Platelet Function Testing For All Patients: ***DEFINITELY!*** *The Data are Strong*

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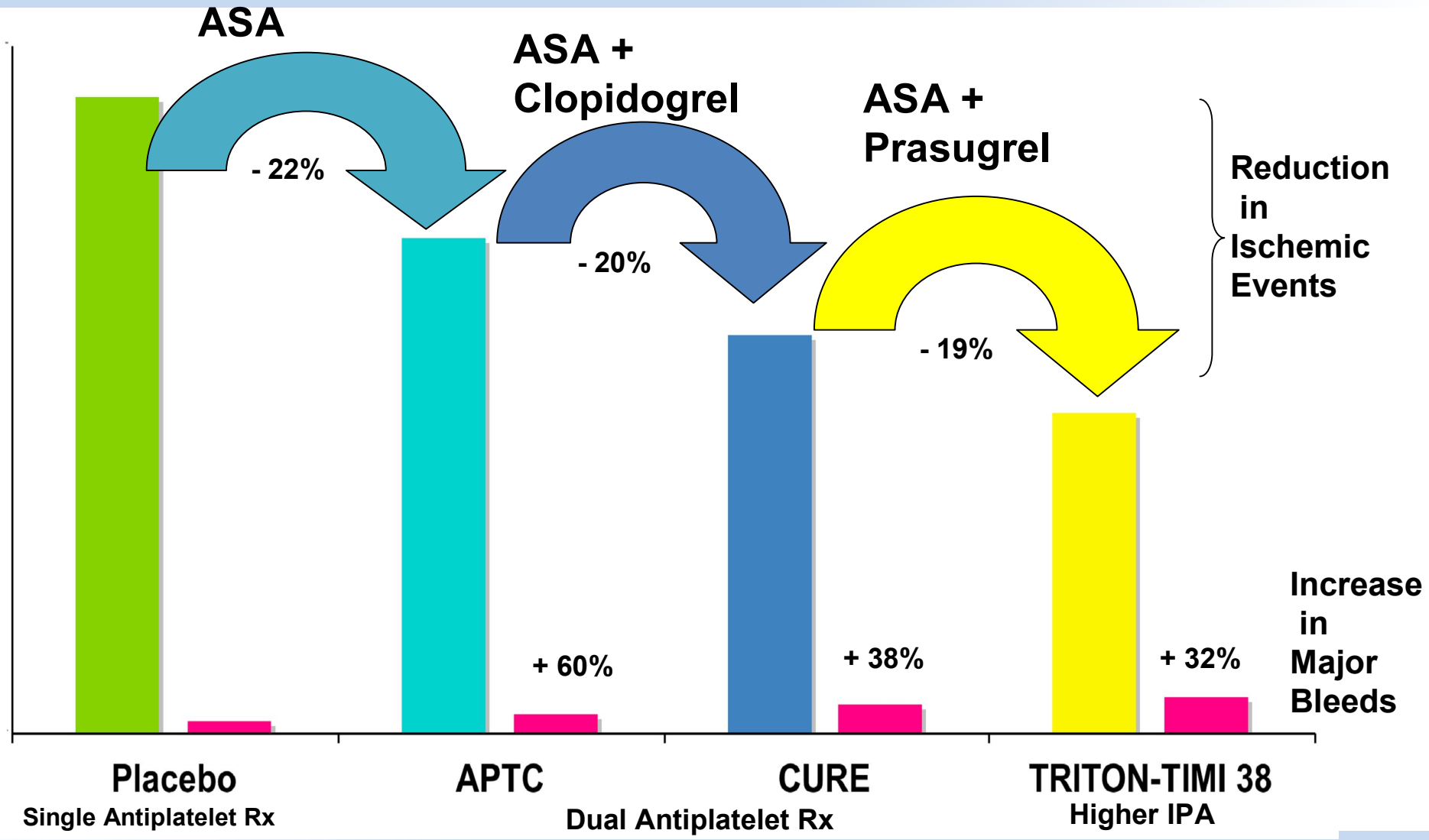
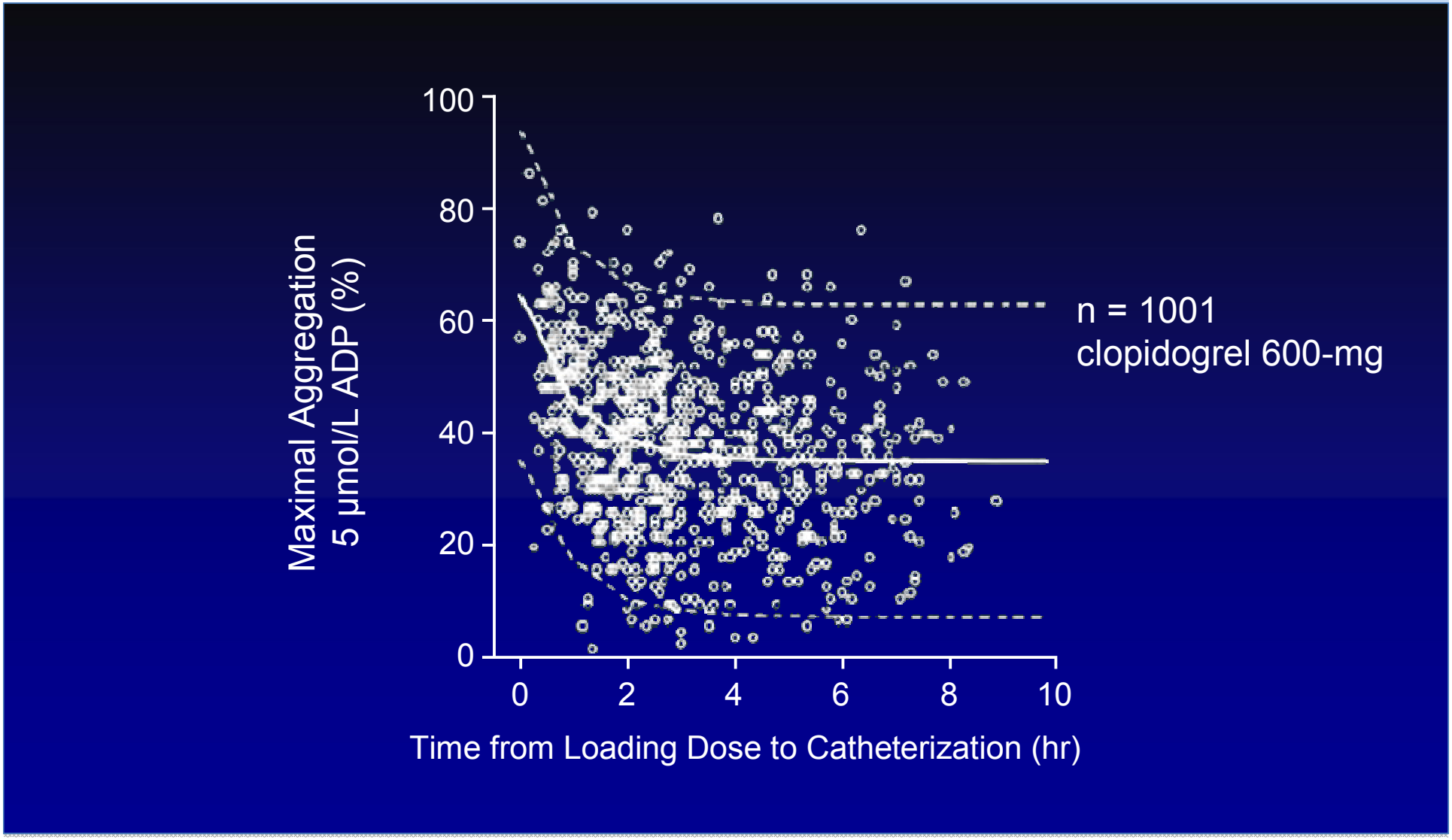
The Current Egalitarian Strategy of Antiplatelet Therapy During And After PCI: *The More The Merrier for Everyone!*



Adapted from Gibson, AHA 2007

Why A One-Size Fits All Aproach?

The Response To A Uniform Dose Of Clopidogrel Is Not Uniform



Hochholzer W et al. Circulation. 2005;111:2560-2564.

SCRIPPS CLINIC

Poor Outcome and Inadequate Clopidogrel Response:
A strong and consistent association across studies

	N	Clinical Setting	Outcomes
Light Transmittance Aggregometry			
Matetzky et al.	60	STEMI undergoing PCI	Post-primary PCI ischemic events (6 months)
Gurbel et al.	192	Nonemergent PCI	Post-PCI ischemic events (6 months)
Gurbel et al.	120	Elective PCI	Post-PCI myonecrosis/inflammation
Cuisset et al.	106	ACS undergoing PCI	Post-PCI ischemic events (30 days)
Lev et al.	120	Elective PCI	Post-PCI myonecrosis
Cuisset et al.	150	Elective PCI	Post-PCI myonecrosis
Hochholzer et al.	802	Elective PCI	Post-PCI ischemic events (30 days)
Geisler et al.	379	Stable and unstable angina undergoing PCI	Post-PCI major cardiovascular events (3 months)
Bliden et al.	100	Chronic clopidogrel undergoing nonemergent PCI	Post-PCI ischemic events (12 months)
Cuisset et al.	190	NSTEACS undergoing PCI	Periprocedural myocardial infarction
Angiolillo et al.	173	Type 2 DM on chronic dual antiplatelet therapy	Ischemic events (24 months)
Marcucci et al.	367	MI undergoing PCI	Post-PCI myonecrosis
Müller et al.	105	Elective PCI	Stent thrombosis
Buonamici et al.	804	PCI with drug eluting stent	Stent thrombosis
VASP-phosphorylation assay			
Bonello et al.	144	Stable angina and low-risk NSTEACS undergoing PCI	Post-PCI major adverse cardiac events (6 months)
Frere et al.	195	NSTEACS undergoing PCI	Post-PCI ischemic events (30 days)
Barragan et al.	46	Subacute stent thrombosis	Stent thrombosis
Gurbel et al.	120	Subacute stent thrombosis	Stent thrombosis
Blindt et al.	99	PCI with high risk for stent thrombosis	Stent thrombosis
VerifyNow $P2Y_{12}$ assay			
Price et al.	380	PCI with drug eluting stents	MACE and stent thrombosis (6 months)
Patti et al.	160	PCI	Major adverse cardiac events (30 days)
Marcucci et al.	683	ACS undergoing PCI	Major adverse cardiac events (12 months)
De Miguel et al.	179	NSTEACS undergoing coronary angiography	Major adverse cardiac events (12 months)
Others			
Sibbing et al.	1608	Elective PCI with drug eluting stent	Stent thrombosis
Ajzenberg et al.	49	Subacute stent thrombosis	Stent thrombosis

Angiollilo et al, Thromb Haemost, in press

Clinically Practical Platelet Function Tests Can Identify Patients At-Risk For Ischemic Events after PCI

VerifyNow (Accumetrics)

TEG Platelet Function Mapping (Haemoscope)

Multiplate Analyzer (Dynabyte)

Clinically-Derived Cut-Offs from Prospective Studies:

Study	N	Device	Primary Endpt	Cutoff	Method
Price et al	**380**	VerifyNow P2Y12	6M CV death, MI, ST	**PRU ≥ 235**	ROC curve
Patti et al	**160**	VerifyNow P2Y12	30-day CV death, MI, TVR	**PRU ≥ 240**	ROC curve
Marcucci et al	**683**	VerifyNow P2Y12	1 yr CV death, MI	**PRU ≥ 240**	ROC curve
Sibbing et al	**1608**	Multiplate Analyzer	30-day Stent thrombosis	**468 AU·min**	ROC curve
Bliden et al	**100**	TEG Platelet Mapping	1 year CV death/MI/TVR/CVA/Non-TVR/Re-hosp Ischemia	nr	ROC curve

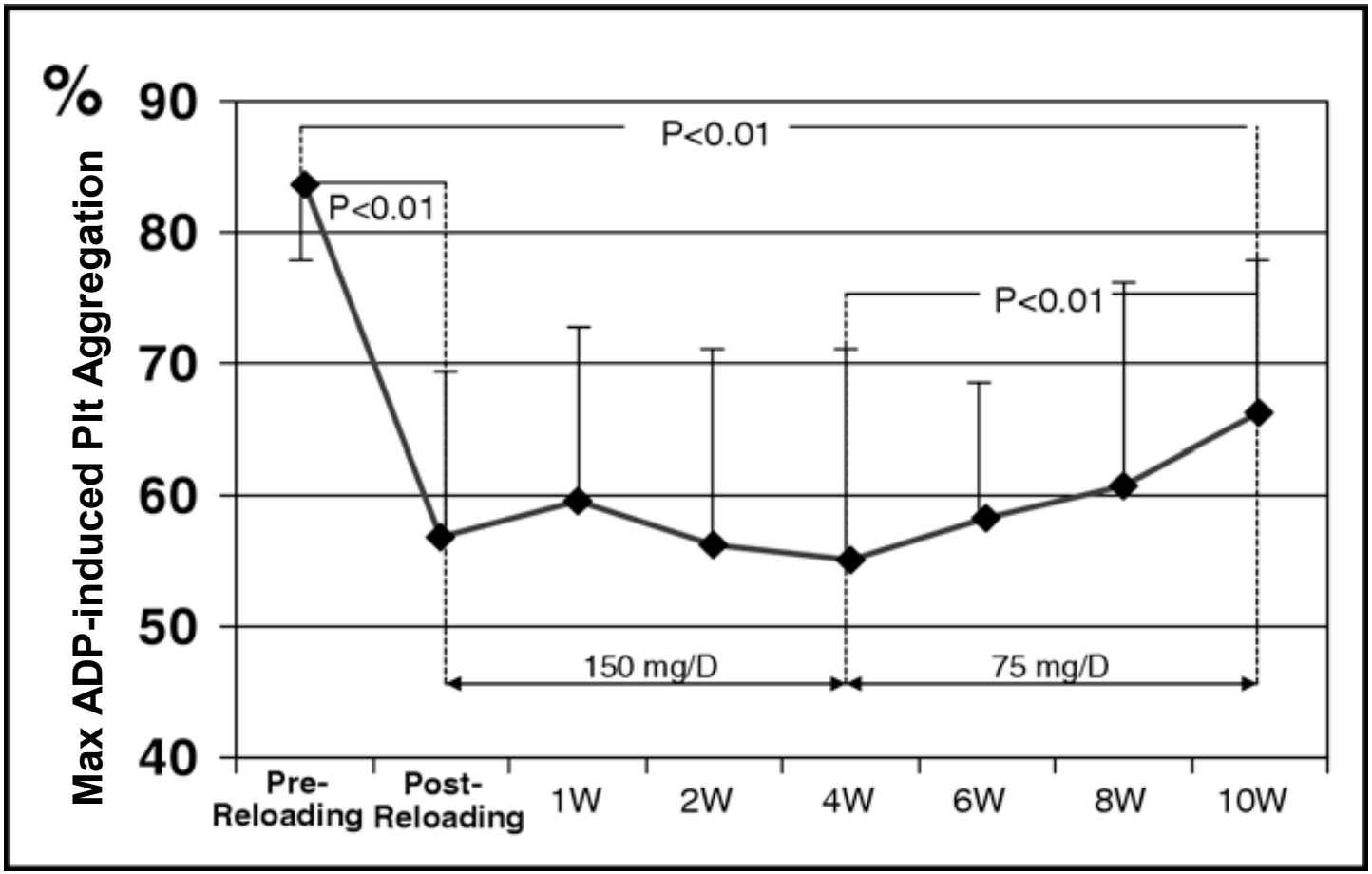
Sibbing et al, J Am Coll Cardiol 2009;53:849-856
Marcucci et al, Circulation 2009; 20;119(2):237-42

Patti, G. et al. J Am Coll Cardiol 2008;52:1128-1133
Price MJ et al. Eur Heart J 2008; 29(8):992-1000

What Can I do If My Patient is A Non-Responder?

Increase the dose of clopidogrel

Re-loading followed by 150-mg/day overcomes "non-responsiveness"

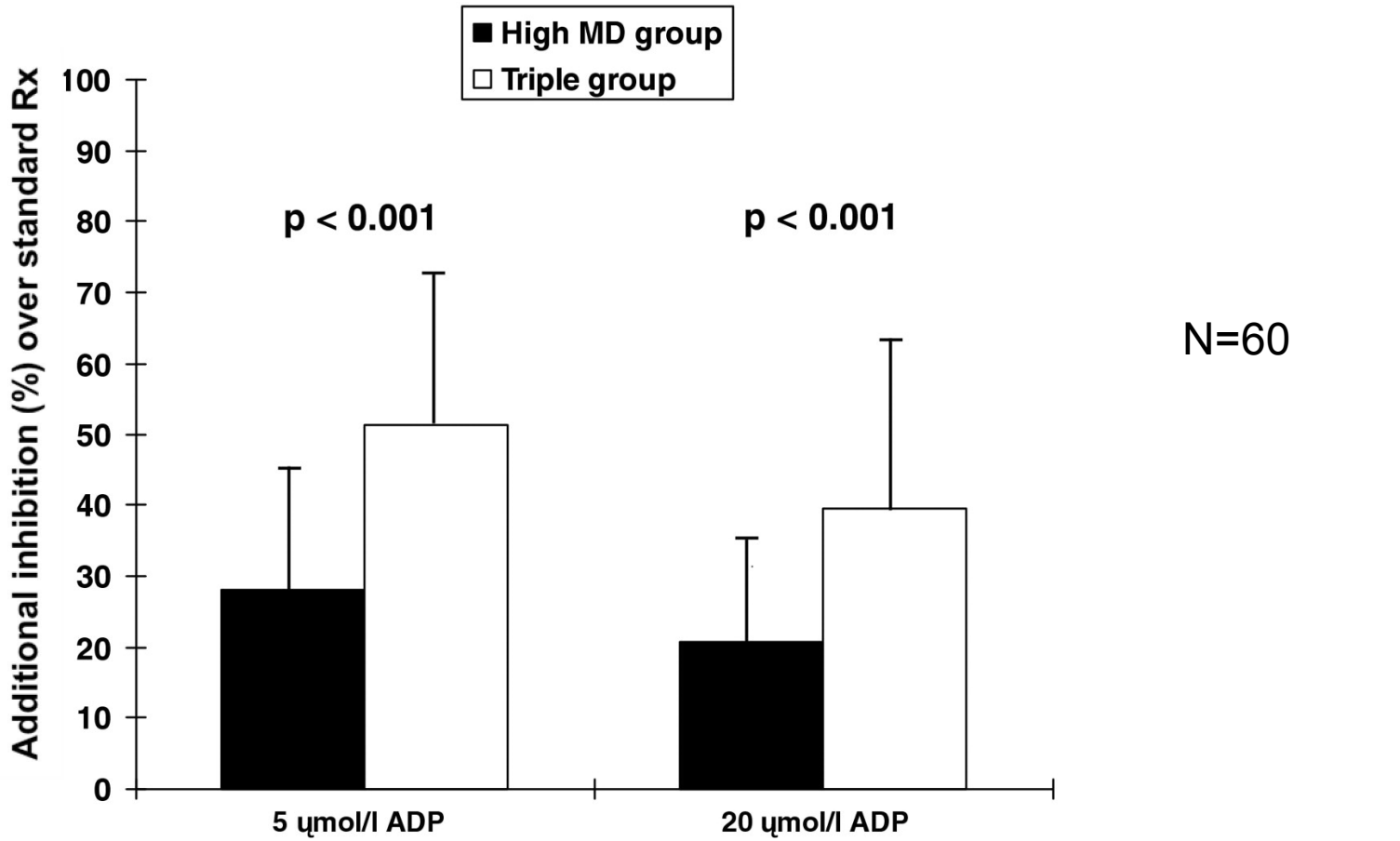


N=30

Matetzky et al, Am J Cardiol 2008; 102(5):524-9

Potential Management Strategies for Patients With High Platelet Reactivity on Standard Clopidogrel Therapy: *Add Cilostazol*

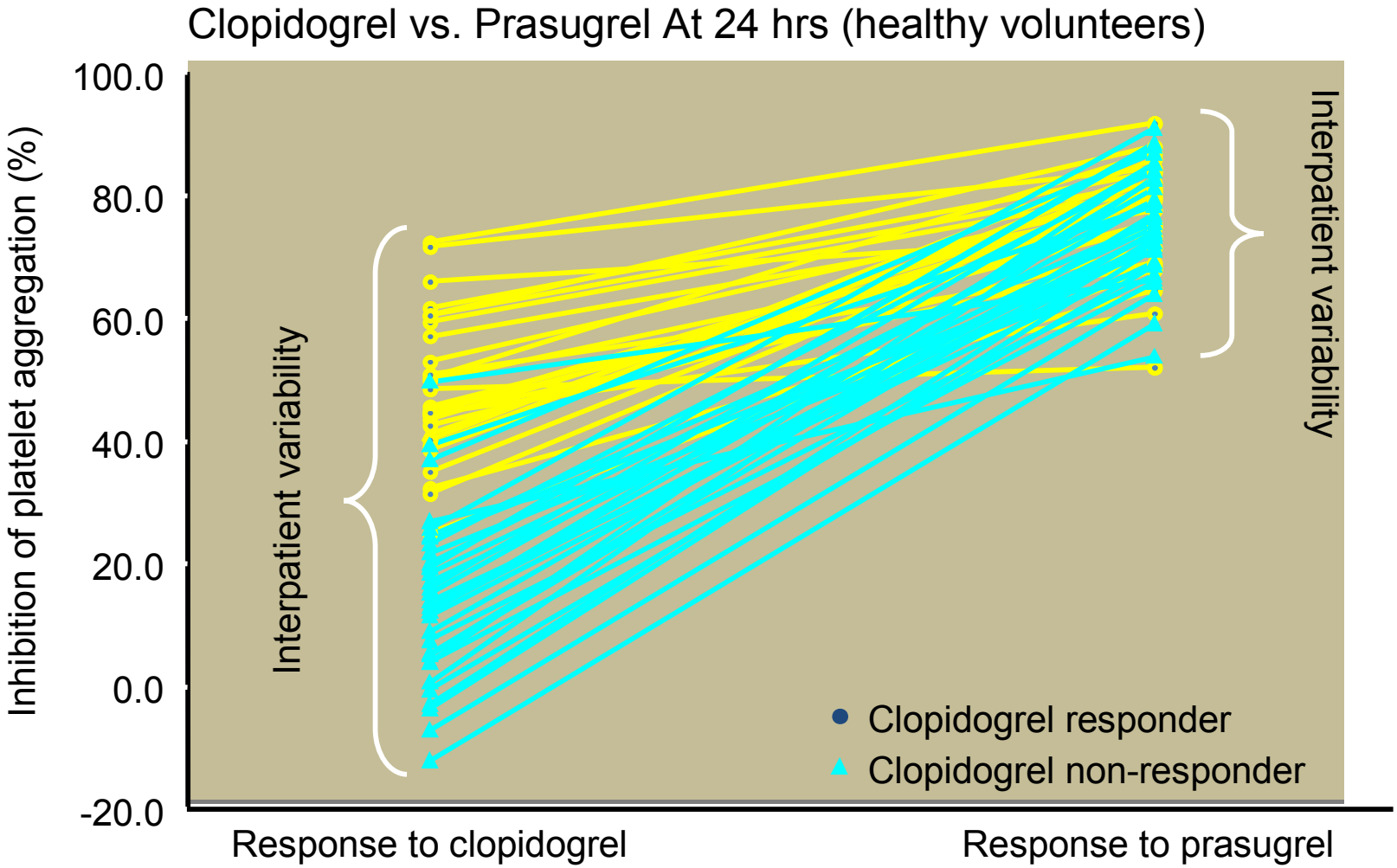
Clopidogrel 150-mg day (**High MD**) vs. Clopidogrel + Cilostazol (**Triple Group***)* in non-responders to standard dosing



NR defined as > 50% Agg (max) with 5uml of ADP at least 12hrs after clop 300-mg

Jeong YH et al, J Am Coll Cardiol, 2009; 53:1101-110

Potential Management Strategies for Patients With High Platelet Reactivity on Standard Clopidogrel Therapy:
Switch to prasugrel

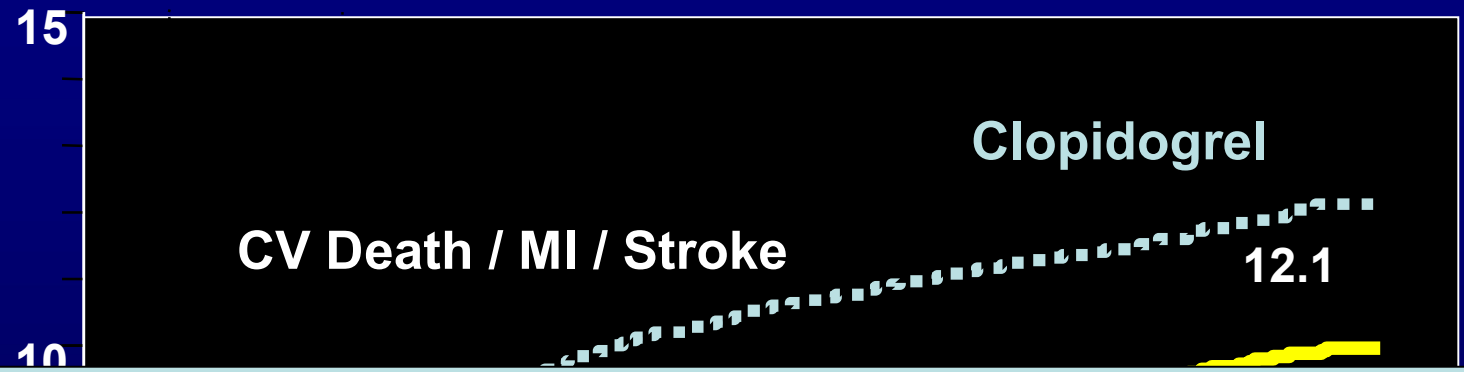


Responder = ≥ 25% IPA at 4 and 24 hours

Brandt JT, et al. *Am Heart J*. 2007;153:66.e9-e16.

TRÎTON TIMI-38

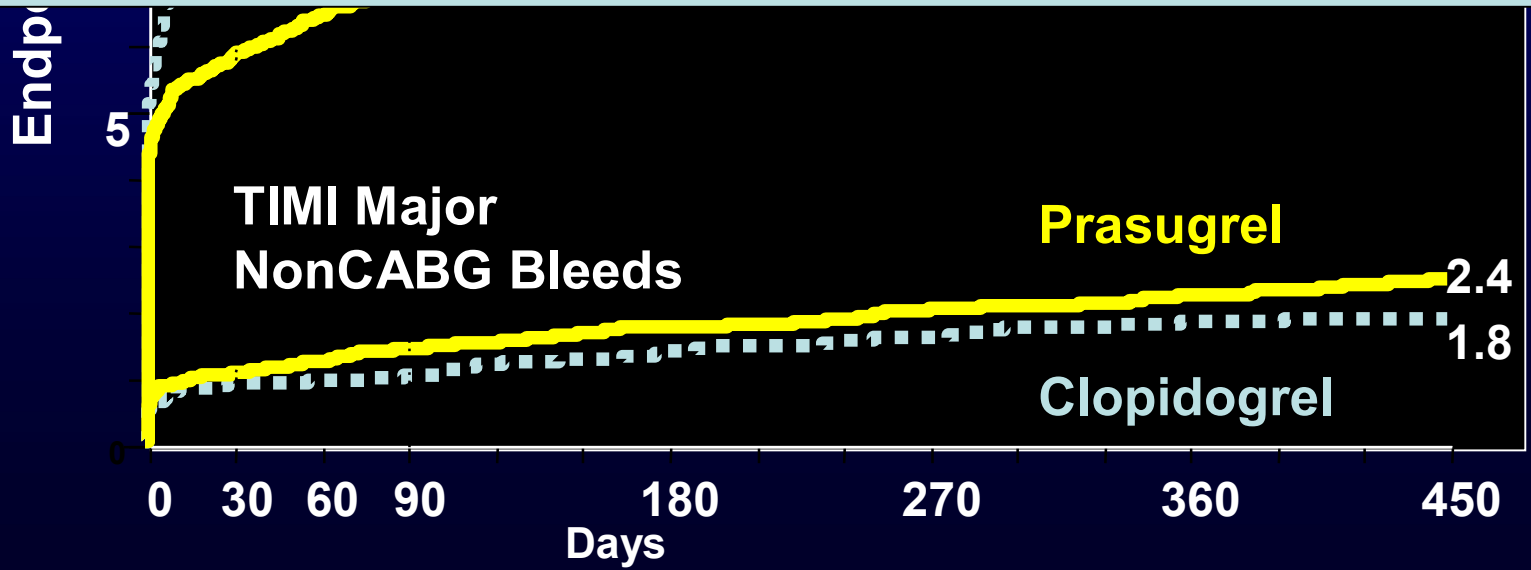
Balance of Efficacy and Safety



138↓ events

HR 0.81
(0.73-0.90)
P=0.0004

Why Not Prasugrel For Everyone?



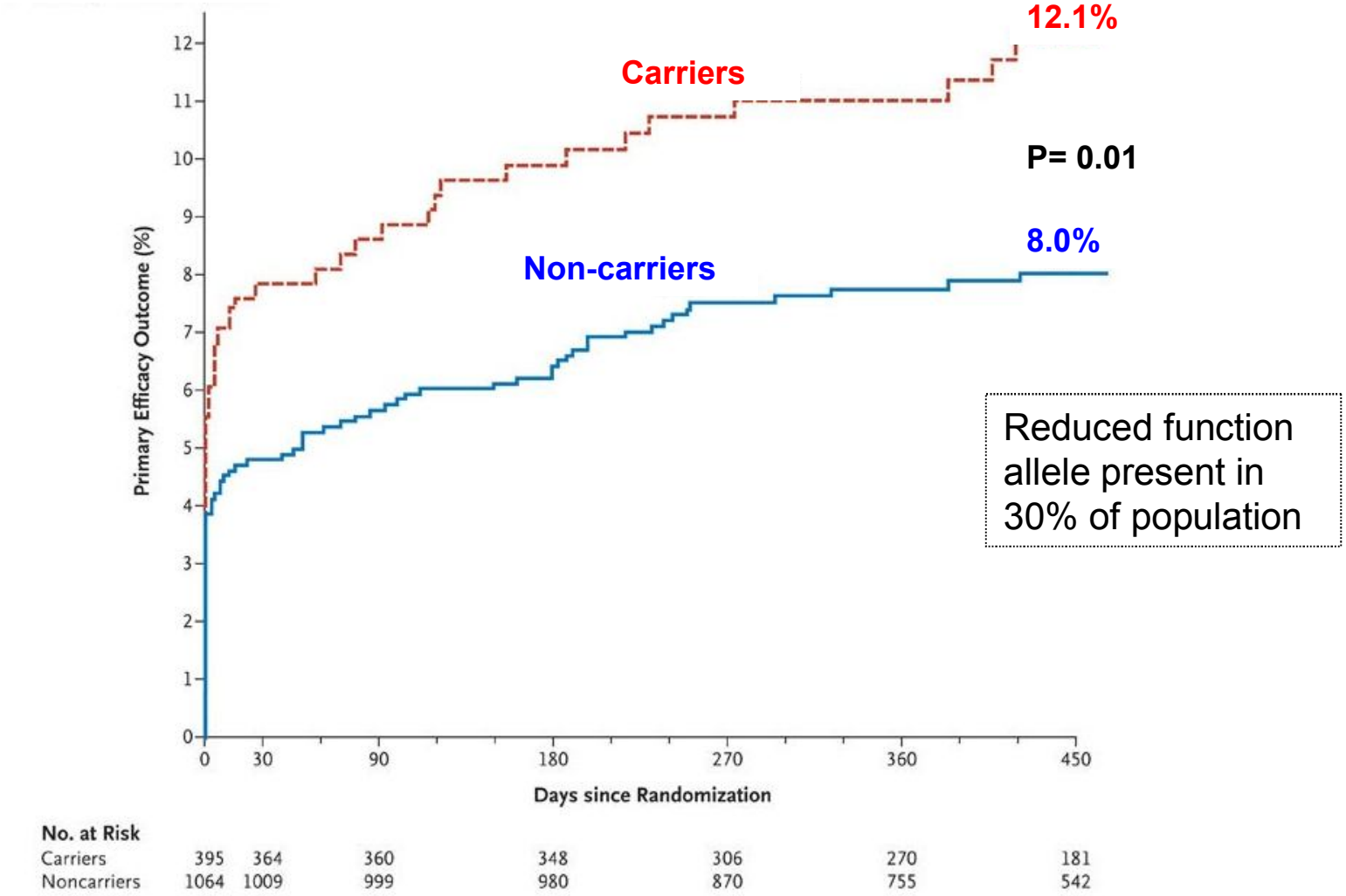
35 ↑ events

HR 1.32
(1.03-1.68)
P=0.03

NNH = 167

Clopidogrel and Outcomes: Prasugrel-like for Most Pts!

TRITON Results According to Carriage of Reduced Fxn CYP2C19 Allele in Pts Receiving Clopidogrel

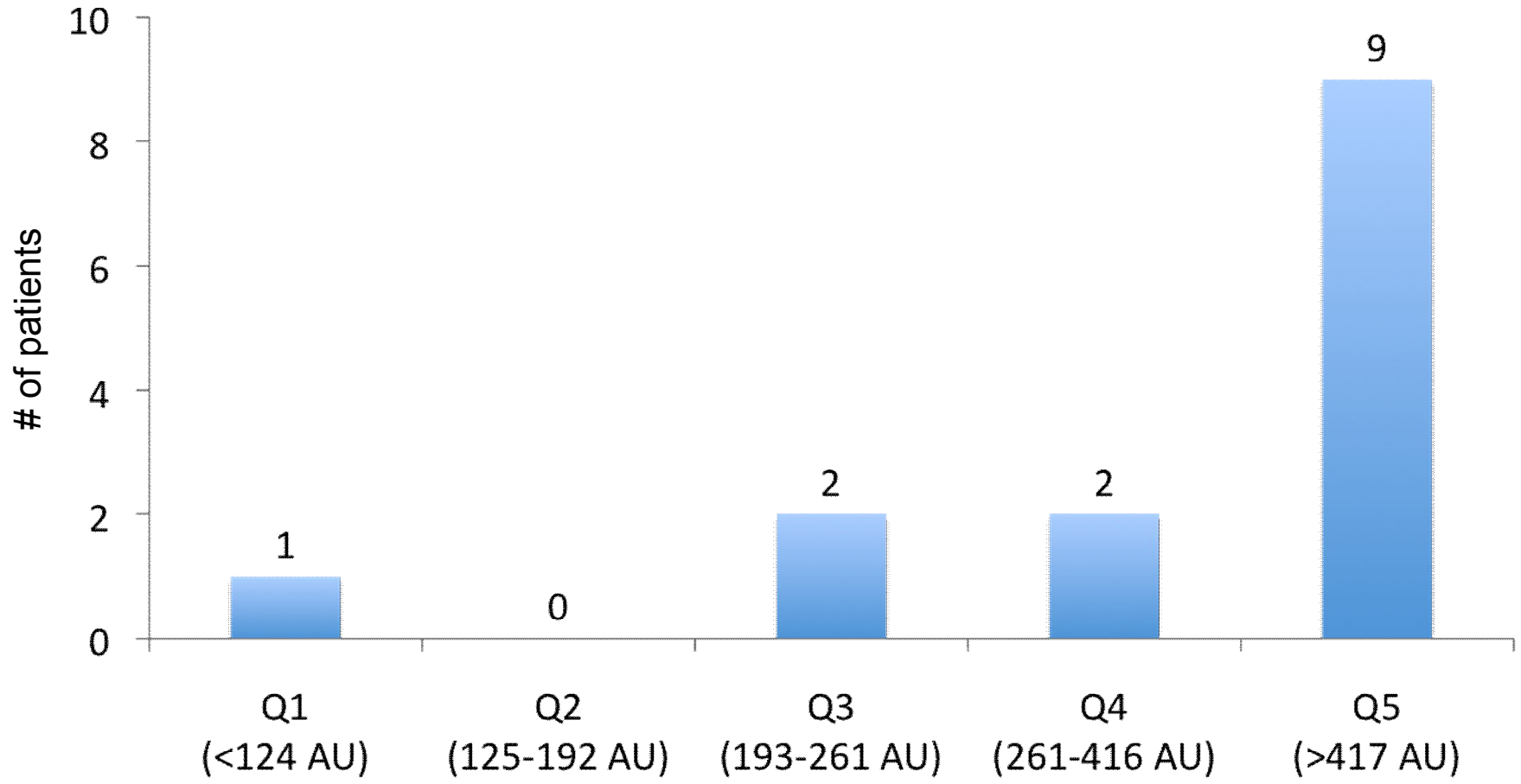


Reduced function allele present in 30% of population

Mega JL et al, NEJM 2009;360:354-62

MEA by Multiplate Analyzer and 30-day Definite/Prob ST

Ischemic Events Cluster in Patients with High Post-treatment Reactivity

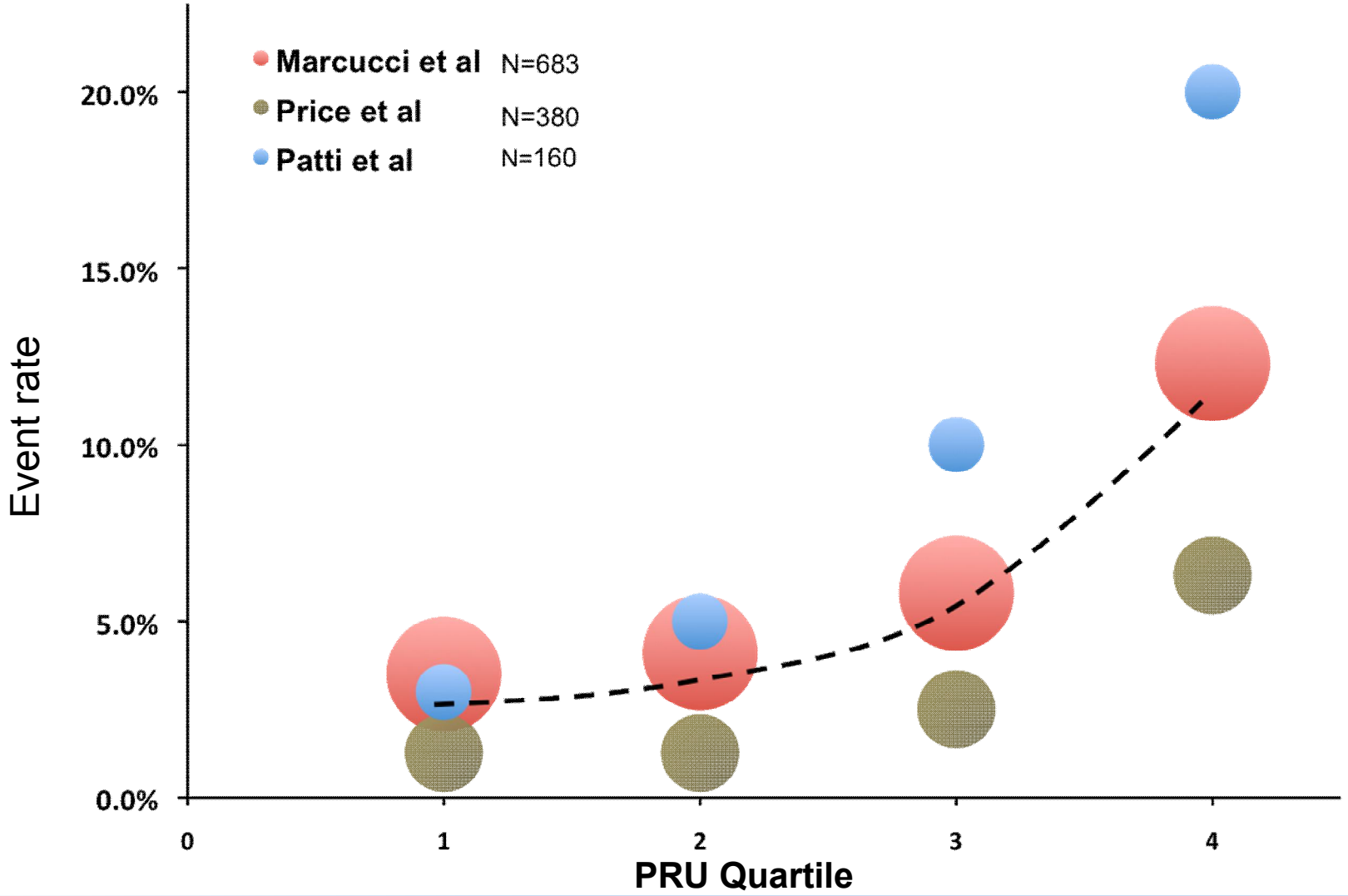


MEA, multiple electrode platelet aggregometry

Sibbing et al, J Am Coll Cardiol 2009;53:849-856

Increasing Risk With Greater Residual Reactivity

Event Rates In Prospective PCI Studies Stratified By PRU Quartile

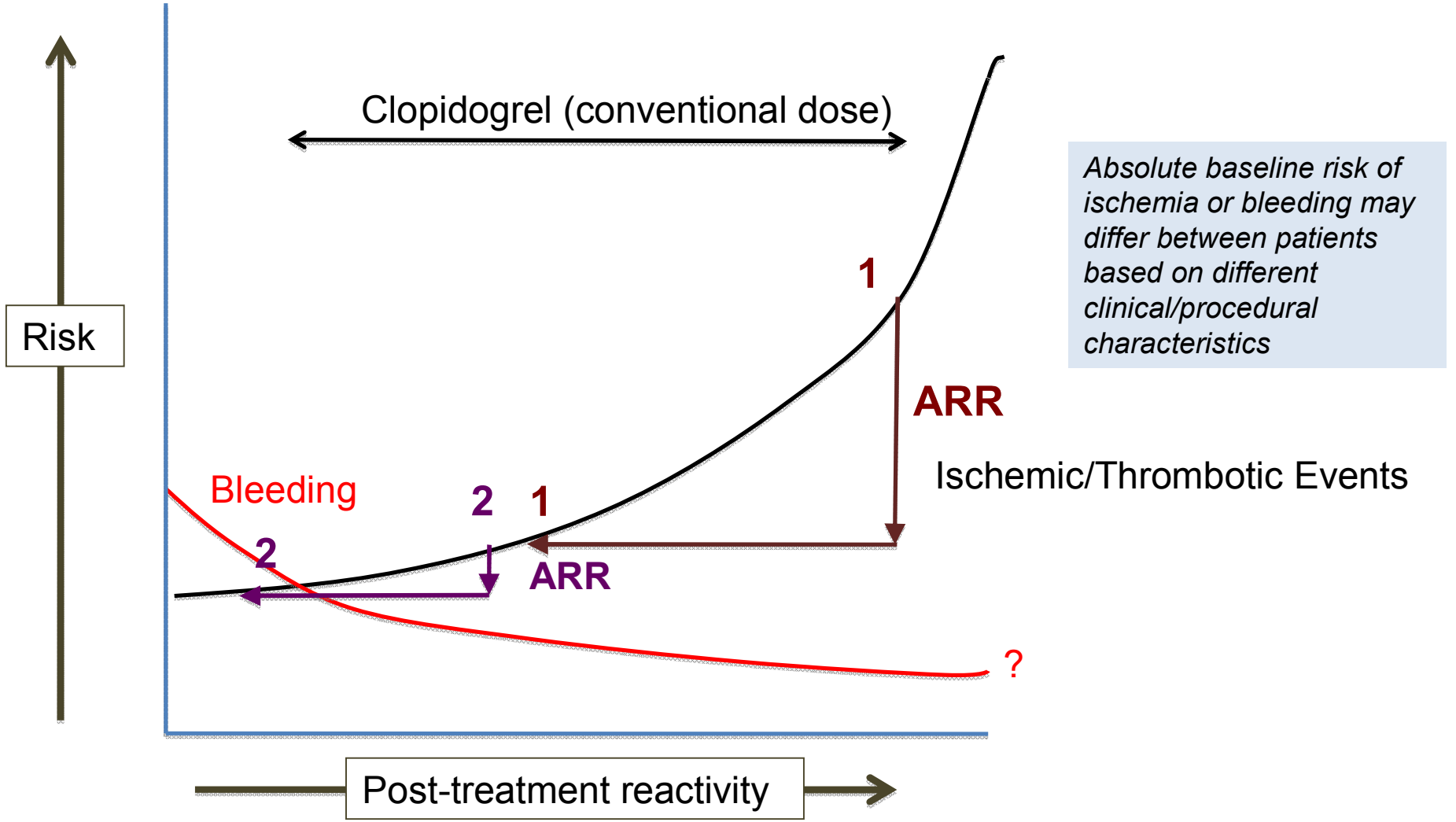


Patti, G. et al. J Am Coll Cardiol 2008;52:1128-1133

Price MJ et al. Eur Heart J 2008; 29:992-1000 Marcucci et al, Circulation 2009

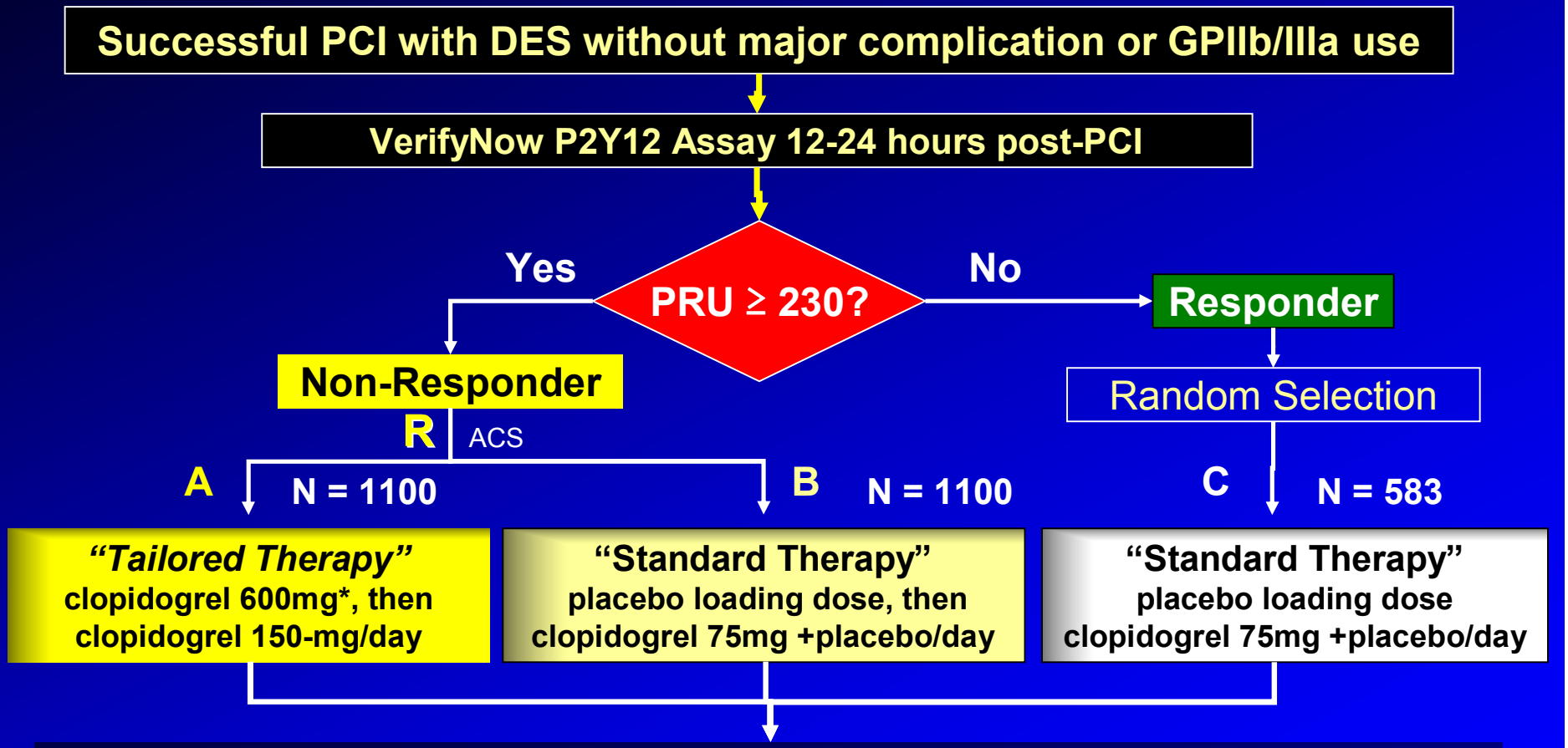
The Balance Between Ischemic and Bleeding Risk

Decreasing Returns With Even Lower Reactivity?



Absolute baseline risk of ischemia or bleeding may differ between patients based on different clinical/procedural characteristics

GRAVITAS



Price MJ et al, Am Heart J, 2009

Does On-Treatment Platelet Reactivity Fulfill the Requirements of *A Risk Factor for Ischemic Events* After PCI?

- Biological plausibility. ✔
- Strong and consistent association between studies. ✔
- Exposure to factor precedes outcome. ✔
- Evidence of a dose-response relationship. ✔

Grimes DA, Schulz KF. Bias and causal associations in observational research. *Lancet.* 2002;359:248-252.

Does POC testing of Platelet Function Fulfill the Criteria For a Screening Tool?

- The test must be practical in the clinical setting. ✔
- The test must accurately characterize low- and high-risk patients. ✔
- Identification of at-risk individuals should lead to a treatment that improves outcome…**GRAVITAS**

Wilson JMG, Jungner G. Principles and practice of screening for disease. Geneva: World Health Organization; 1968.


RON – COME TO LA JOLLA AND
RIDE THE WAVE OF PLATELET
FUNCTION TESTING!