When and why should we use platelet function testing?

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What do we know?

- **Platelet inhibition varies substantially in patients treated with clopidogrel**

  Gurbel PA, Circulation 2003;107:2908-2913.

- **High residual platelet activity is associated with a higher rate of ischemic events than lower platelet reactivity**

  Hochholzer W, J Am Coll Cardiol 2006;48:1742-1750.

- **Genetic factors may affect platelet inhibition by clopidogrel**

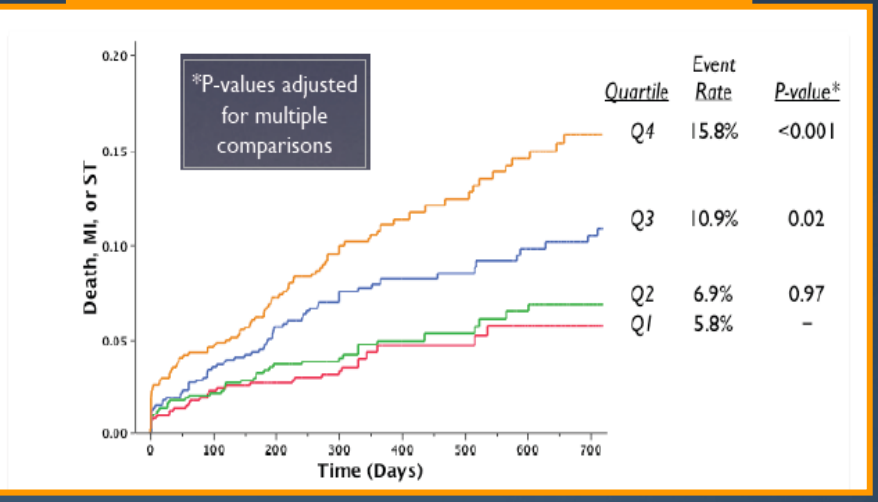
  Mega JL, N Engl J Med 2009;360:354-362.

- **Newer $P2Y_{12}$ blocking agents are less likely to be associated with variable platelet inhibition**

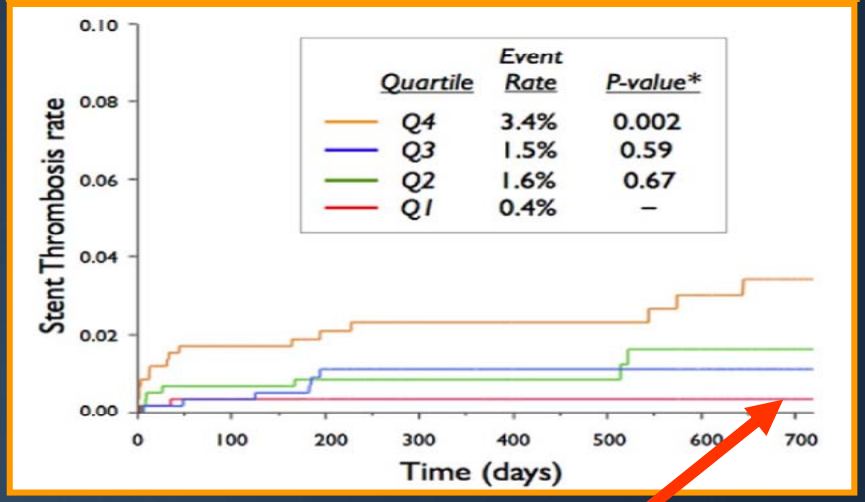
  Gurbel PA, Circulation 2009;120:2577-2585.

Platelet Function is Clearly Related To Post-PCI Ischemic Risk
VerifyNow Analysis of 6 Studies (n=3,059)

2 Yr MACE by PRU Quartile



2 Yr Stent Thrombosis by PRU Quartile



Very low event rate

Brar SS, Et al. *J Am Coll Cardiol.* 2011;58:1945–54

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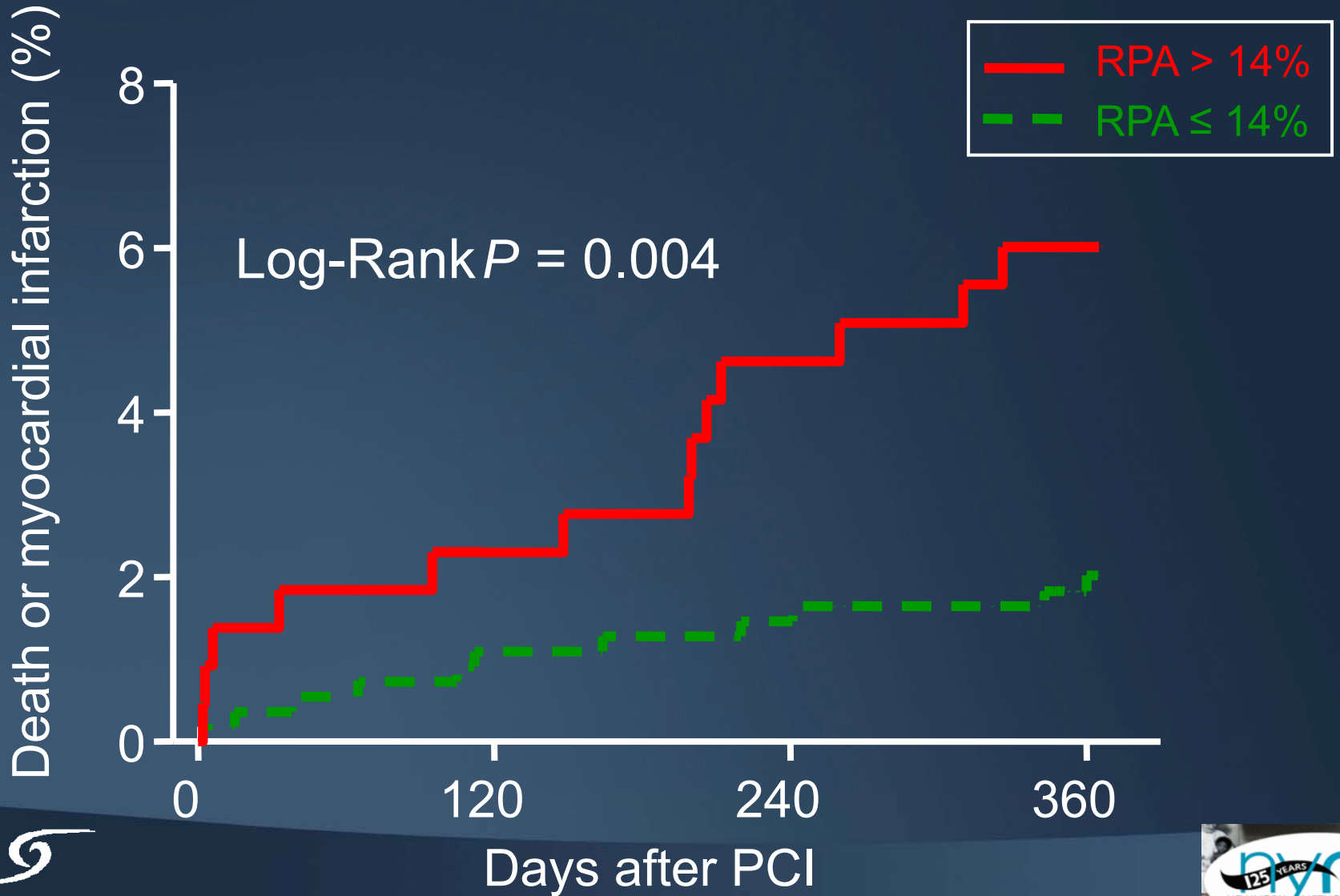
Prognostic impact of on-treatment platelet reactivity in EXCELSIOR



Trenk et al., J Am Coll Cardiol 2008; 51: 1925

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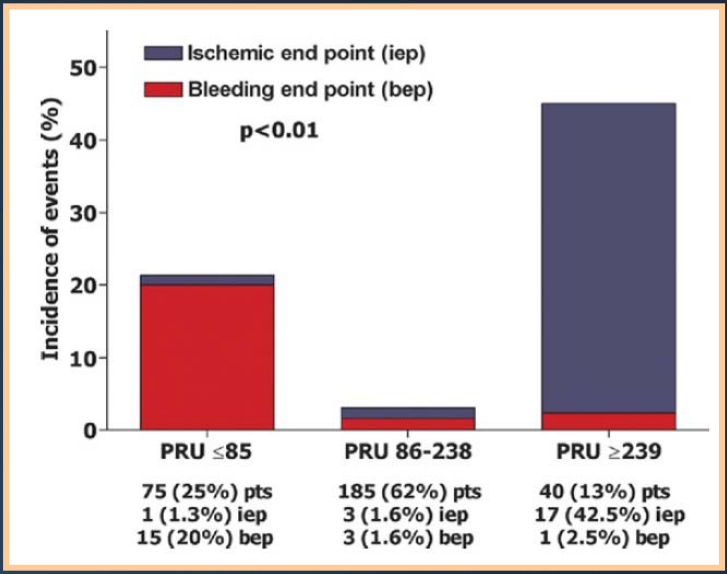
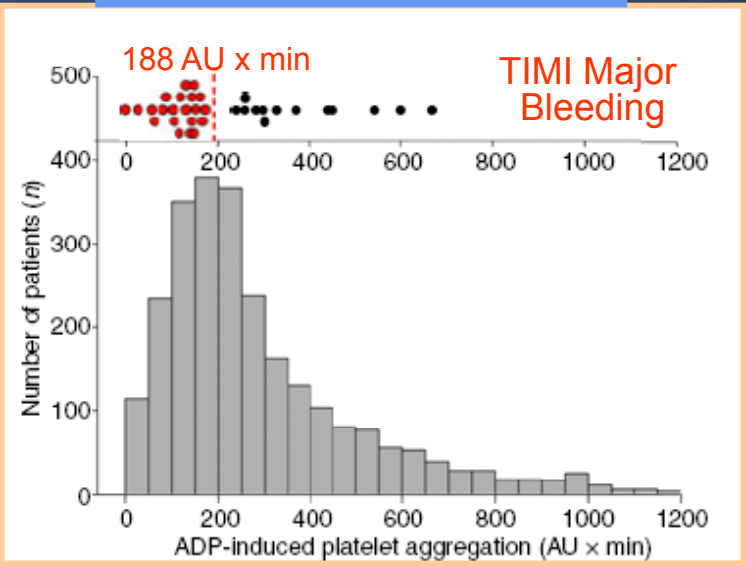
Bleeding risk increases below a platelet reactivity threshold

VerifyNow Assay

Campo G, et al. *J Am Coll Cardiol* 2011;57:2474–83

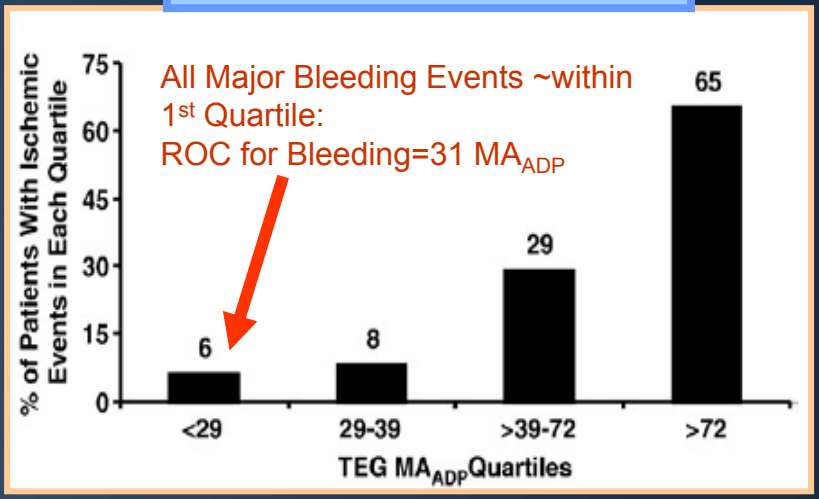


Multiplatele Analyzer



Sibbing D, et al. *J Thromb Haemost.* 2010;250-6

Thrombelastography



Gurbel PA, et al. *Am Heart J.* 2010;

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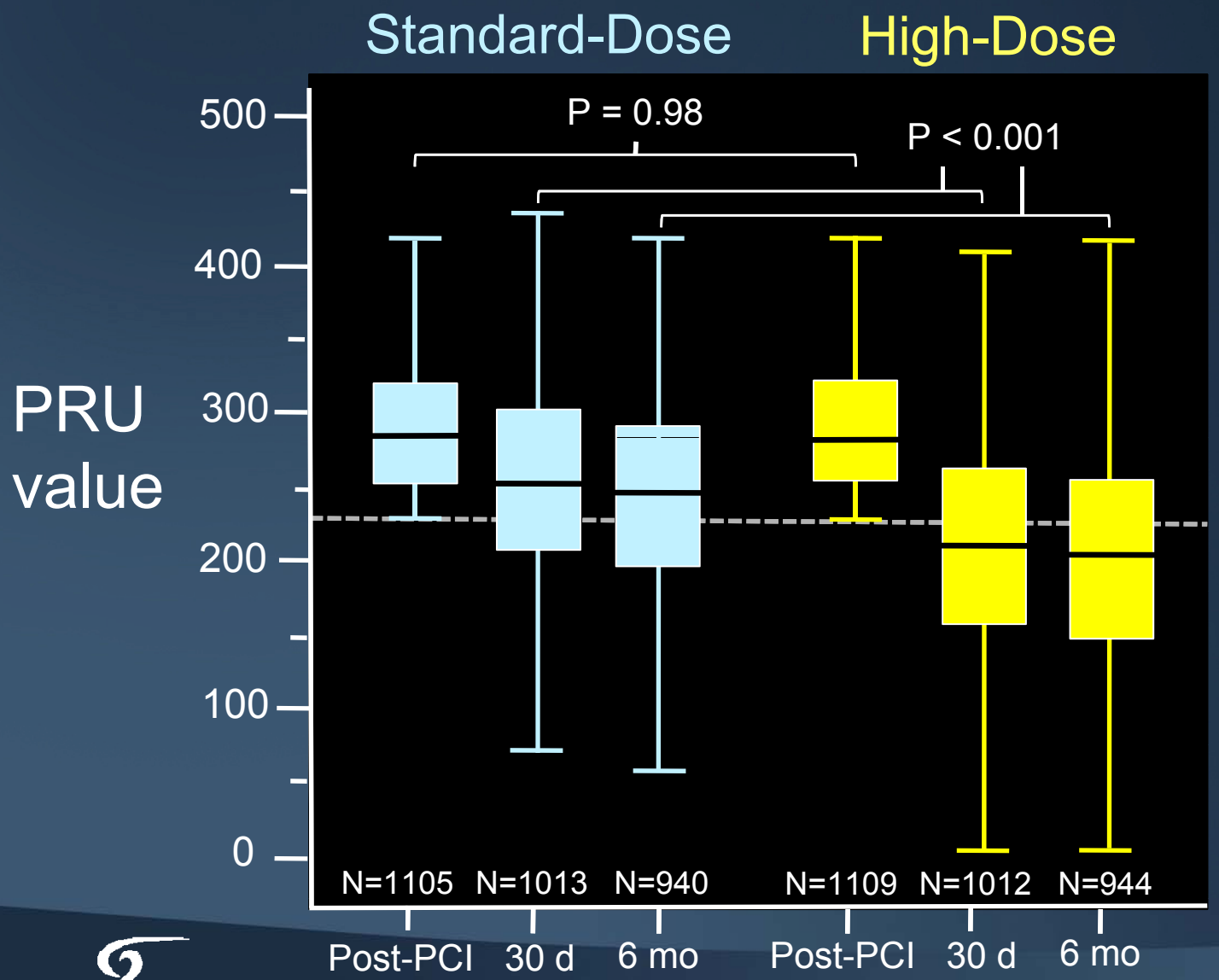
GRAVITAS



Persistently high reactivity @ 30 days: 62% vs 40%, p<0.001

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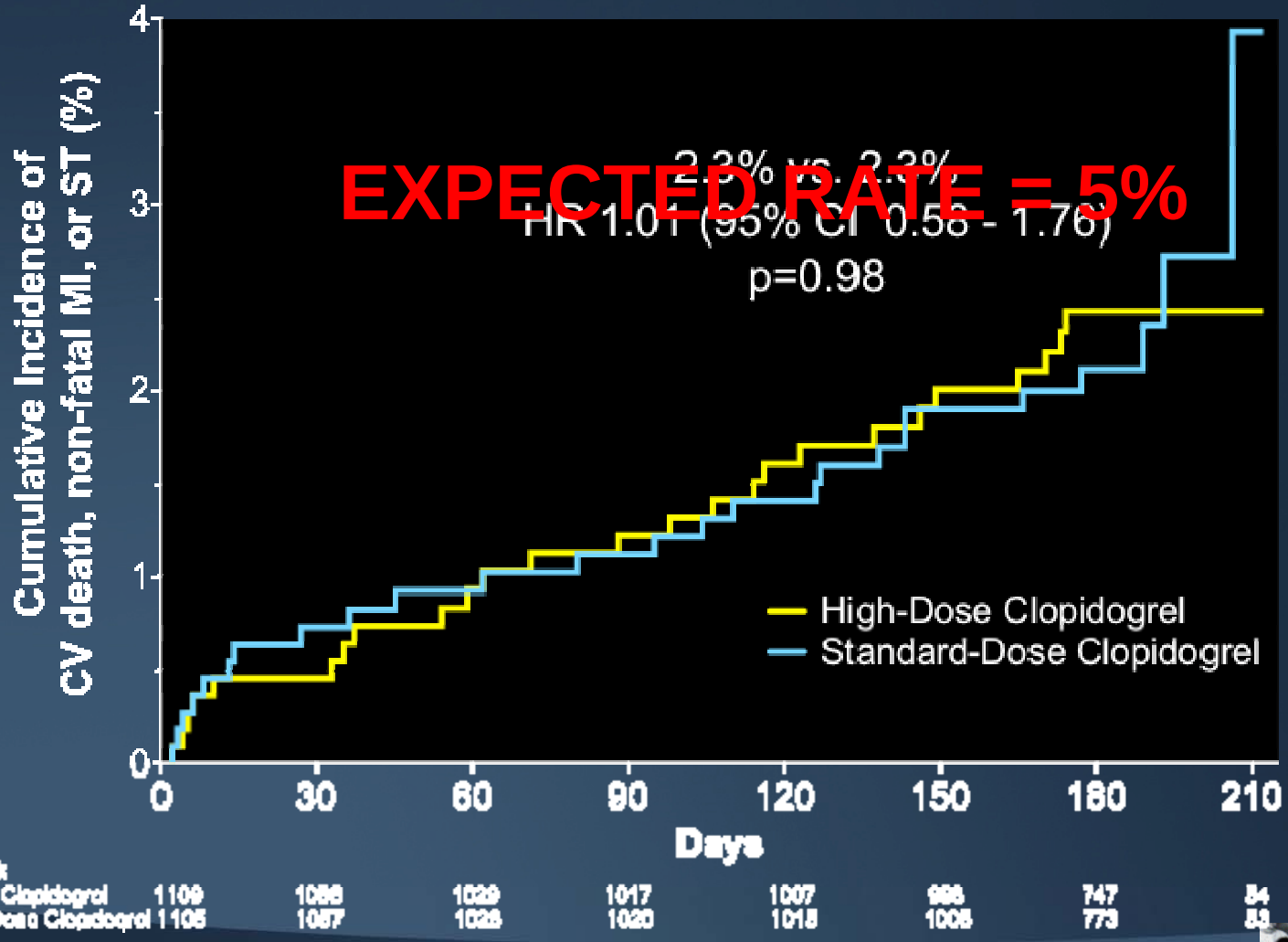
GRAVITAS – Primary endpoint



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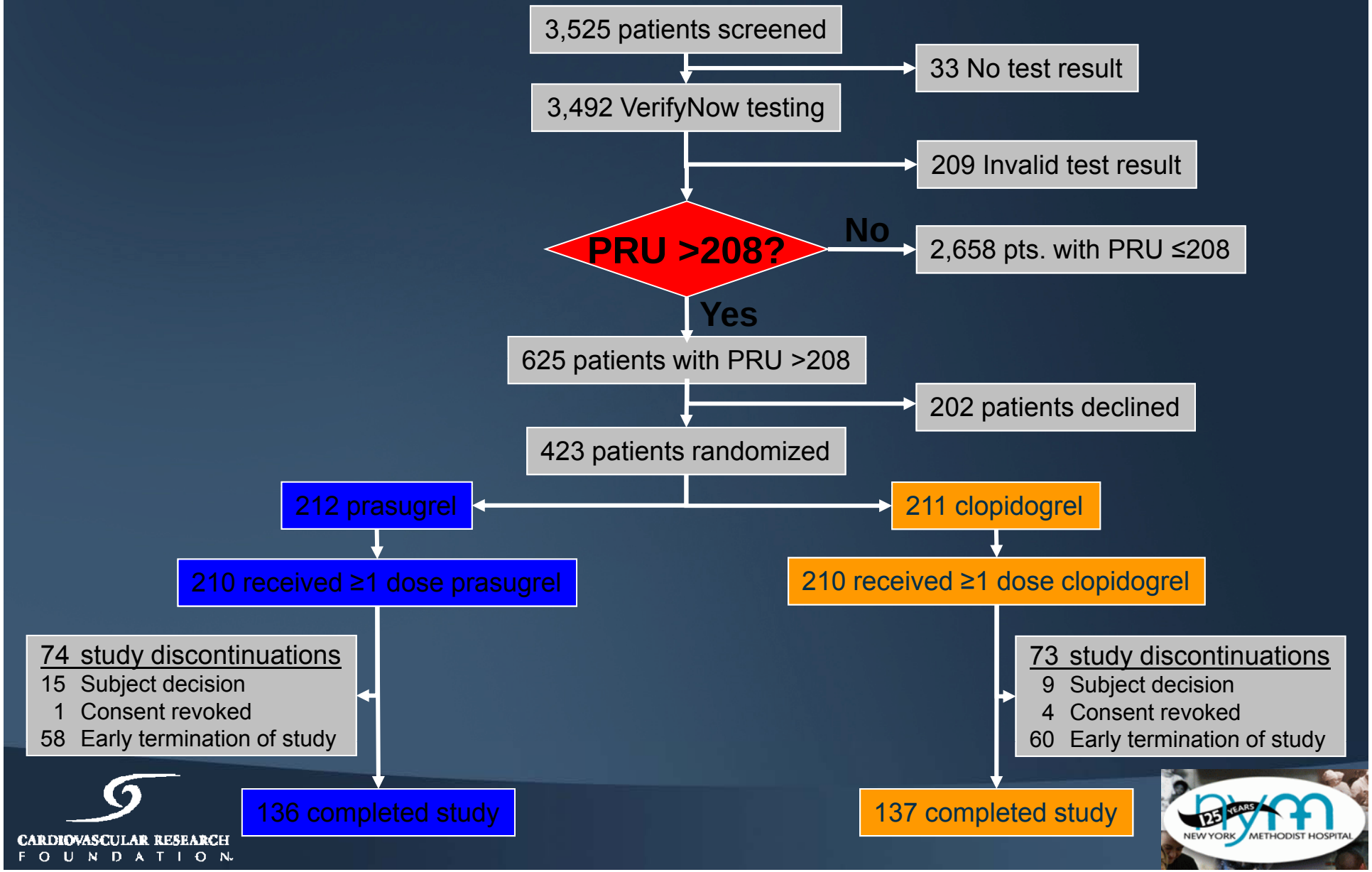
TRIGGER-PCI



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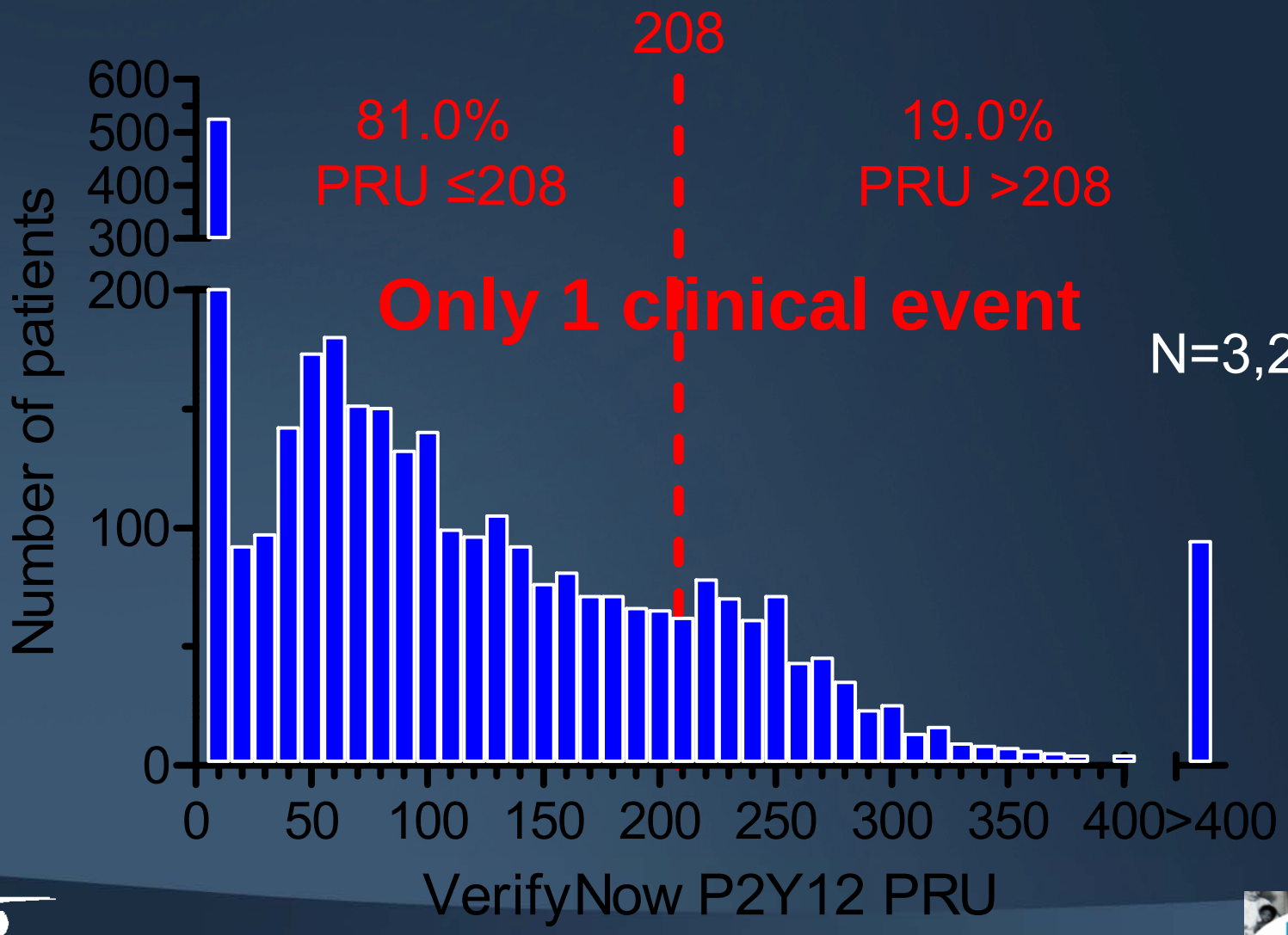
Frequency distribution of VerifyNow P2Y12 PRU after loading with Clopidogrel 600mg and 1st MD



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CYP 2C19

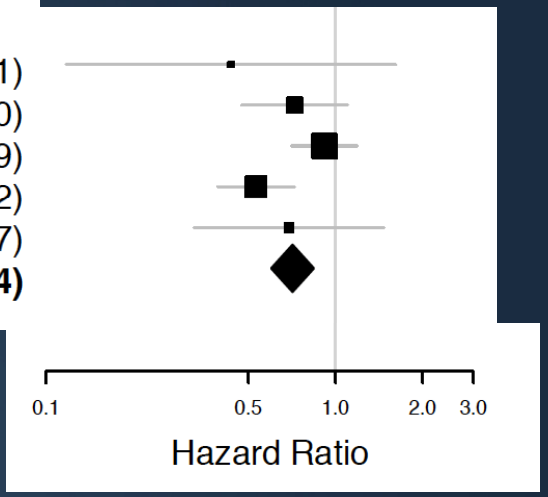
3 allele classes
- "Wild type" (*1): 63%
- Loss-of-function (*2, *3): 13%
- Gain-of-function (*17): 24%

5 metabolizer phenotypes
- Poor: 2 loss-of-function alleles (2%)
- Intermediate: 1 loss-of-function and 1wild type alleles (16%)
- Extensive: 2 wild types alleles (39%)
- Ultra: 1 or 2 gain-of-function alleles (37%)
- Unknown: 1 gain-of-function and 1 loss-of-function alleles (6%)

2 carrier status
- Loss-of-function carriers (1 or more *2, *3): 24%
- Gain-of-function carriers (1 or more *17): 41%

CURE – Genetic analysis

Metabolizer Phenotype	Placebo Event Rate	Clopidogrel Event Rate	Hazard Ratio (95% CI)
Poor	10.9% (6/55)	6.6% (4/61)	0.44 (0.12–1.61)
Intermediate	12.2% (54/442)	8.5% (37/437)	0.72 (0.48–1.10)
Extensive	12.3% (121/987)	10.8% (112/1033)	0.92 (0.71–1.19)
Ultra	13.6% (112/826)	7.8% (66/847)	0.53 (0.39–0.72)
Unknown	10.2% (18/176)	7.2% (11/152)	0.69 (0.33–1.47)
Total	**12.5% (311/2486)**	**9.1% (230/2530)**	**0.71 (0.60–0.84)**



Heterogeneity P-value = 0.12

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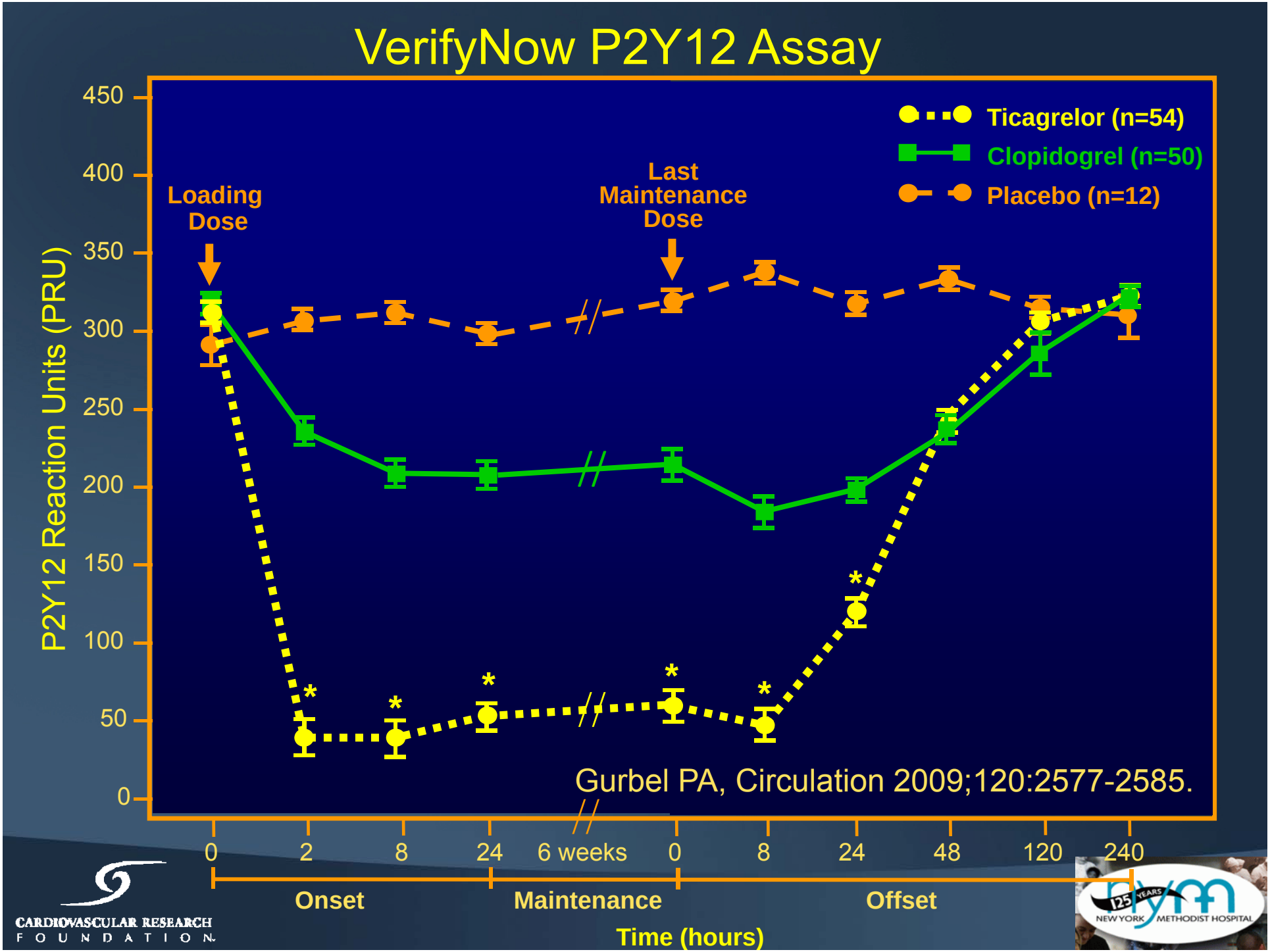
VerifyNow P2Y12 Assay



Platelet FunctionTesting

No Benefit

Platelet function testing may be considered in patients at high risk for poor clinical outcomes.

In clopidogrel-treated patients with high platelet reactivity, alternative agents, such as prasugrel or ticagrelor, might be considered.

The routine clinical use of platelet function testing to screen clopidogrel-treated patients undergoing PCI is not recommended.

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Clopidogrel Genetic Testing

Genetic testing might be considered to identify whether a patient at high risk for poor clinical outcomes is predisposed to inadequate platelet inhibition with clopidogrel.

When a patient predisposed to inadequate platelet inhibition with clopidogrel is identified by genetic testing, treatment with an alternate $P2Y_{12}$ inhibitor (e.g., prasugrel or ticagrelor) might be considered.

No Benefit

The routine clinical use of genetic testing to screen clopidogrel-treated patients undergoing PCI is not recommended.

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Conclusions

- Residual platelet activity after $P2Y_{12}$ inhibition has excellent NPV, but poor PPV for future ischemic events
- Intensification of platelet inhibition with clopidogrel does not result in fewer ischemic events
- Newer $P2Y_{12}$ inhibitors alleviate the need for platelet function testing