

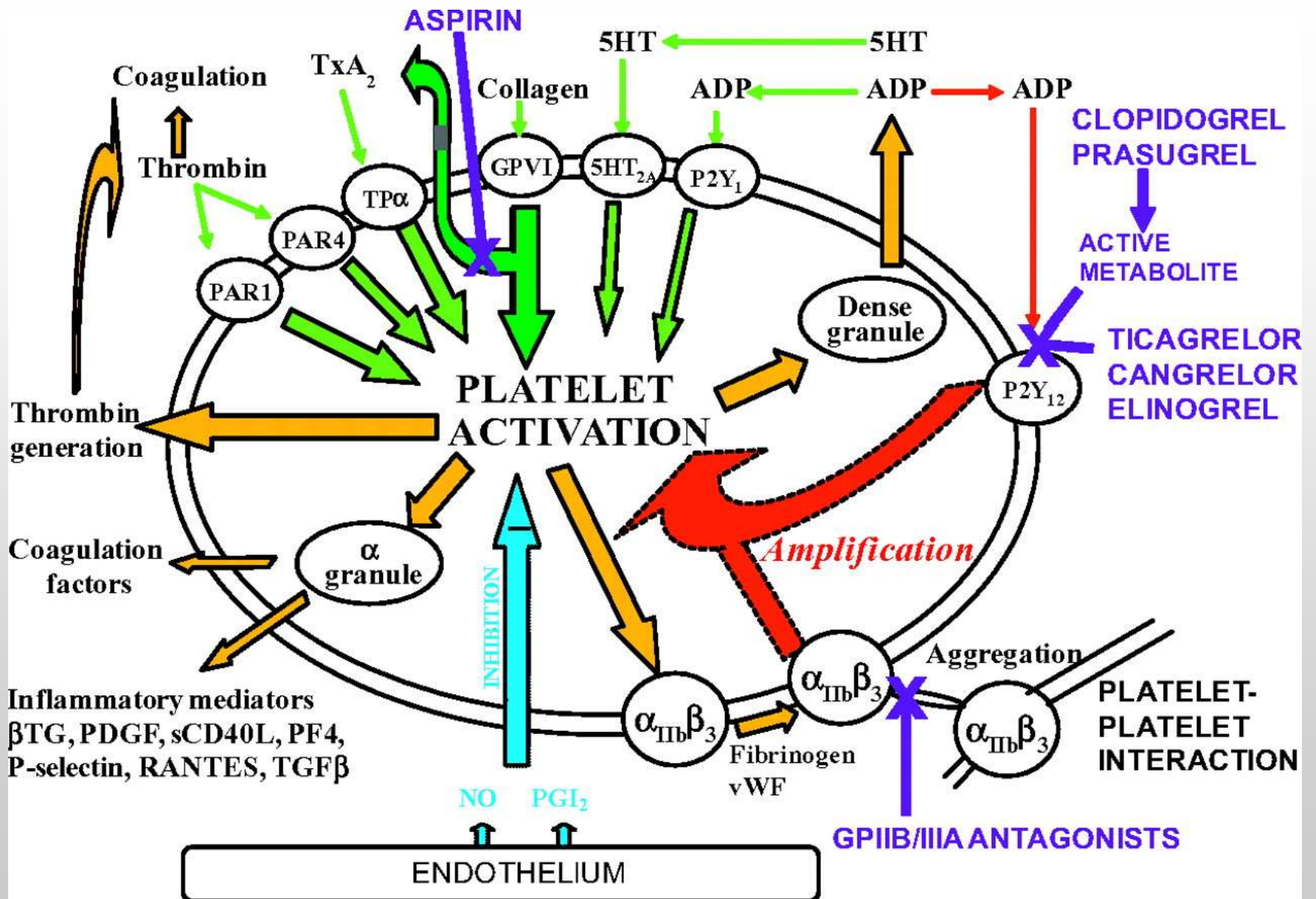
Prasugrel y ticagrelor en el SCA

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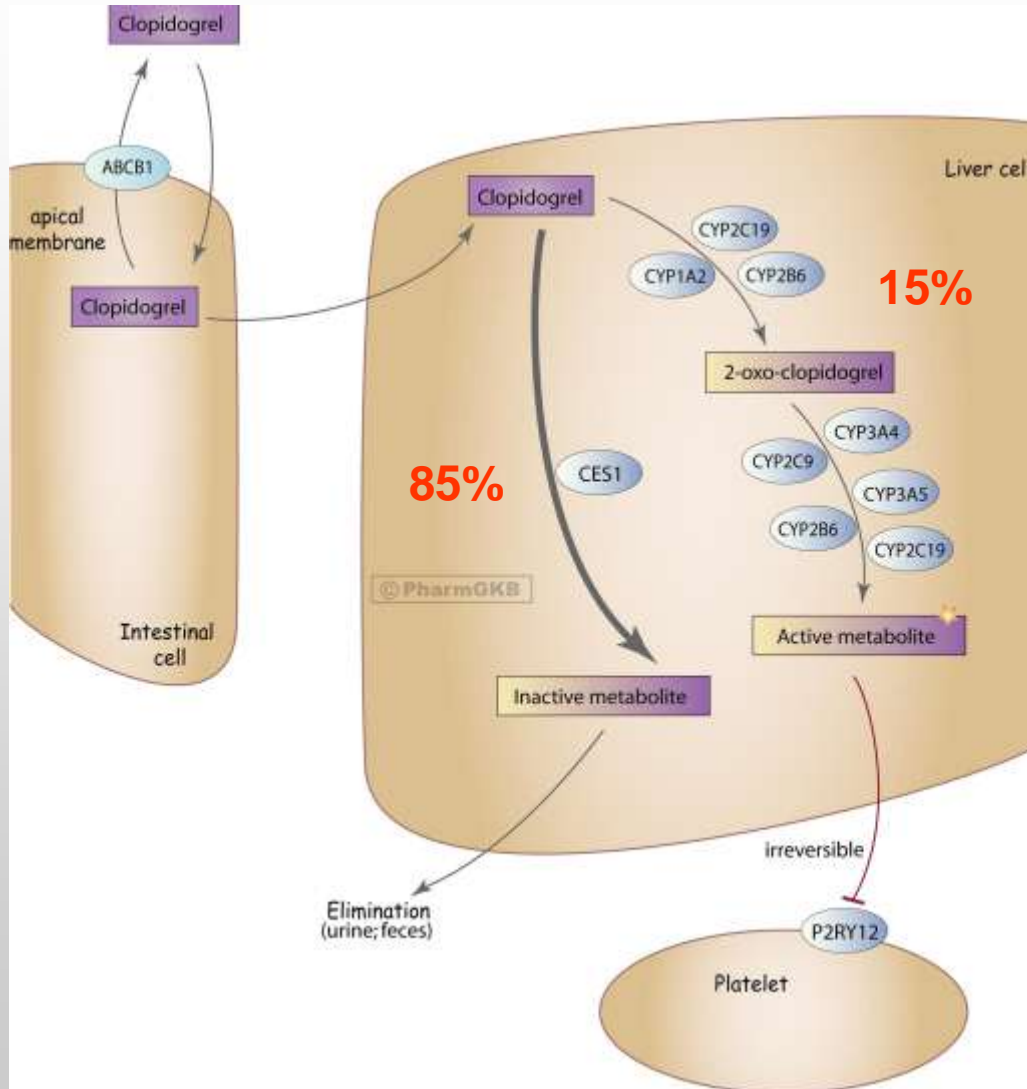
**Curso Casa del Corazón
Madrid
15 junio 2012**

Conflicto de intereses:

Honorarios (modestos) por consultoría y/o charlas de: ASTRA-ZENECA, BAYER, BMS, CHIESI, DAIICHI-SANKYO, URIACH

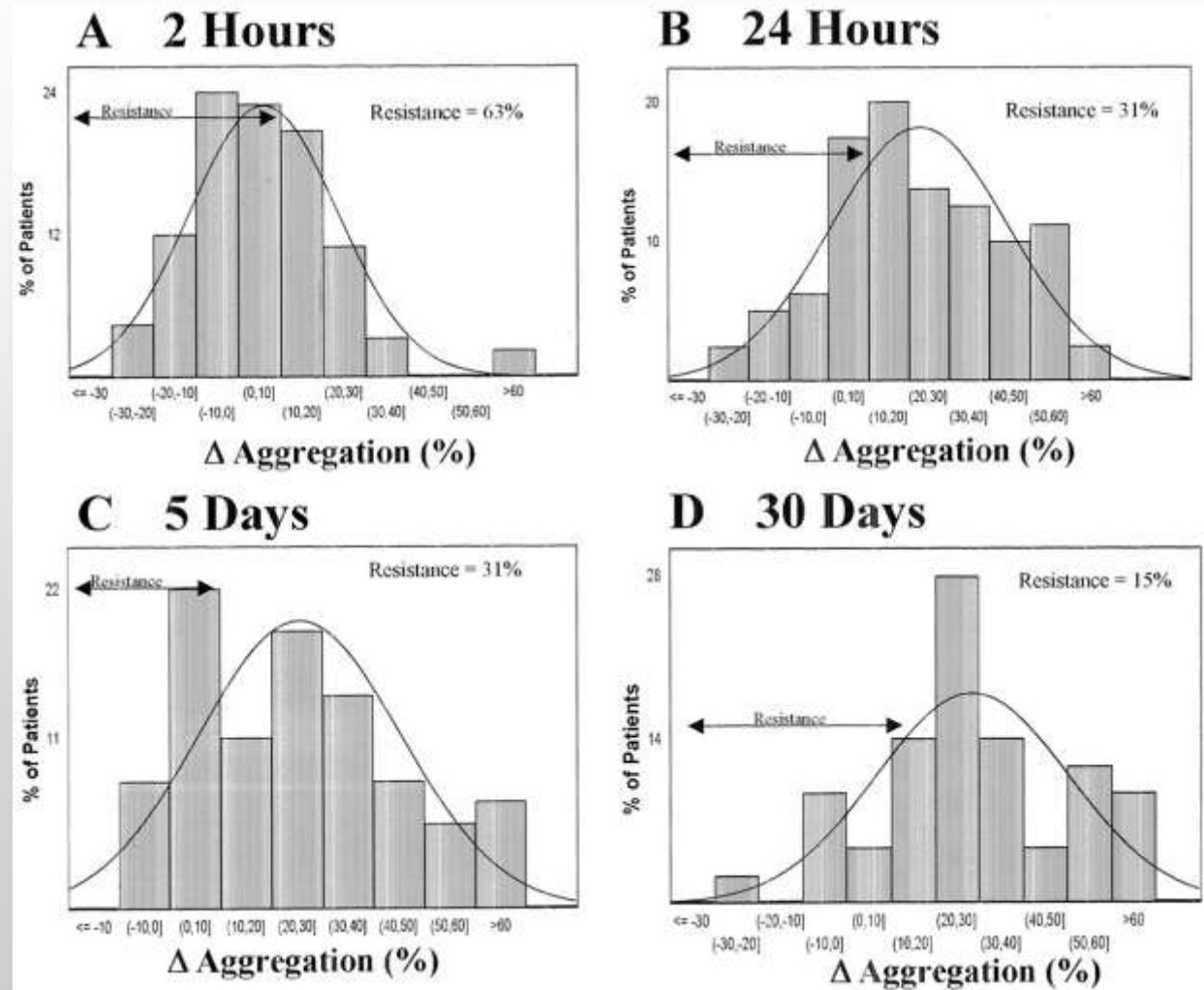


Absorción y metabolismo del clopidogrel



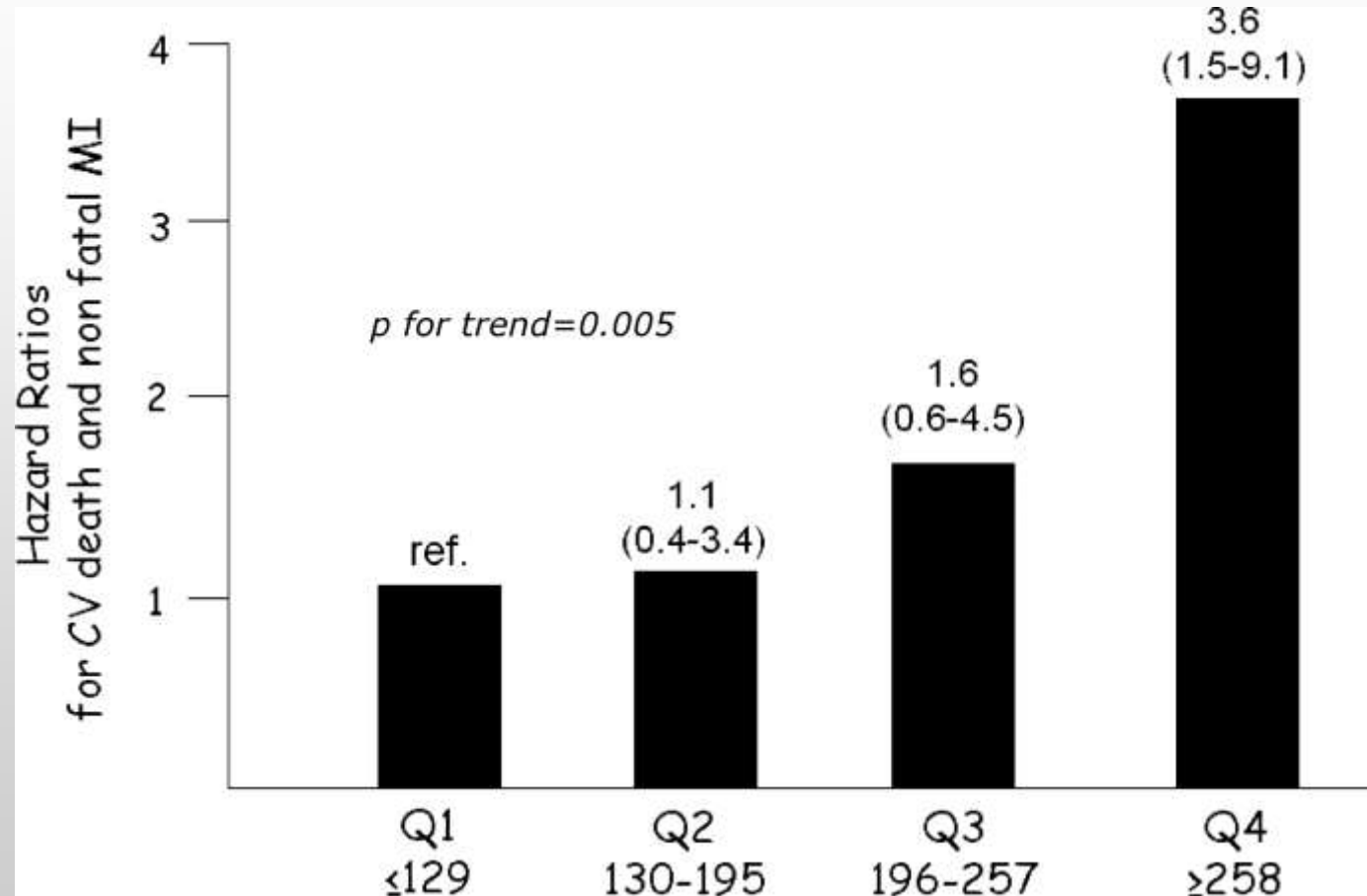
Variabilidad de la inhibición plaquetaria con clopidogrel

- 96 pts stent electivo
- CLOPI
 - 300 mg carga
 - 75 mg/d
- Ag PLA 5 uM ADP
- 'Resistencia': no reducción de la AP >10% respecto a la basal

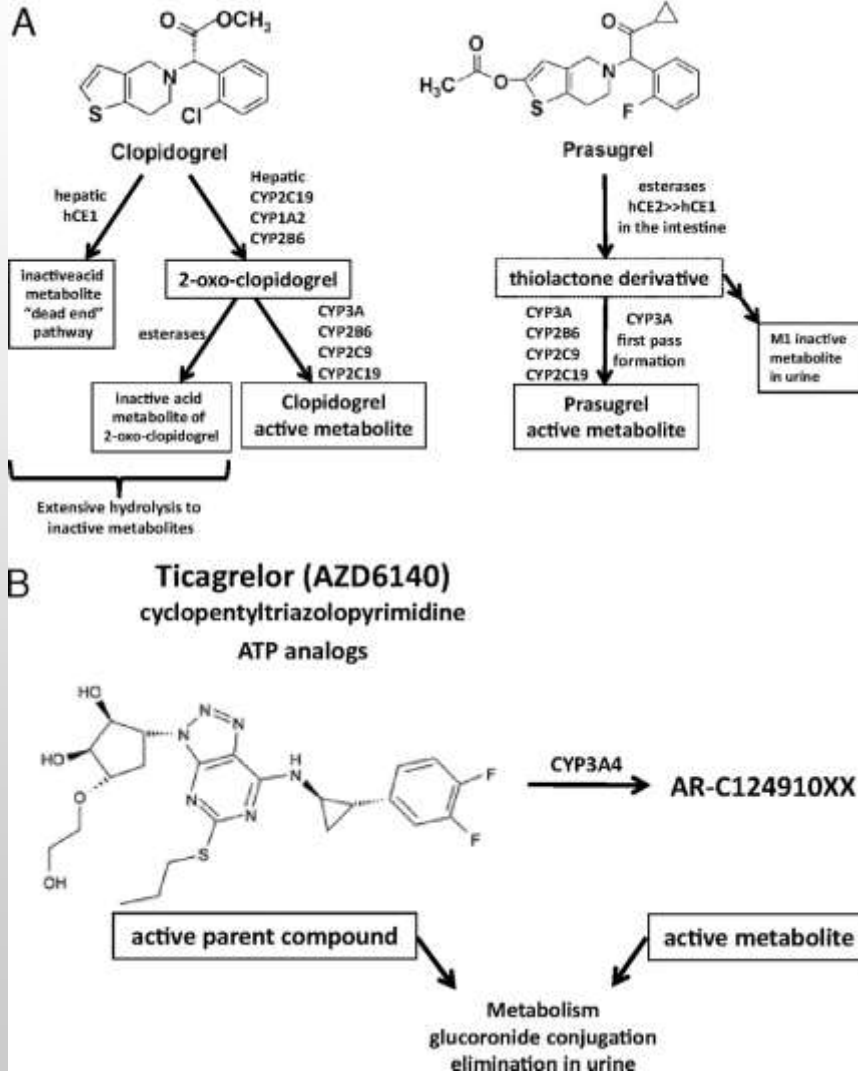


La reactividad plaquetaria residual se asocia con eventos adversos

- 683 pts SCA+stent
- CLOPI 600+75/d
- VerifyNow P2Y12 en 24 h (o 6 d)
- PRU >240: predictor de complicaciones



Clopidogrel, prasugrel y ticagrelor



CLOPIDOGREL

- pro-fármaco, metabolismo complejo
- niveles metabolito activo variables
- efecto poco predecible

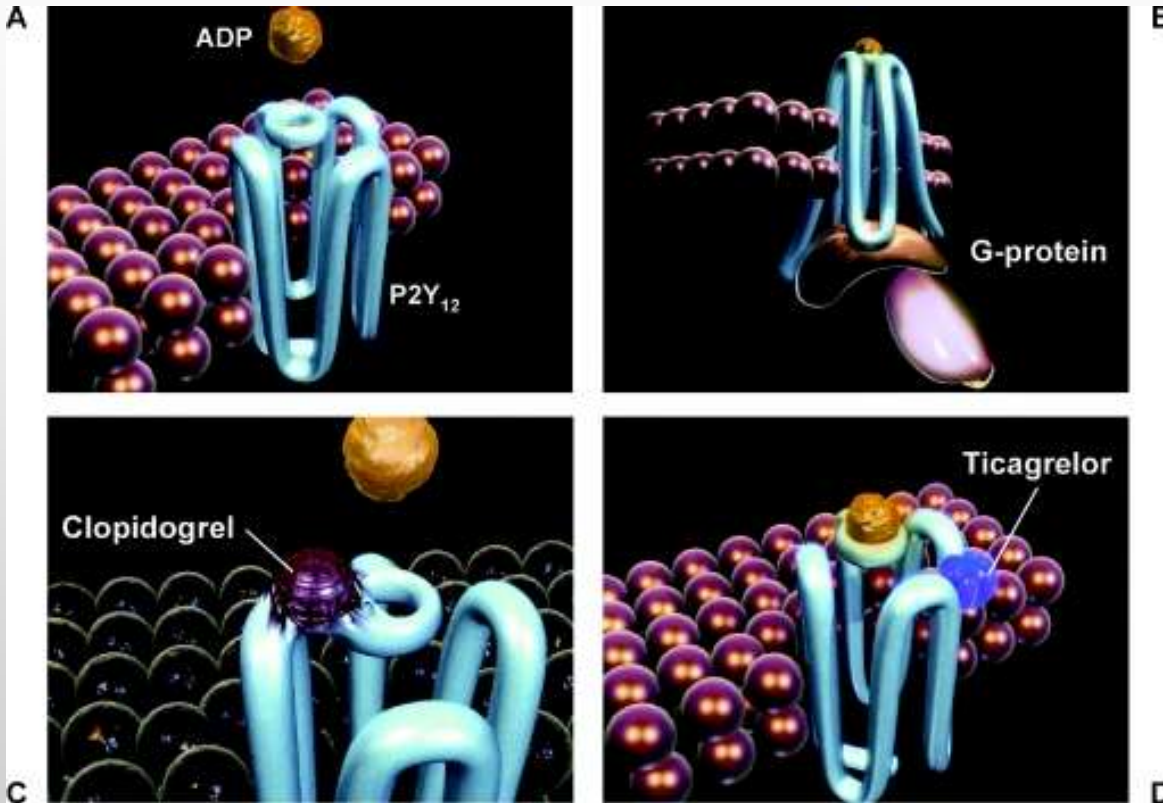
PRASUGREL

- pro-fármaco, metabolismo simple
- niveles metabolito activo predecibles
- efecto predecible

TICAGRELOR

- fármaco activo
- efecto predecible

Clonidogrel, prasugrel y ticagrelor



CLOPIDOGREL

- irreversible
- administración c/24 h

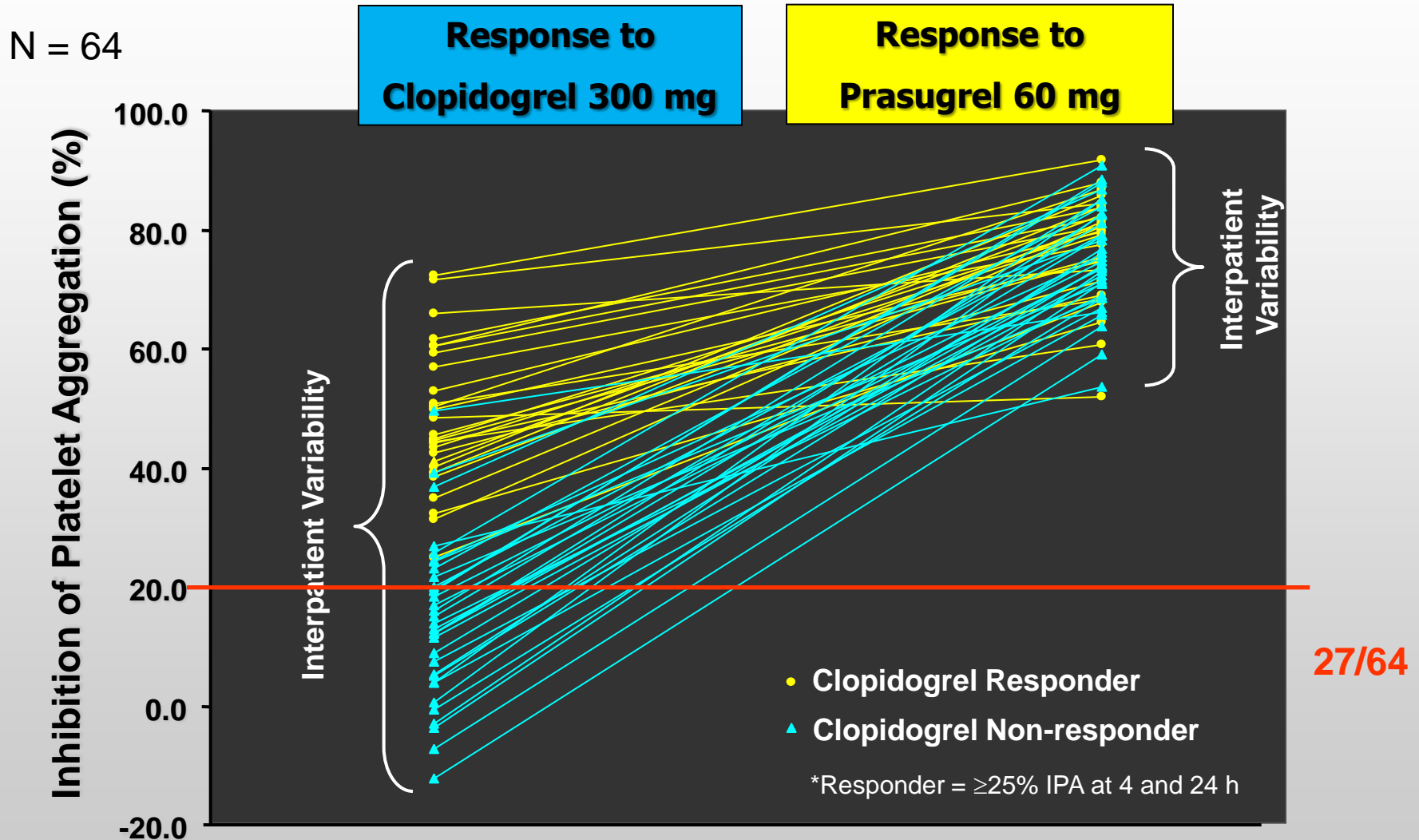
PRASUGREL

- irreversible
- administración c/24 h

TICAGRELOR

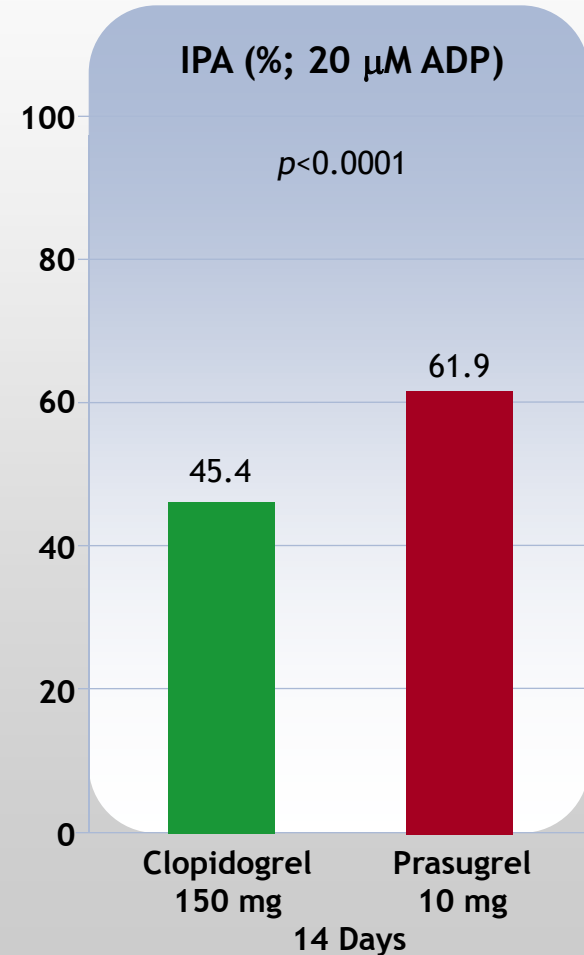
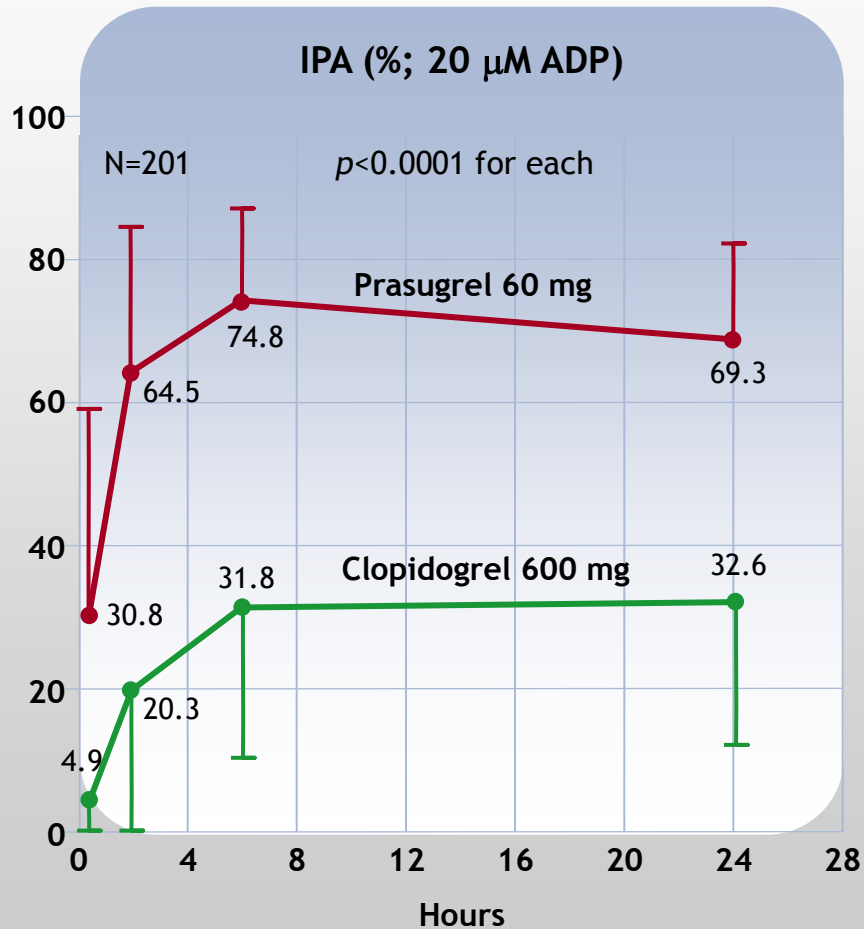
- reversible
- administración c/12 h

PRASUGREL 60 mg vs CLOPIDOGREL 300 mg Inhibición agregación plaquetar (20 uM ADP) a 24 h



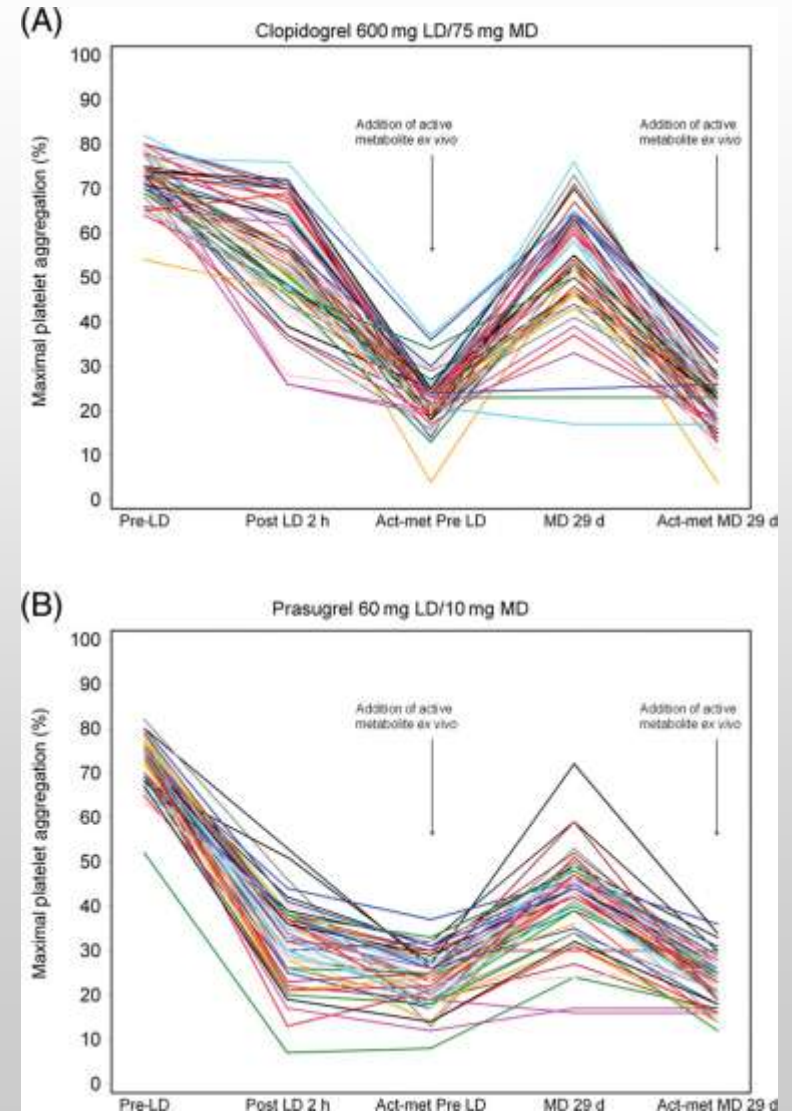
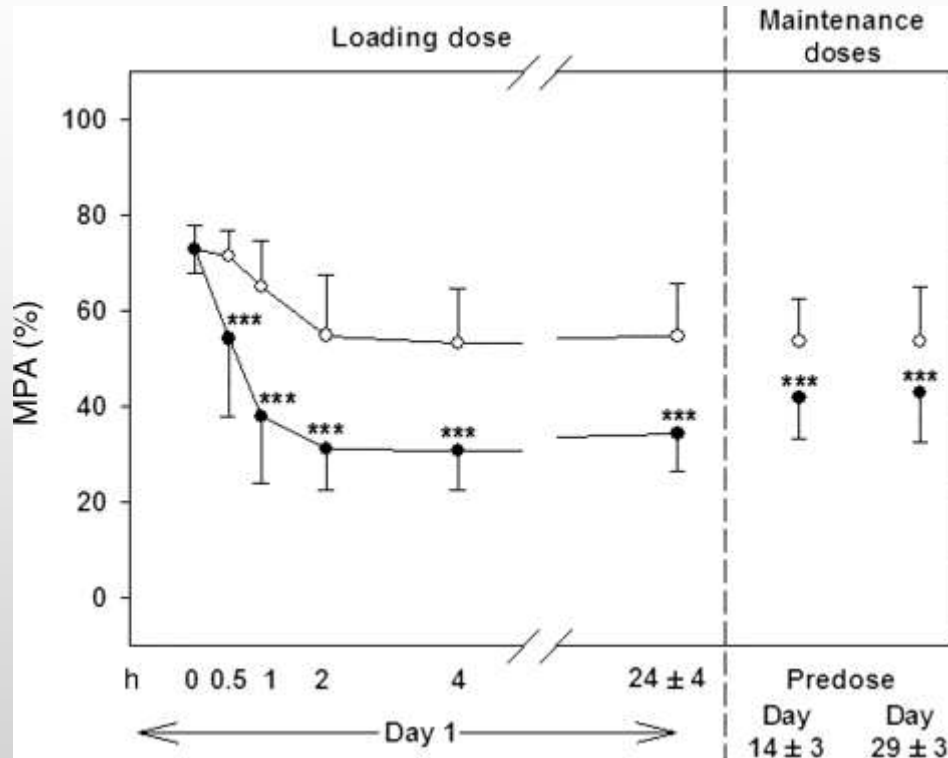
PRASUGREL 60 mg vs CLOPIDOGREL 600 mg Inhibición agregación plaquetar (20 μ M ADP)

PRINCIPLE-TIMI 44 Study



PRASUGREL 60/10 mg vs CLOPIDOGREL 600/75 mg

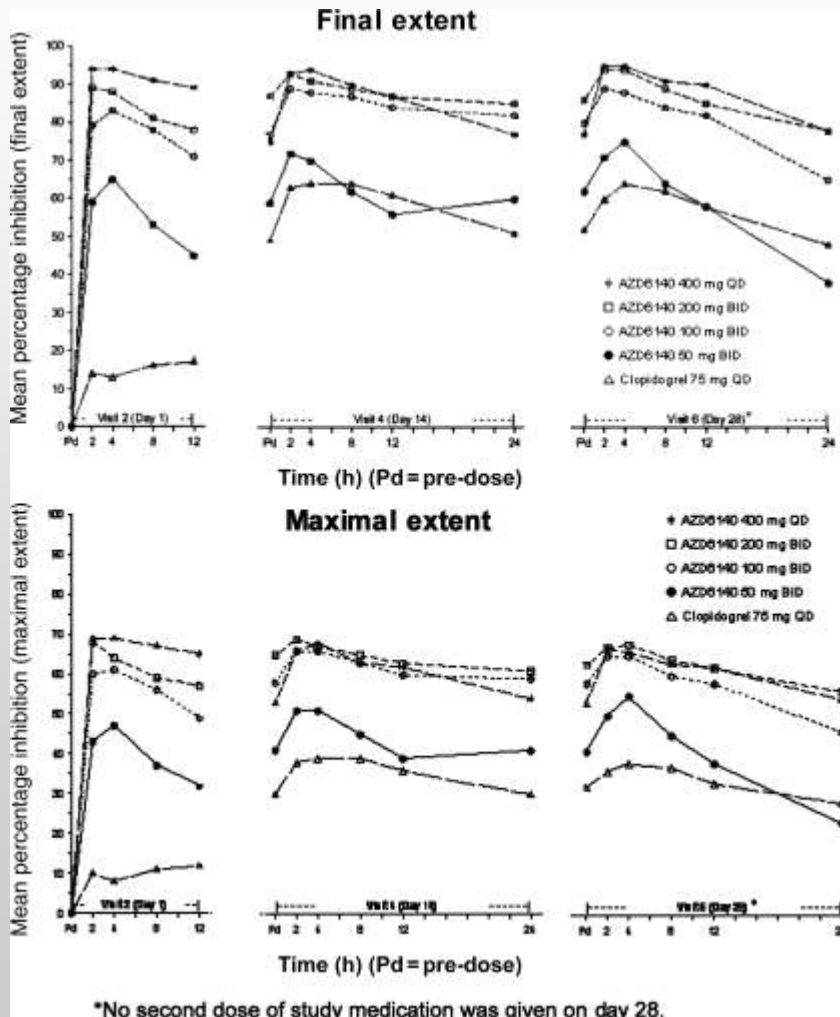
Efecto de añadir el metabolito activo



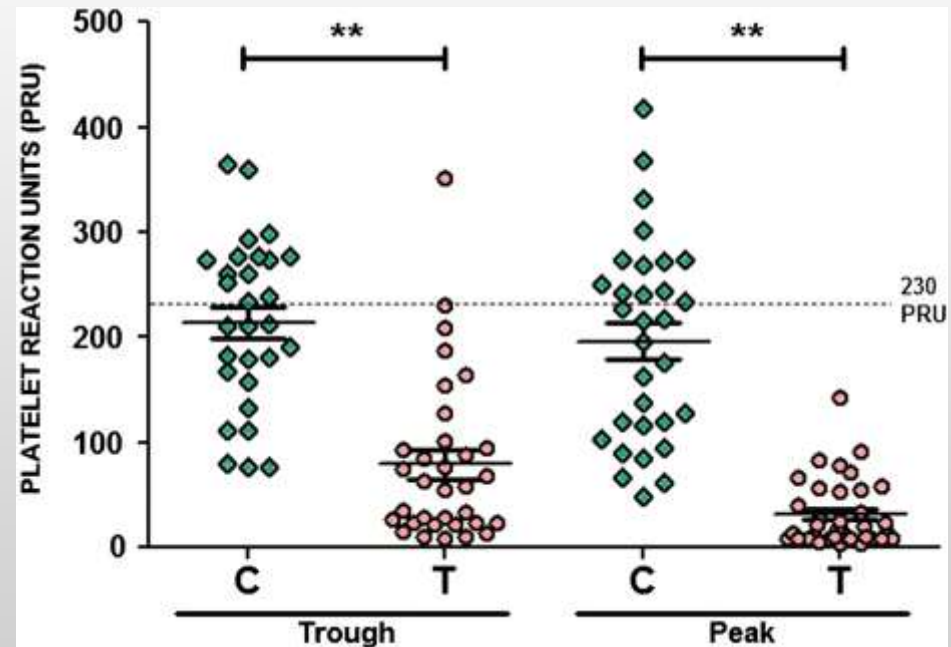
TICAGRELOR vs CLOPIDOGREL

Efecto antiagregante plaquetario

DISPERSE Study



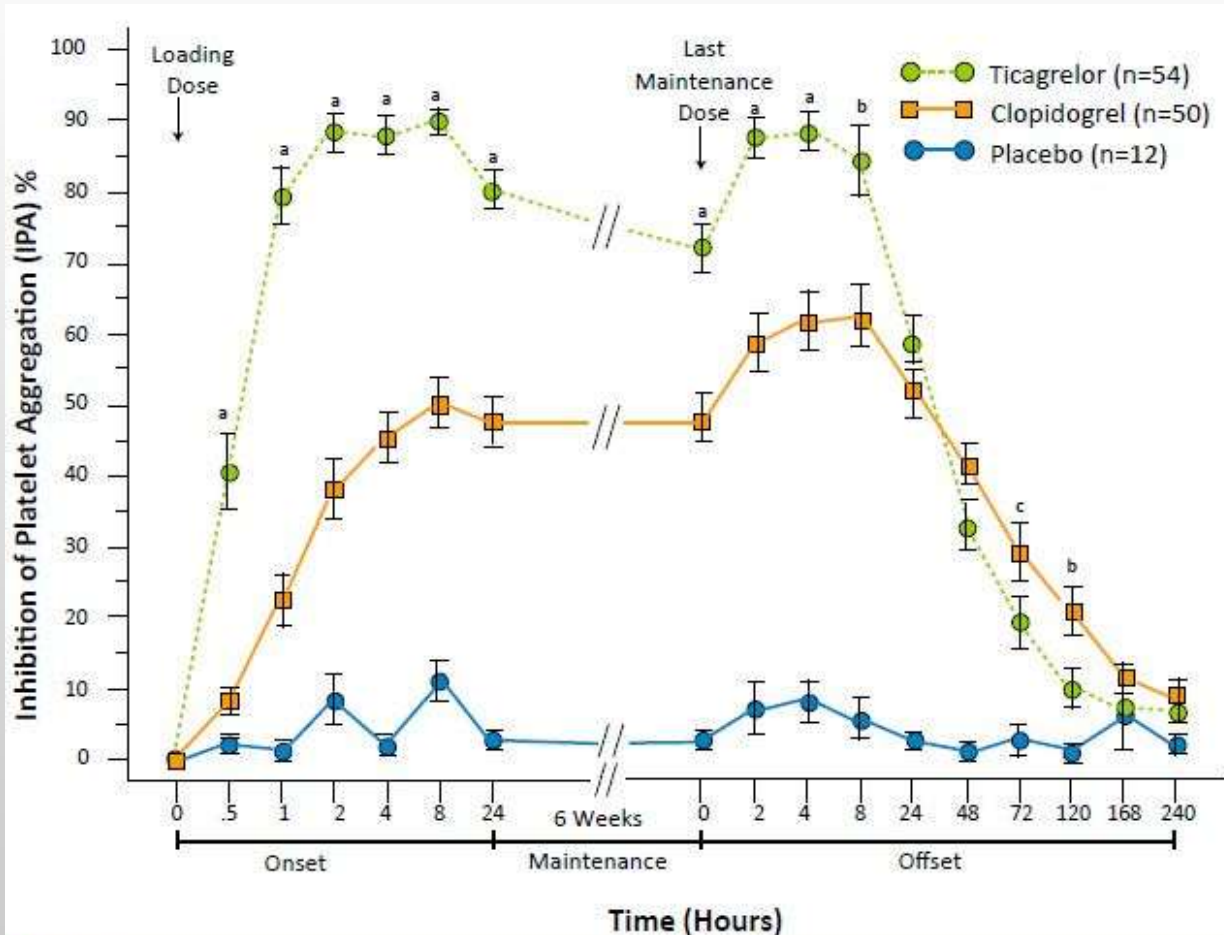
PLATO-PLATELET Substudy



TICAGRELOR vs CLOPIDOGREL

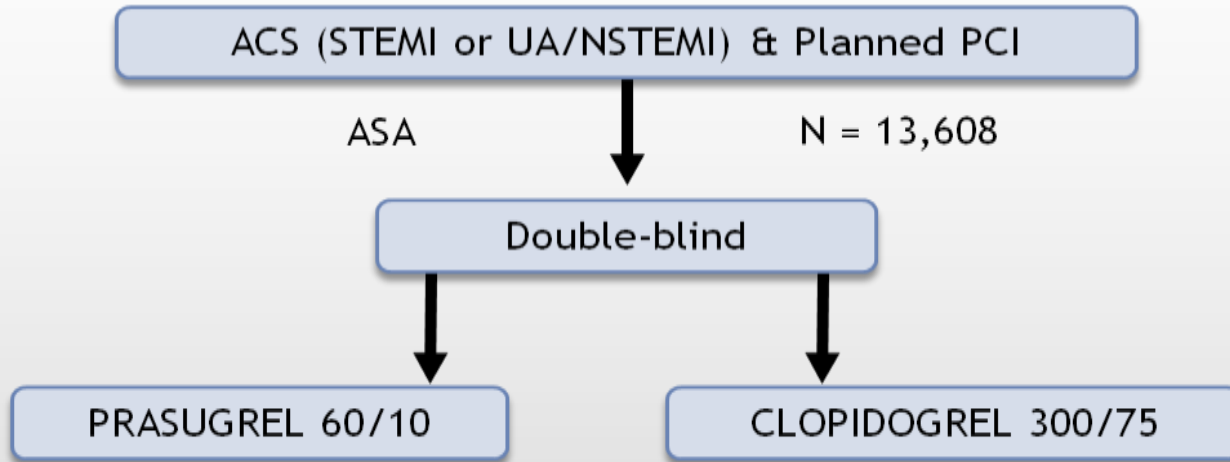
Duración efecto tras suspender el tratamiento

ONSET-OFFSET Study



- N = 123
- CI estable con AAS
- TICAGRELOR
180 mg + 90 mg/12h
- CLOPIDOGREL
600 mg + 75 mg/d
- PLACEBO

PRASUGREL vs CLOPIDOGREL en SCA tratado con ICP: TRITON-TIMI 38 Study



Duration of therapy: 6-15 months

1° endpoints:

2° endpoint:

Safety:

CV death, MI, Stroke

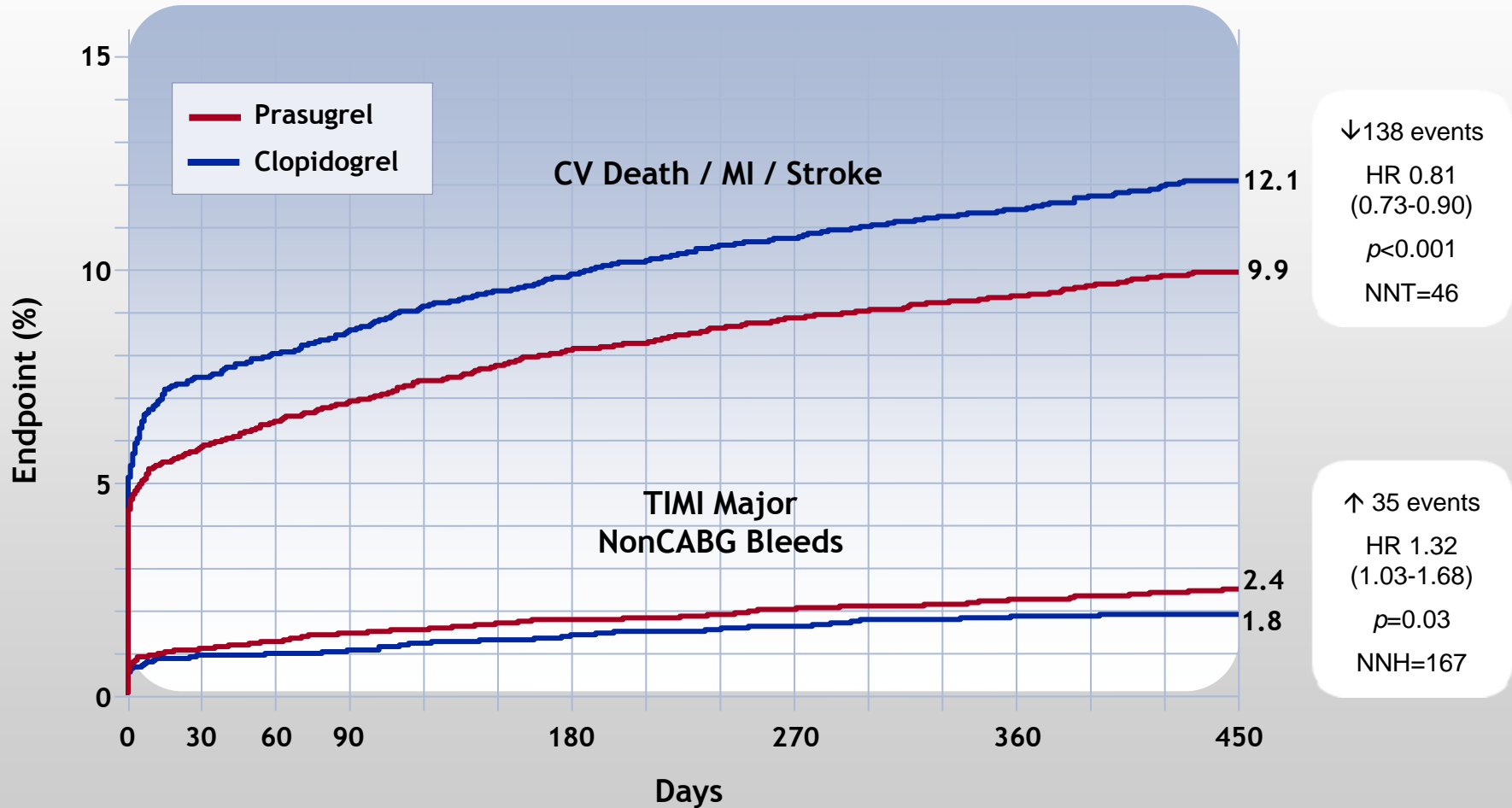
Stent thrombosis

TIMI major bleed, life-threatening bleed

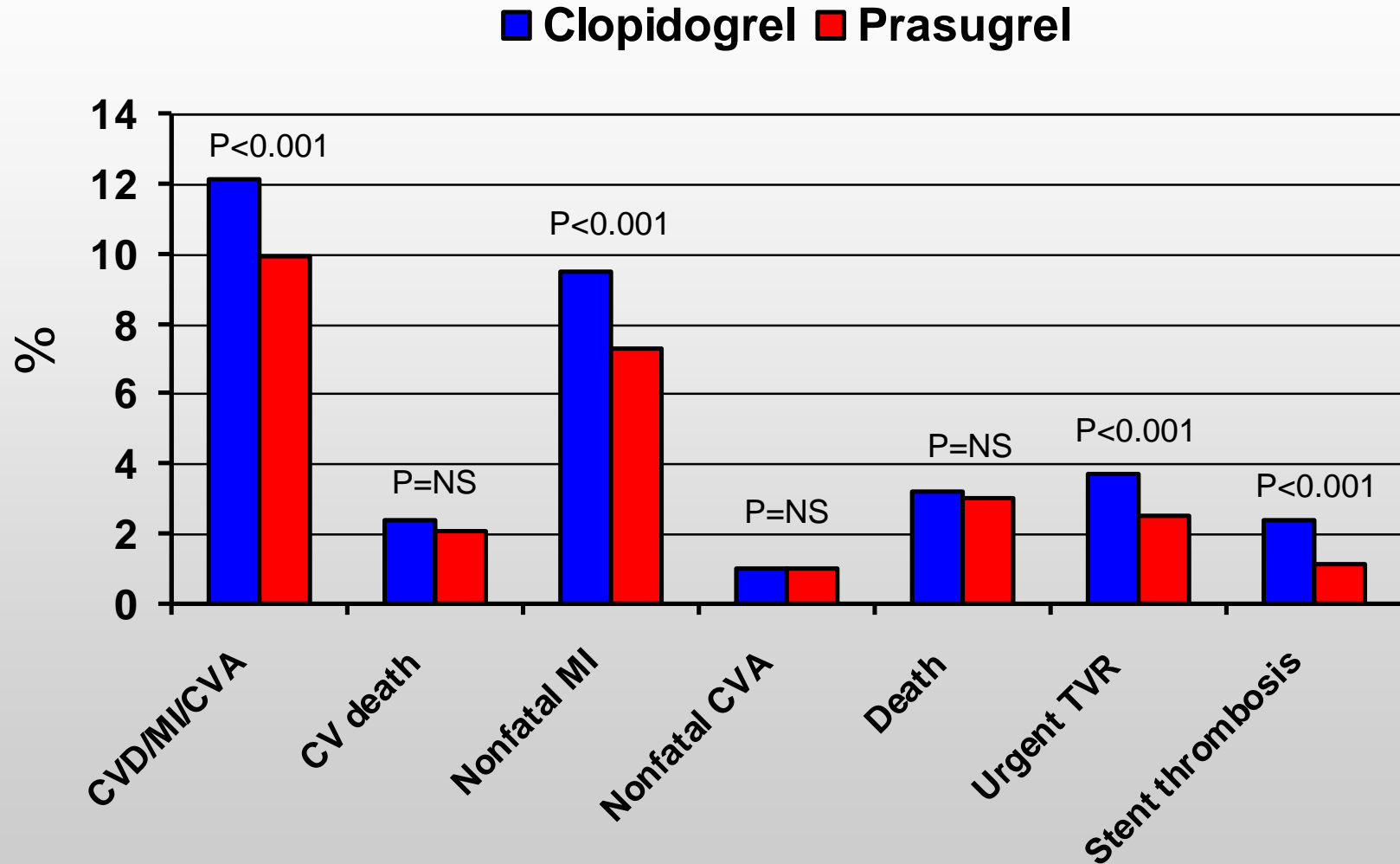
Wiviott SD et al. Am Heart J 2006;152:627-35

Wiviott SD et al. N Engl J Med 2007;357:2001-15

PRASUGREL 60/10 vs CLOPIDOGREL 300/75 en SCA tratado con ICP: TRITON-TIMI 38 Study

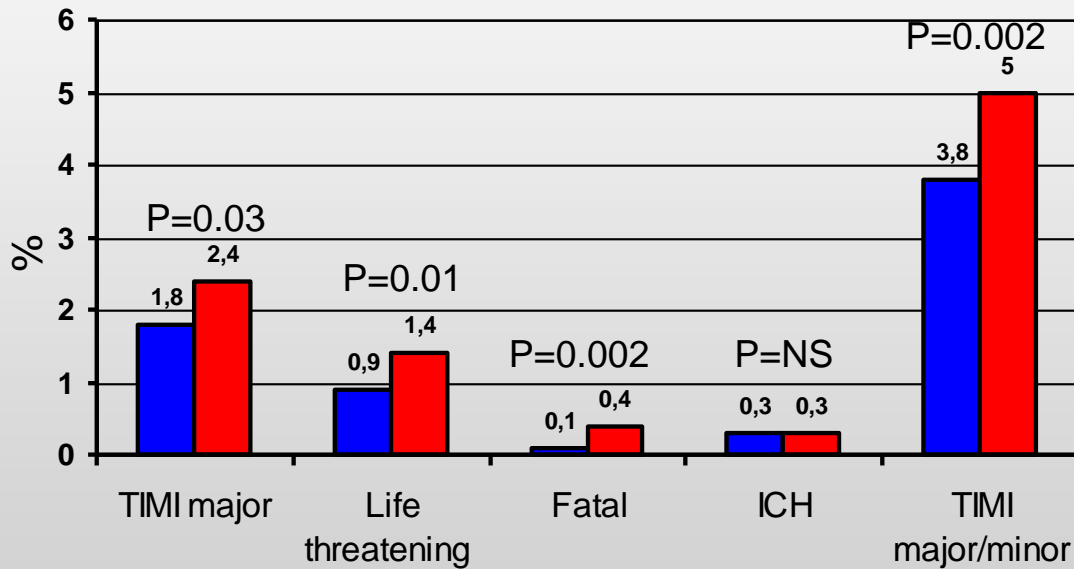


TRITON-TIMI 38 Study: Efficacy end points

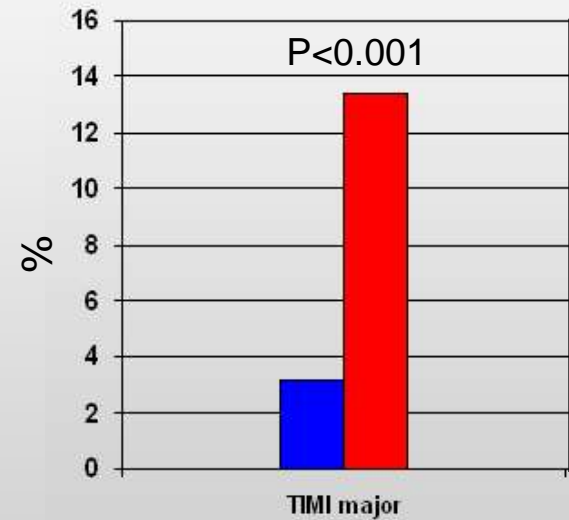


TRITON-TIMI 38 Study: Bleeding end points

■ Clopidogrel ■ Prasugrel



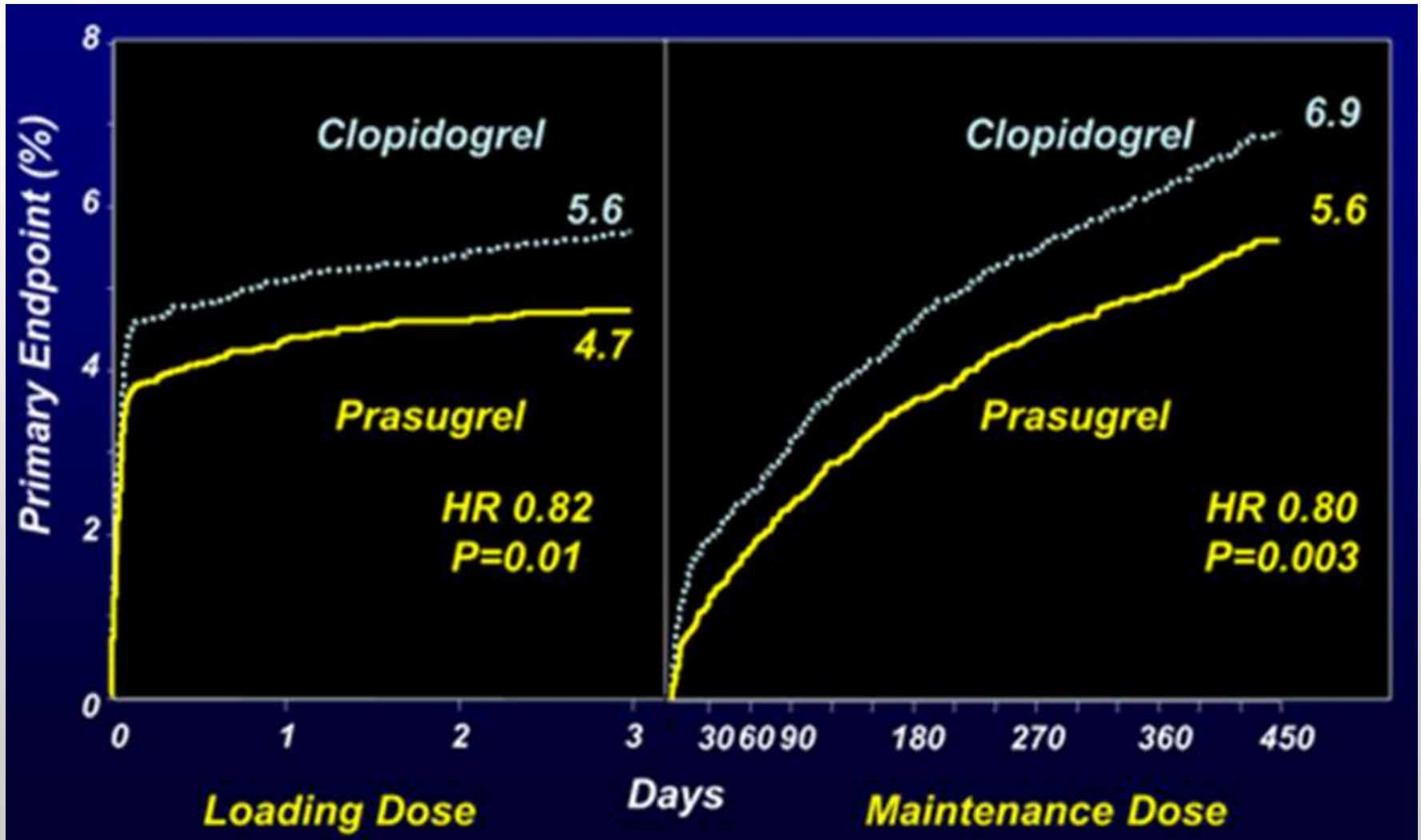
Non-CABG-related



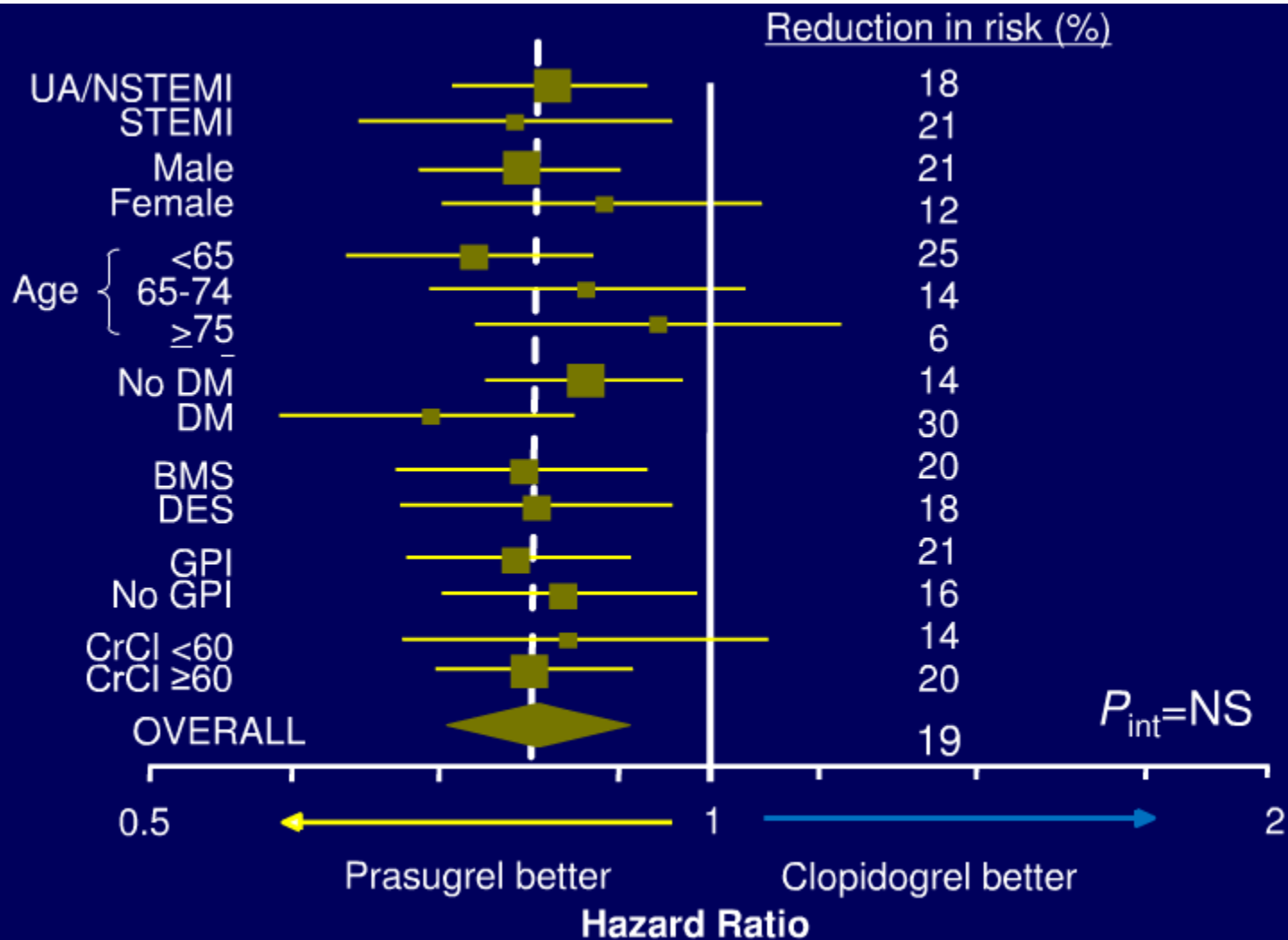
CABG-related

ICH in pts w/ previous stroke/TIA (n=518):
0 vs 2.3% (P=0.02)

TRITON-TIMI 38 Study: Timing of benefit

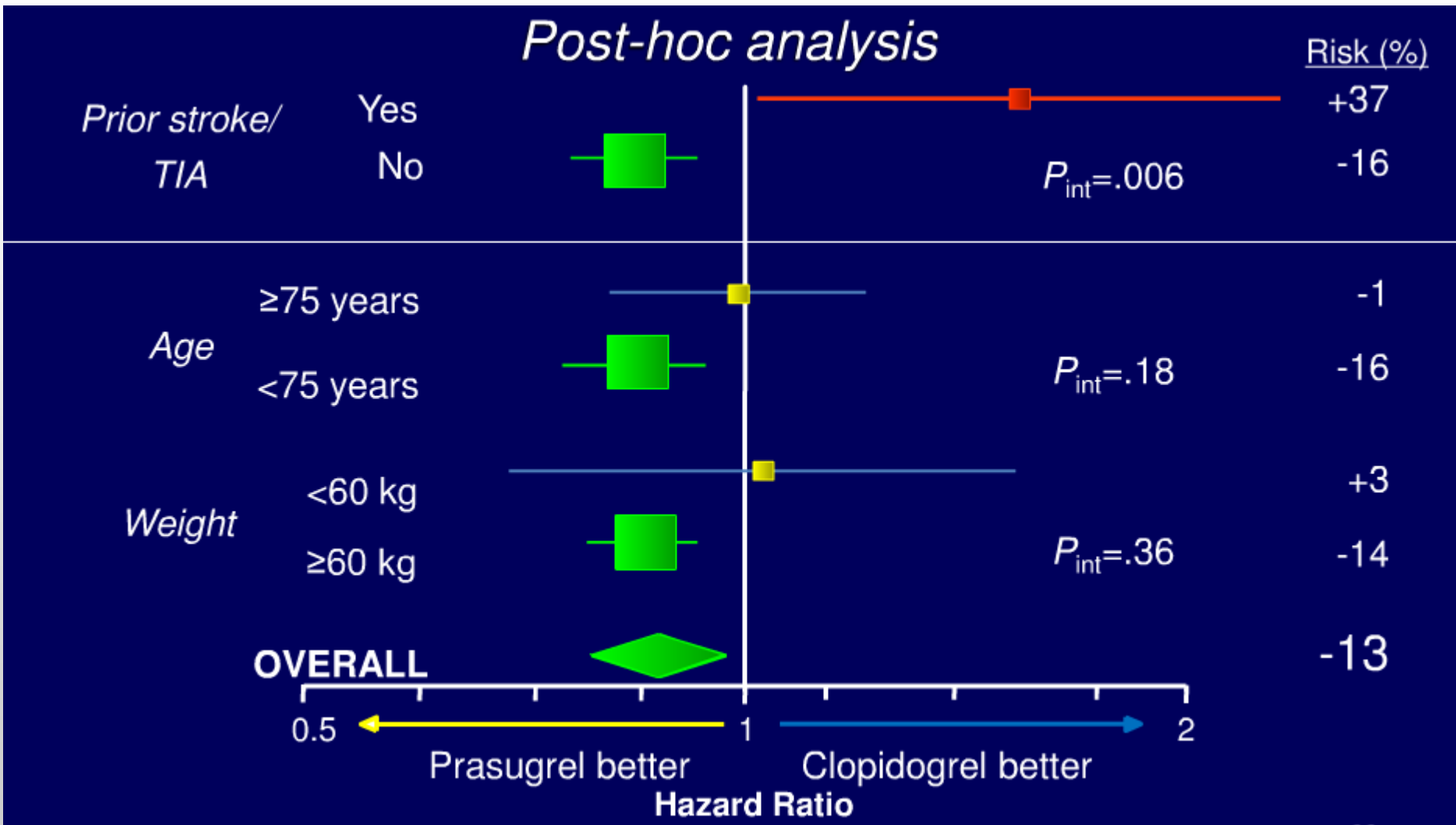


TRITON-TIMI 38 Study: Subgroup analysis



TRITON-TIMI 38 Study

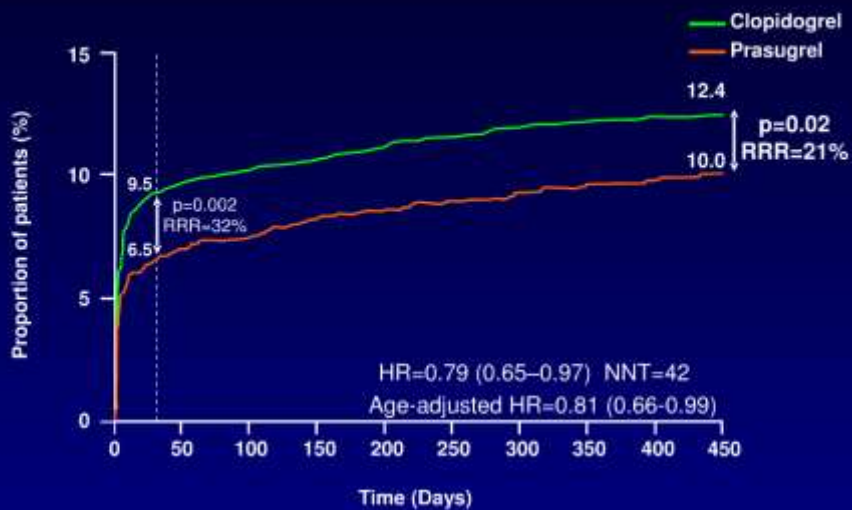
Subgroup analysis by bleeding risk



TRITON-TIMI 38 Study STEMI cohort

TRITON TIMI-38 STEMI cohort

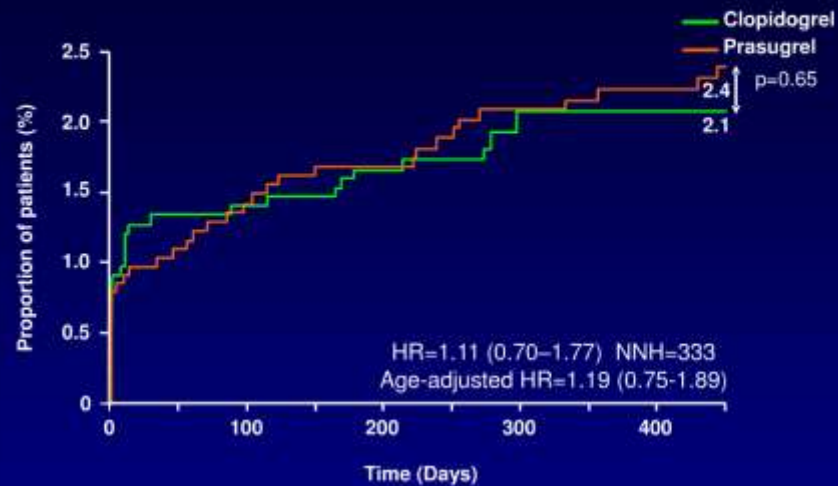
Primary EP (CV death, MI and stroke at 15 months)



Montalescot et al. ESC 2008

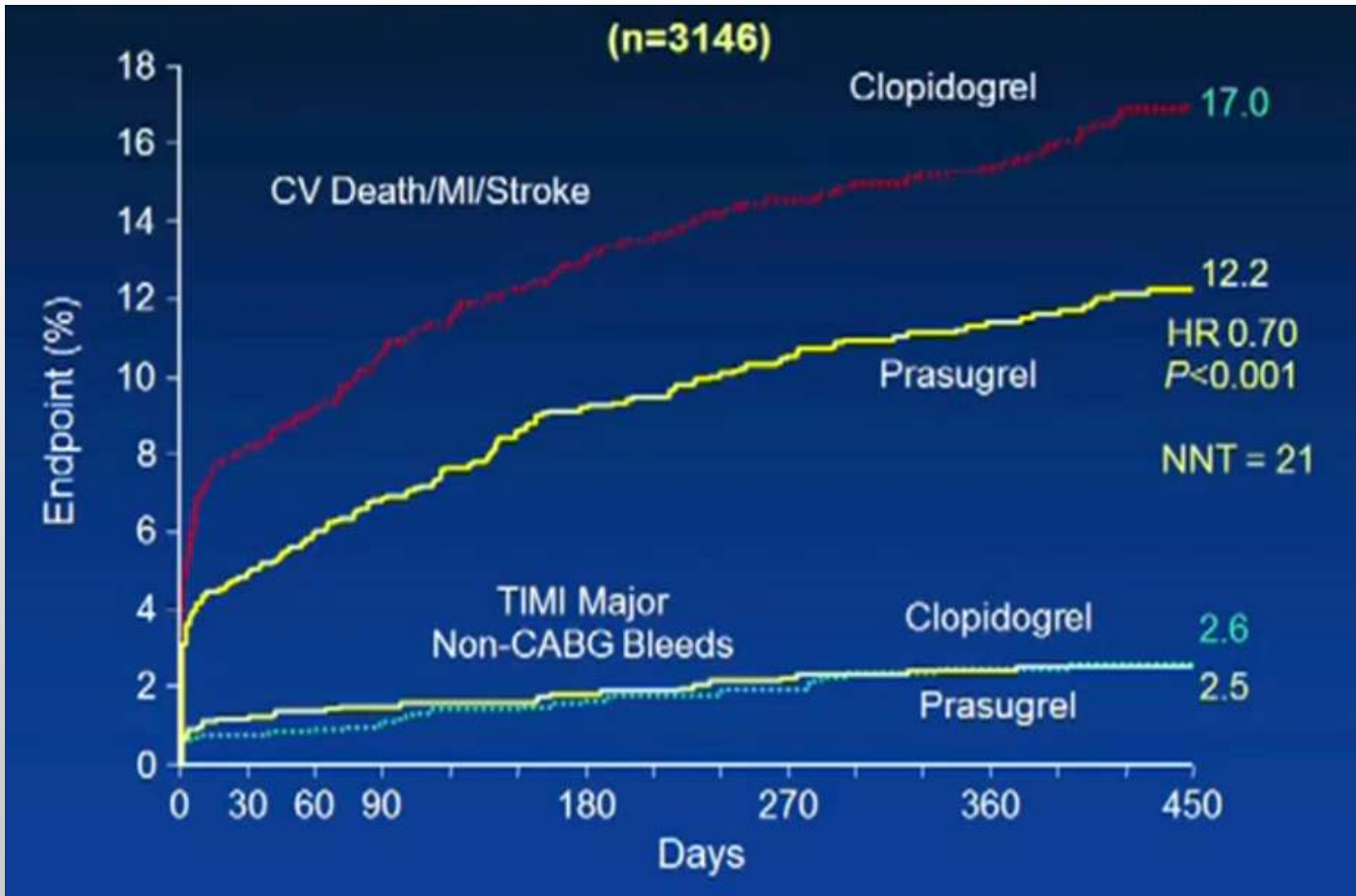
TRITON TIMI-38 STEMI cohort

TIMI major non-CABG bleeding

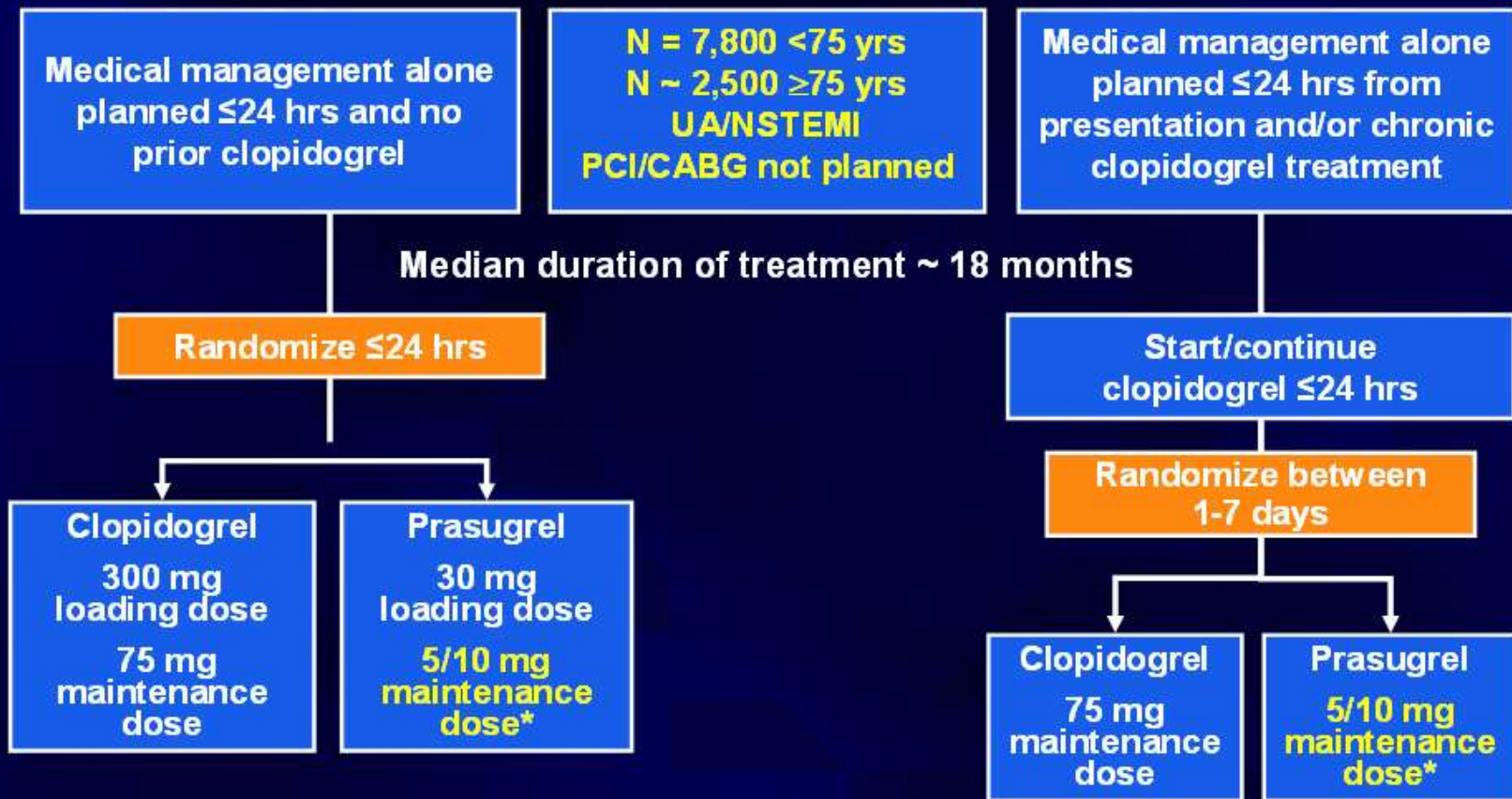


Montalescot et al. ESC 2008

TRITON-TIMI 38 Study Diabetic subgroup



TRILOGY ACS: Study design



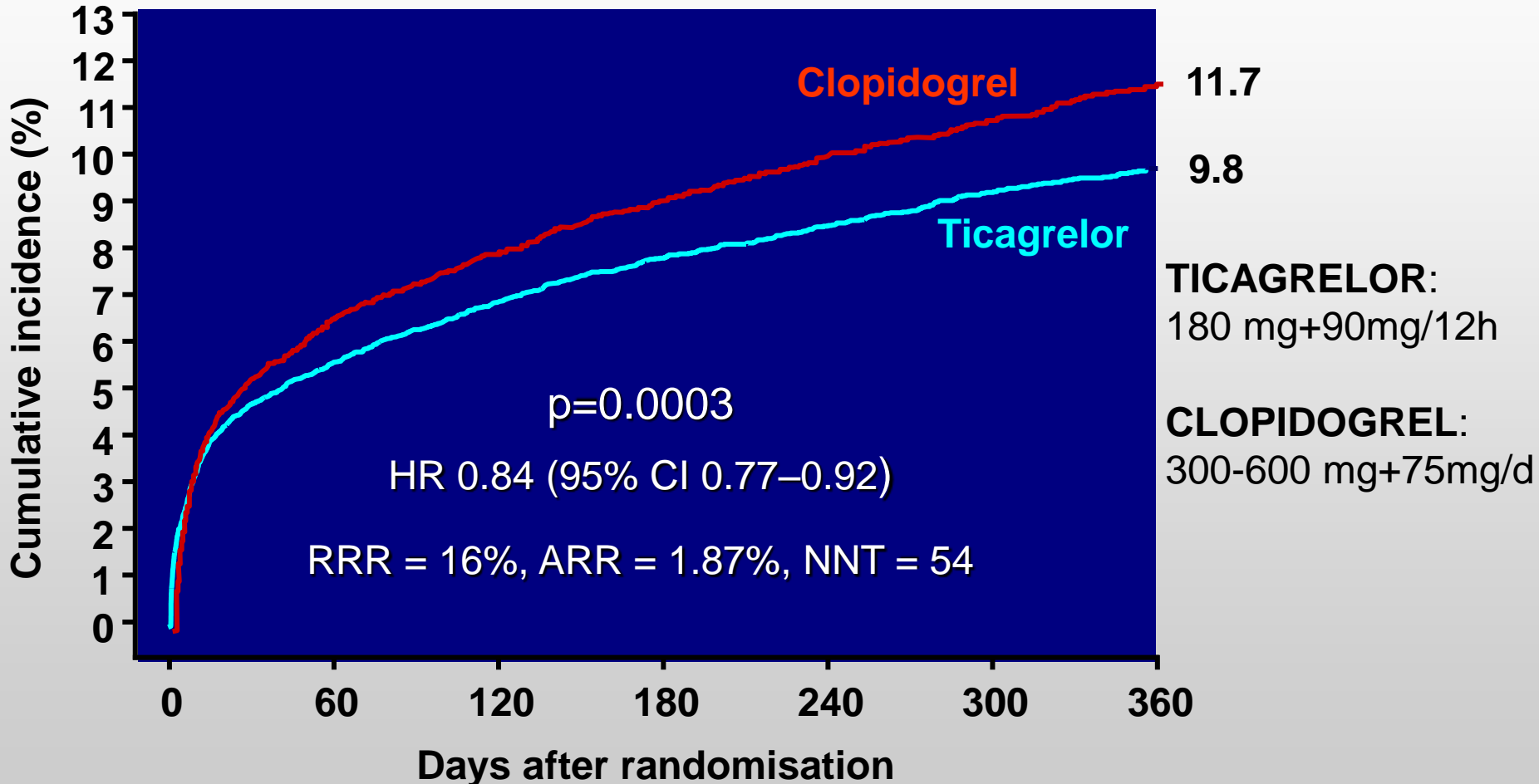
*5 mg maintenance dose of prasugrel for age ≥75 yrs or weight <60 kg

Courtesy of MT Roe, MD
NIH. www.clinicaltrials.gov.

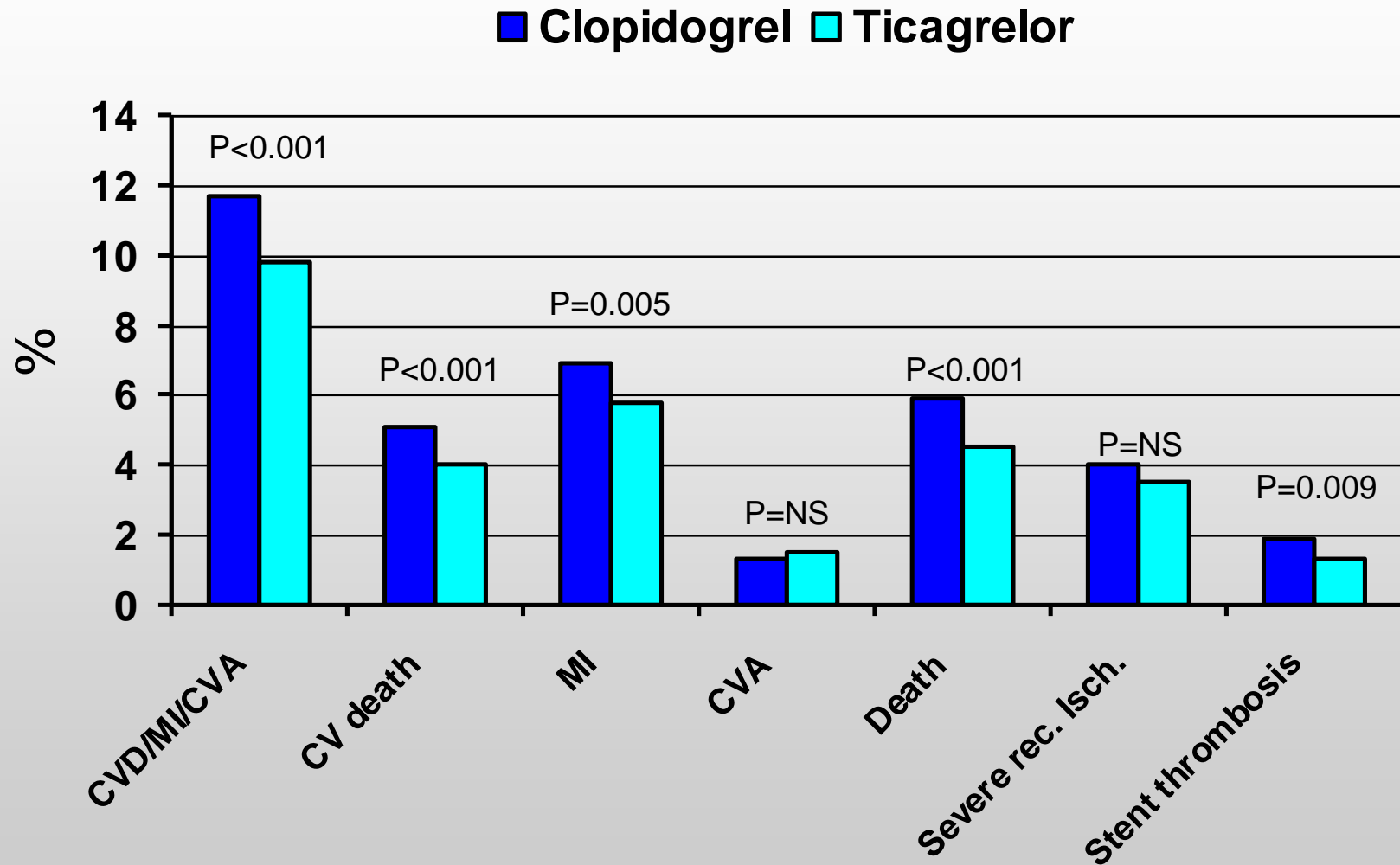
Ticagrelor vs. clopidogrel en pacientes con SCA: PLATO Study

N=18.624

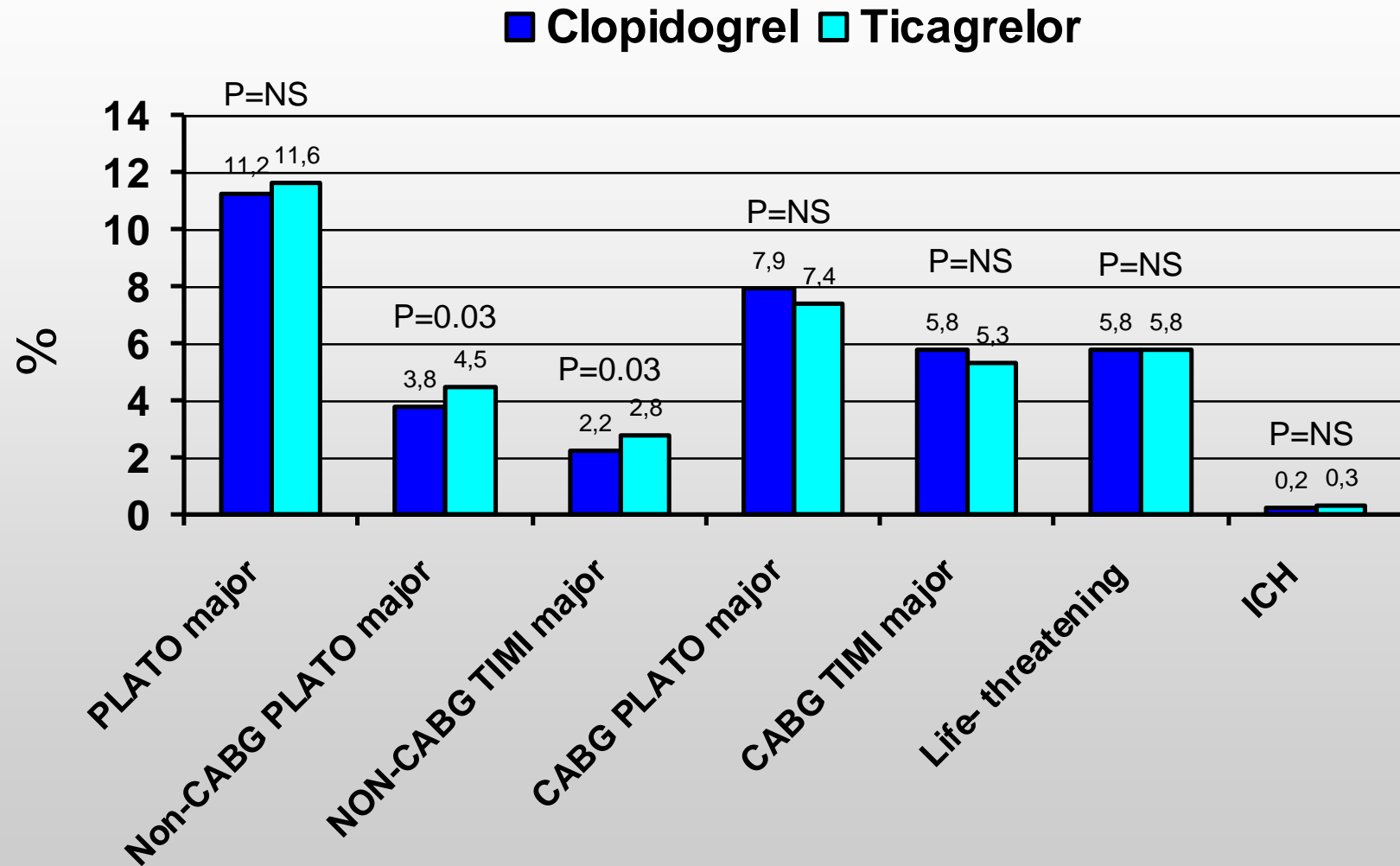
CV death, MI or stroke



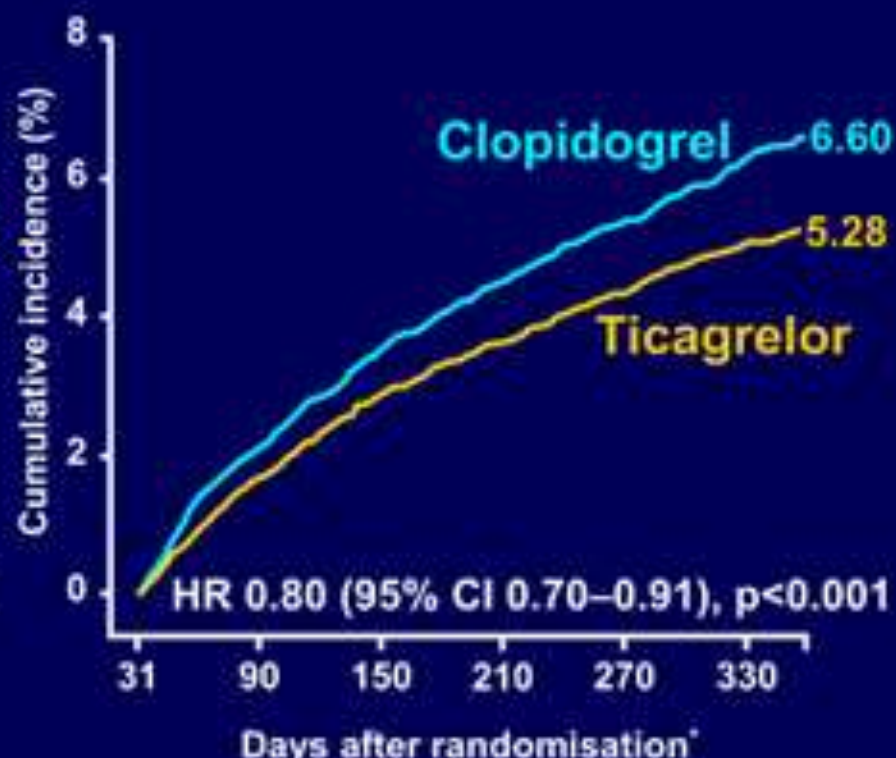
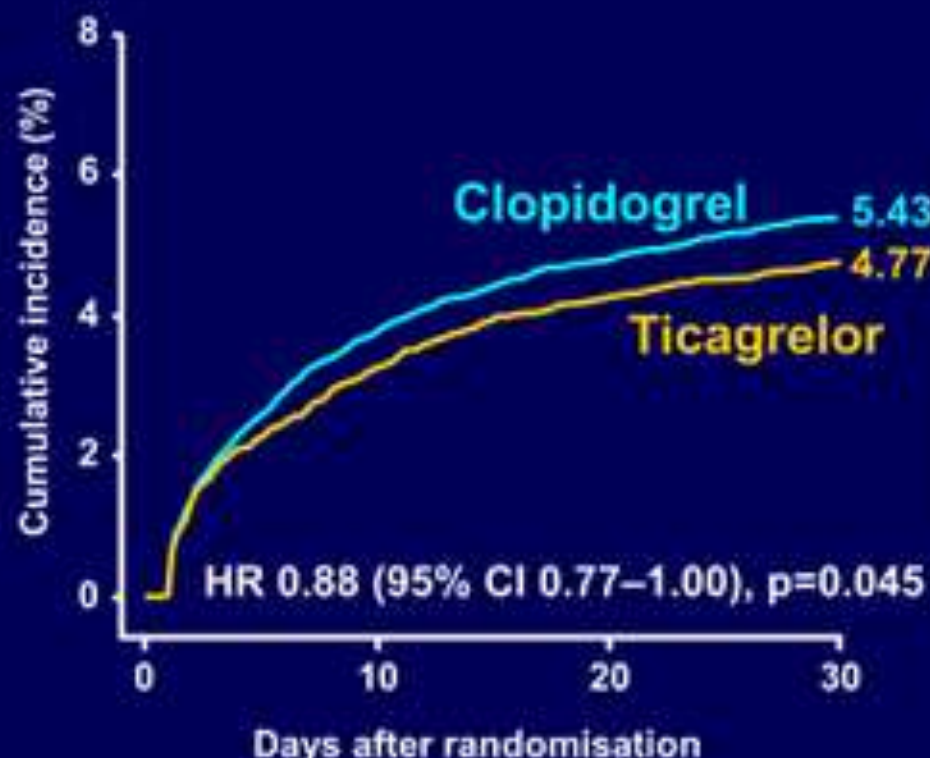
PLATO Study: Efficacy end points



PLATO Study: Bleeding end points



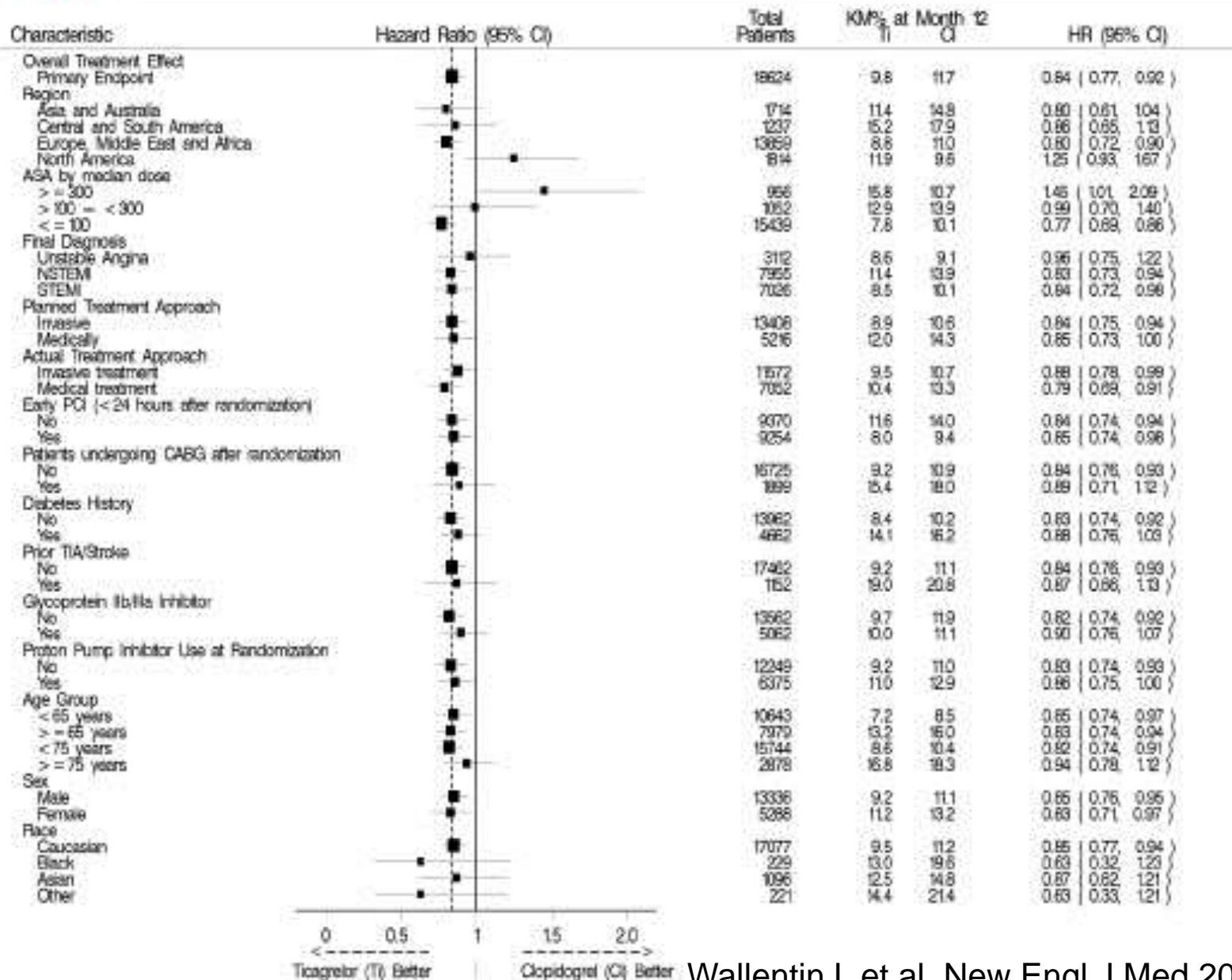
Primary efficacy endpoint over time (composite of CV death, MI or stroke)



No. at risk	0	10	20	30	31	90	150	210	270	330
Ticagrelor	9,333	8,942	8,827	8,763	8,673	8,543	8,397	7,028	6,480	4,822
Clopidogrel	9,291	8,875	8,763	8,688	8,688	8,437	8,286	6,945	6,379	4,751

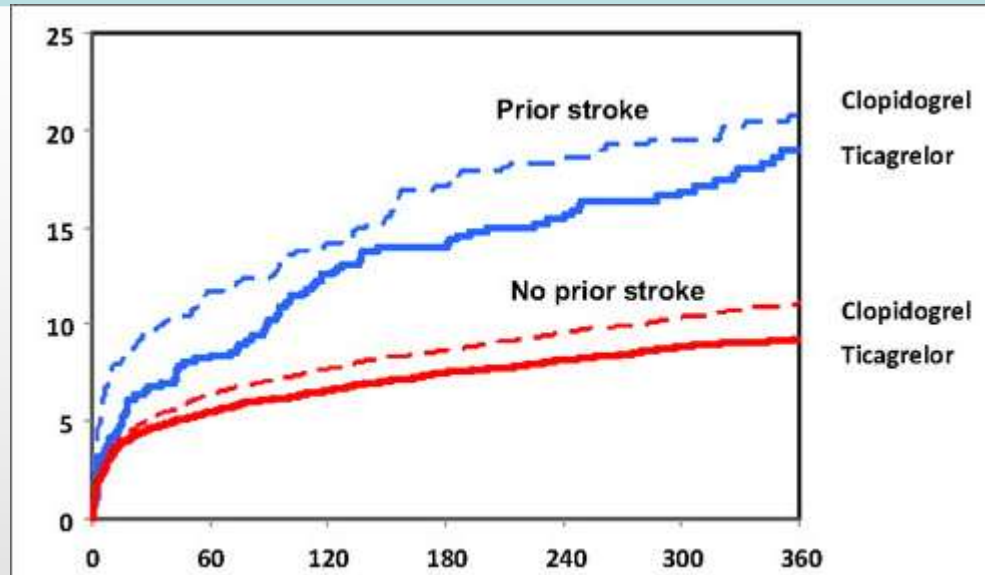
*Excludes patients with any primary event during the first 30 days

PLATO Study: Subgroup analysis

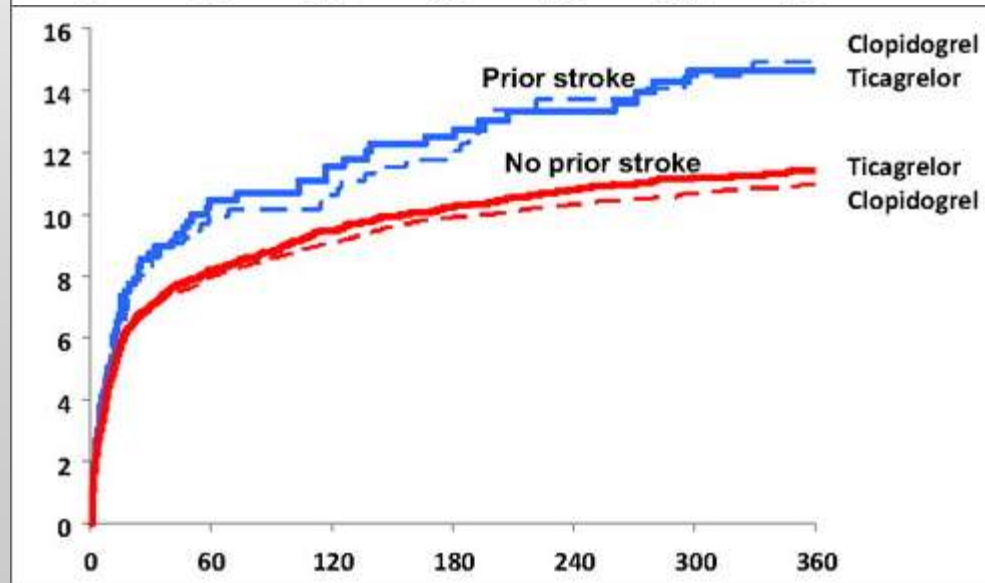


PLATO Study: Patients with prior stroke

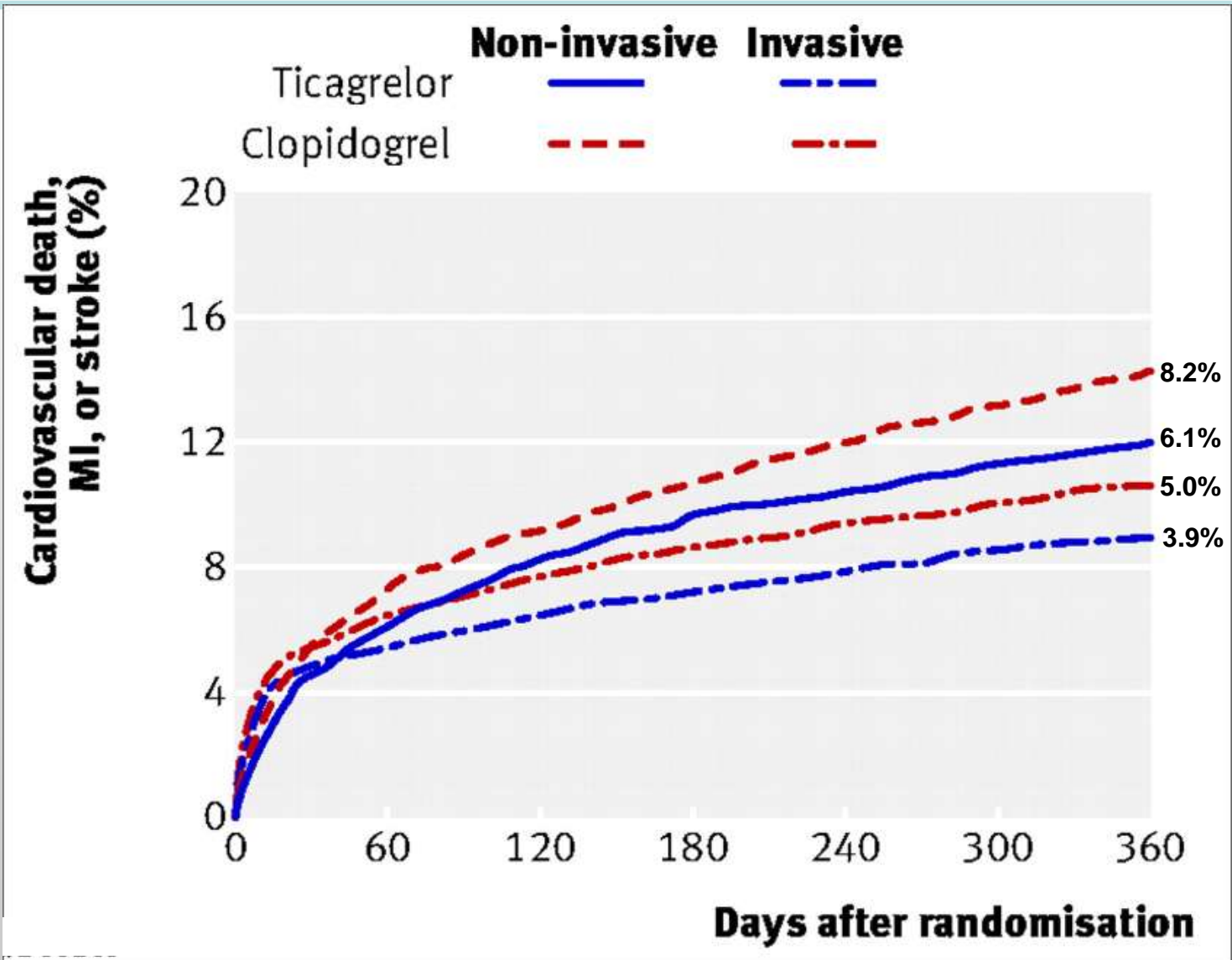
**Primary
endpoint**



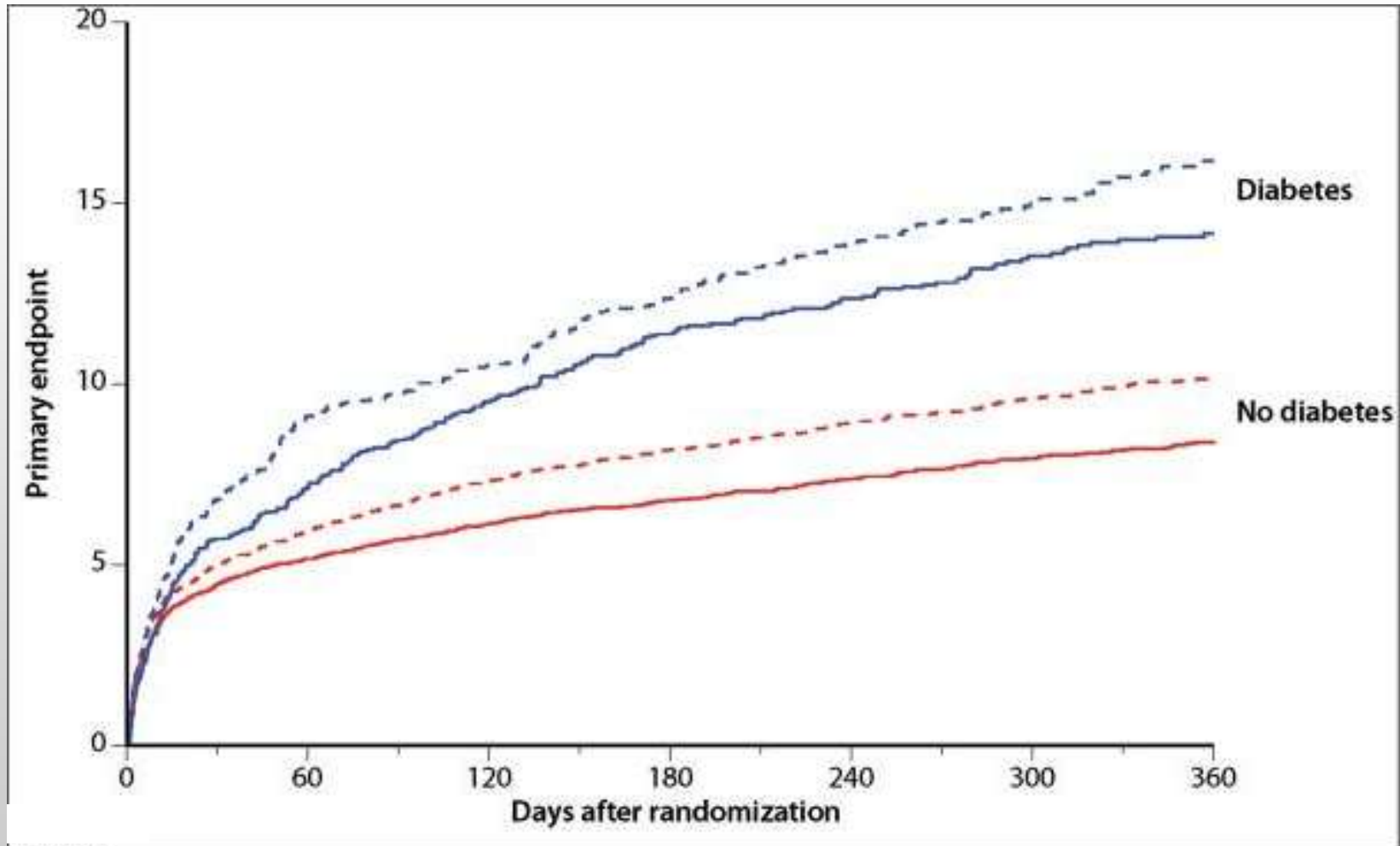
**Major
bleeding**



PLATO Study: Invasive vs noninvasive strategy



PLATO Study: Diabetic subgroup



PLATO: Ventricular Pauses and Dyspnea

	Ticagrelor (n = 9235)	Clopidogrel (n = 9186)	<i>P</i> value
Ventricular pauses \geq 3 sec First week	5.8% 84/1451	3.6% 51/1415	.01
Ventricular pauses \geq 3 sec At 30 days	2.1% 21/985	1.7% 17/1006	.52
Dyspnea	13.8% 1270/9235	7.8% 721/9186	< .001

TRITON vs PLATO: Diferencias metodológicas

	TRITON	PLATO
POBLACIÓN	SCA que se trata con ICP	SCA (manejo invasivo o no)
TTO PREVIO	No	Permitido
Dosis clopidogrel	300 mg	300-600 mg
CABG	2.7%	10.2%
Manejo médico	0%	16.9%
Duración estudio (mediana)	14.5 meses	9 meses

Prasugrel vs clopidogrel: contraindicaciones y precauciones

	PRASUGREL	CLOPIDOGREL
CONTRAINDICACIONES	Alto riesgo sangrado	Alto riesgo sangrado
	Ictus hemorrágico previo	Ictus hemorrágico previo
	ACV/AIT previo	Disfunción hepática severa
PRECAUCIONES	Ancianos	Posible cirugía próxima
	Bajo peso	Bradiarritmia
	Posible cirugía próxima	Hiperuricemia
		Drogas CYP-450 3A

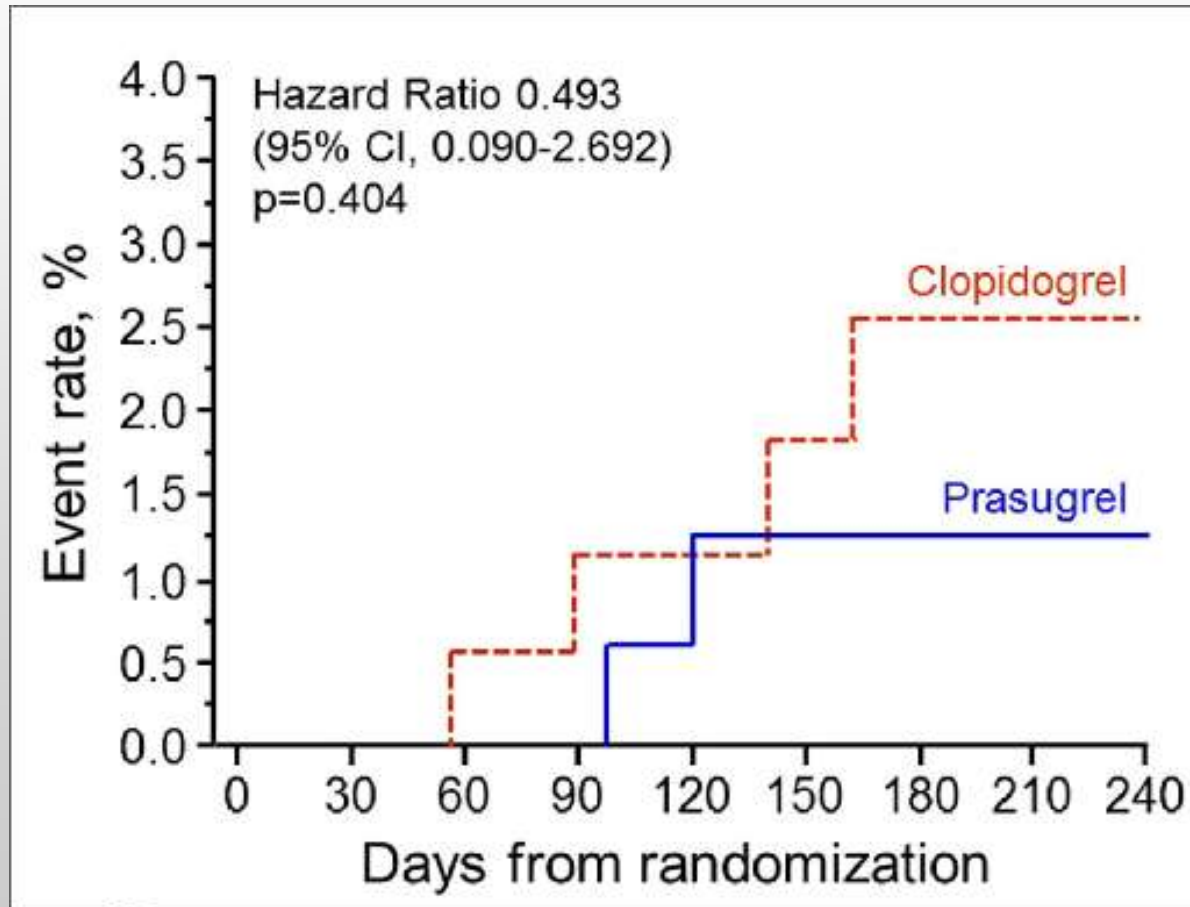
Prasugrel vs clopidogrel: indicaciones

<p>Ticagrelor (180-mg loading dose, 90 mg twice daily) is recommended for all patients at moderate-to-high risk of ischaemic events (e.g. elevated troponins) , regardless of initial treatment strategy and including those pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced).</p>	I	B
<p>Prasugrel (60-mg loading dose, 10-mg daily dose) is recommended for P2Y₁₂-inhibitor-naïve patients (especially diabetics) in whom coronary anatomy is known and who are proceeding to PCI unless there is a high risk of life-threatening bleeding or other contraindications.^d</p>	I	B
<p>Clopidogrel (300-mg loading dose, 75-mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel.</p>	I	A

Prasugrel vs clopidogrel: sólo en SCA!!

TRIGGER PCI Study

423 pts tras SFA por CI estable y con reactividad plaquetaria elevada con clopidogrel



Muchas gracias