



Clopidogrel vs New Antiplatelet Therapy (Prasugrel)

Adnan Kastrati, MD

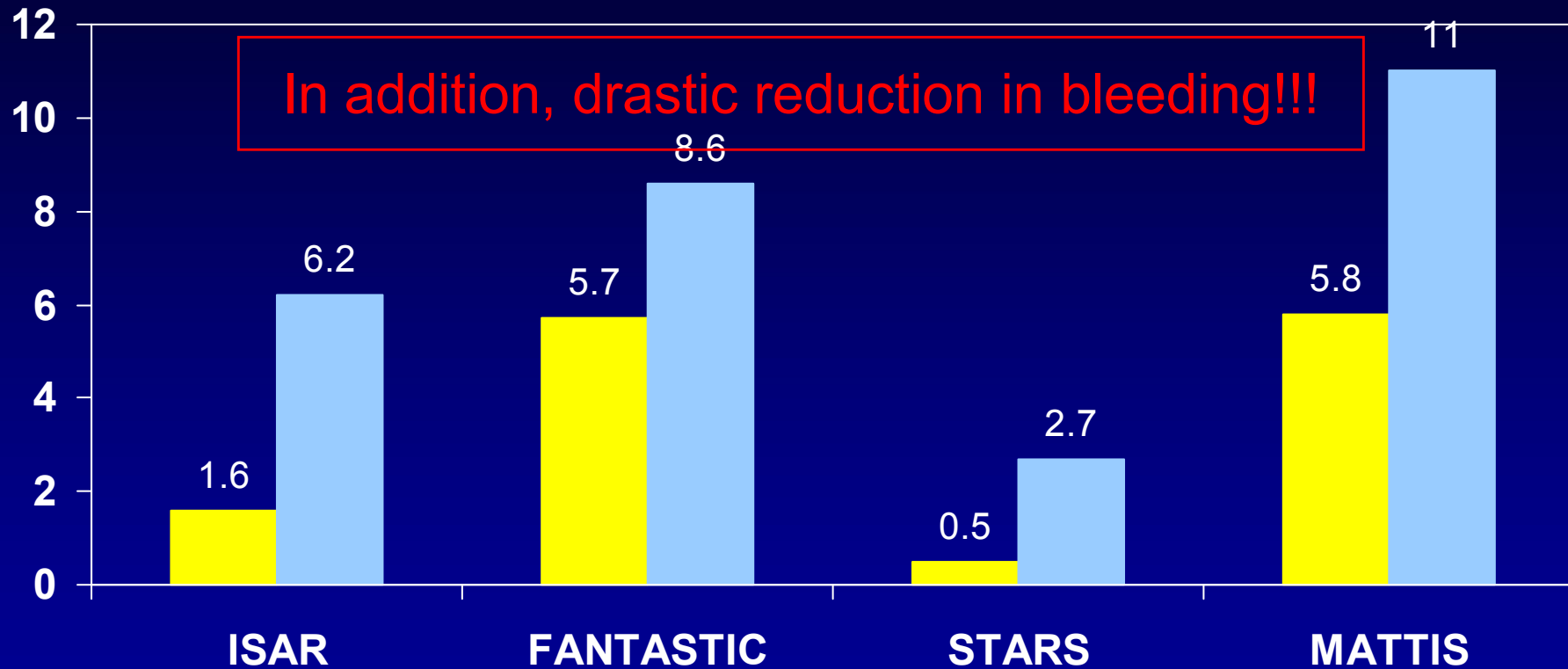
Deutsches Herzzentrum, Technische Universität München, Germany

Seoul, April 30, 2010

Dual Antiplatelet Therapy for Stenting



MACE, %



 Dual Antiplatelet Therapy

 Oral Anticoagul. Therapy

ISAR, NEJM 1996

FANTASTIC, Circ 1998

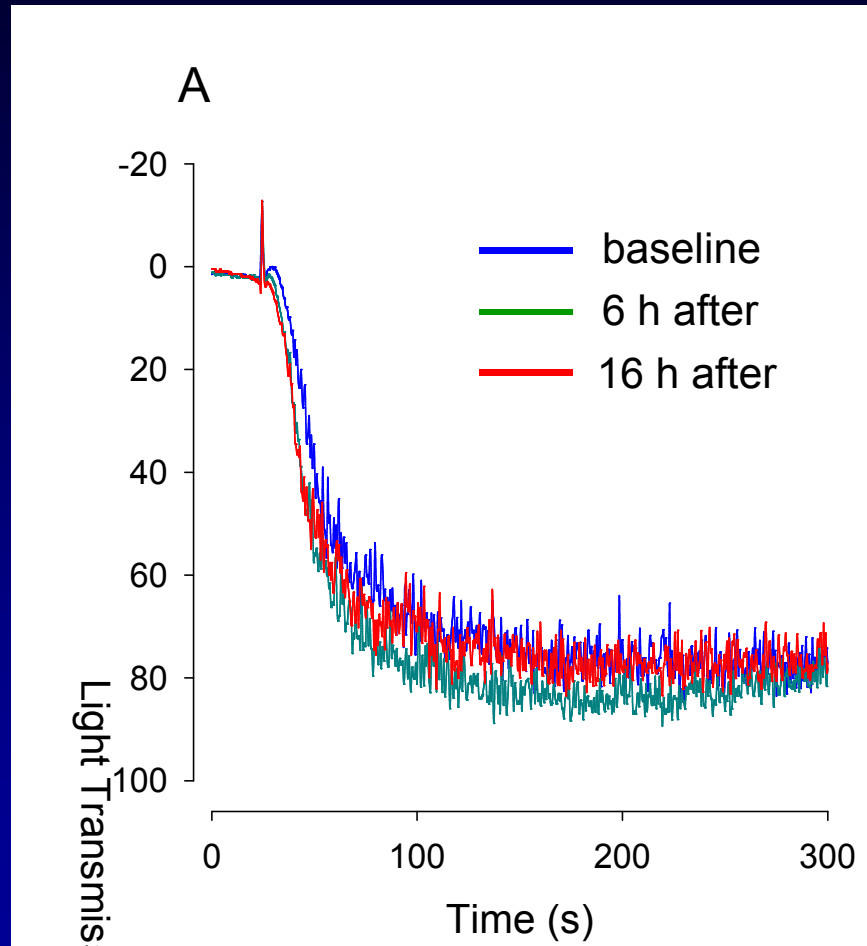
STARS, NEJM 1998

MATTIS, Circ 1998

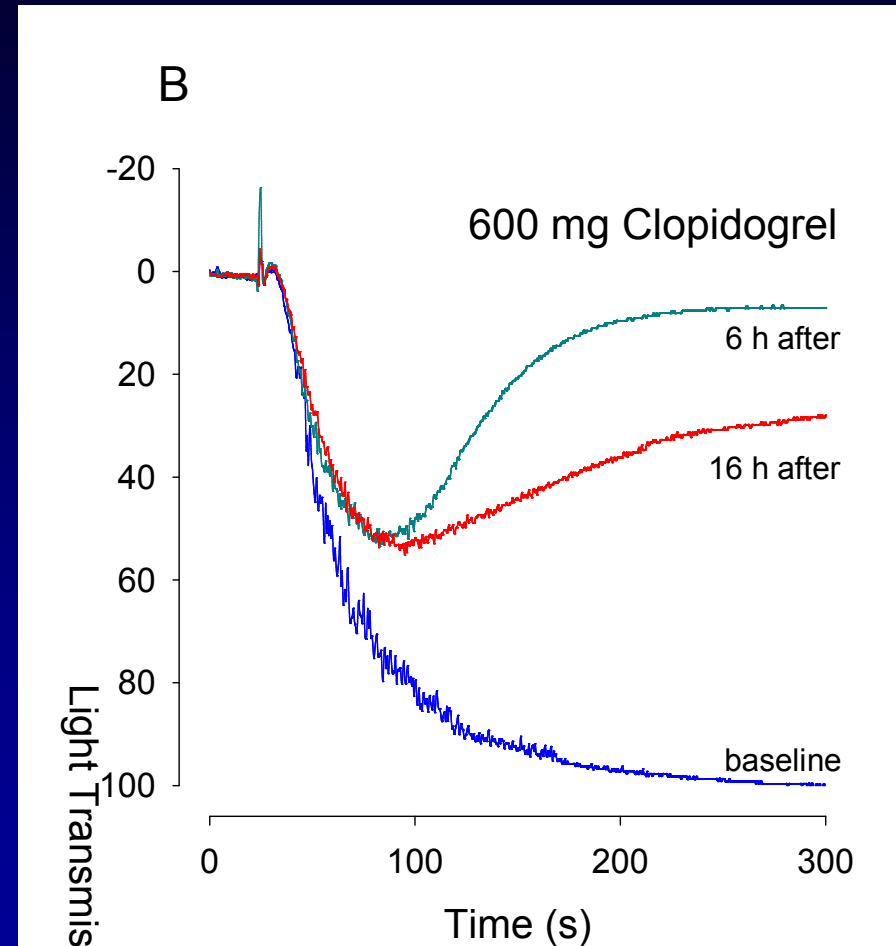
A Patient with Stent Thrombosis and Clopidogrel Resistance



A Patient with Stent Thrombosis and Clopidogrel Resistance



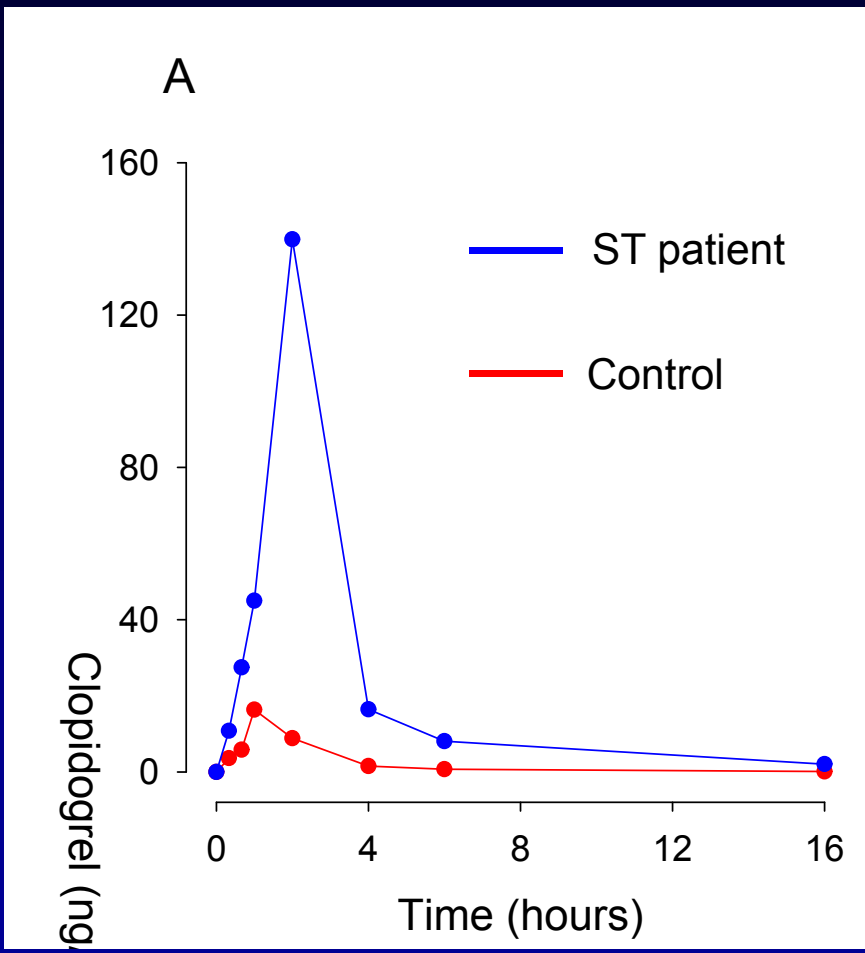
Stent Thrombosis Patient



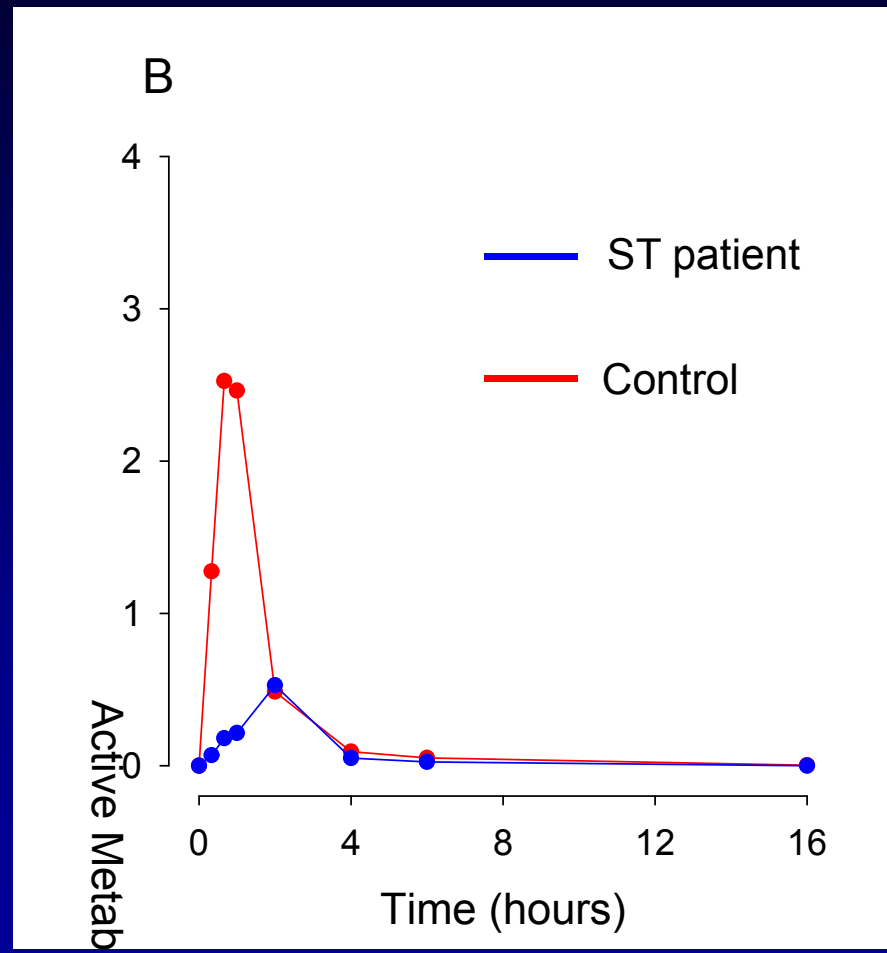
Control Individual



A Patient with Stent Thrombosis and Failed Metabolization of Clopidogrel



Clopidogrel



Active Metabolite

Beckerath et al, Thromb Haemost 2005

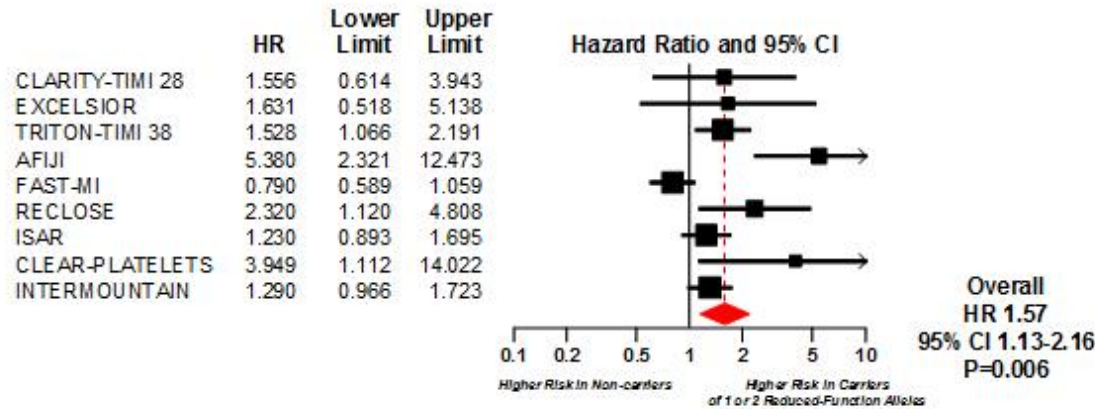
Prasugrel

A New Alternative to Clopidogrel



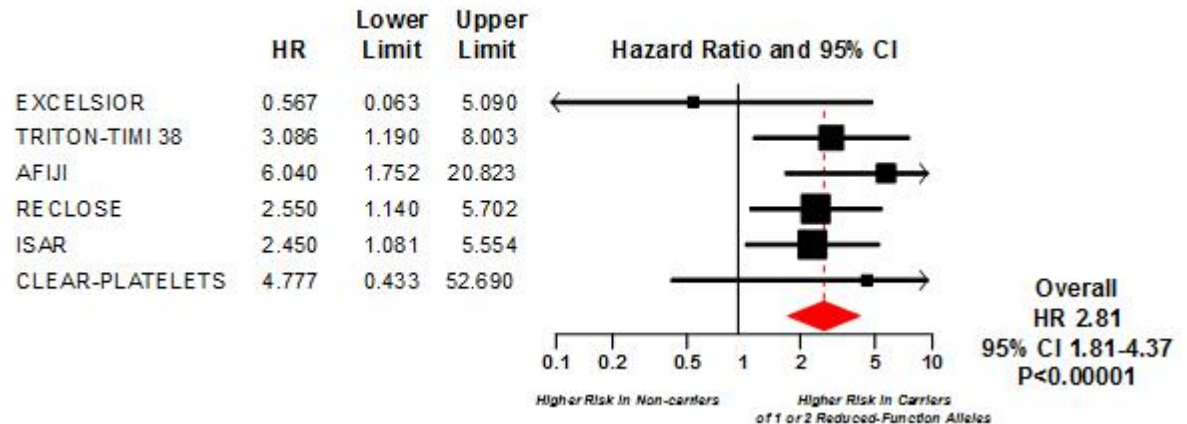
Cardiovascular Death, MI, or Ischemic Stroke by CYP2C19 Genotype

A. Carriers of One or Two CYP2C19 Reduced-Function Alleles versus Non-Carriers



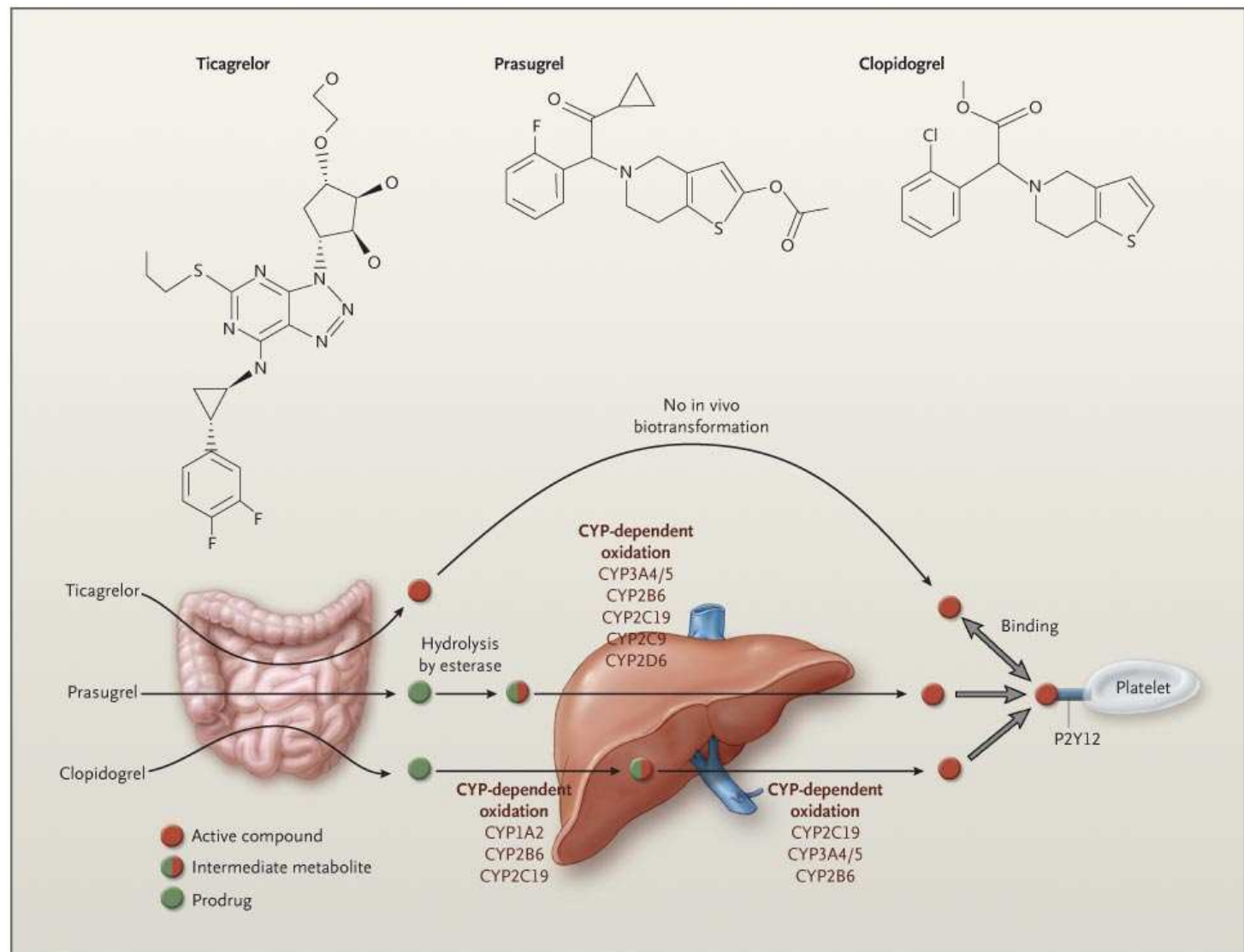
Stent Thrombosis by CYP2C19 Genotype

A. Carriers of One or Two CYP2C19 Reduced-Function Alleles versus Non-Carriers

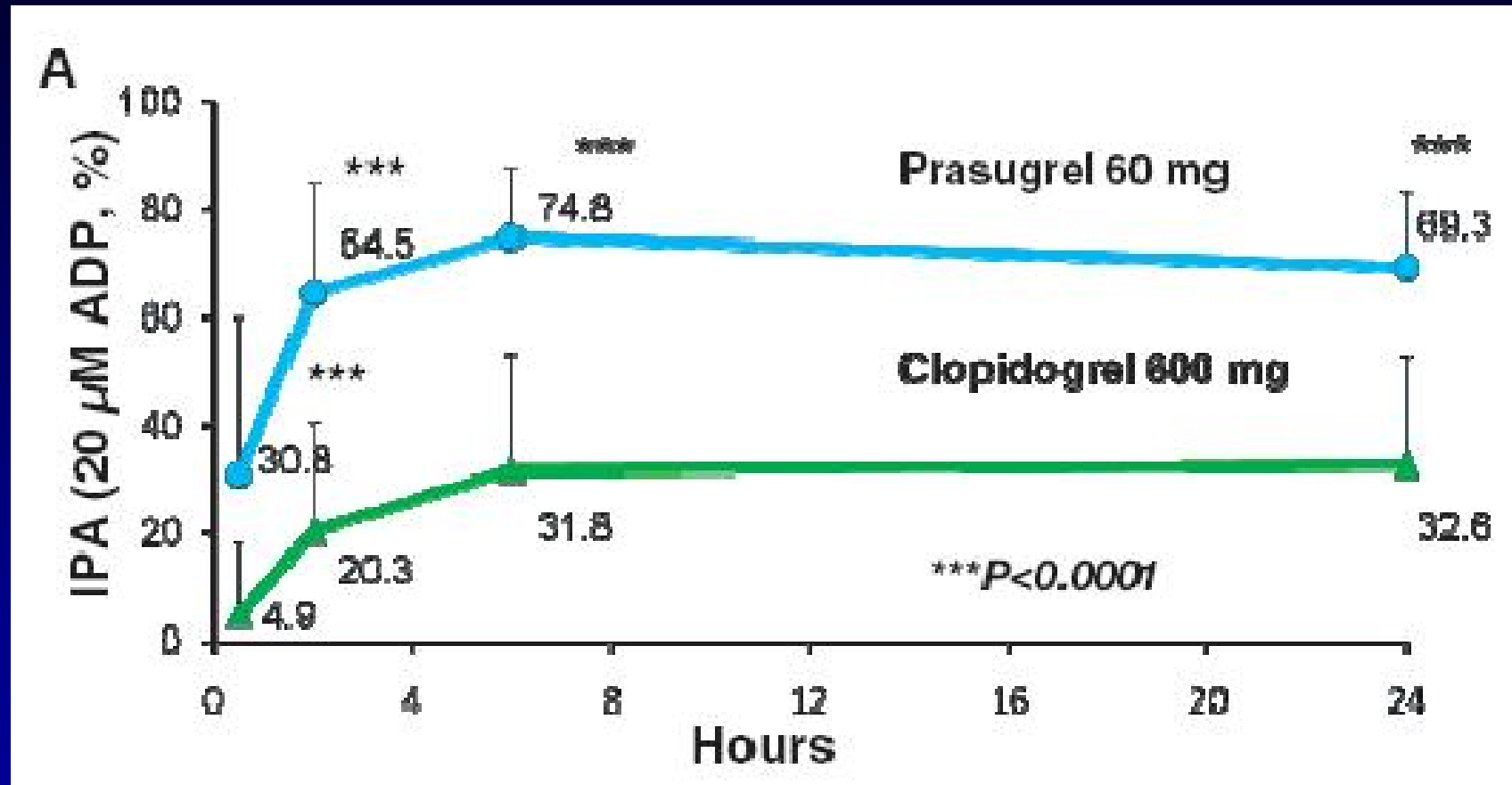


Prasugrel

A New Alternative to Clopidogrel



Prasugrel vs. Clopidogrel Platelet Inhibition



Prasugrel

PRINCIPLE-TIMI 44, Circ 2007

Prasugrel vs. Clopidogrel TRITON-TIMI 38



ACS (STEMI or UA/NSTEMI) & Planned PCI

ASA

13,608 patients

Double-blind

CLOPIDOGREL
300 mg LD/ 75 mg MD

PRASUGREL
60 mg LD/ 10 mg MD

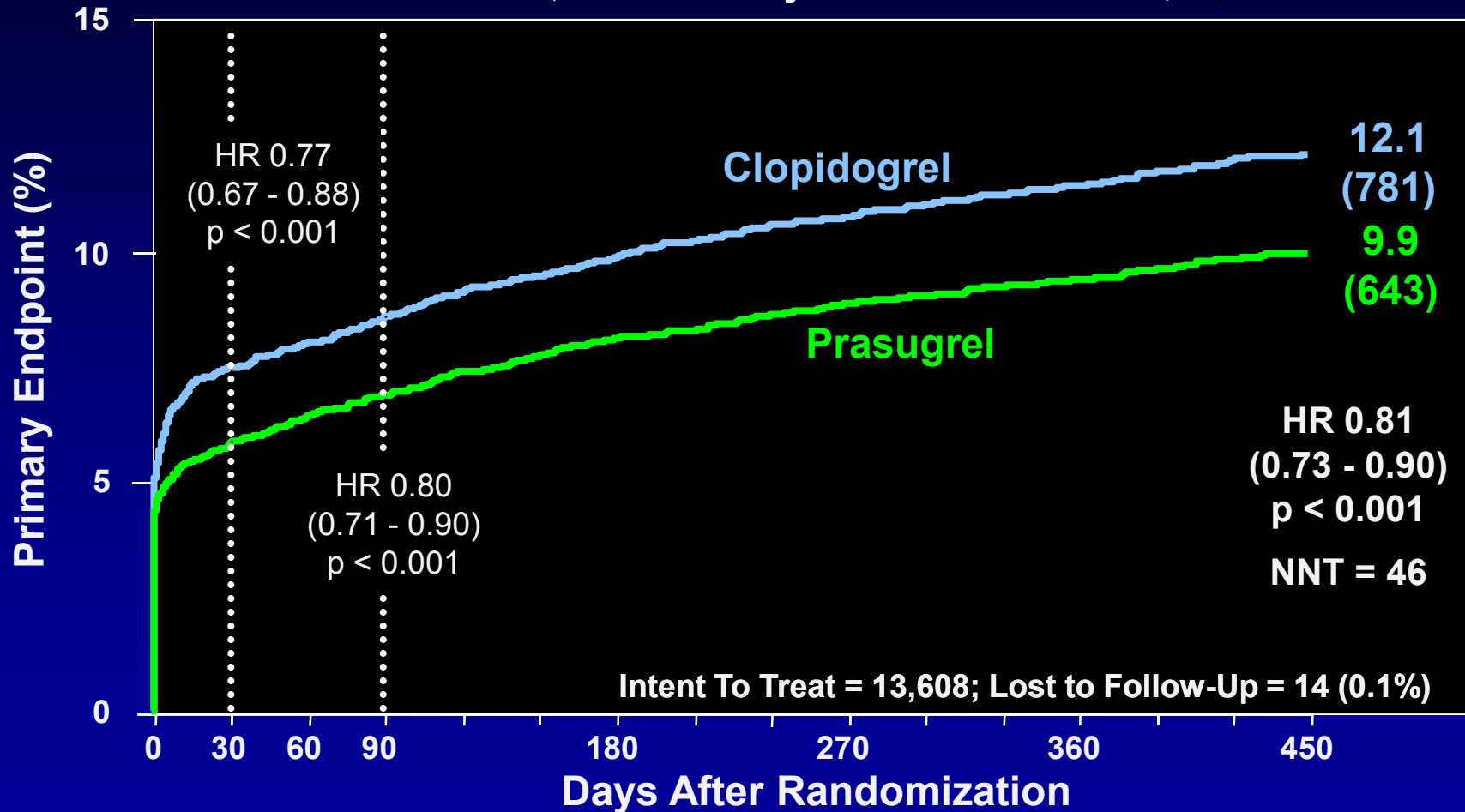
Median duration of therapy - 12 months

1° endpoint: CV death, MI, Stroke
2° endpoints: CV death, MI, Stroke, Rehosp-Rec Isch
CV death, MI, UTVR
Stent Thrombosis (ARC definite/prob.)
Safety endpoints: TIMI major bleeds, Life-threatening bleeds
Key Substudies: Pharmacokinetic, Genomic

TRITON-TIMI 38 Primary Endpoint



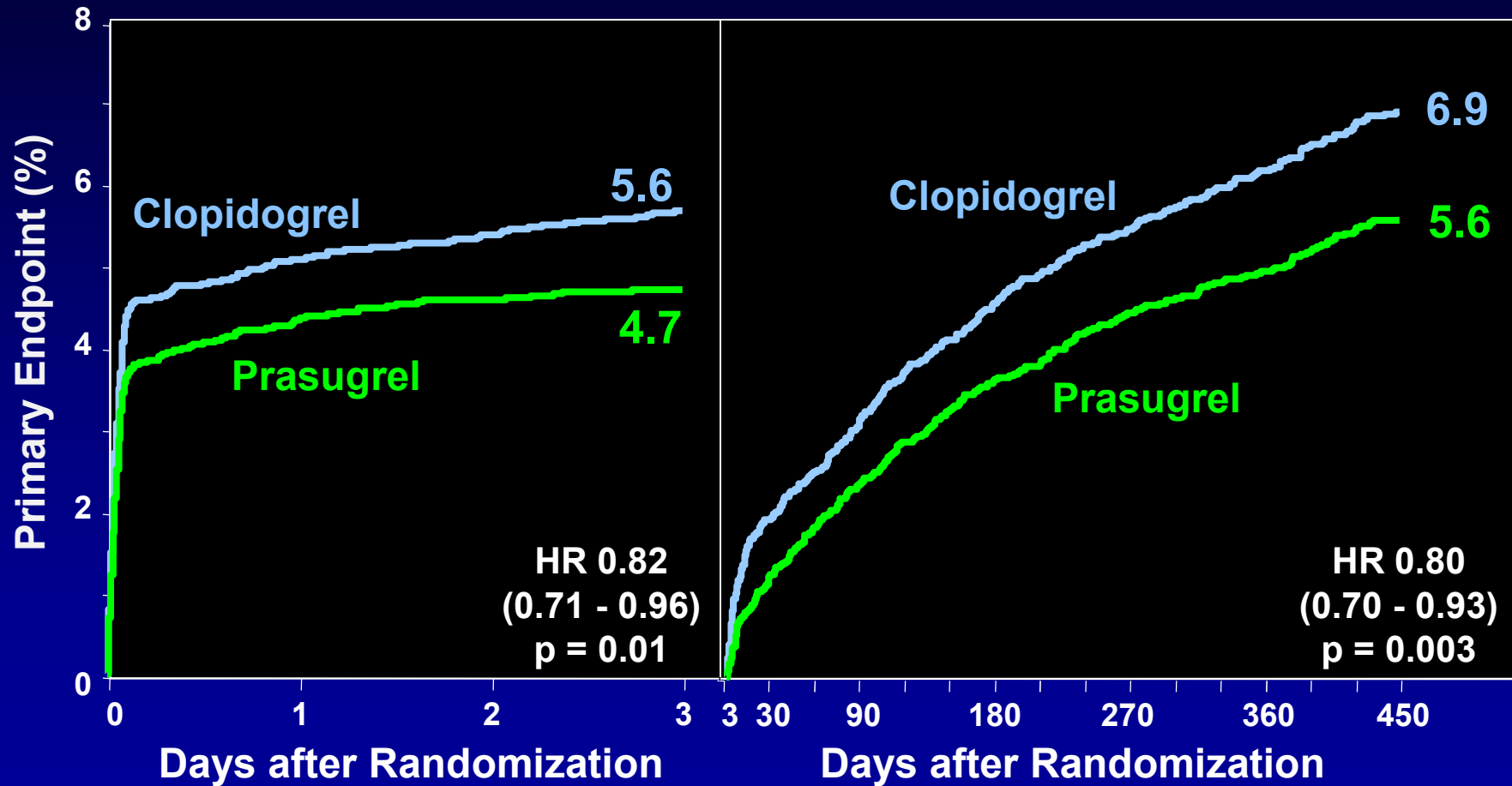
Cardiovascular Death, Nonfatal Myocardial Infarction, Nonfatal Stroke



TRITON-TIMI 38 Primary Endpoint



Cardiovascular Death, Nonfatal Myocardial Infarction, Nonfatal Stroke

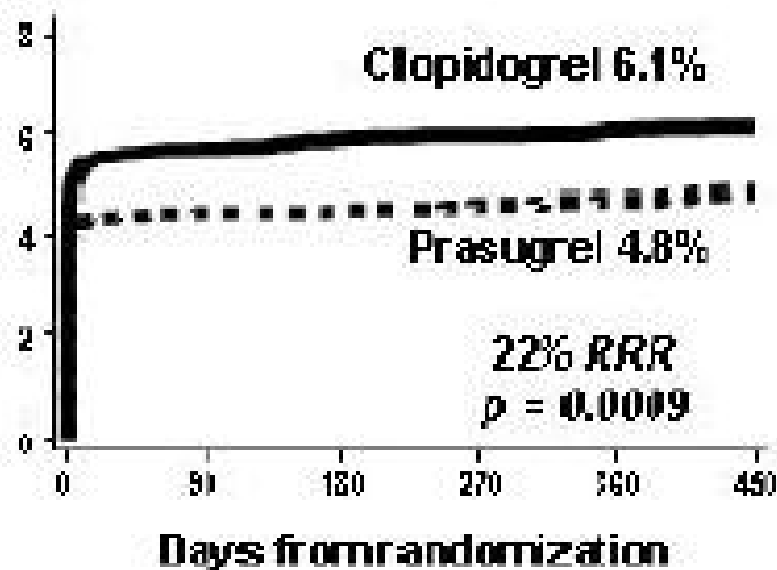


TRITON-TIMI 38

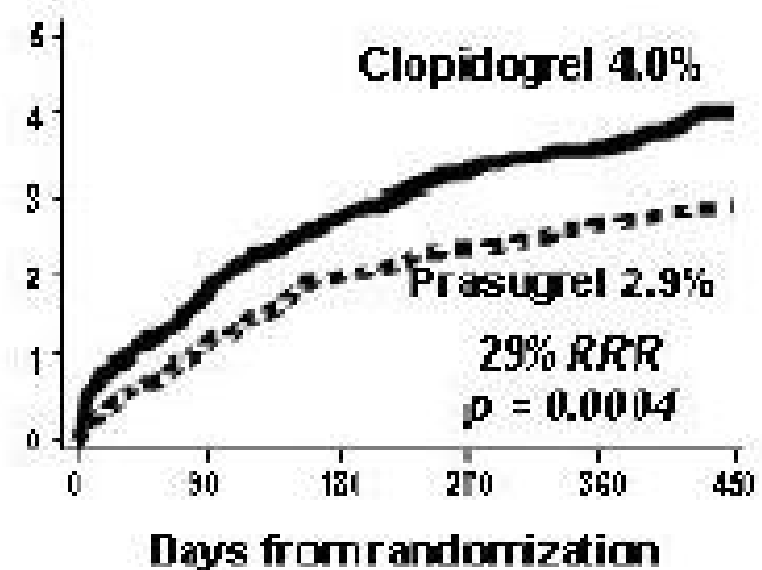
Periprocedural and Spontaneous MI



Peri-procedural MI (%)

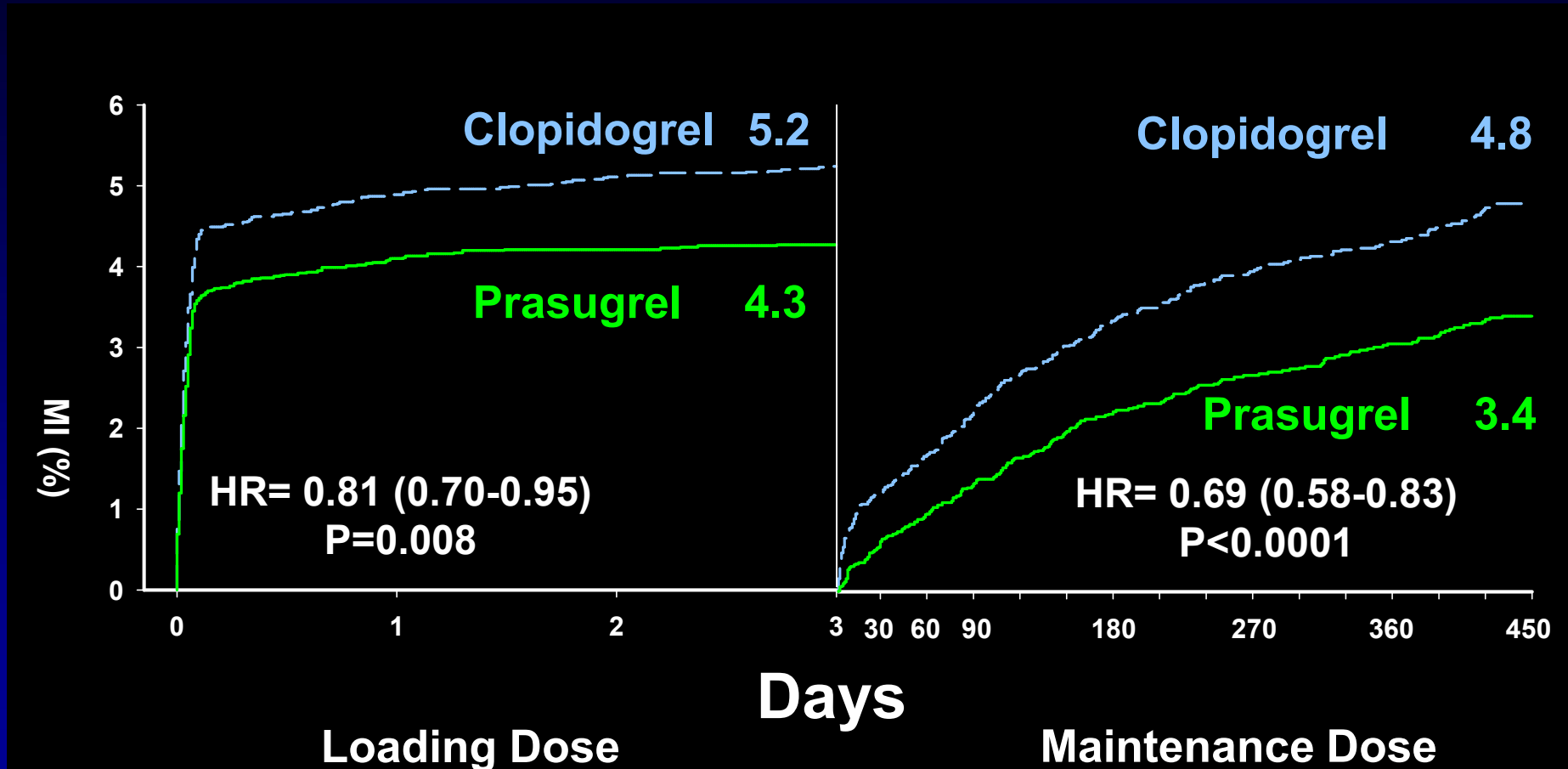


Spontaneous MI (%)

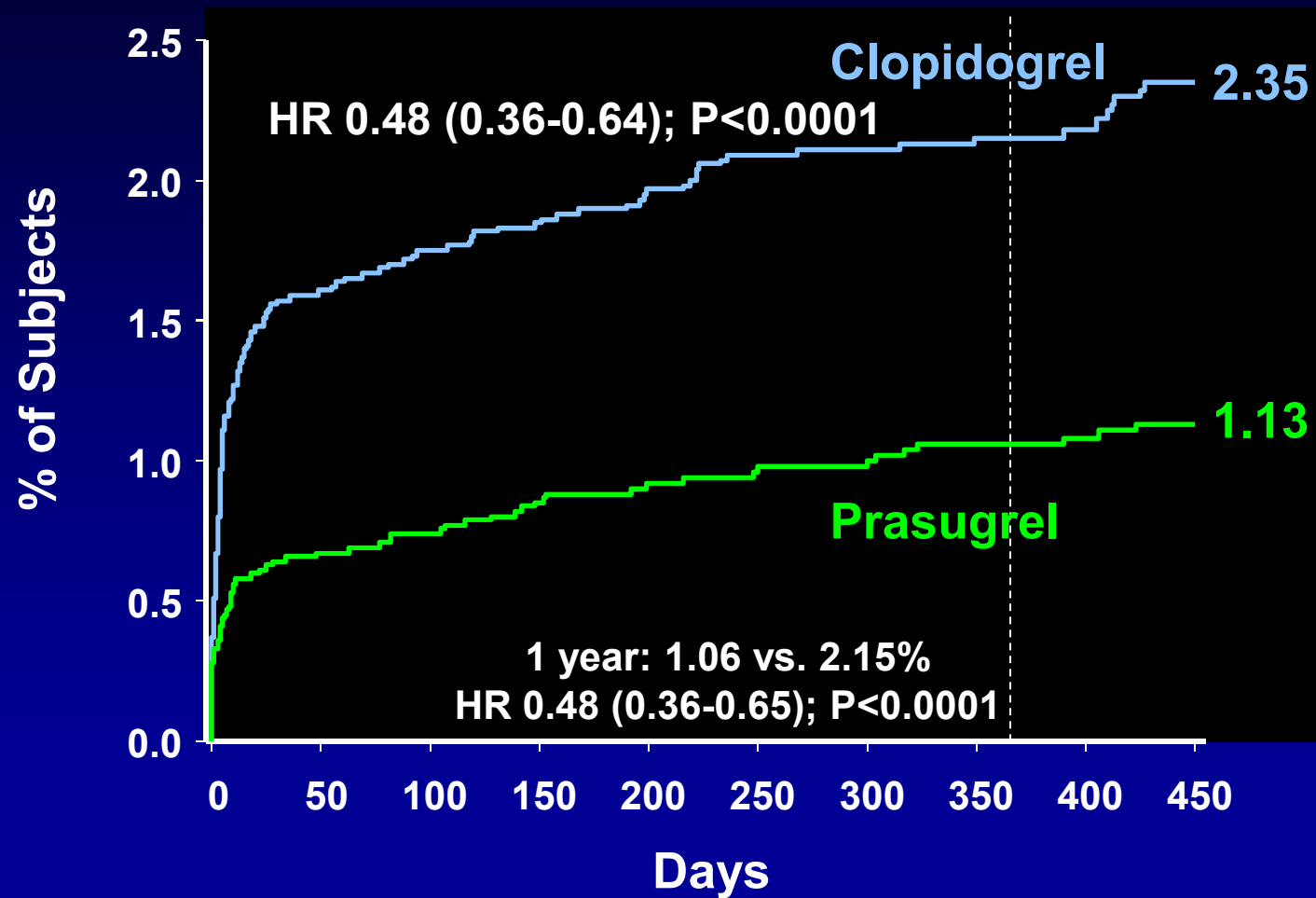


TRITON-TIMI 38

Early and Late MI

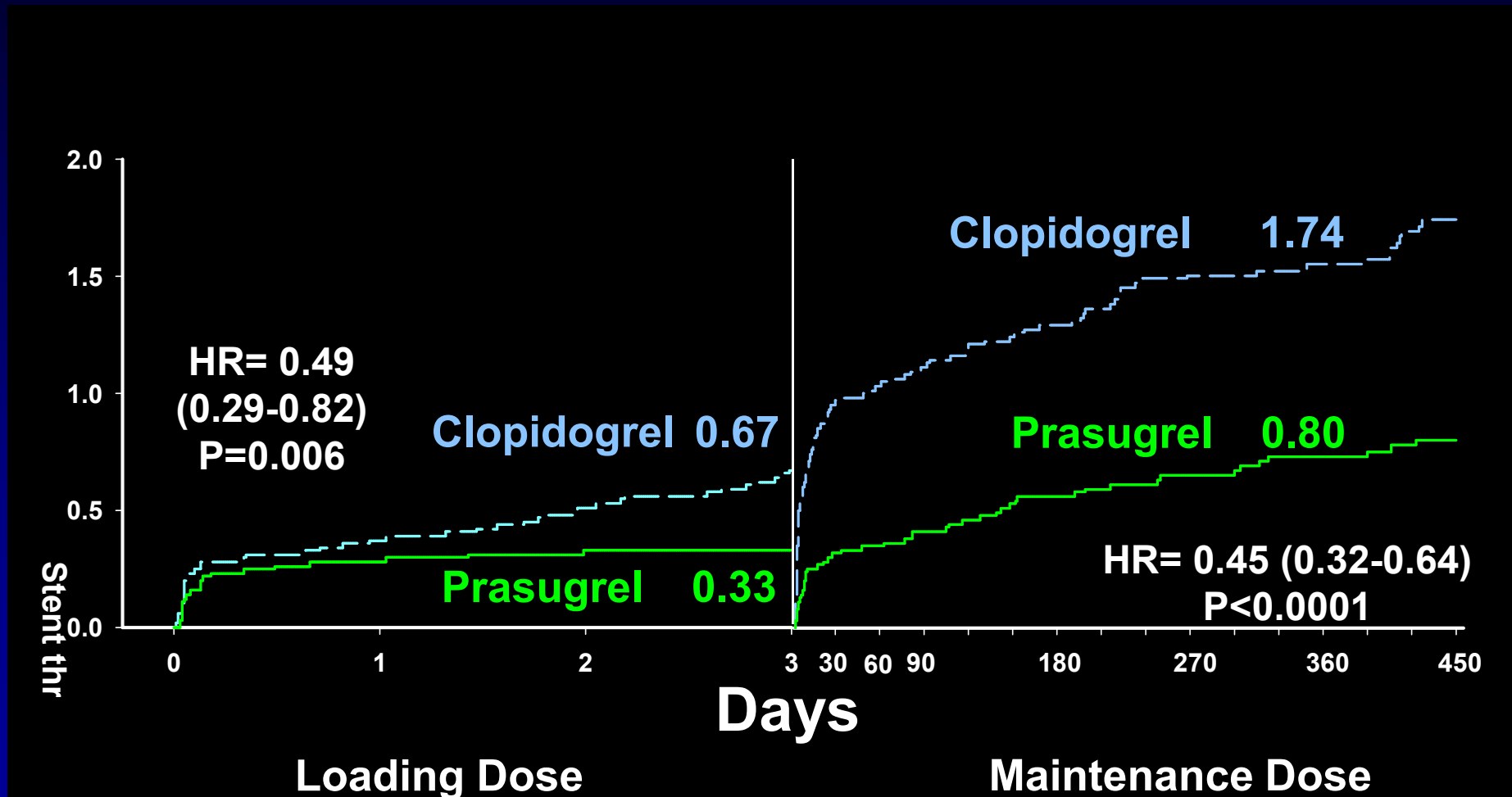


TRITON-TIMI 38 Stent Thrombosis

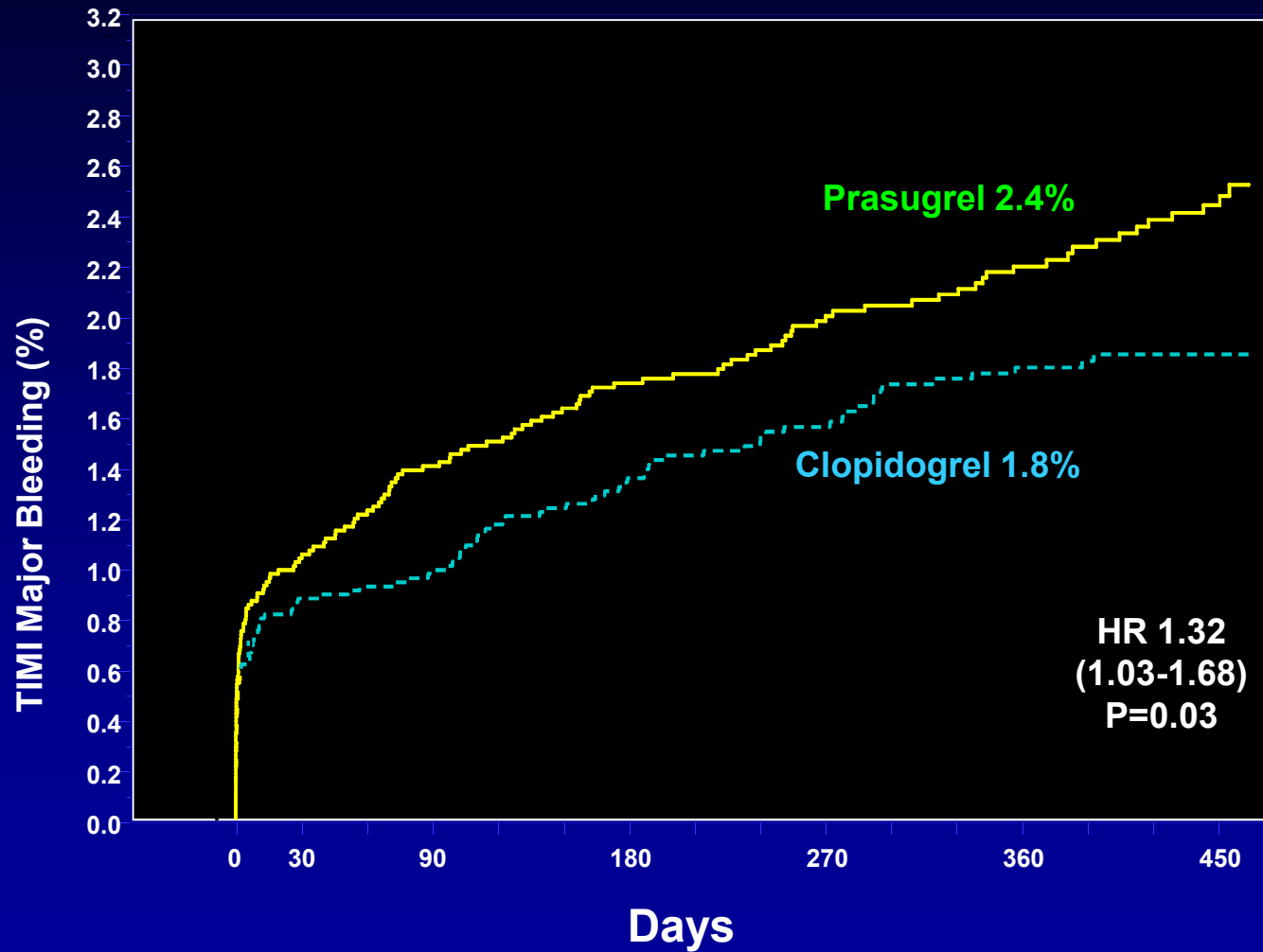


TRITON-TIMI 38

Early and Late Stent Thrombosis



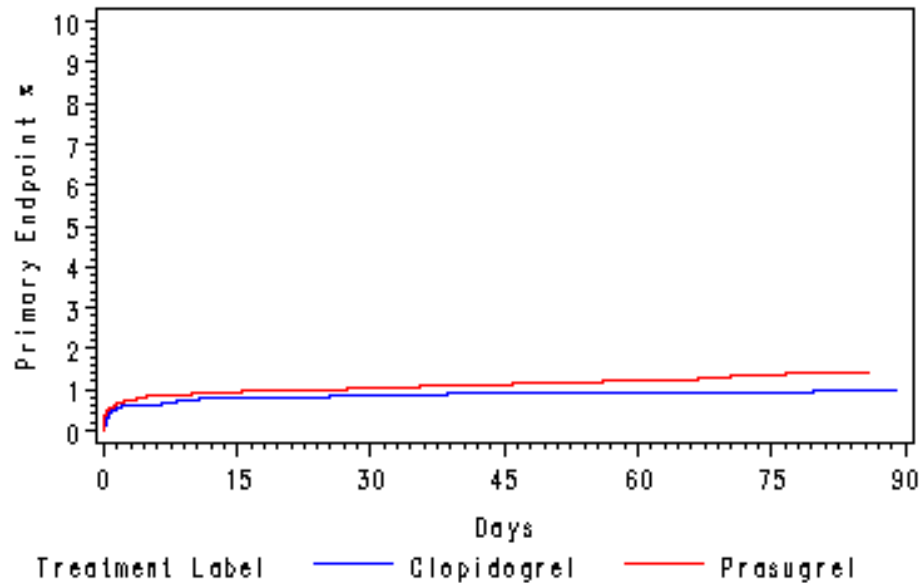
TRITON-TIMI 38 Safety Endpoint



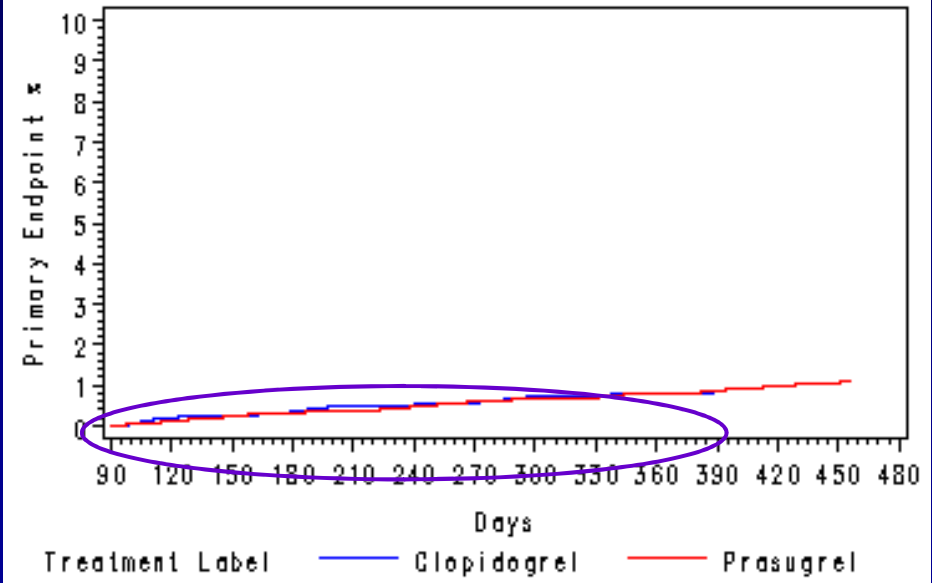
TRITON-TIMI 38 Safety Endpoint



Non-CABG TIMI Major Bleeding LTE 90
All Patients

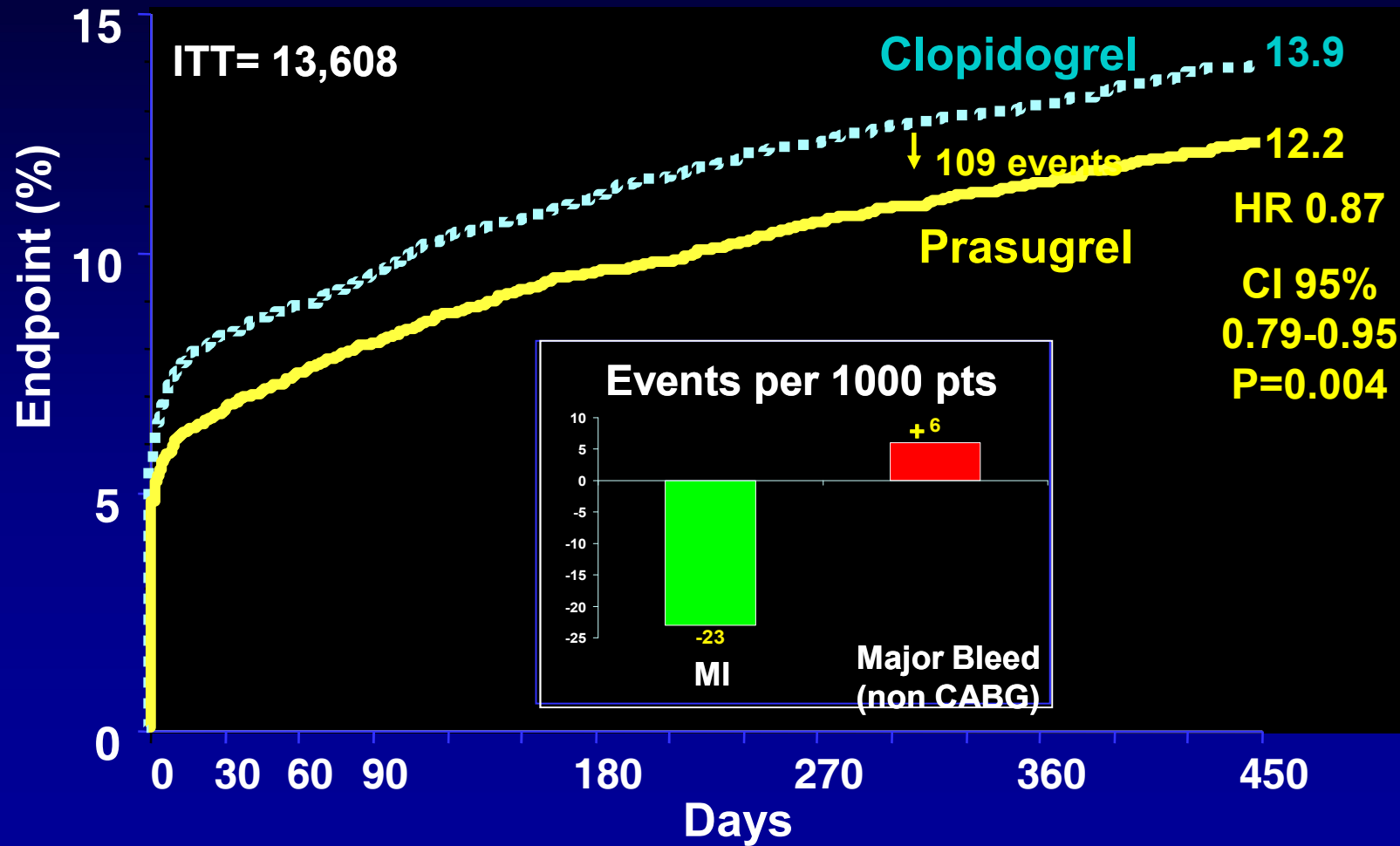


Non-CABG TIMI Major Bleeding GT 90
All Patients



TRITON-TIMI 38

Net Clinical Benefit



TRITON-TIMI 38

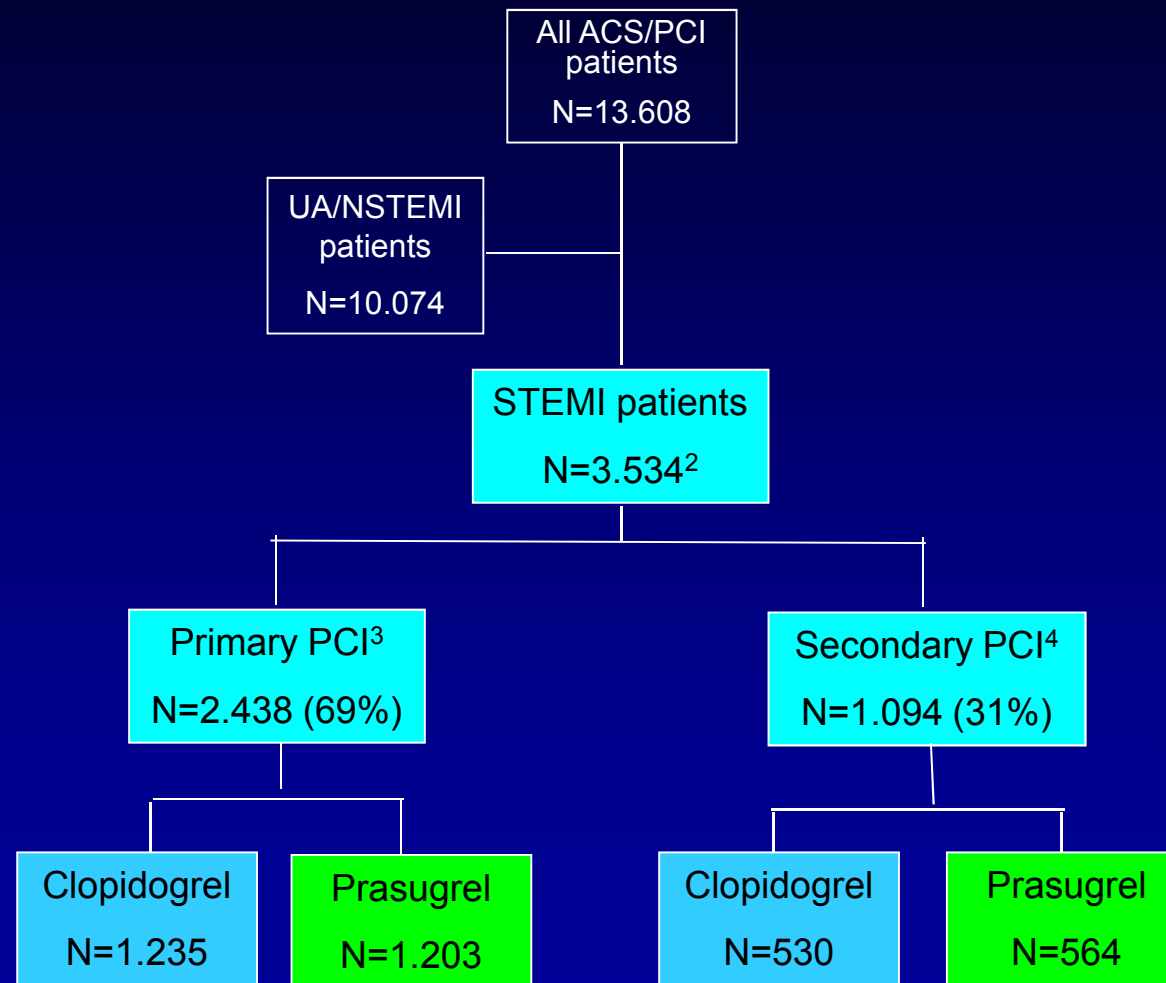
Net Clinical Benefit



Table 4. The Balance of Efficacy and Safety in Selected Subgroups.*

End Point	Prasugrel <i>no. of patients/total no. (%)</i>	Clopidogrel <i>no. of patients/total no. (%)</i>	Hazard Ratio for Prasugrel (95% CI)	P Value	P Value for Interaction†
Age <75 yr, body weight \geq60 kg, and no history of stroke or TIA					
Death from cardiovascular causes, nonfatal MI, or nonfatal stroke (primary efficacy end point)	433/5421 (8.3)	569/5383 (11.0)	0.74 (0.66–0.84)	<0.001	0.008
Non-CABG-related TIMI major bleeding	91/5390 (2.0)	73/5337 (1.5)	1.24 (0.91–1.69)	0.17	0.64
Death from any cause, nonfatal MI, nonfatal stroke, or non-CABG-related nonfatal TIMI major bleeding	522/5421 (10.2)	641/5383 (12.5)	0.80 (0.71–0.89)	<0.001	0.006

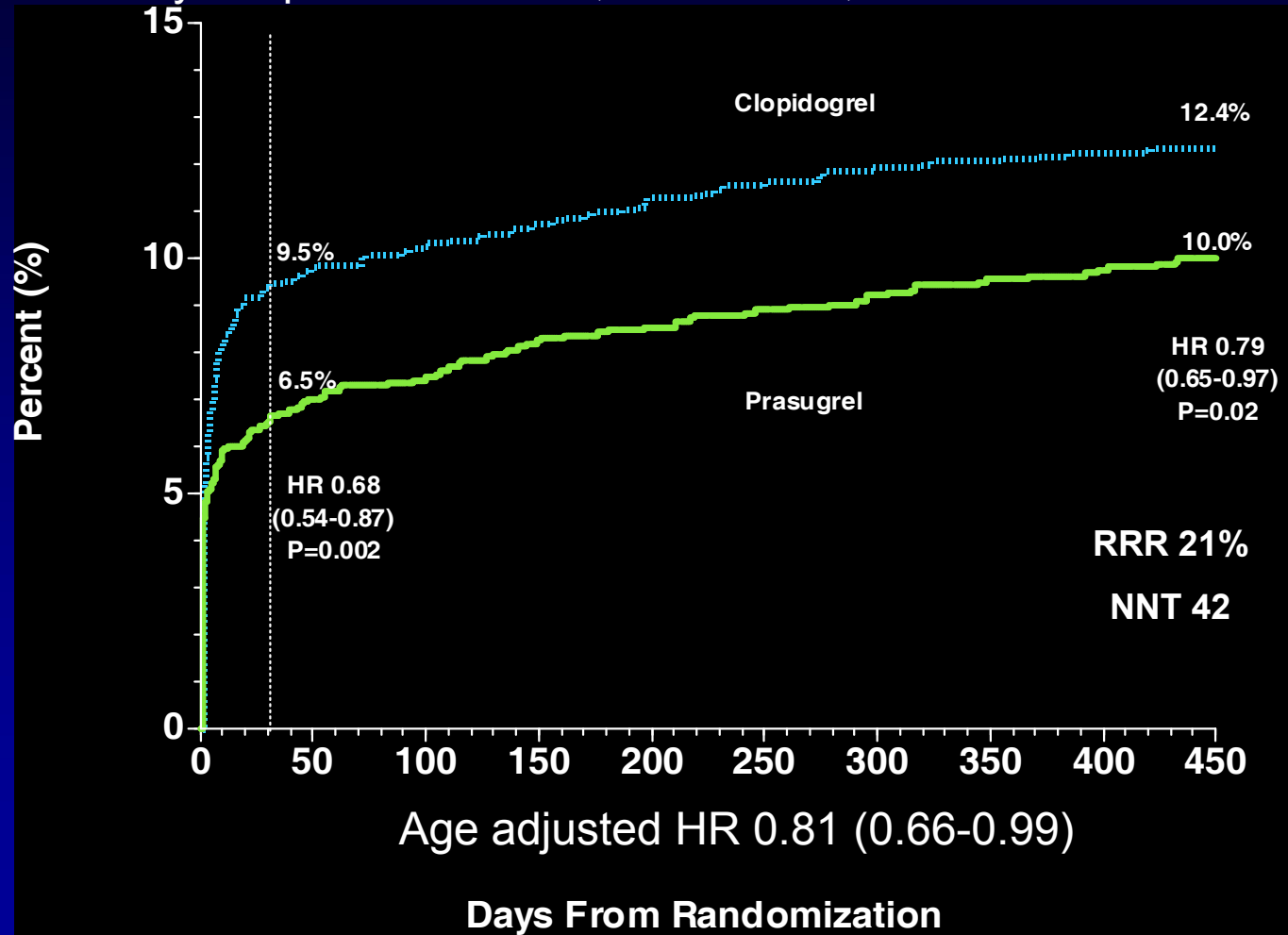
TRITON-TIMI 38 STEMI Subset



TRITON-TIMI 38 STEMI Subset



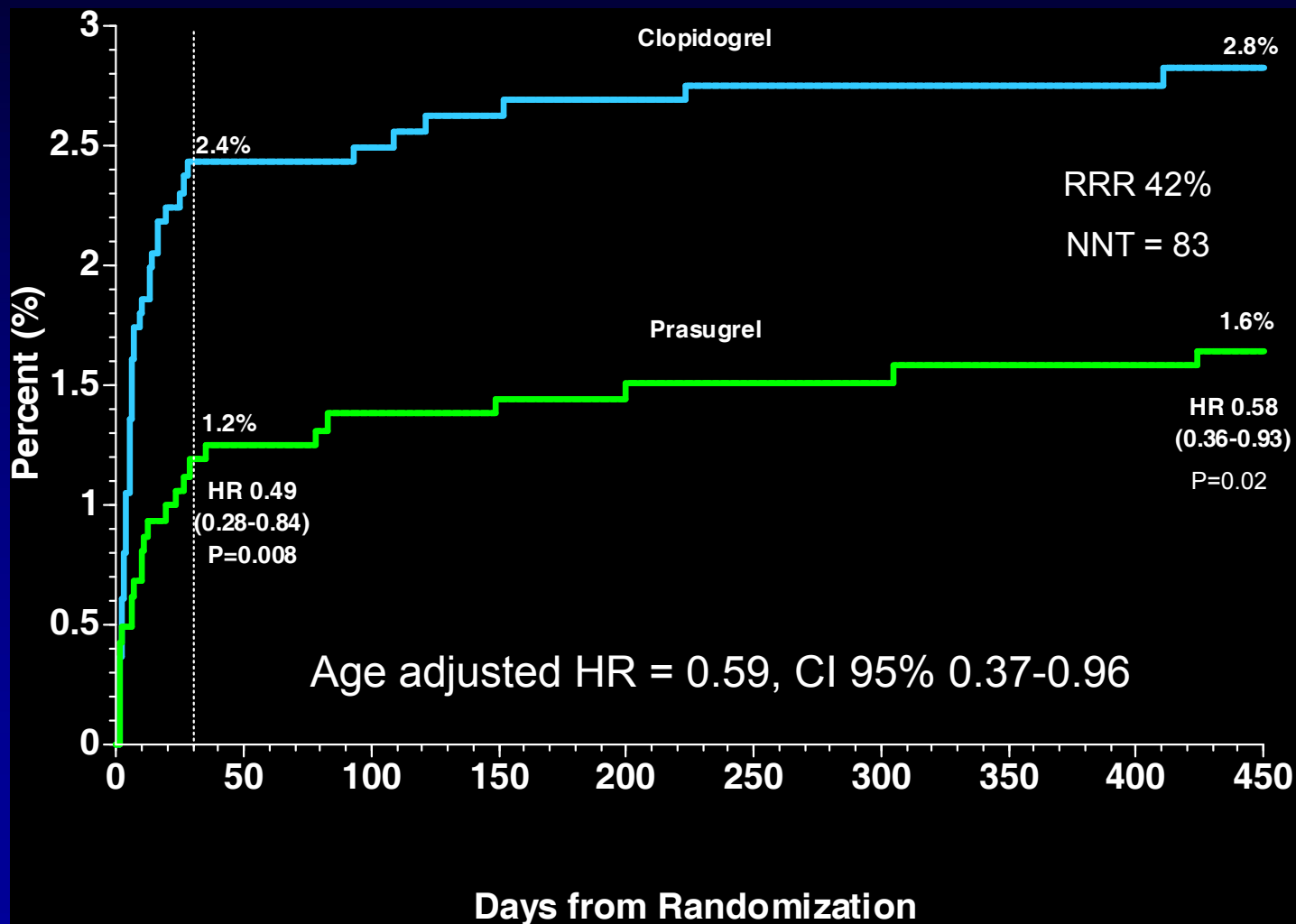
Primary endpoint: CV death, nonfatal MI, nonfatal stroke



TRITON-TIMI 38 STEMI Subset



Stent thrombosis – ALL STEMI patients

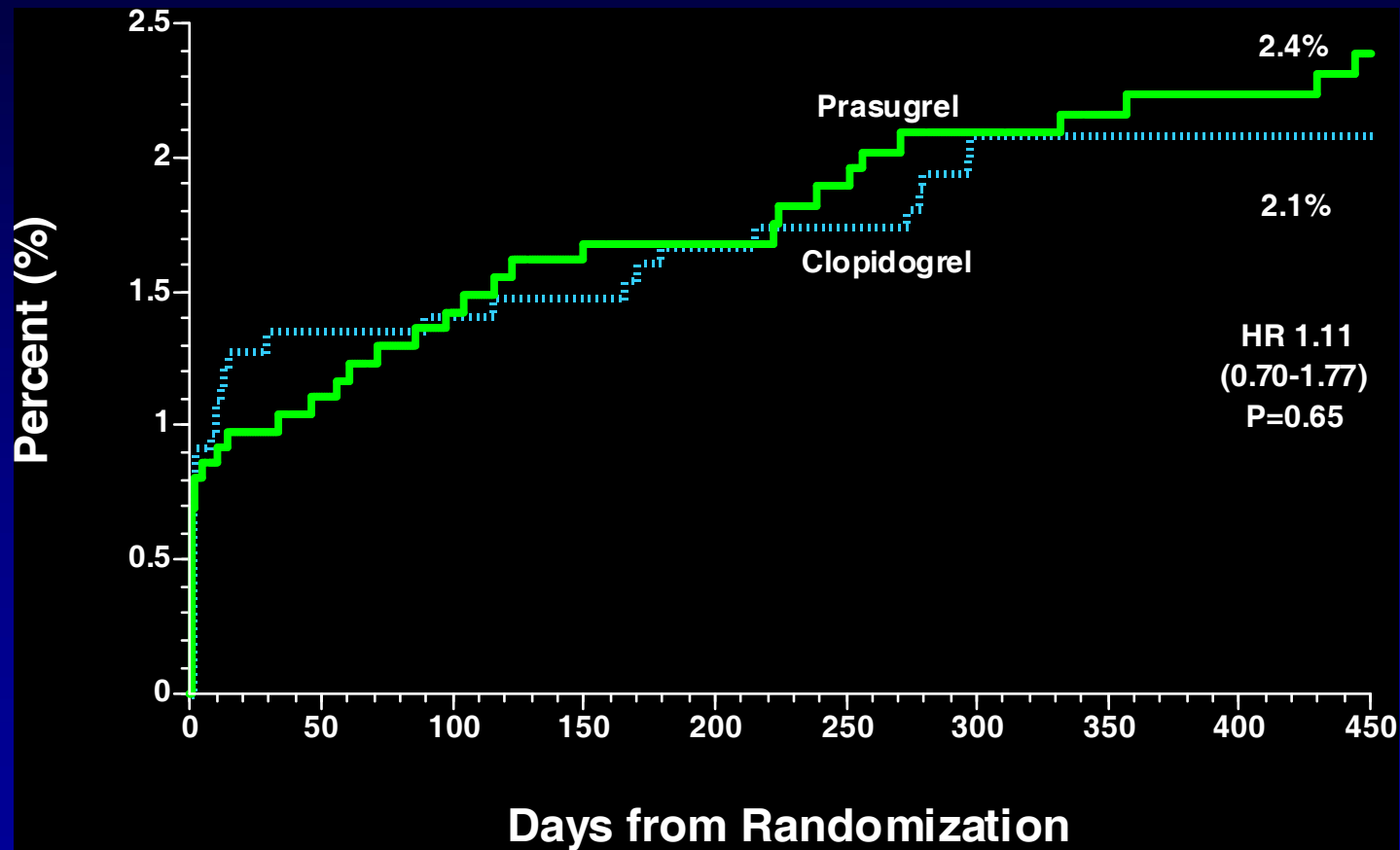


TRITON-TIMI 38 STEMI Subset



Main safety endpoint (TIMI major non-CABG bleedings)

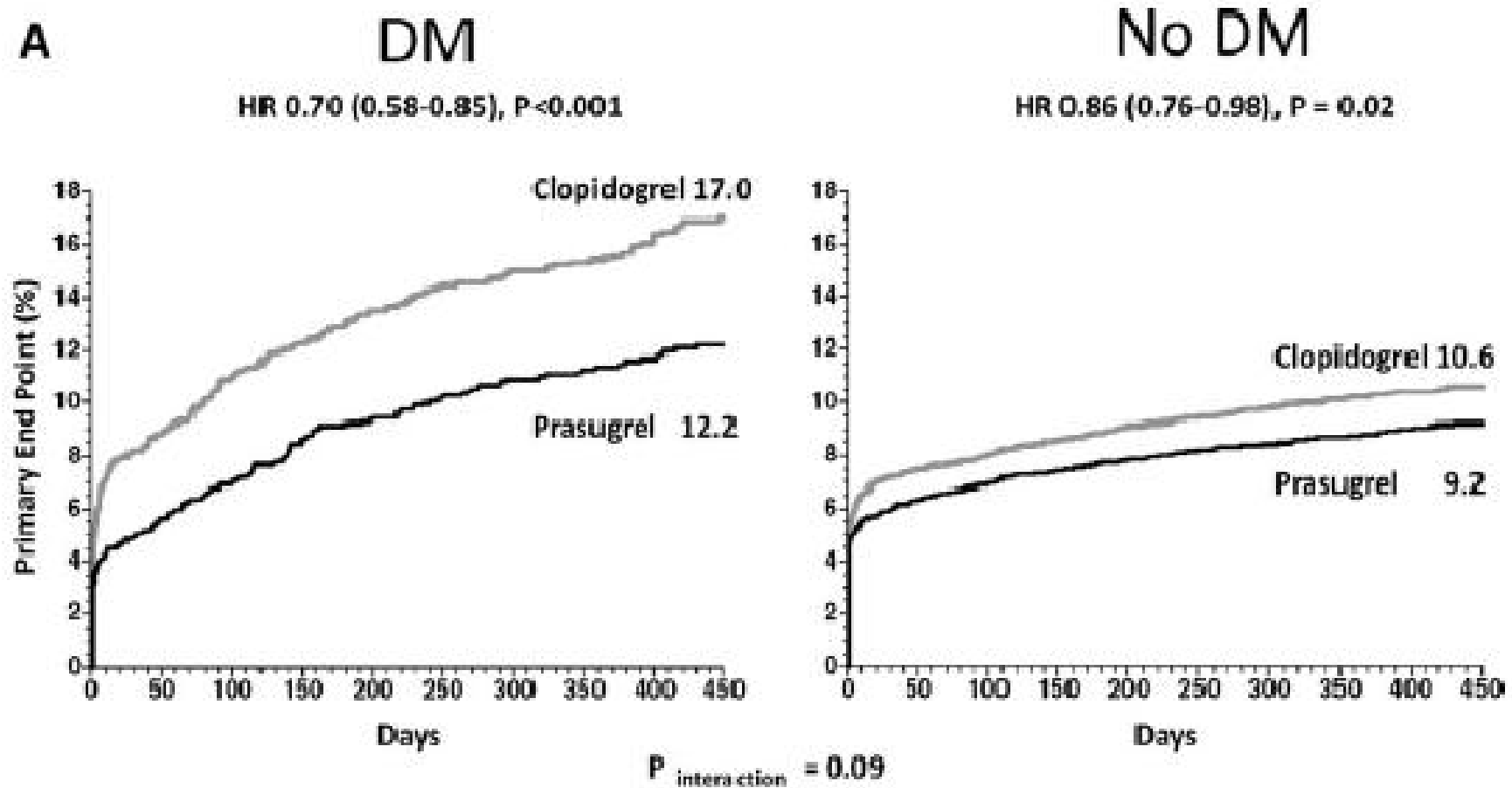
All STEMI patients



TRITON-TIMI 38 Diabetic Subset



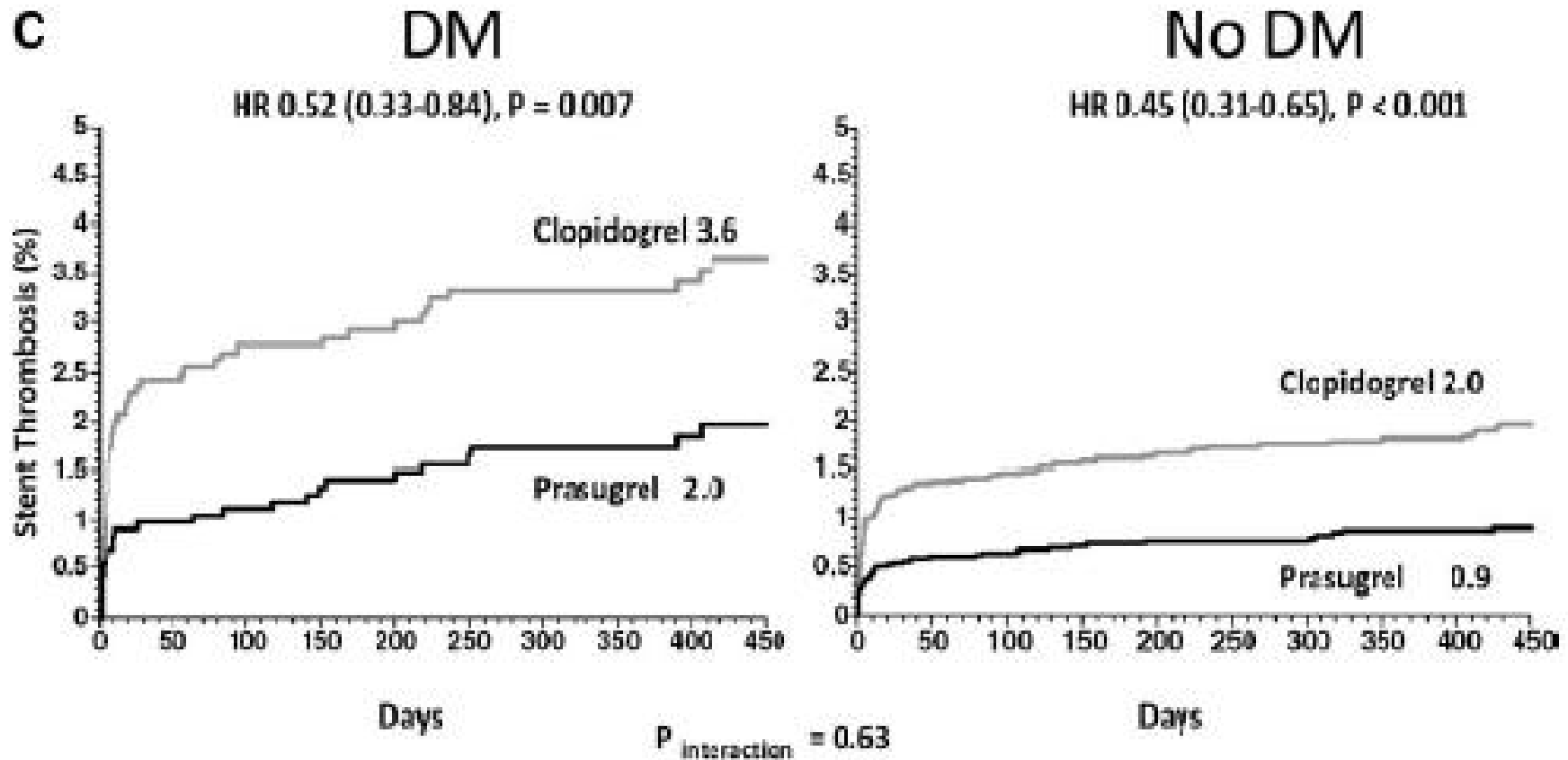
Primary endpoint: CV death, nonfatal MI, nonfatal stroke



TRITON-TIMI 38 Diabetic Subset



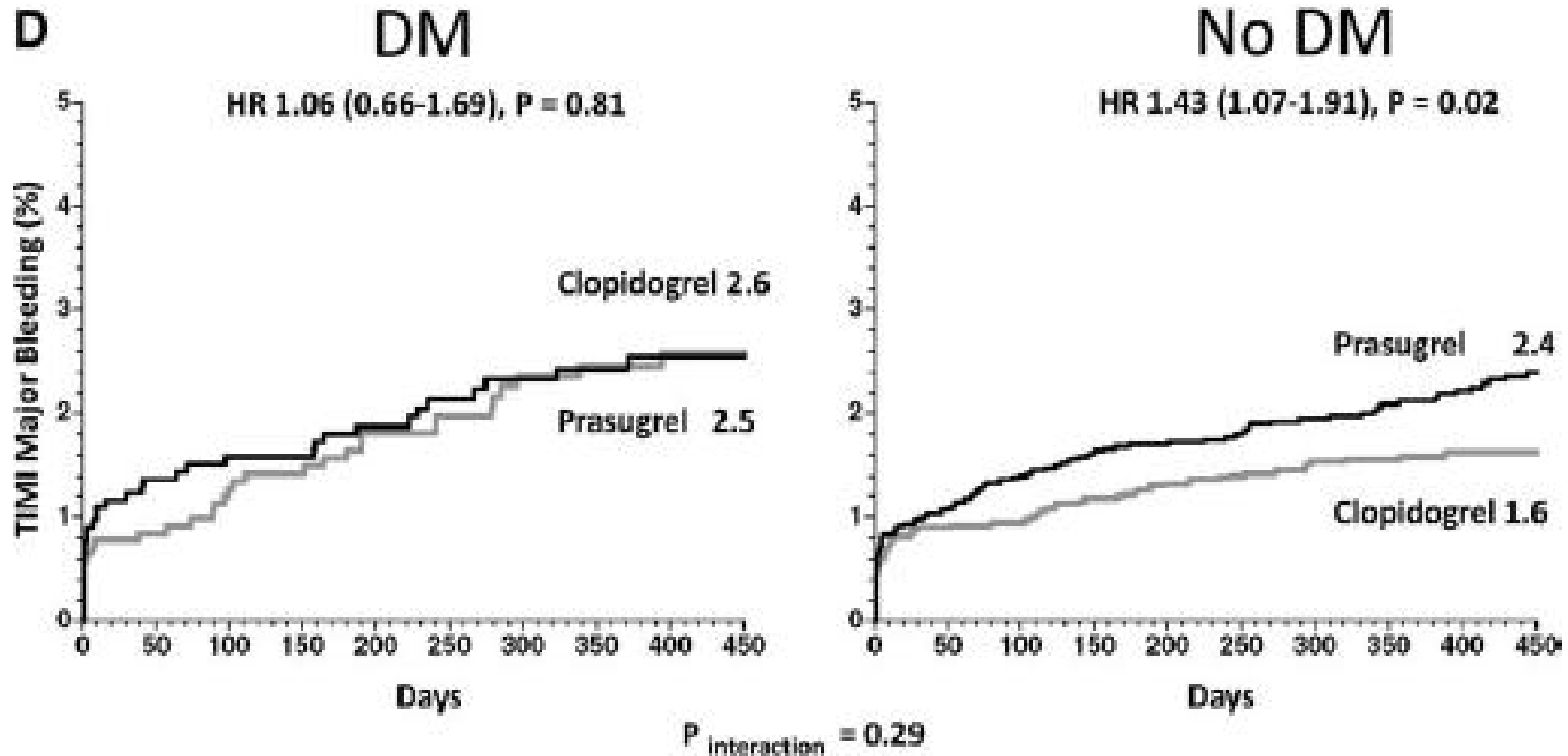
Stent Thrombosis



TRITON-TIMI 38 Diabetic Subset



TIMI Major Bleeding



Prasugrel vs Clopidogrel



In the majority of patients with ACS undergoing PCI, prasugrel is a superior alternative to clopidogrel

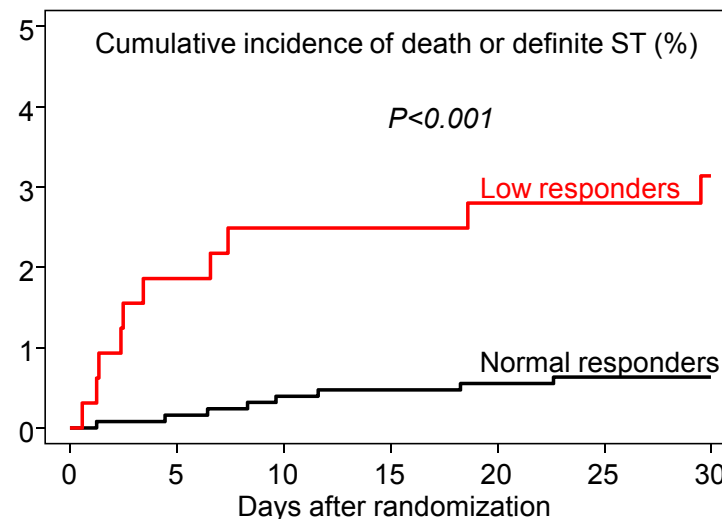
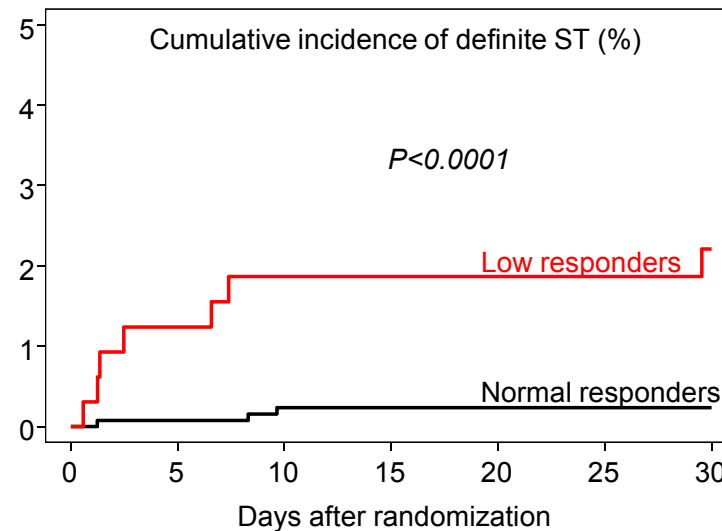
The role of prasugrel in patients with stable CAD undergoing PCI waits for evaluation



Platelet Function Testing After Clopidogrel Hyporesponsiveness and Thrombosis



n=1608 pts





Flow-chart TRIGGER-PCI Study

