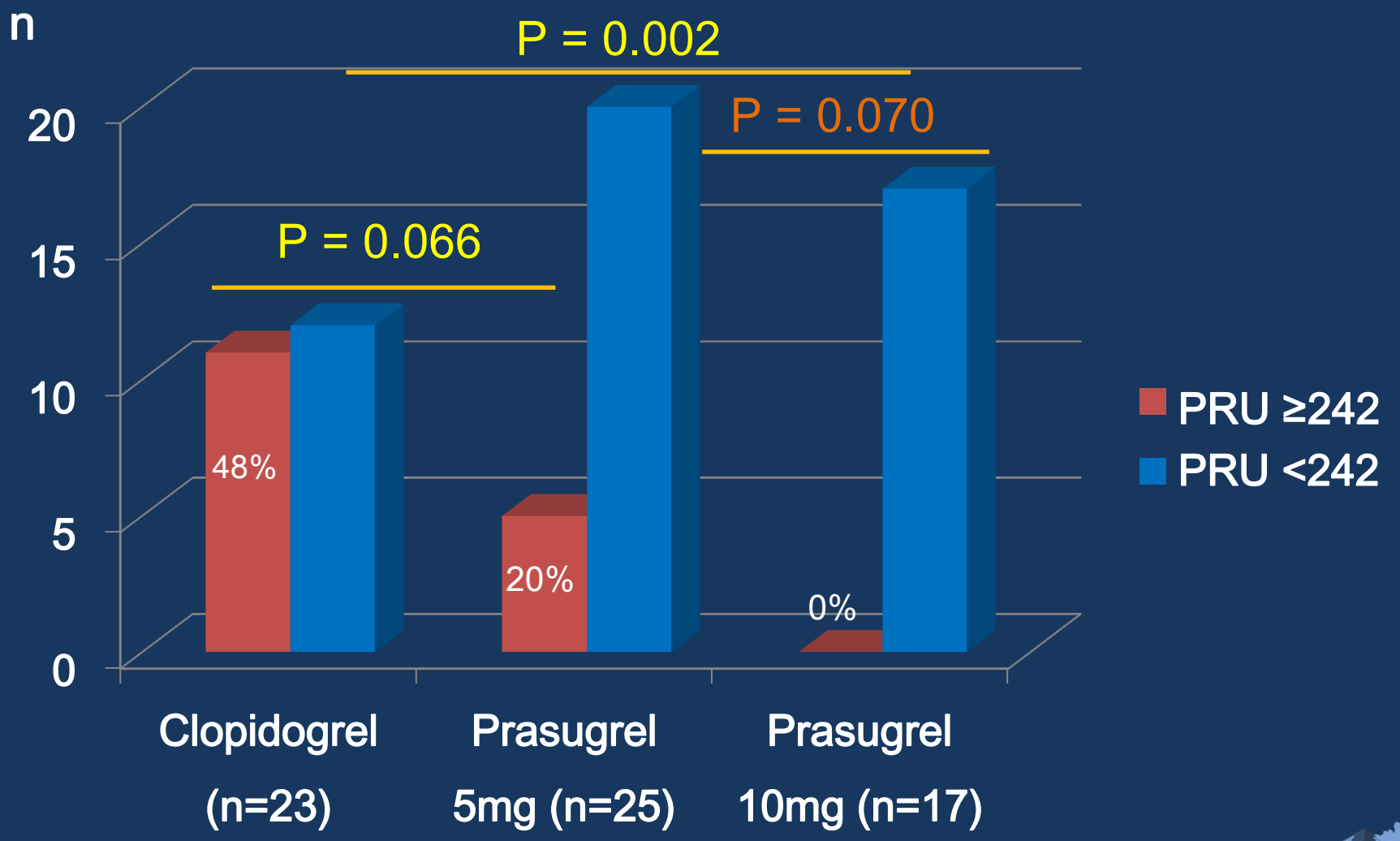
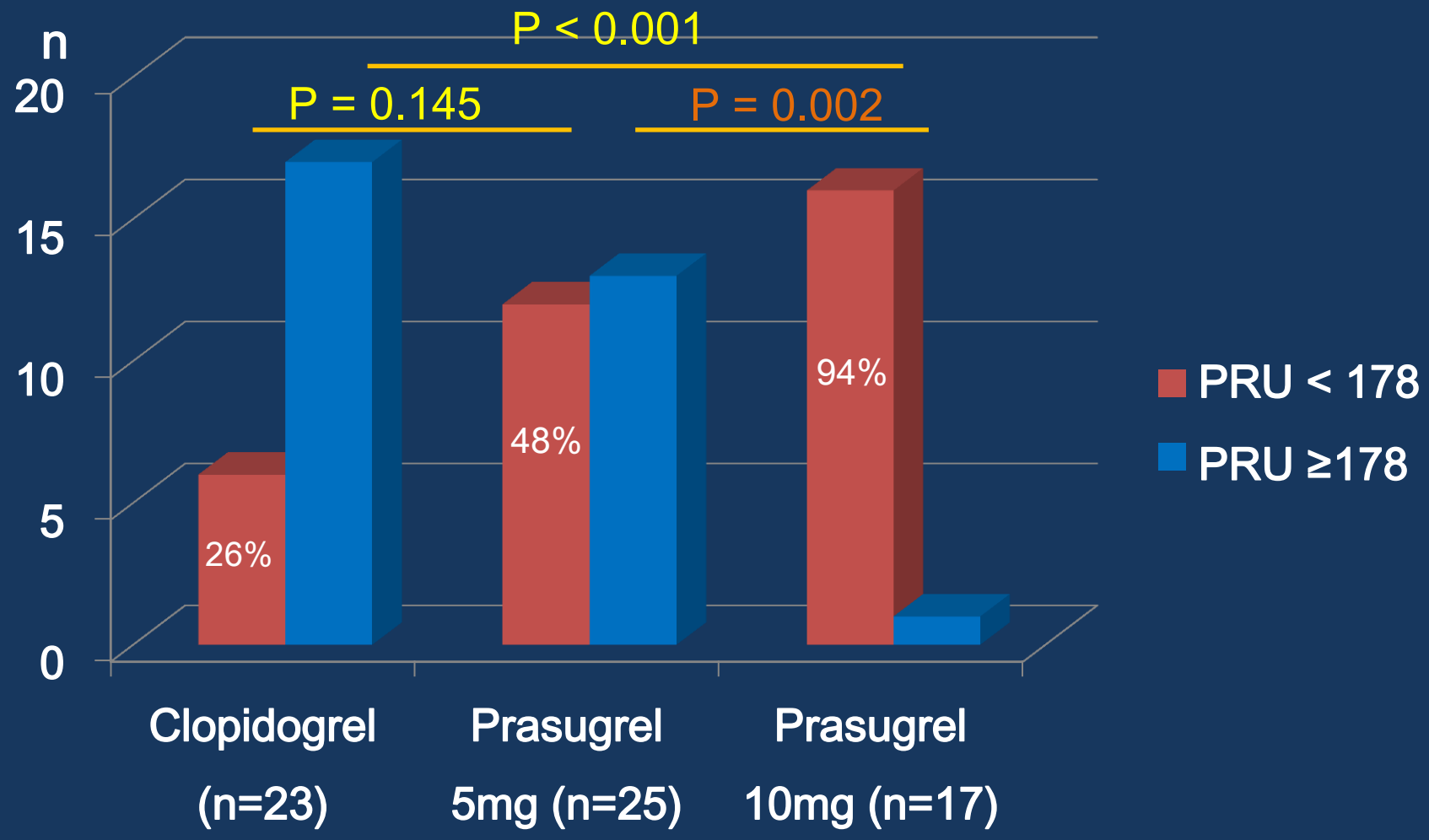
HPR - PRU ≥242



LPR - PRU ≤ 178


P < 0.001
P = 0.145
P = 0.002
n
20
15
10
5
0
26%
48%
94%
PRU < 178
PRU ≥178
Clopidogrel (n=23)
Prasugrel 5mg (n=25)
Prasugrel 10mg (n=17)

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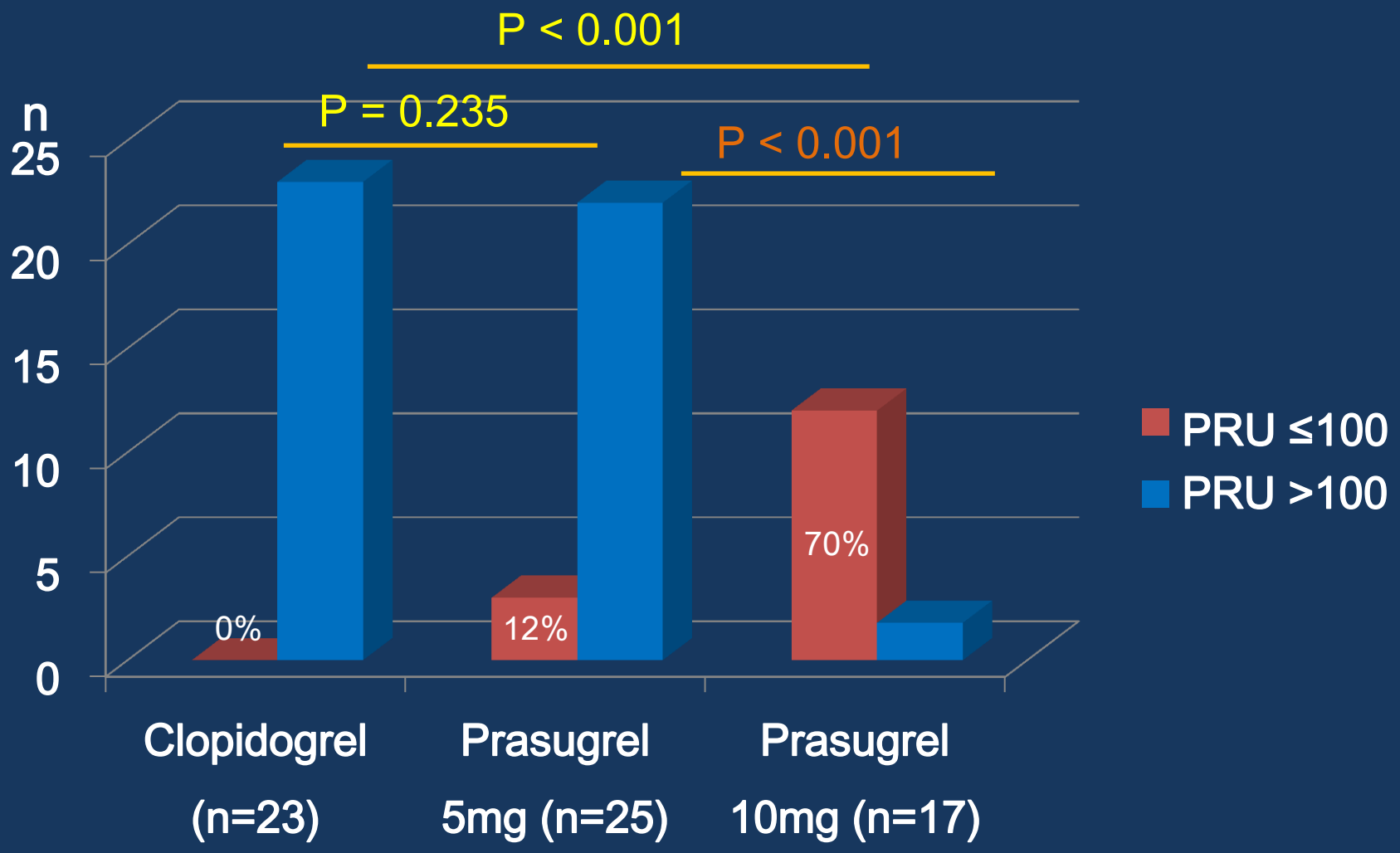
LPR - PRU ≤ 100



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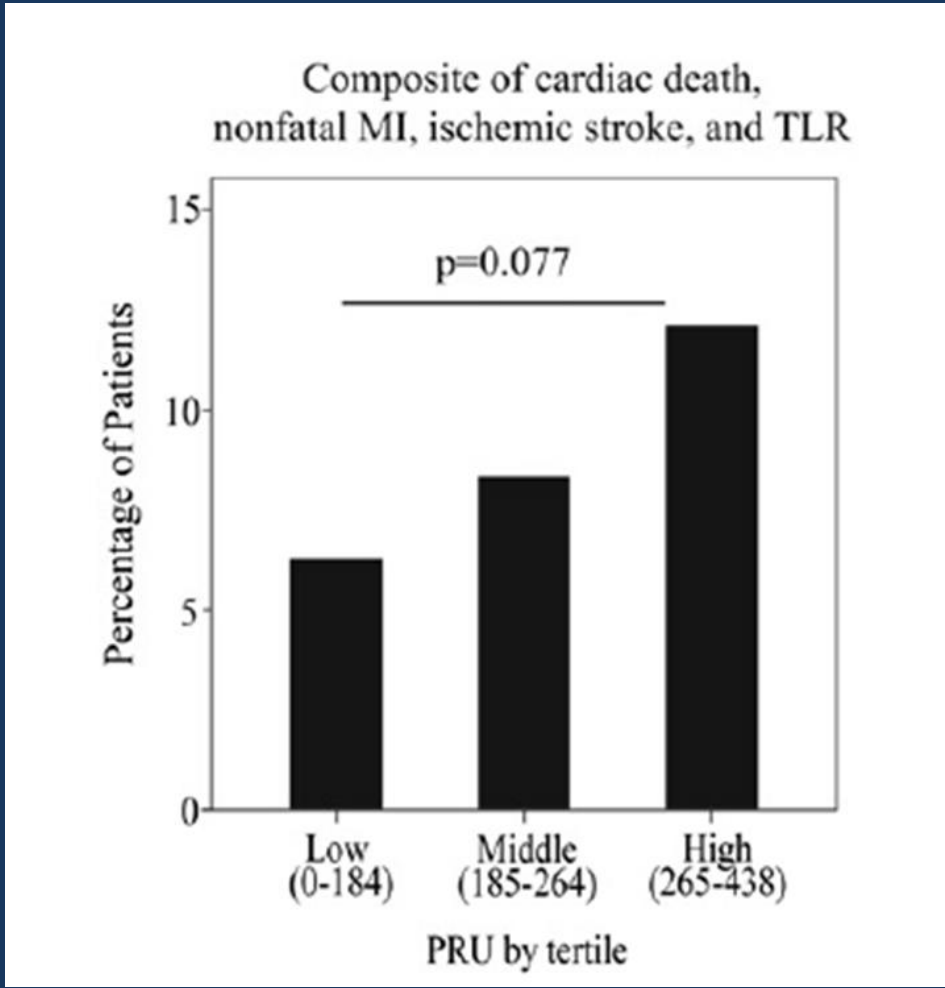
Clinical events

Events	Total (n)	Clopidogrel 75 mg/day	Prasugrel 5 mg/day	Prasugrel 10 mg/day	P value
MACE *	1	0	0	1	0.238
Bleeding (BARC# ≥ Type 2)	4	1	2	1	0.870

*Major adverse cardiovascular events (MI, Stroke, revascularization)
Bleeding Academic Research Consortium

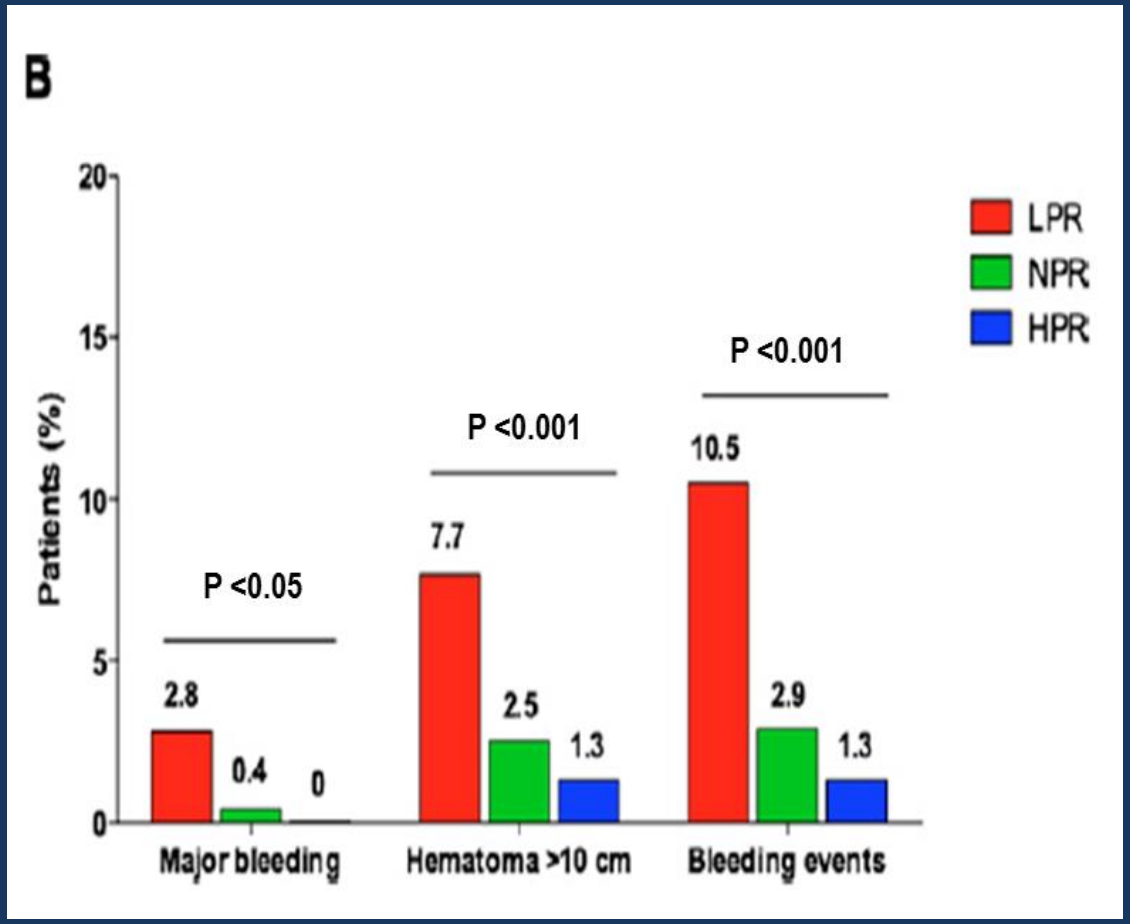
DISCUSSION

HPR & MACE in Korean



Suh et al. JACC Vol. 57, No. 3, 2011

LPR & Bleeding



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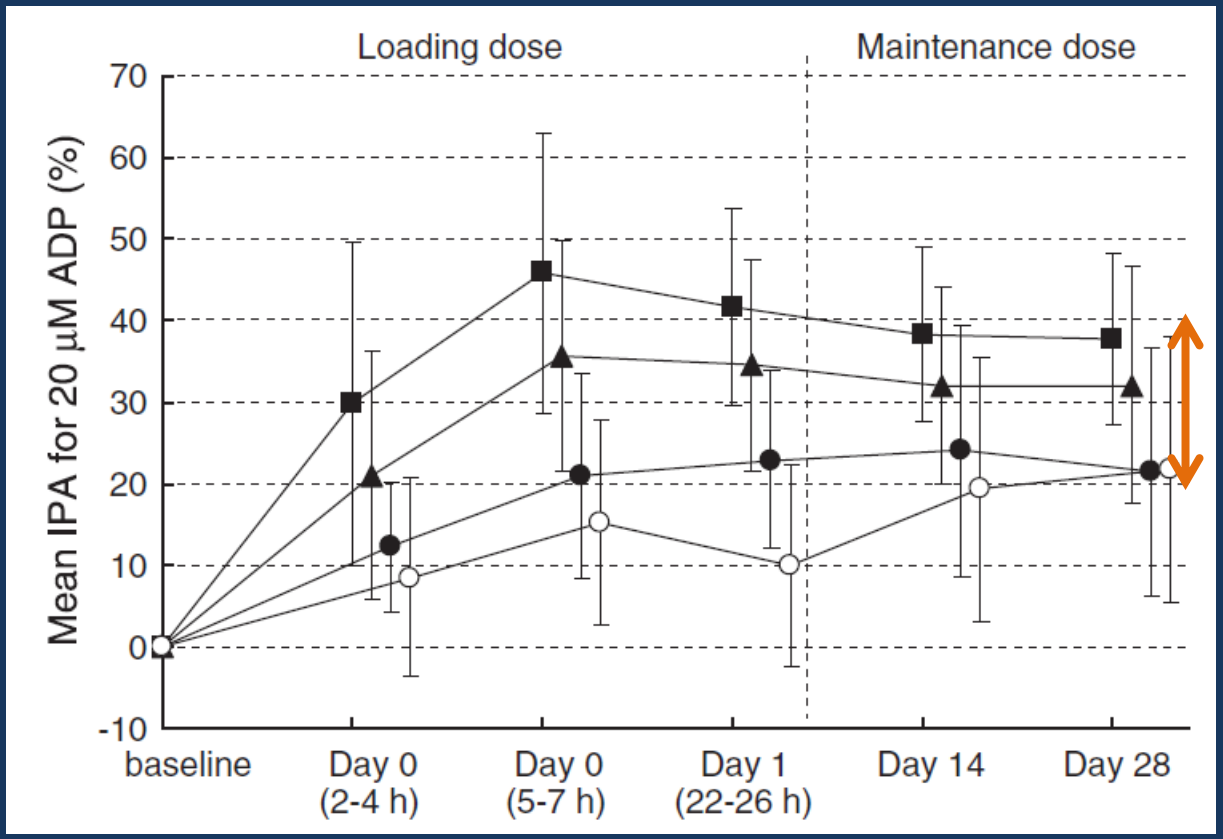
Prasugrel dose in Asian



- Prasugrel 20/5(n=17)
- Prasugrel 15/3.75(n=23)
- Prasugrel 10/2.5(n=20)
- Clopidogrel 300/75(n=24)

H. Yokoi et al., Thrombosis Research 2012

Ideal dose of Prasugrel ?

2.5mg? 5mg? 7.5mg?

Asian is different

- Better response & More bleeder

Ideal therapeutic window

- Large prospective study is needed

Limitations

Small sample size

Short term follow – up data

Selection Bias

Conclusion

Prasugrel 5 mg as a maintenance dose

- Showed significantly low incidence of LPR

- Did not increase HPR


THANK YOU FOR YOUR ATTENTION