



Antiplatelet Therapy After PCI: How Much and How Long?

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Antiplatelet Therapy after PCI: How much and how long?



The simplest and extreme response:

Give the highest possible dose for life!!!

Safety concerns related to bleeding risk.

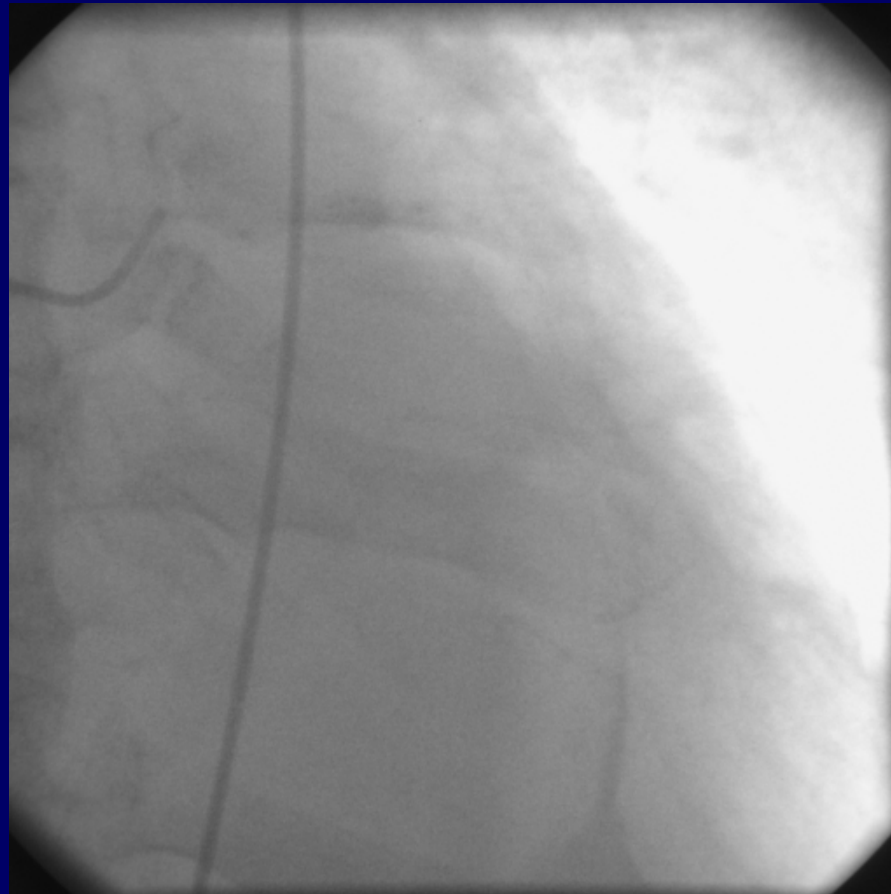
No proven effectiveness.

Antiplatelet Therapy after PCI: How much and how long?

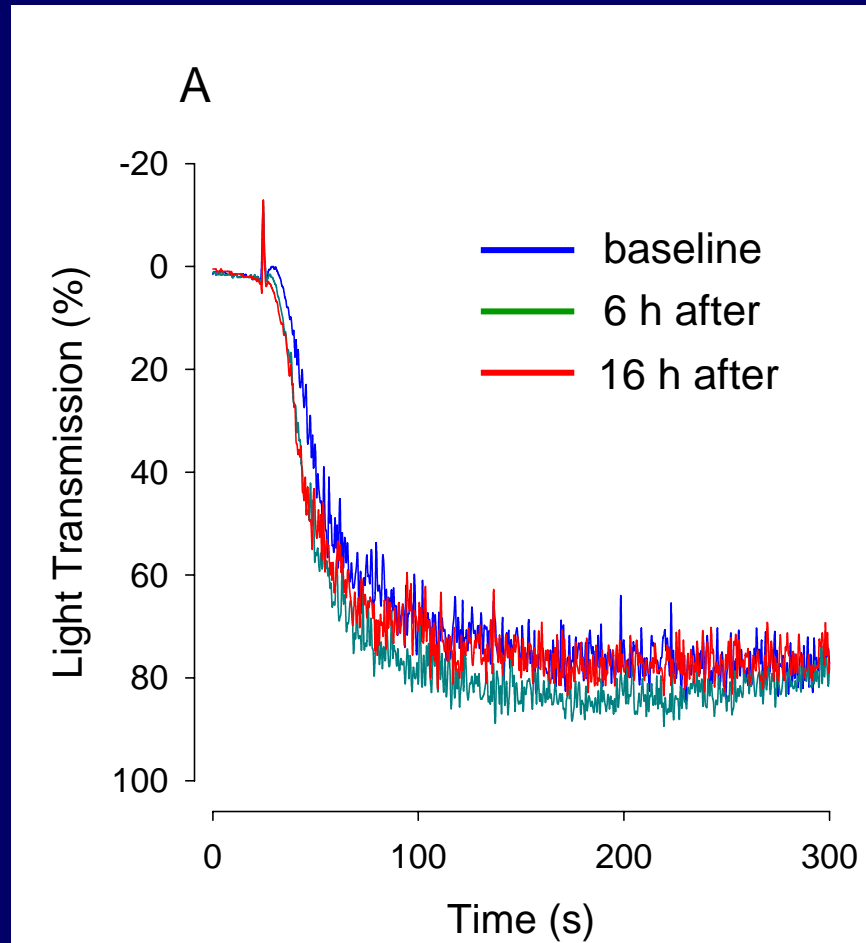


- Maintenance Dose
- Duration of Therapy

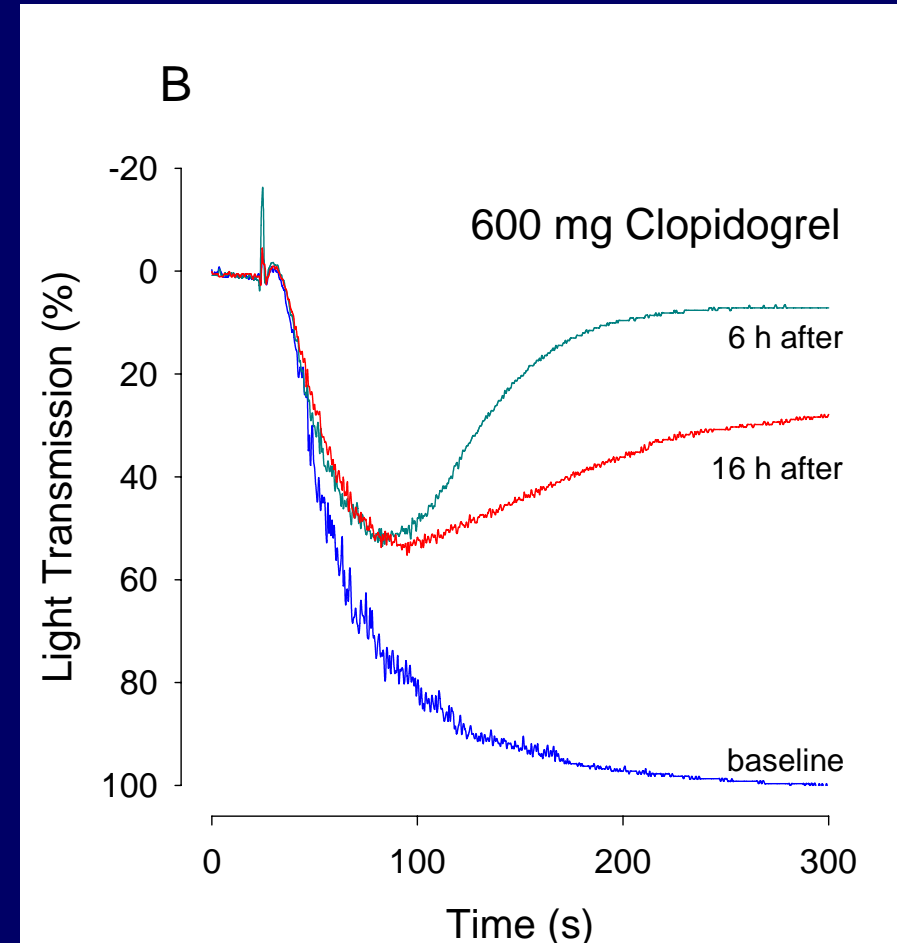
A Patient with Stent Thrombosis While on Clopidogrel Therapy



A Patient with Stent Thrombosis and Clopidogrel Resistance



Stent Thrombosis Patient



Control Individual

Antiplatelet Therapy after PCI: How much and how long?

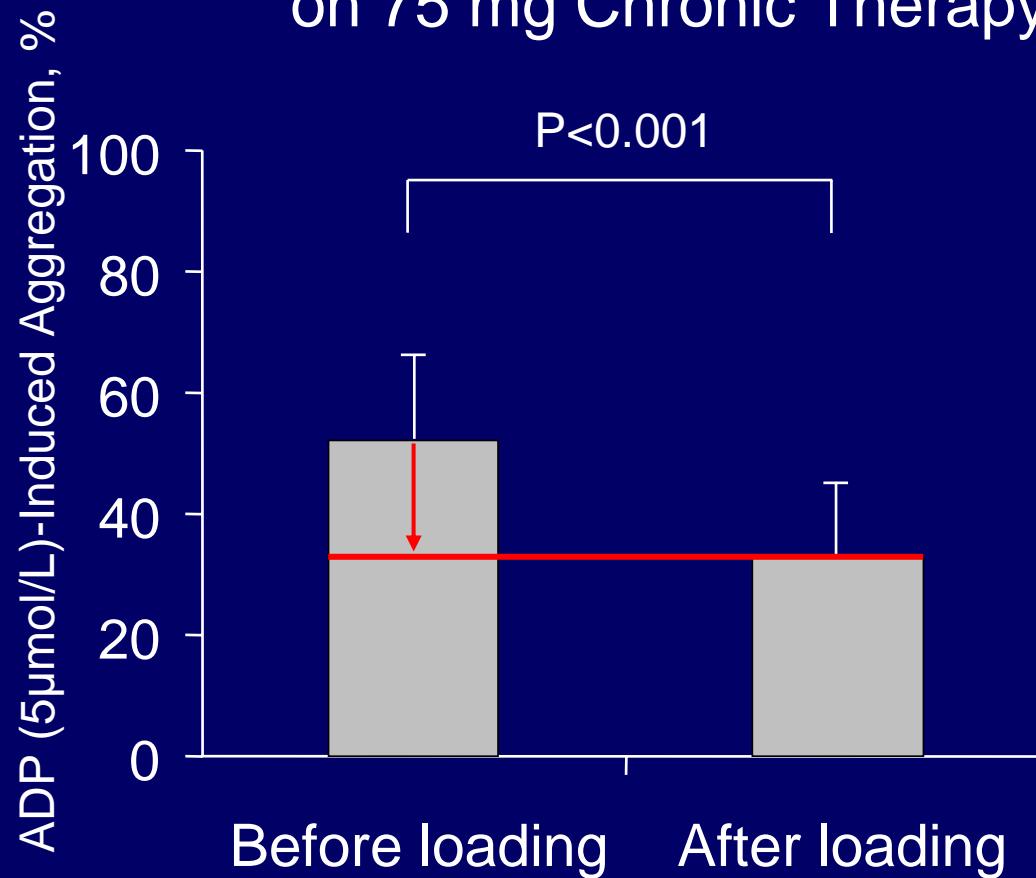


Does increased maintenance dose help ?

Are 75 mg of Clopidogrel the Optimal Dose ?



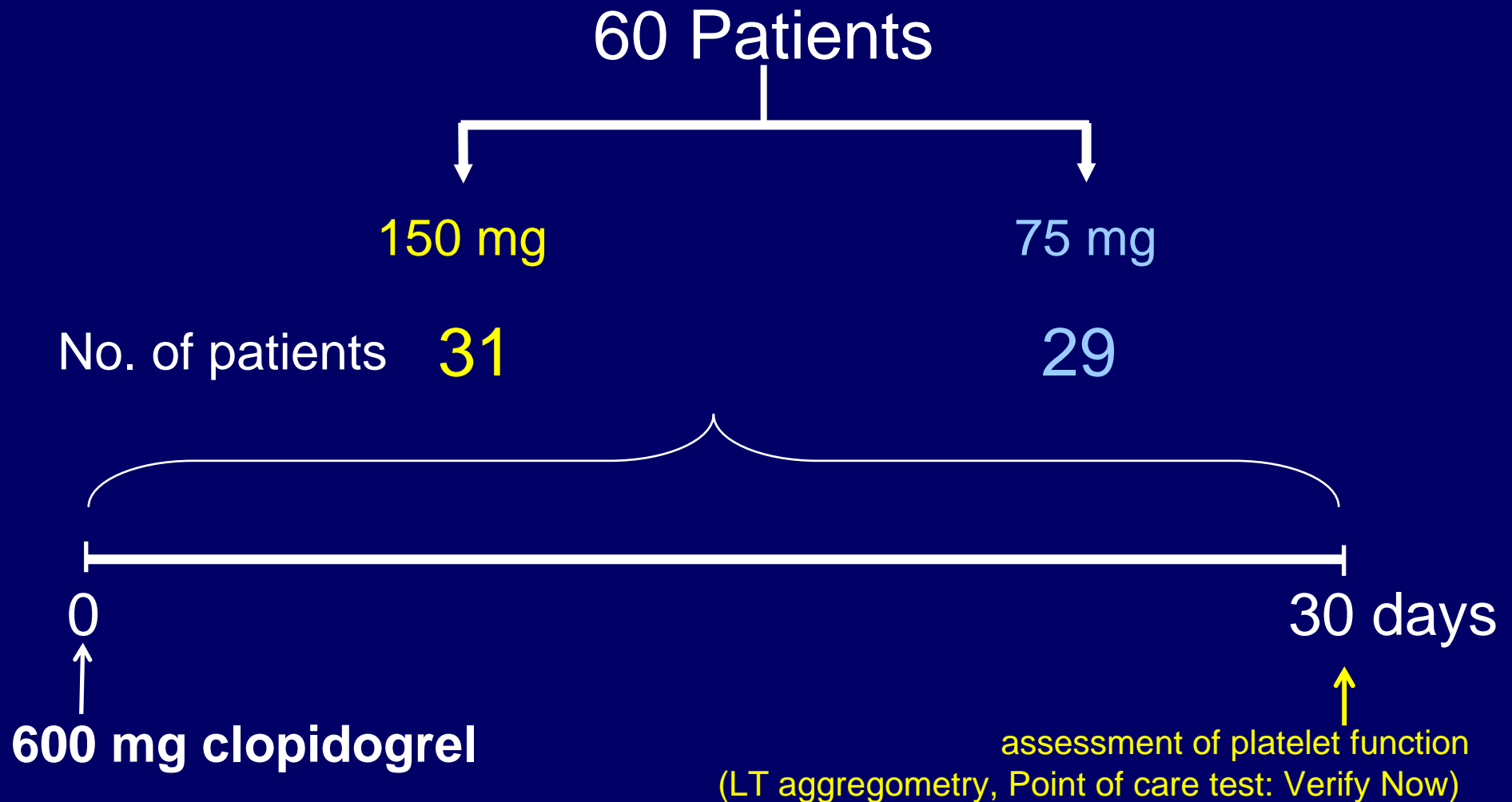
600 mg Loading in Pts
on 75 mg Chronic Therapy



600 mg Clopidogrel

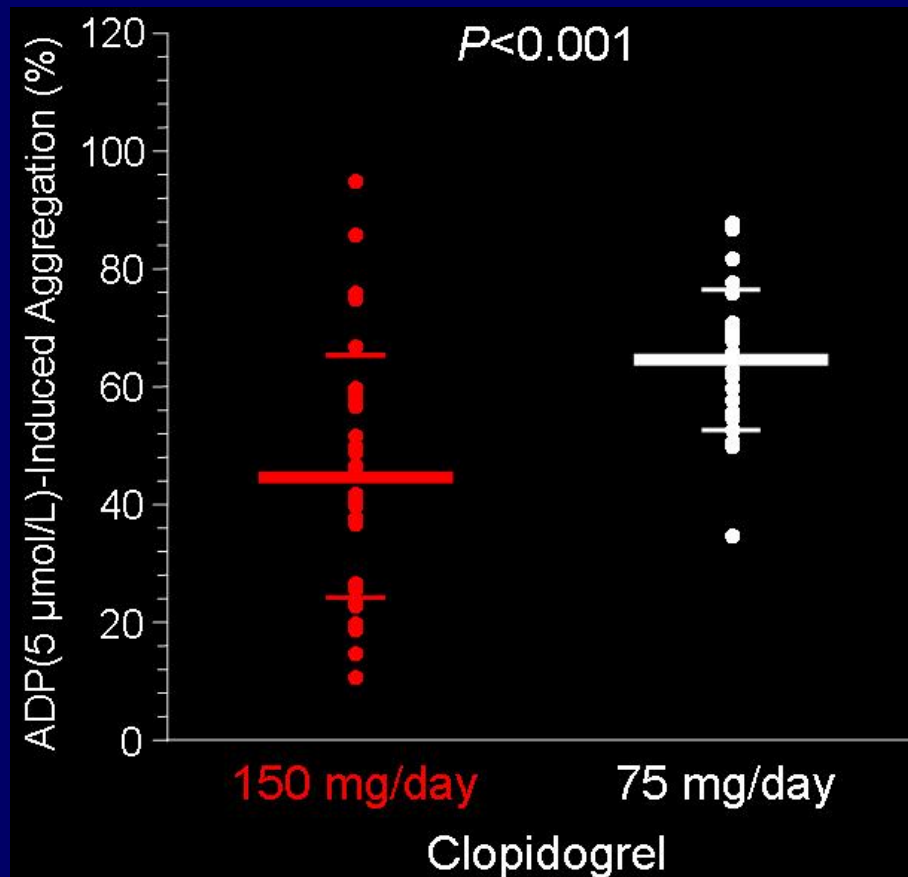
Kastrati et al, Circulation 2004

Are 75 mg of Clopidogrel the Optimal Dose ? - ISAR-CHOICE 2 -

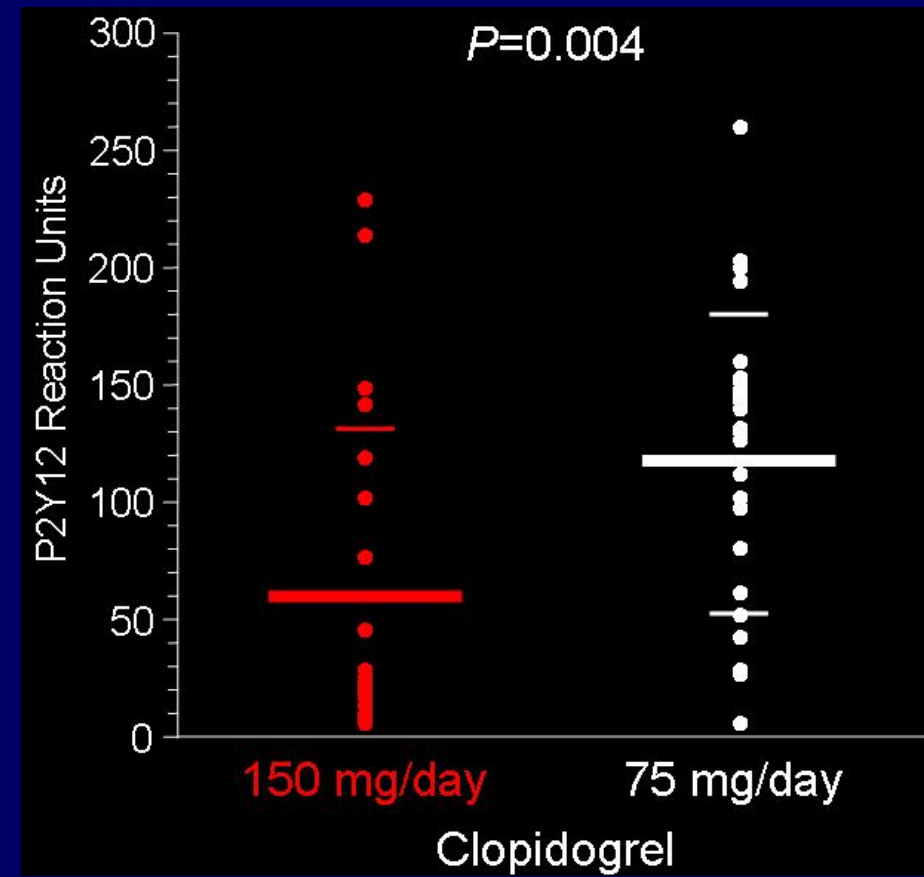




LT Aggregometry

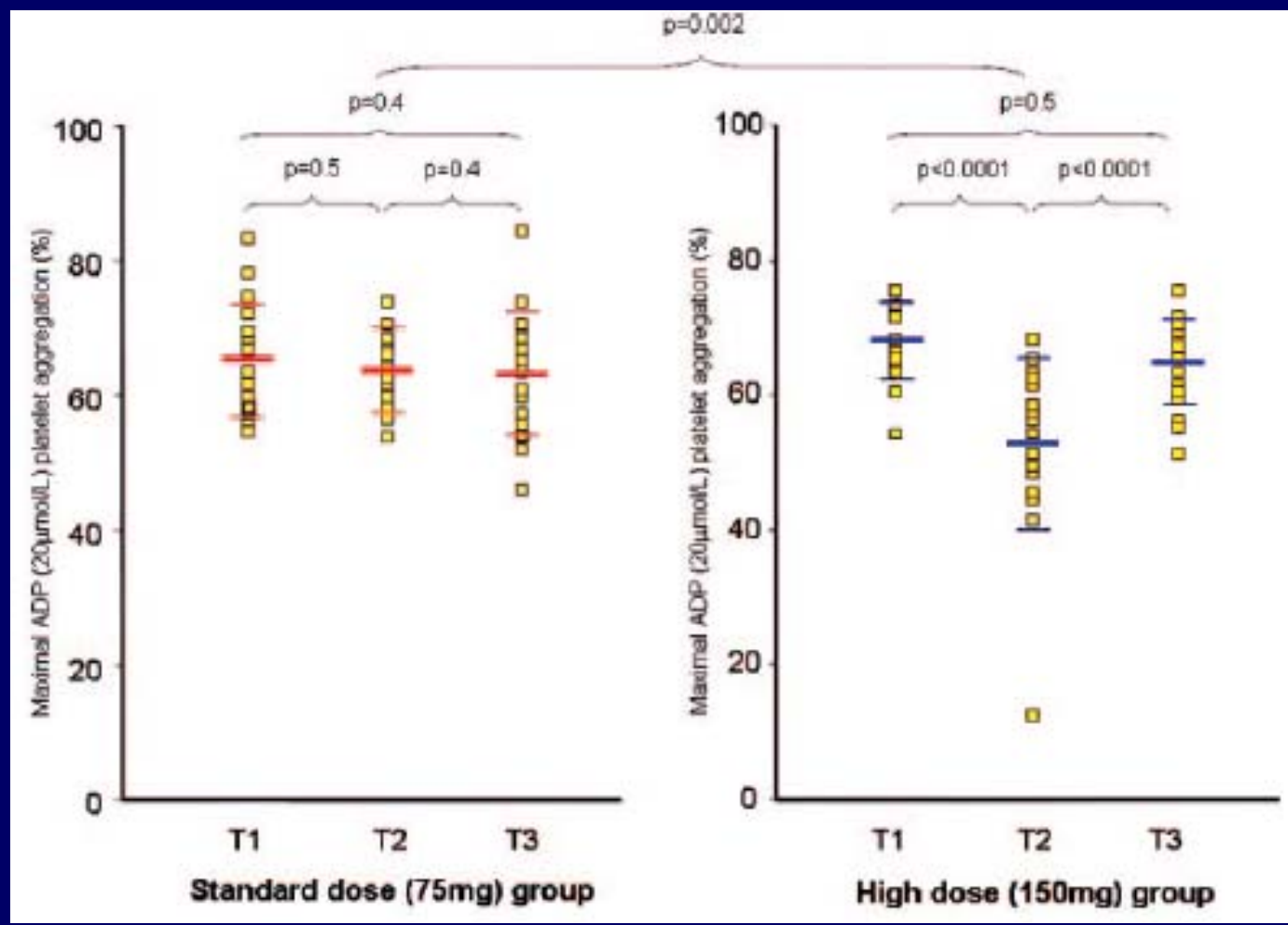


VerifyNow™ P2Y12 Assay





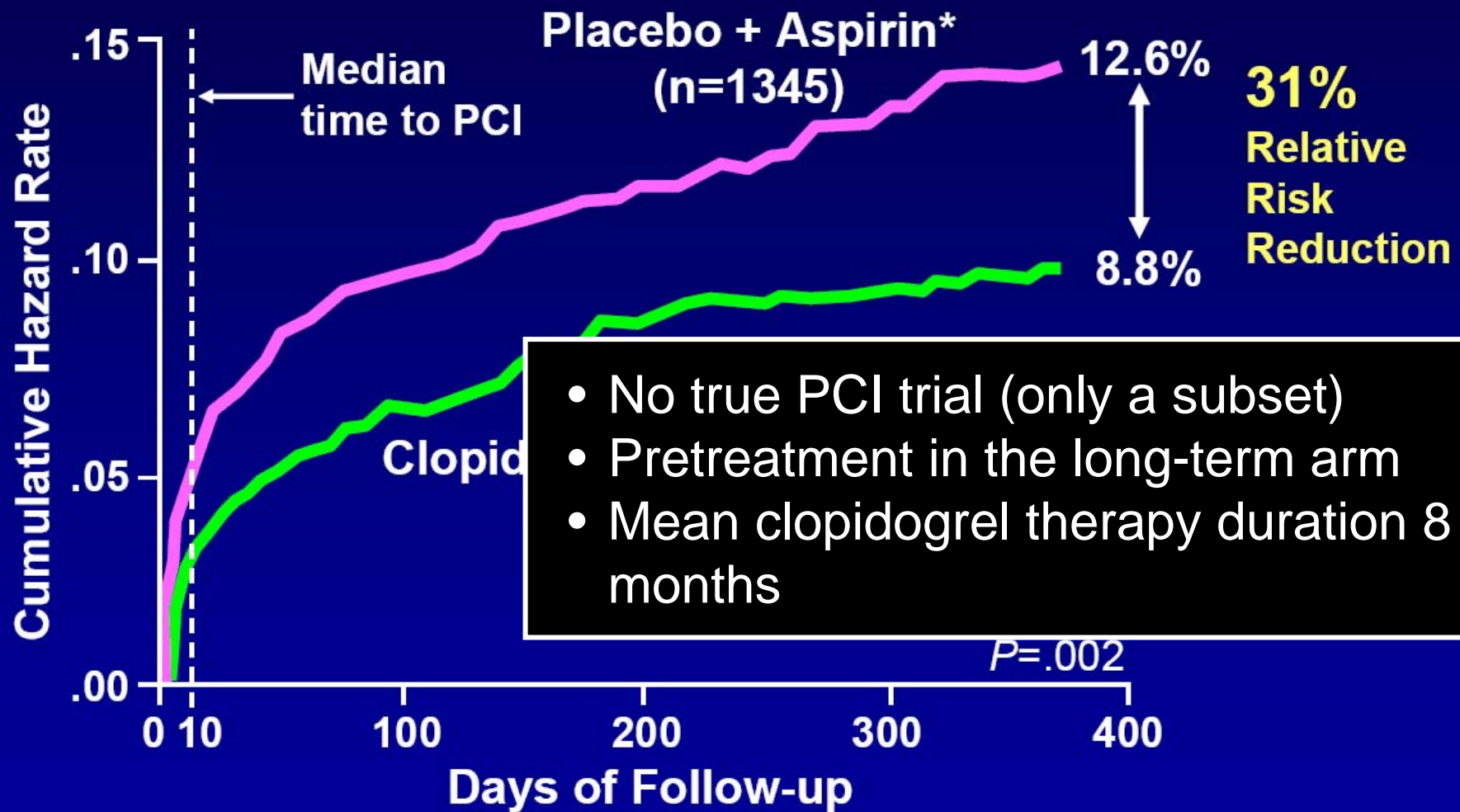
Fighting Low-Response by Increased Dose - OPTIMUS Trial -





The clinical benefit of an increased maintenance dose of clopidogrel is not known and 75 mg still remain the standard dose for chronic therapy.

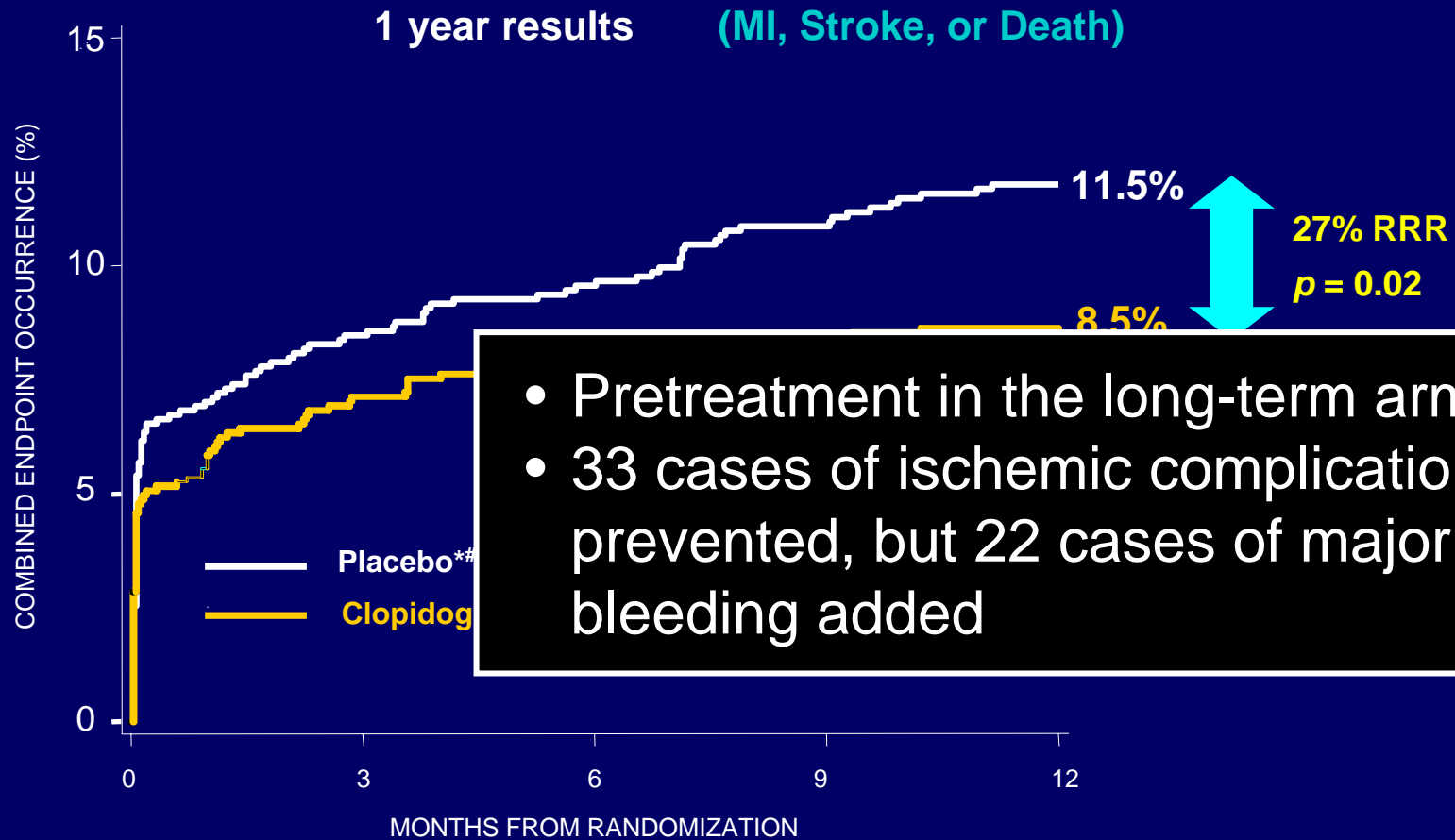
Duration of Therapy in PCI Patients - PCI-CURE -



- No true PCI trial (only a subset)
- Pretreatment in the long-term arm
- Mean clopidogrel therapy duration 8 months

*In combination with standard therapy.
Mehta SR, et al. *Lancet*. 2001;358:527-533.

Duration of Therapy in PCI Patients - CREDO -





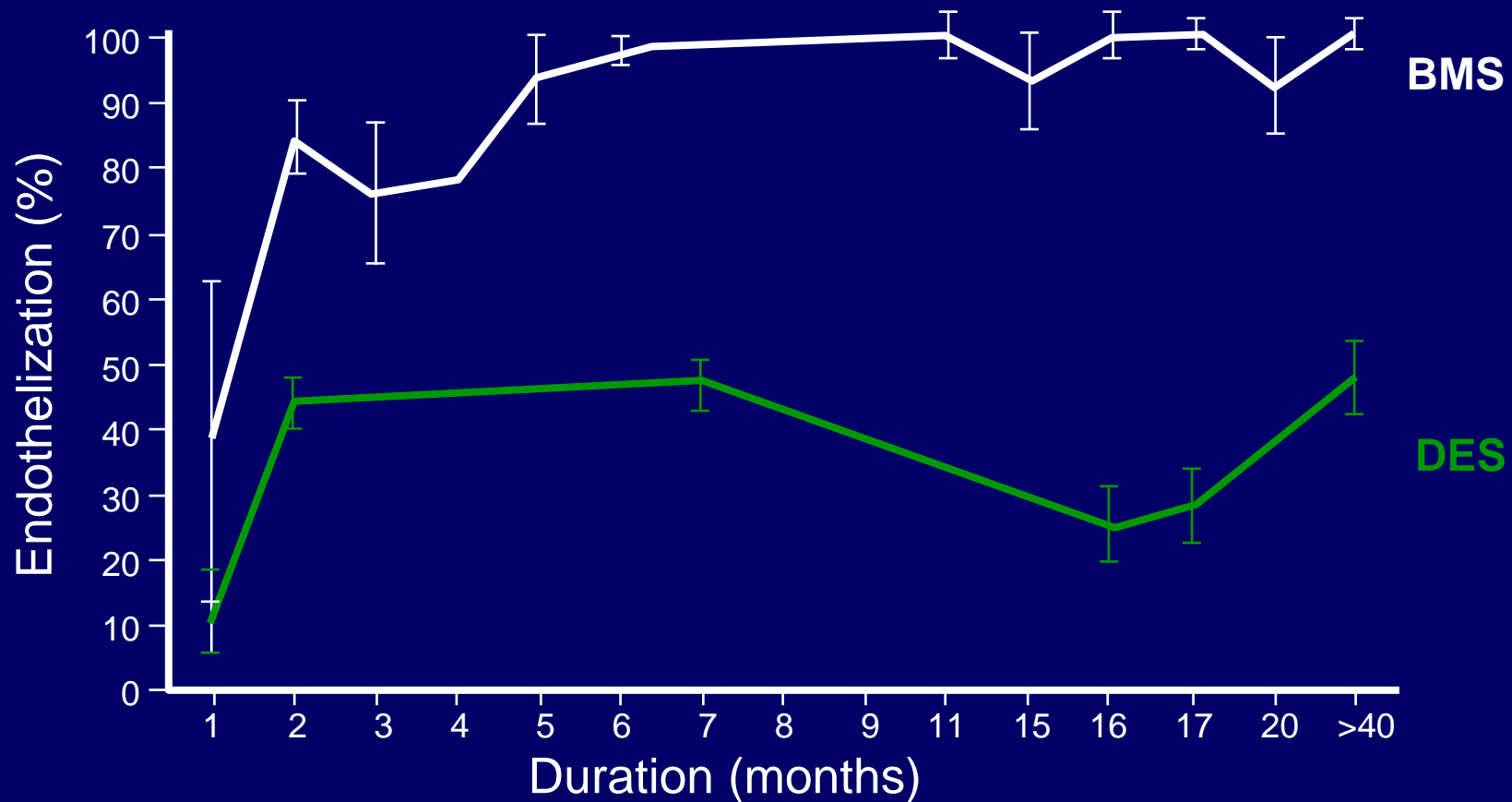
AHA/ACC/SCAI/ACS/ADA Science Advisory (cardiologists, surgeons, dentists)

Abstract—Dual antiplatelet therapy with aspirin and a thienopyridine has been shown to reduce cardiac events after coronary stenting. However, many patients and healthcare providers prematurely discontinue dual antiplatelet therapy, which greatly increases the risk of stent thrombosis, myocardial infarction, and death. This advisory stresses the importance of 12 months of dual antiplatelet therapy after placement of a drug-eluting stent and educating the patient and healthcare providers about hazards of premature discontinuation. It also recommends postponing elective surgery for 1 year, and if surgery cannot be deferred, considering the continuation of aspirin during the perioperative period in high-risk patients with drug-eluting stents. (*Circulation*. 2007;115:813-818.)

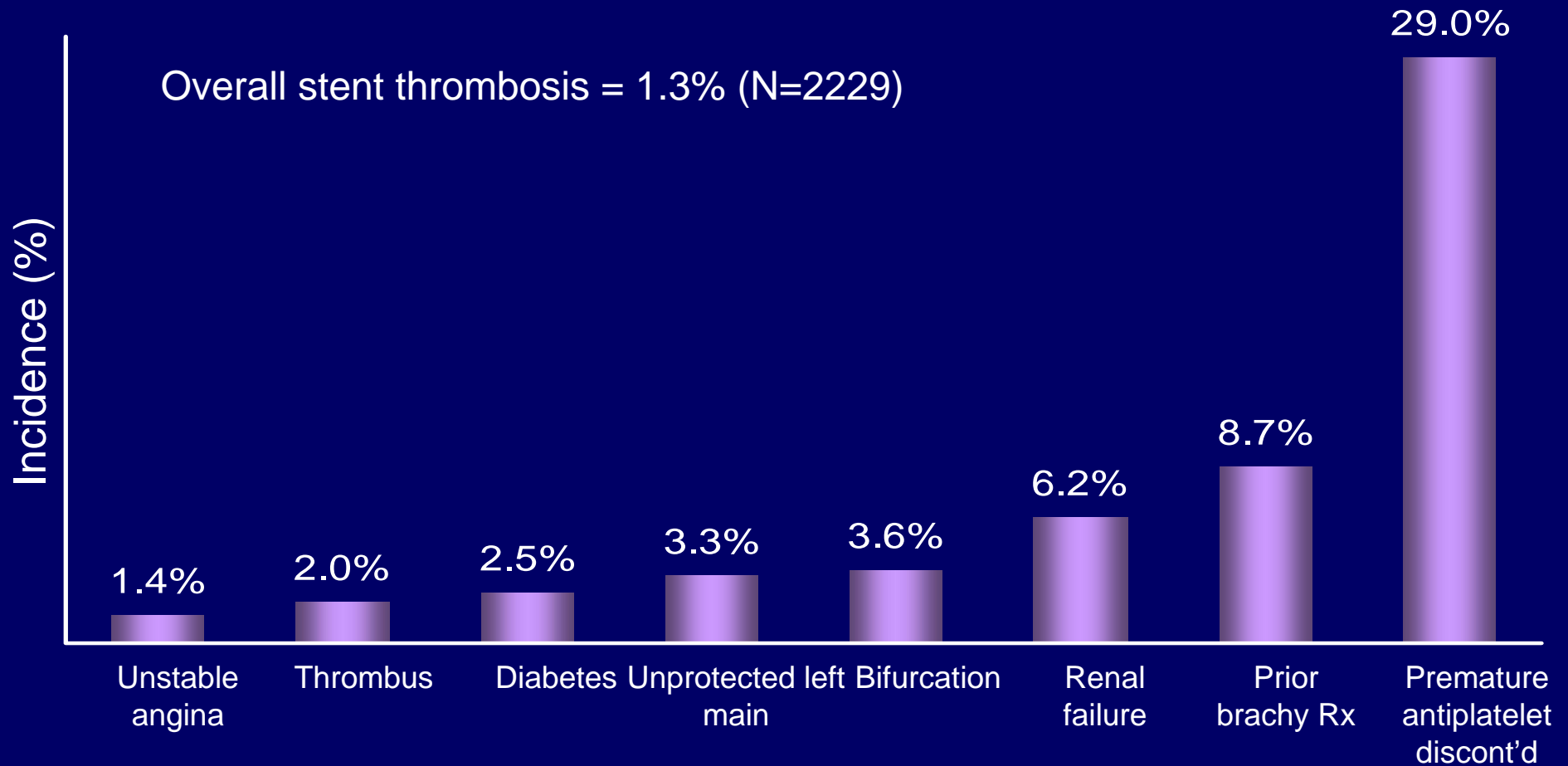
Endothelialization in DES vs BMS



From autopsies of 23 patients treated with DES > 30 days and 25 matched BMS-treated autopsies.



Early Discontinuation of Antiplatelet Therapy and DES Thrombosis



Minimum Duration of Clopidogrel Therapy in DES Pivotal Randomized Trials



- SIRIUS (Cypher): 3 months
- TAXUS IV (Taxus): 6 months
- ISAR-TEST (ISAR I DES): 6 months
- ENDEAVOR II (Endeavor): 3 months
- SPIRIT III (Xience): 6 months



Is an excess of risk of stent thrombosis with
DES vs. BMS ?

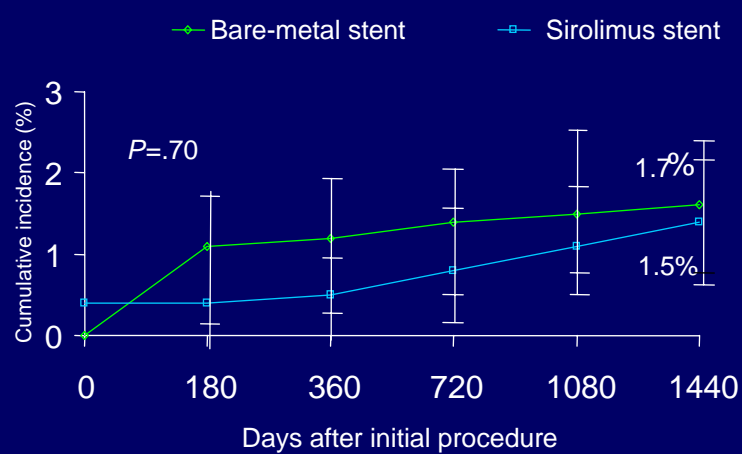


DES vs BMS Thrombosis

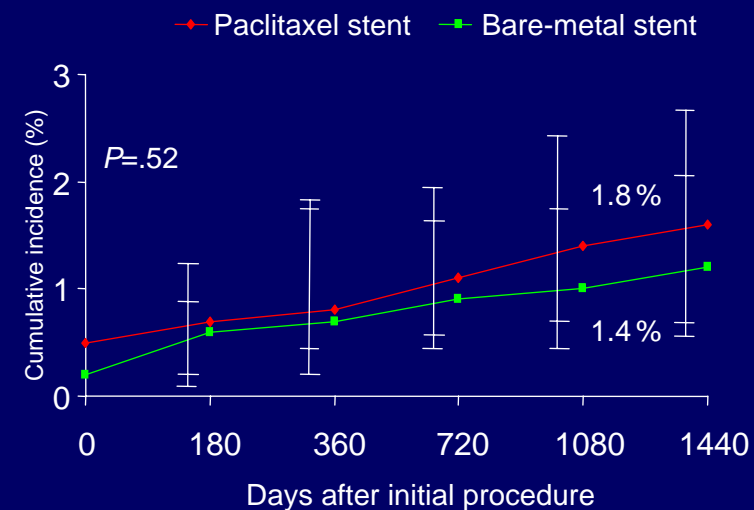
The Truth in the Light of ARC Definition



Sirolimus Stent (ARC)



Paclitaxel Stent (ARC)



No. at risk		0	180	360	720	1080	1440
Sirolimus stent	878	863	848	823	788		
Bare-metal stent	870	853	842	825	789		

No. at risk		0	180	360	720	1080	1440
Paclitaxel stent	878	863	848	823	788		
Bare-metal stent	870	853	842	825	789		



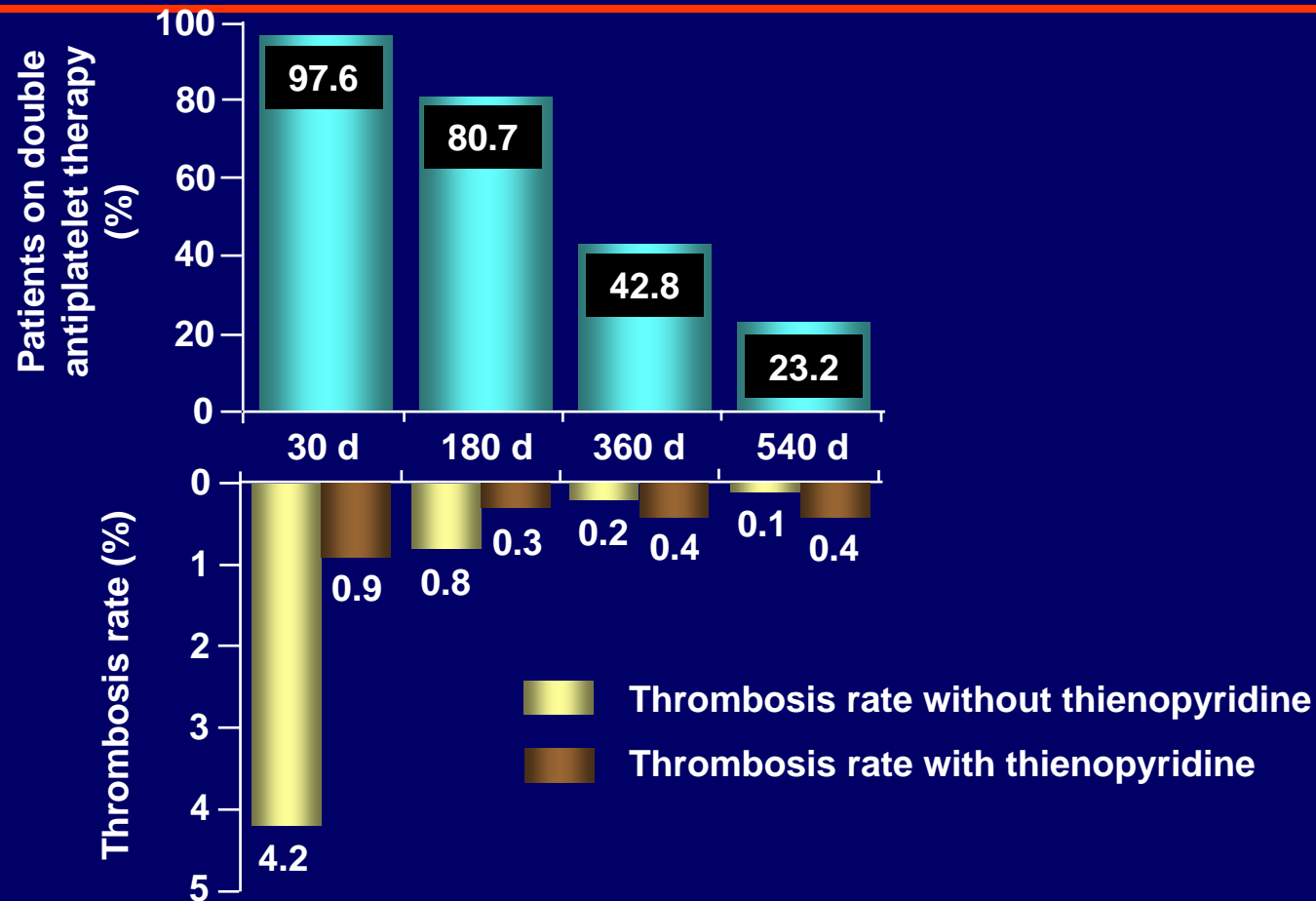
Off-Label Use and Safety of DES - Meta-Analysis of Cypher vs. BMS Trials -



Cypher vs BMS Off-Label (13 Trials)

Death	0.97 (0.70-1.33)
Stent Thrombosis	0.88 (0.51-1.52)

Do We Need Dual Antiplatelet Therapy Beyond 6 Months After DES?



Discontinuation of thienopyridine therapy was the major determinant of ST within the first 6 months, but insufficient information is available to determine whether there is benefit in continuing a thienopyridine beyond 6 months.

Optimal Duration of Clopidogrel Therapy After DES

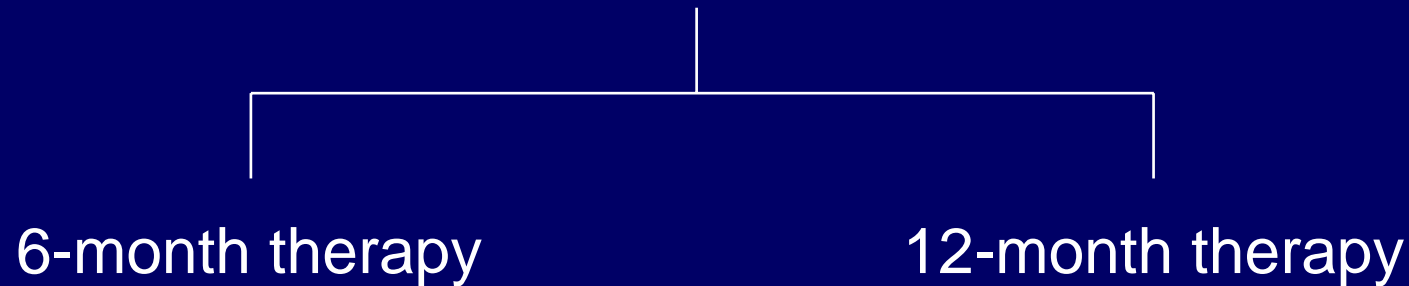


ISAR-SAFE

A Multi-Center, Randomized, Double-Blind Trial

6000

DES Patients



Primary end point at 15 months

A composite of death, MI, stent thrombosis, stroke, major bleeding



Incidence of Death and Acute Myocardial Infarction Associated With Stopping Clopidogrel After Acute Coronary Syndrome

JAMA, February 6, 2008—Vol 299, No. 5

Design, Setting, and Patients Retrospective cohort study of 3137 patients with ACS discharged from 127 Veterans Affairs hospitals between October 1, 2003, and March 31, 2005, with posthospital treatment with clopidogrel.



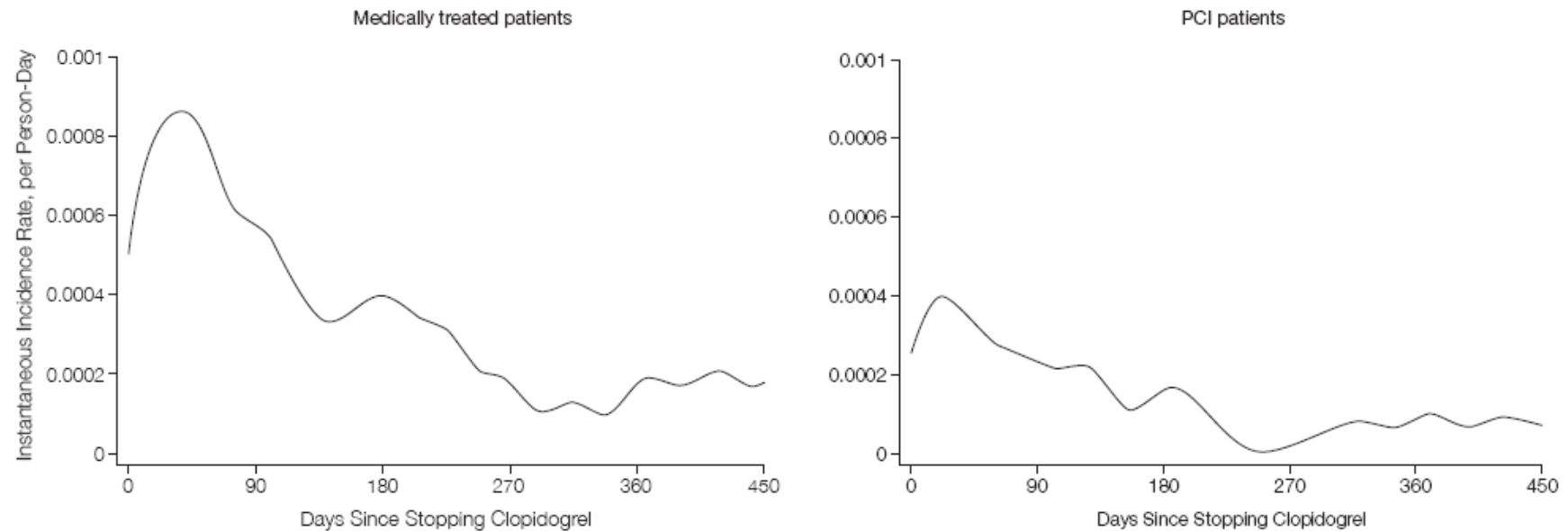
Table 1. Baseline Characteristics of the Study Cohort

Variables	All (n = 3137)	Medical Therapy (n = 1568)	PCI (n = 1569)
Demographics			
Age, y			
Mean (SD)	66.0 (11.7)	68.5 (11.7)	63.5 (11.1)
Median (range)	65 (57-76)	70 (60-79)	62 (56-73)
Male sex, No. (%)	3080 (98.2)	1543 (98.4)	1537 (98.0)
White race, No. (%)	1669 (53.2)	853 (54.4)	816 (52.0)
Comorbidities, No. (%)			
Heart failure	715 (22.8)	487 (31.1)	228 (14.5)
Diabetes	659 (21.0)	376 (24.0)	283 (18.0)
Prior myocardial infarction	809 (25.8)	485 (30.9)	325 (20.7)
PCI within prior 6 mo	272 (8.7)	98 (6.2)	174 (11.1)
Prior CABG	710 (22.6)	449 (28.6)	261 (16.6)
Cerebrovascular disease	228 (7.3)	153 (9.8)	75 (4.8)
Peripheral vascular disease	805 (25.7)	518 (33.0)	287 (18.3)
Renal disease	504 (16.1)	338 (21.6)	166 (10.6)
COPD	472 (15.1)	290 (18.5)	182 (11.6)
Dementia	358 (11.4)	225 (14.4)	133 (8.5)
Cancer	202 (6.4)	123 (7.8)	79 (5.0)
Current smoker	1068 (34.0)	468 (29.9)	600 (38.2)
Medications, No. (%)			
Prior clopidogrel use	620 (19.8)	452 (28.8)	168 (10.7)
Aspirin at discharge	2866 (91.4)	1381 (88.1)	1485 (94.7)
β-Blocker at discharge	2907 (92.7)	1439 (91.8)	1468 (93.6)
ACE inhibitor at discharge	2365 (75.4)	1111 (70.9)	1254 (79.9)
Statin at discharge	2540 (81.0)	1198 (76.4)	1342 (85.5)
ACS presentation factors			
TIMI risk score, mean (SD)	3.2 (1.3)	3.2 (1.3)	3.2 (1.3)
Left ventricular ejection fraction <40%, No. (%)	786 (25.1)	441 (28.1)	345 (22.0)
Unstable angina, No. (%)	402 (12.8)	326 (20.8)	76 (4.8)
ACS treatment, No. (%)			
Glycoprotein IIb/IIIa use	1437 (45.8)	408 (26.0)	1029 (65.6)
Duration receiving clopidogrel following hospital discharge, d			
Mean (SD)	290 (161)	278 (169)	302 (151)
Median (range)	298 (163-413)	281 (120-417)	310 (182-410)

Incidence of Death and Acute Myocardial Infarction Associated With Stopping Clopidogrel After Acute Coronary Syndrome



Figure. Risk-Adjusted Instantaneous Incidence Rates of Death or AMI Over Time After Stopping Treatment With Clopidogrel Among Medically Treated and PCI-Treated Patients With ACS Using Multivariable Cox Regression Models



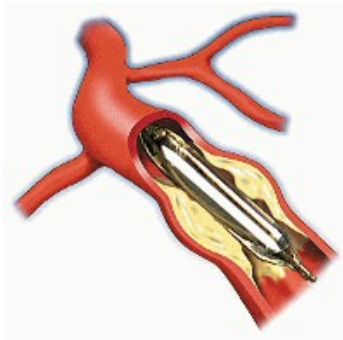
ACS indicates acute coronary syndrome; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention.

The findings of this study, coupled with prior physiological studies, support the hypothesis of a **possible clopidogrel rebound effect from rebound platelet activation following clopidogrel withdrawal.**

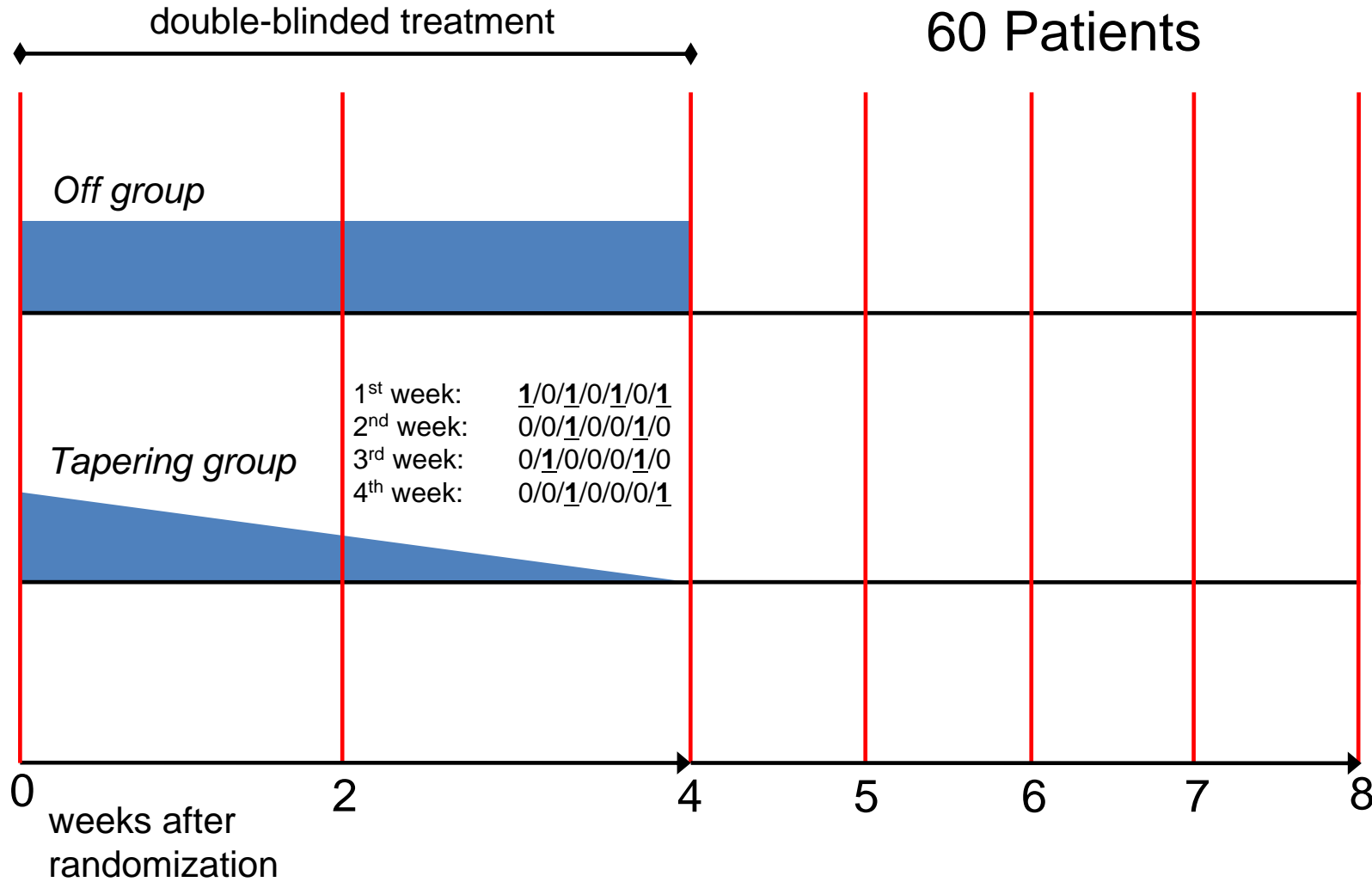


ISAR-REBOUND

Intracoronary **S**tenting and **A**ntithrombotic **R**egimen:
REBOUND Platelet Aggregation After
Discontinuation of Long-Term Clopidogrel Treatment



Protocol Overview





CAUTION

... in discontinuing clopidogrel therapy

Optimal Duration of Clopidogrel Therapy After DES

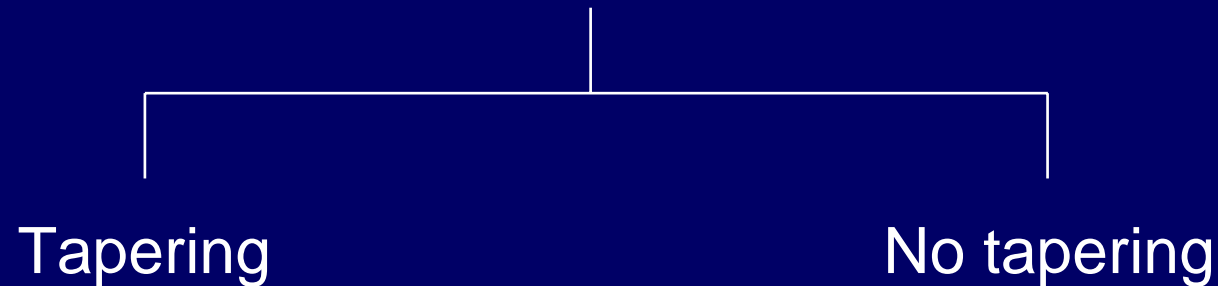


ISAR-CAUTION

A Randomized, Double-Blind Trial

3000

DES Patients



Primary end point at 3 months

A composite of cardiac death, MI, stent thrombosis, stroke, major bleeding or rehospitalization for ACS

ISAR-CAUTION



Randomization:

Tapered vs. abrupt interruption of clopidogrel therapy

