Tratamiento antiagregante en la trombosis del stent

Alvaro Merino Otermin

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Stent Thrombosis

David R. Holmes, JR, MD,* Dean J. Kereiakes, MD,† Scot Garg, MD,§
Patrick W. Serruys, MD, PHD,§ Gregory J. Dehmer, MD,‖ Stephen G. Ellis, MD,‡
David O. Williams, MD,¶ Takeshi Kimura, MD,# David J. Moliterno, MD**

ARC Definition of ST to Standardize ST and Ensure Unified Assessment Across Trials

Term	Definition
"Definite" ST	The highest level of certainty Either angiographic or post-mortem evidence of thrombotic stent occlusion
"Probable" ST	Any unexpected death within 30 days of stent implantation, or any myocardial infarction in the territory of the implanted stent irrespective of time
"Possible" ST	Any unexplained death beyond 30 days until the end of follow-up
Early ST	ST occurring in the first 30 days after stent implantation
Late ST	ST occurring between 1 month and 1 yr after stent implantation
Very late ST	ST occurring beyond 1 yr

JACC Vol. 56, No. 17, 2010 October 19, 2010:1357–65

JACC White Paper

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Selected Multifactorial Causes of ST

	Precipitant of Stent Thrombosis
Stent factors	Hypersensitivity to drug coating or polymer Incomplete endothelialization Stent design Covered stents (64,65)
Patient factors	PCI for acute coronary syndrome/ST-segment elevation MI Diabetes mellitus Renal failure Impaired left ventricular function Premature cessation of dual antiplatelet therapy Aspirin nonresponsiveness Clopidogrel nonresponsiveness Glycoprotein IIb/IIIa inhibitors Prior brachytherapy Malignancy Saphenous vein graft disease
Lesion characteristics	Lesion/stent length Vessel/stent diameter Complex lesions (bifurcation lesions, chronic total occlusions) Saphenous vein graft target lesion Stasis
Procedural factors	Inadequate stent expansion/sizing Incomplete stent apposition Stent deployment in necrotic core Residual edge dissection

JACC Vol. 56, No. 17, 2010 October 19, 2010:1357–65

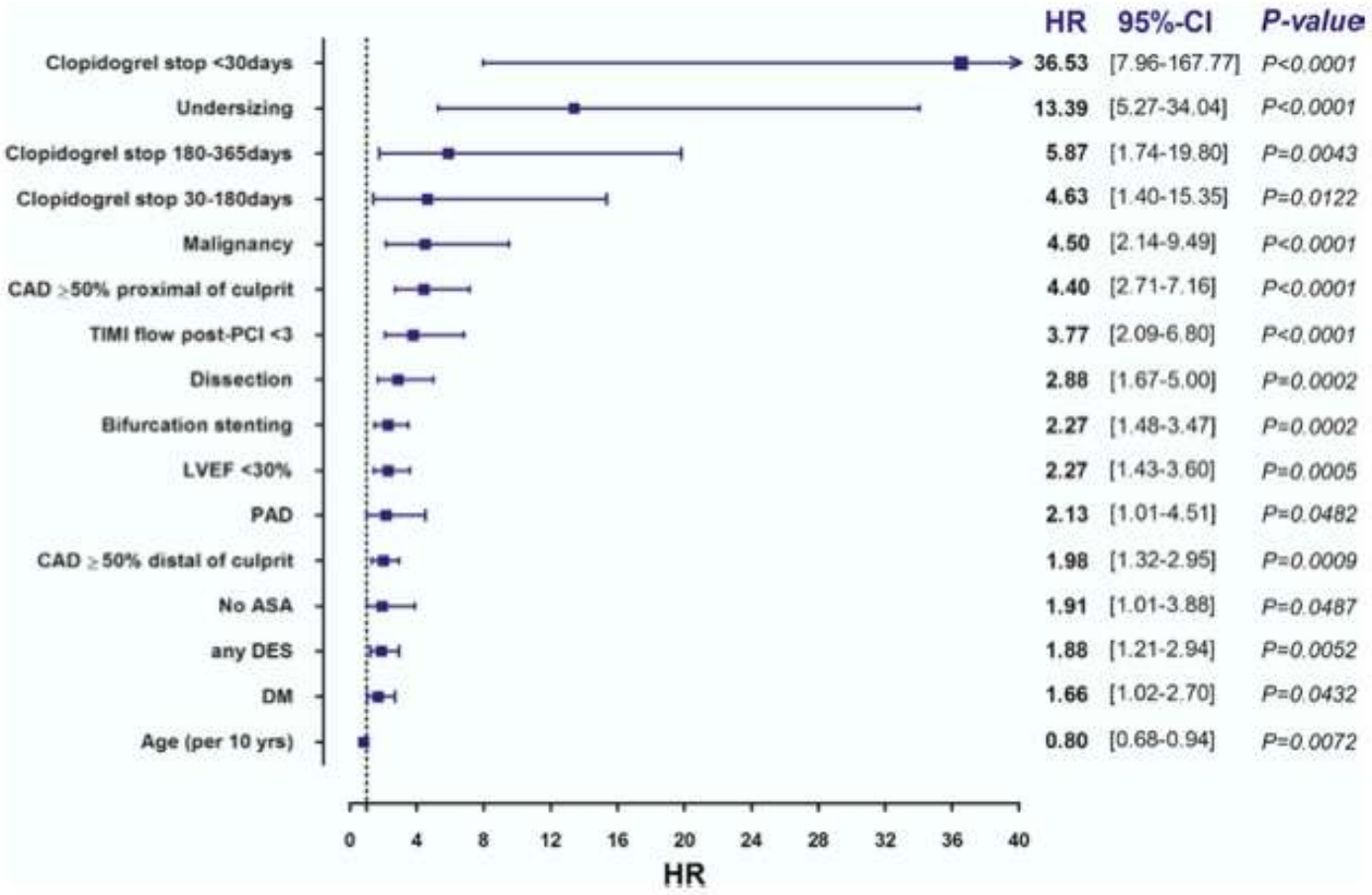
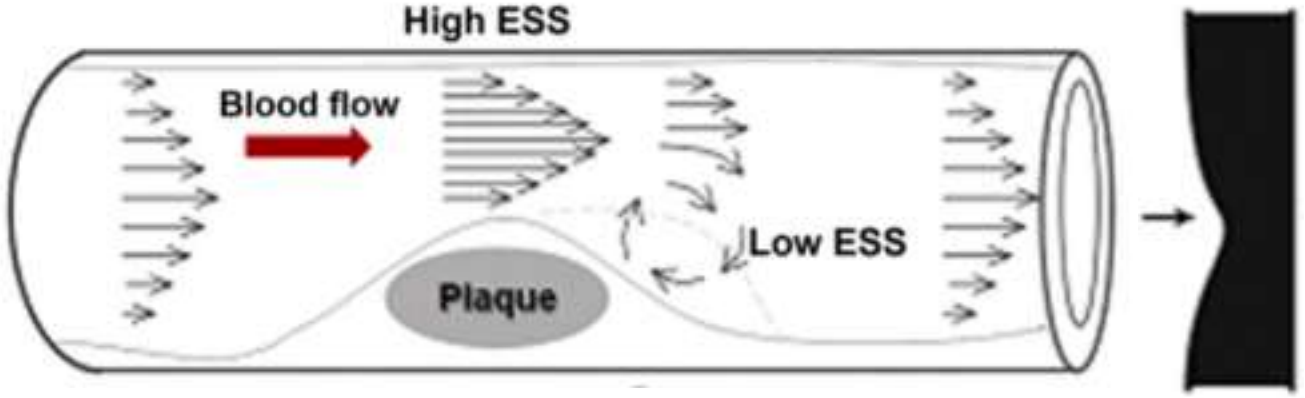
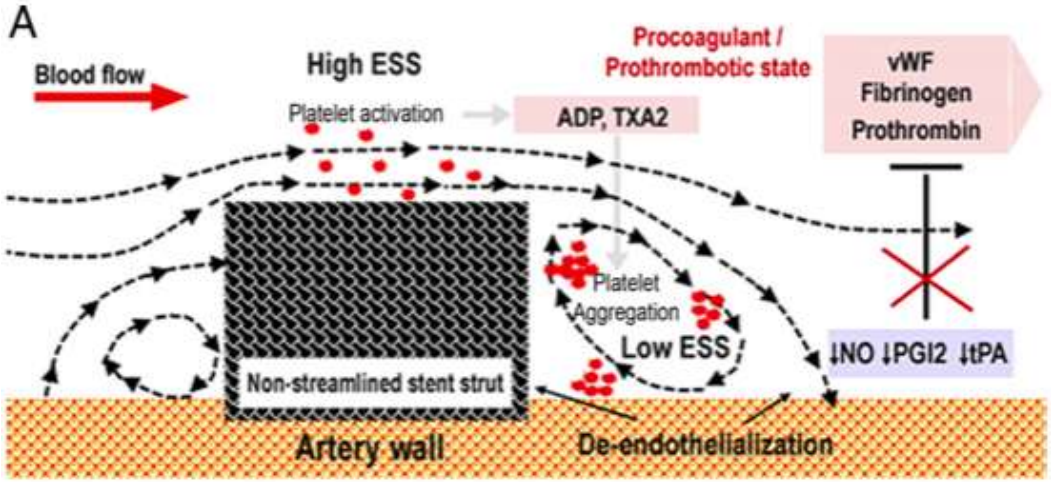
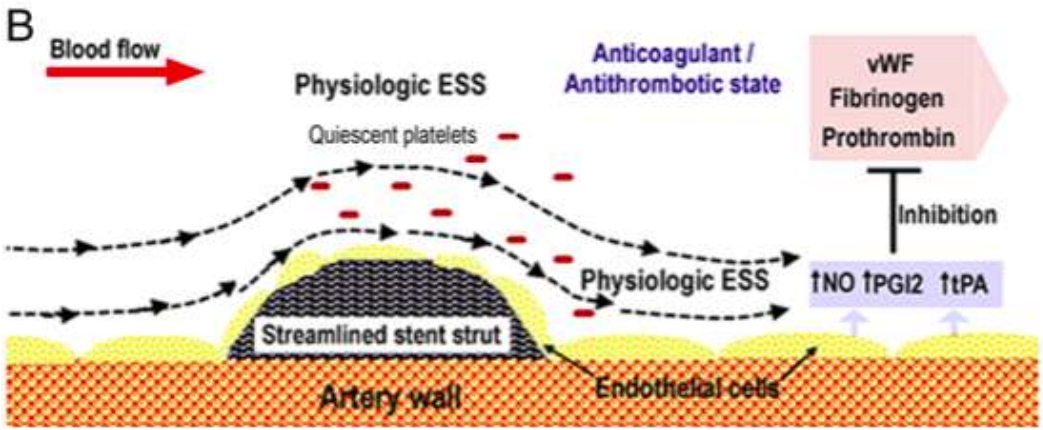


Figure 1 **Independent Risk Factors for ST**

A comparison of the total group of patients with stent thrombosis (ST) with all matched-control subjects. Represented by hazard ratio (HR) and 95% confidence interval (CI). ASA = acetyl salicylic acid; CAD = coronary artery disease; DES = drug-eluting stent(s); DM = diabetes mellitus; LVEF = left ventricular ejection fraction; PAD = peripheral artery disease; PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.







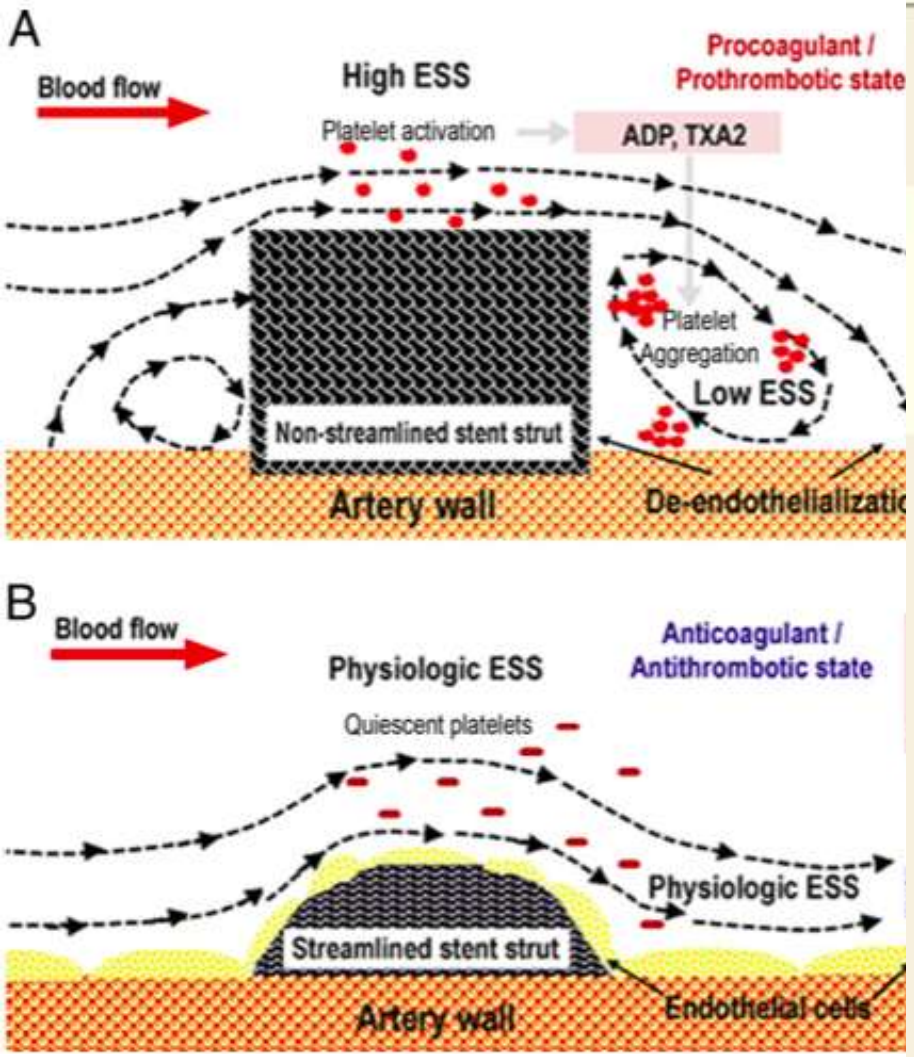
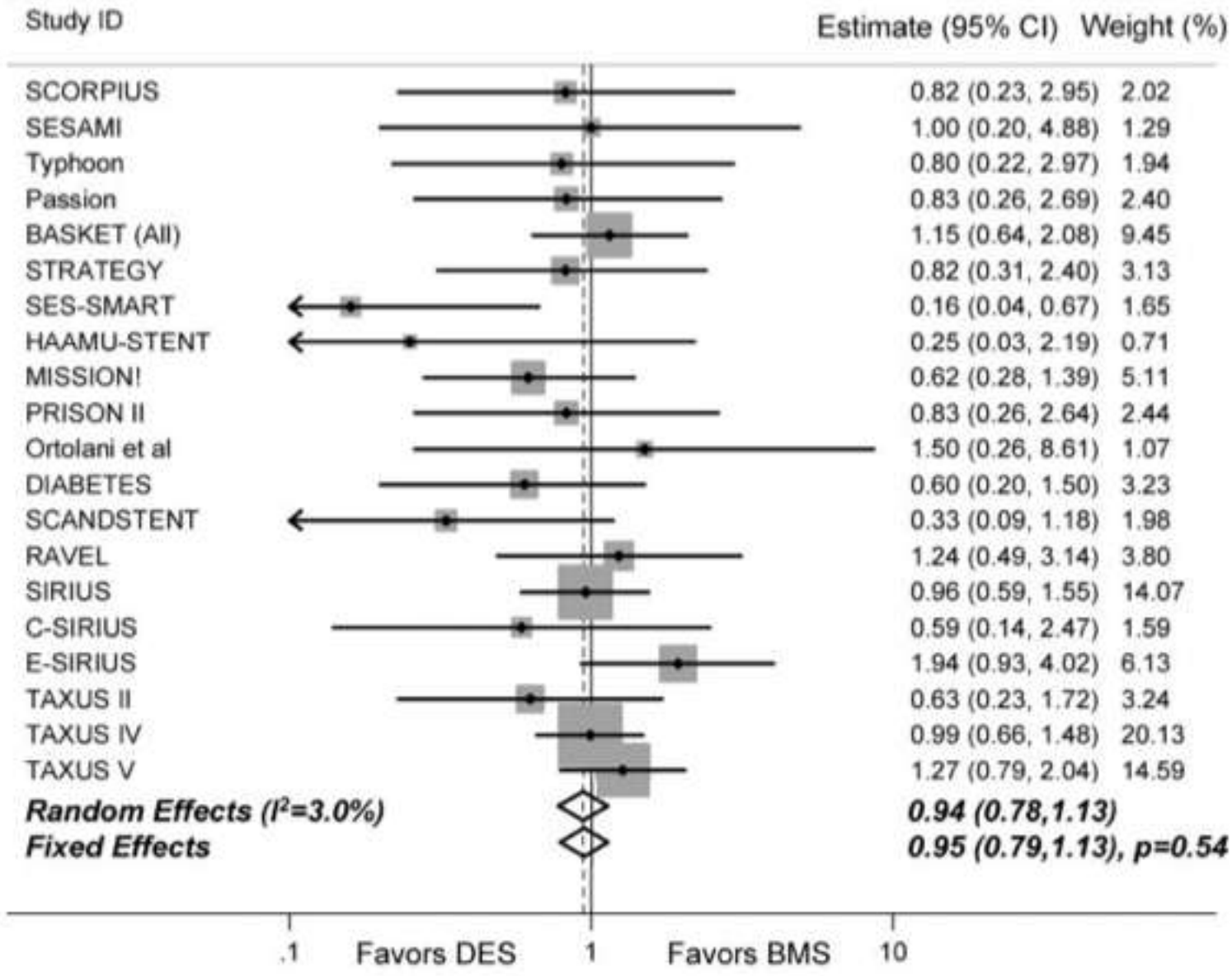


Table 1 Risk Factors of Late Stent Thrombosis and Potential Role of ESS

Risk Factor	Effect on In-Stent ESS/ Endothelial Response to ESS
Patient factors	
Diabetes	
Renal failure	
Acute coronary syndrome	
Stent factors	
Incomplete endothelialization	→ Attenuation of physiologic ESS-induced endothelial production of PGI_2, tPA, eNOS (2)
Hypersensitivity to the drug or polymer	
Procedural factors	
Bifurcation stenting	→ Adverse hemodynamic impact on the inherently complex ESS environment (68–70)
Lesion complexity	
Multivessel disease	
Excessive stent length	
Stent undersizing	→ Gaps between stent struts and arterial wall → increased flow resistance → low ESS (12)
Incomplete stent expansion (underexpansion)	
Overlapping stents	
Expansive vascular remodeling	→ Reduced flow rate → low ESS (2,4)
Antiplatelet therapy	
Premature discontinuation	
Clopidogrel resistance	

Infarto: DES vs BMS



(*Circulation*. 2009;119:3198-3206.)

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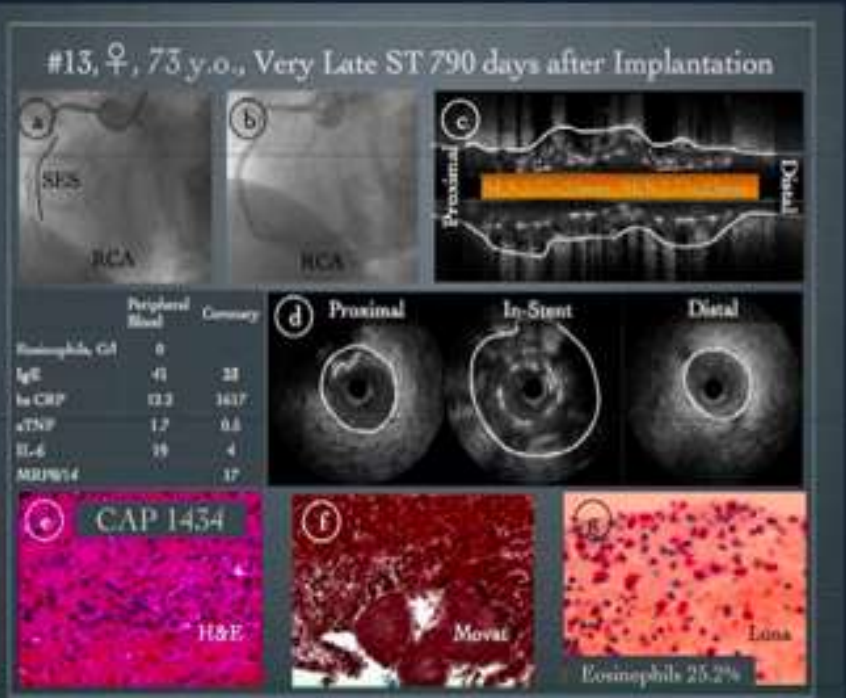
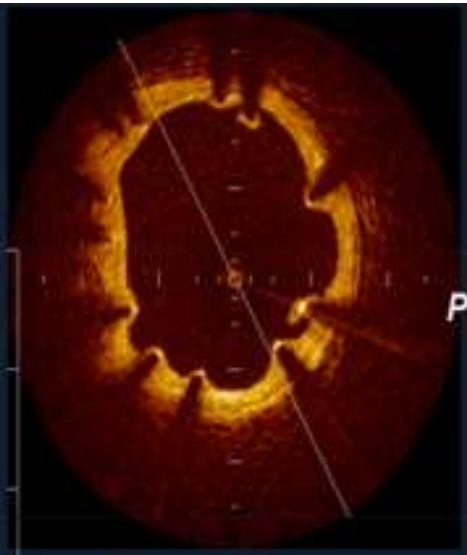
Eosinophilic Infiltrates



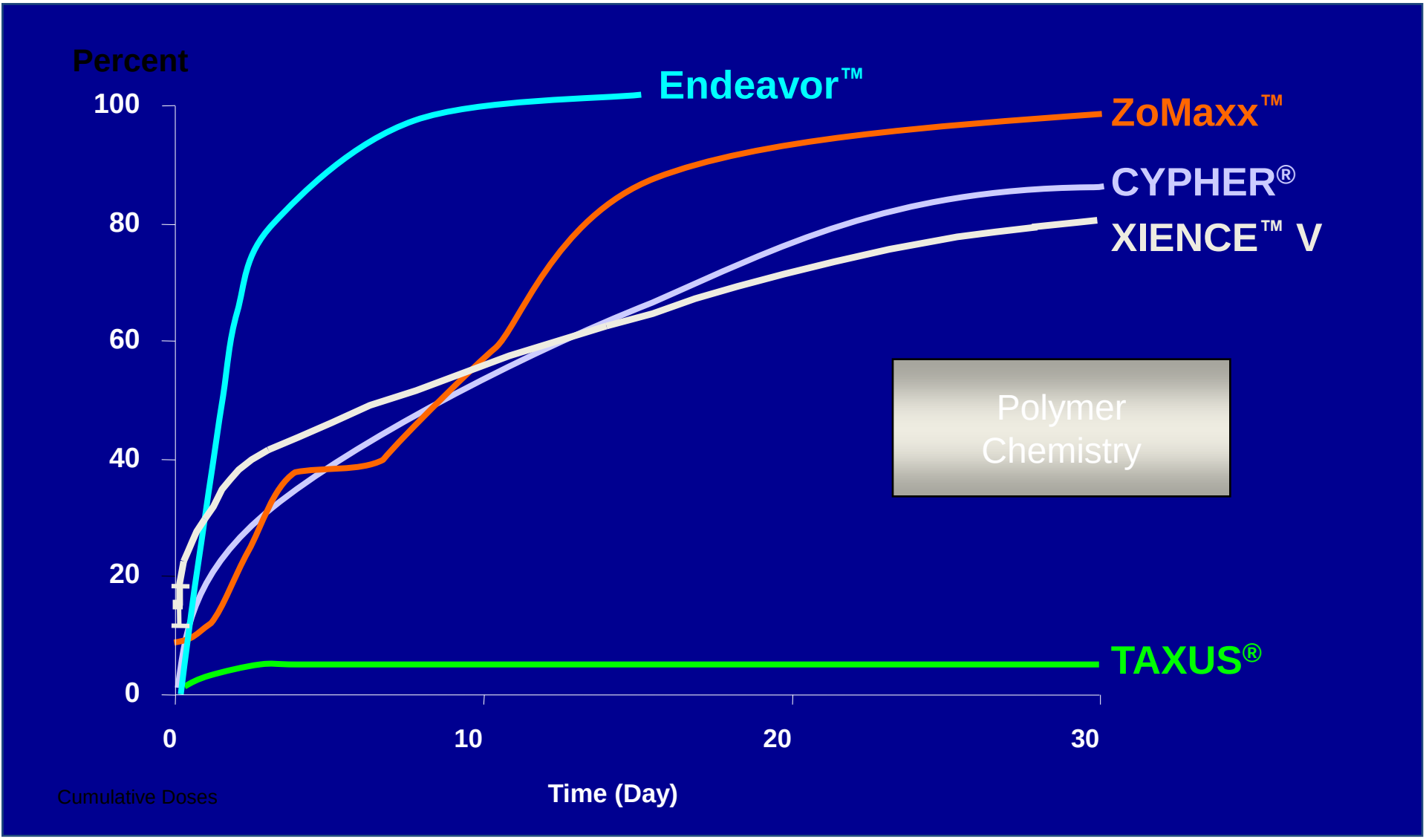
Cook et al. *Circulation* 2009

Delayed Healing

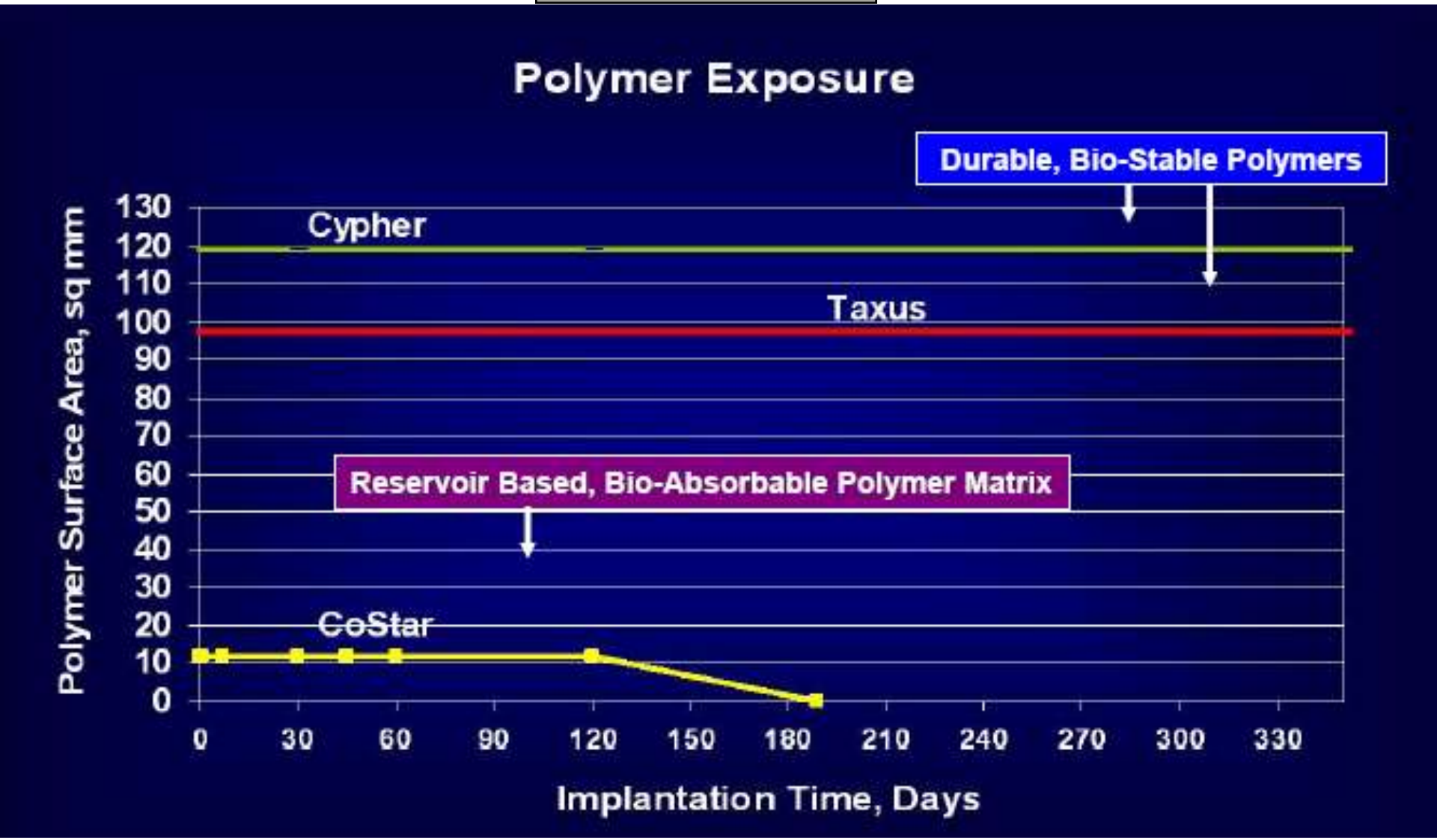


Guagliumi et al. *Circulation* 2011

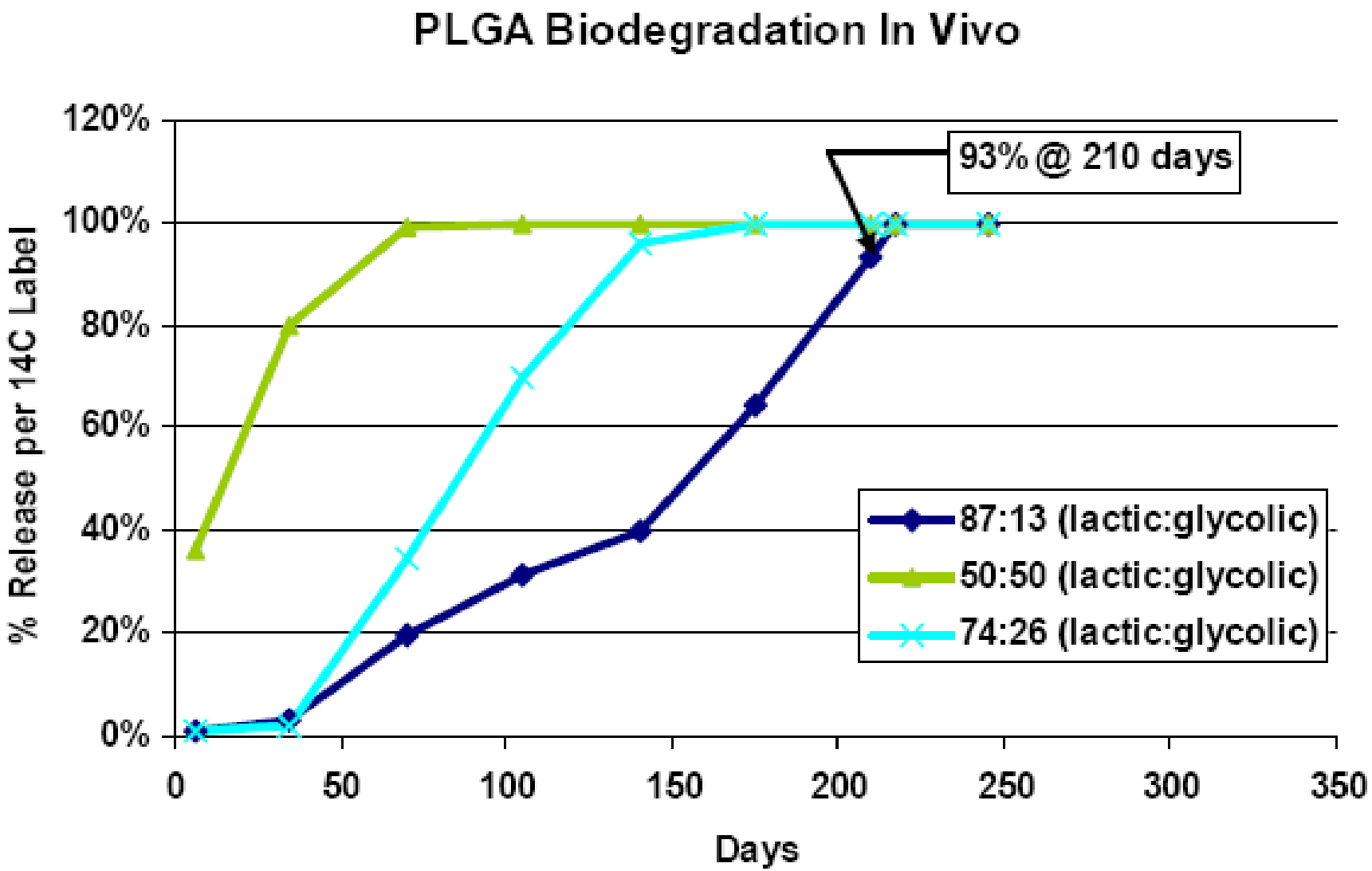
Drug Release Profiles *(in vivo)*



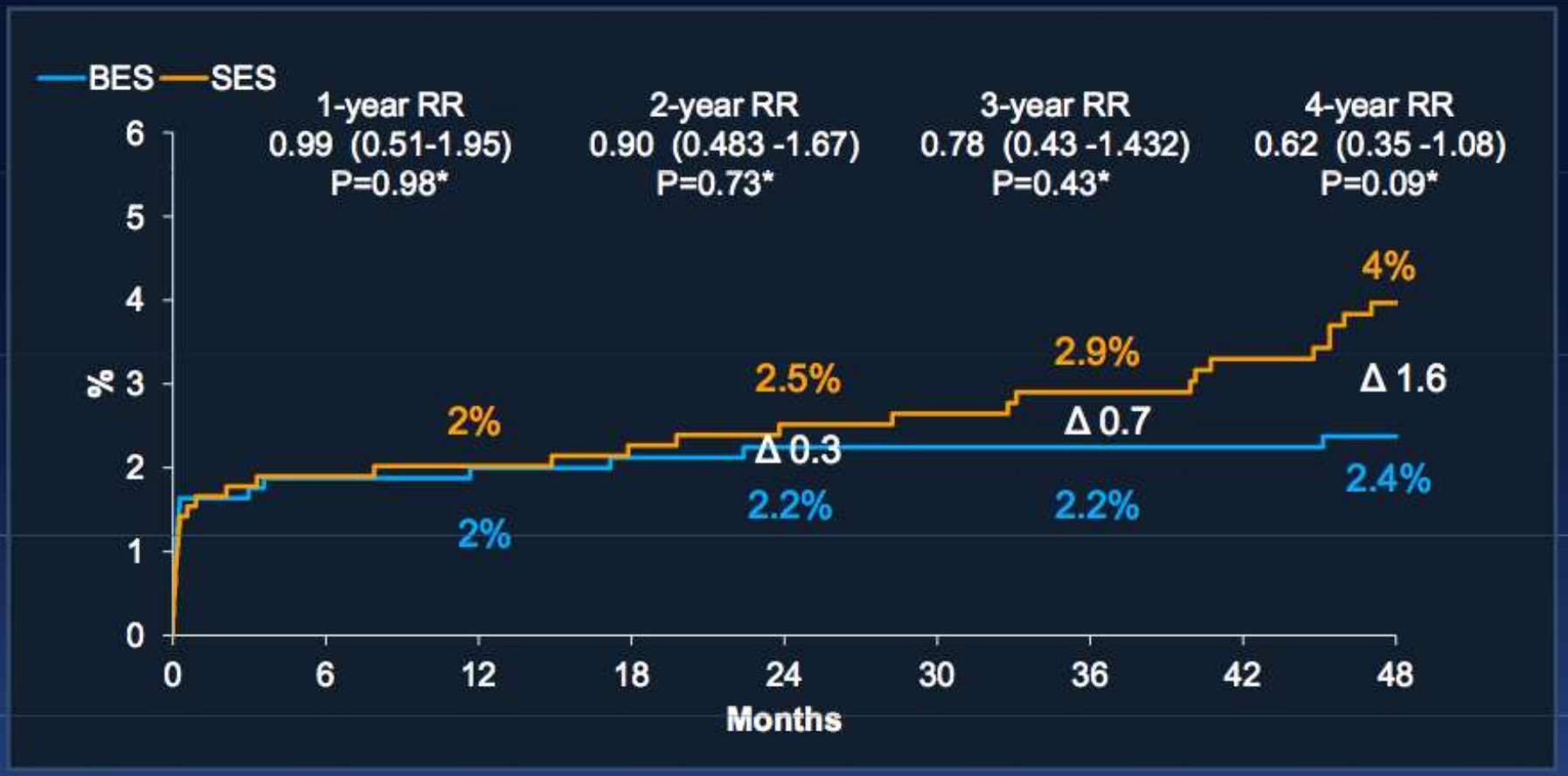
Polymer Chemistry



PLGA Resorption Controlled by Varying Co-polymer Ratios



Definite Stent Thrombosis (ARC)



Numbers at risk

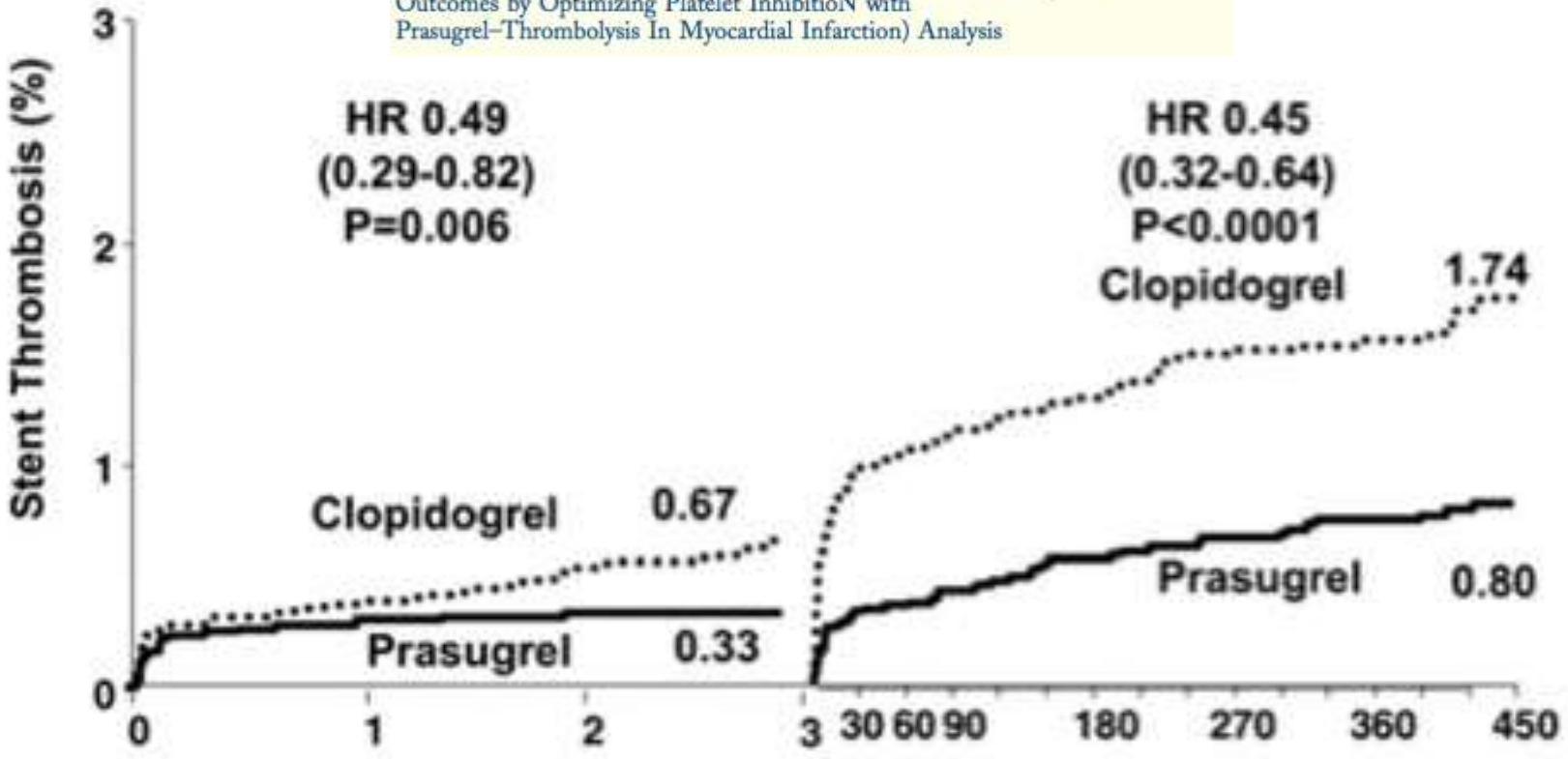
SES	850	817	801	787	776	759	750	730	714
BES	857	821	804	792	787	780	774	757	746

* P values for superiority

Tto. antiagregante post ICP

Early and Late Benefits of Prasugrel in Patients With Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention

A TRITON–TIMI 38 (TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitioN with Prasugrel–Thrombolysis In Myocardial Infarction) Analysis



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Stent thrombosis

PLATO Invasive

	Ticagrelor (n=6,732)	Clopidogrel (n=6,676)	HR for ticagrelor (95% CI)	p value*
Stent thrombosis, %				
Definite	1.0	1.6	0.62 (0.45–0.85)	0.003
Probable or definite	1.7	2.3	0.72 (0.56–0.93)	0.01
Possible, probable, or definite	2.2	3.1	0.72 (0.58–0.90)	0.003

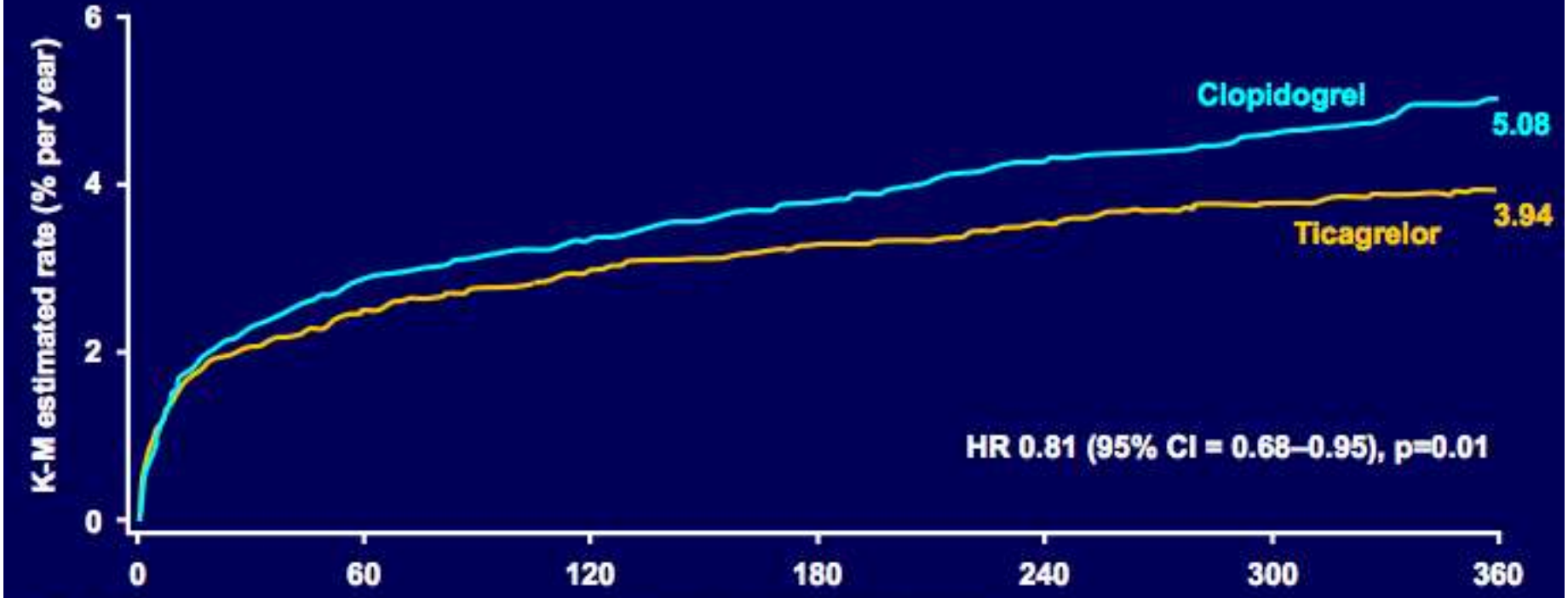
¶ Evaluated in patients with any stent during the study

Time-at-risk is calculated from the date of first stent insertion in the study or date of randomization

* By univariate Cox model

All-cause mortality

PLATO
Invasive



No. at risk							
Ticagrelor	6,732	6,439	6,375	6,241	5,141	3,951	3,233
Clopidogrel	6,676	6,376	6,331	6,209	5,114	3,917	3,164

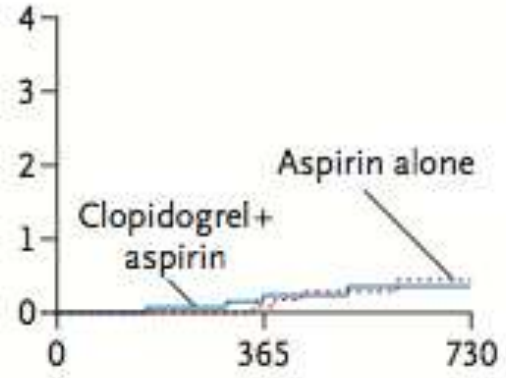
Optimal Duration of Clopidogrel Use after Implantation of Drug-Eluting Stents — Still in Doubt

Peter B. Berger, M.D.

ORIGINAL ARTICLE

Duration of Dual Antiplatelet Therapy after Implantation of Drug-Eluting Stents

Seung-Jung Park, M.D., Duk-Woo Park, M.D., Young-Hak Kim, M.D.,



Safety and Efficacy of Six Months Dual Antiplatelet Therapy After Drug-Eluting Stenting (ISAR-SAFE)

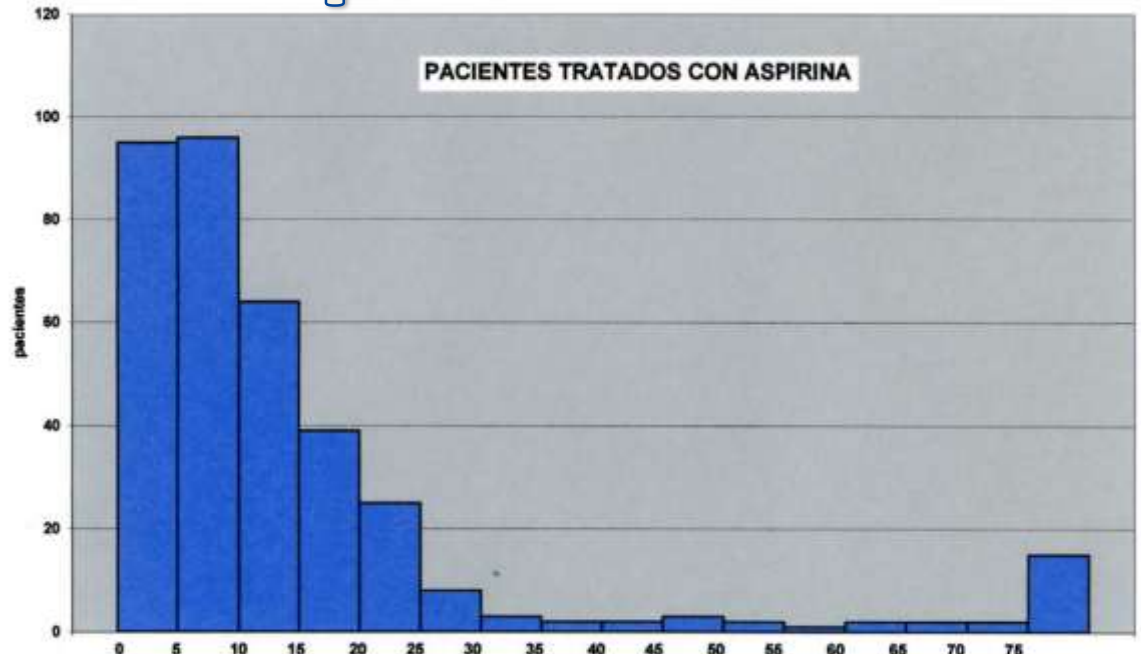
This study is currently recruiting participants.
Verified April 2012 by Deutsches Herzzentrum Muenchen

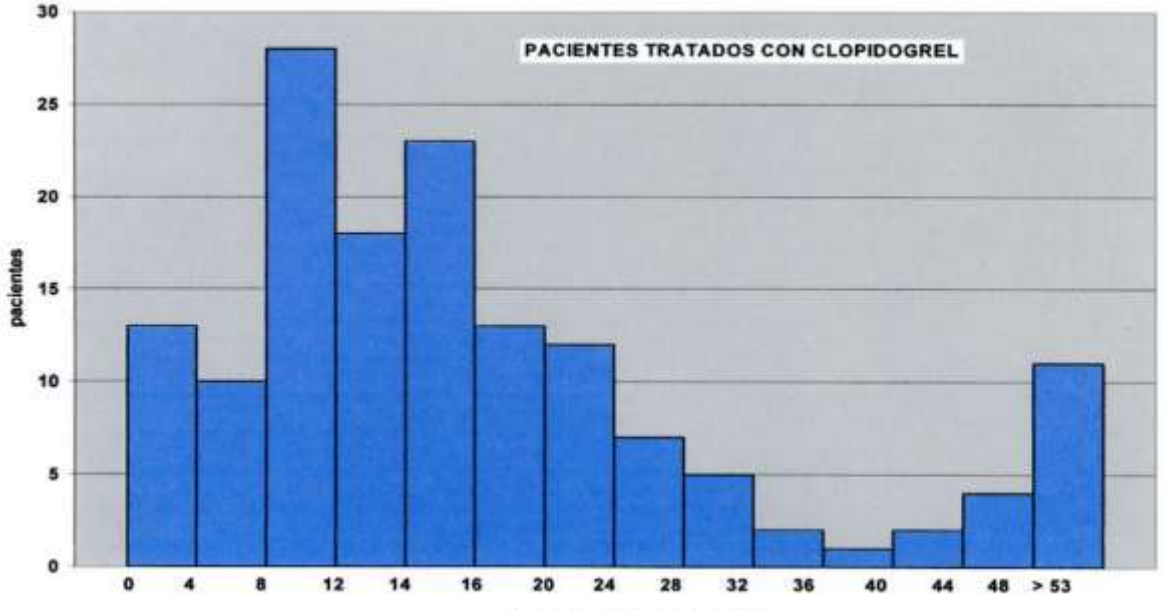
First Received on April 15, 2008. Last Updated on April 19, 2012 History of Changes

Optimized Duration of Clopidogrel Therapy Following Treatment With the Endeavor Zotarolimus - Eluting Stent in the Real World Clinical Practice - Optimize Trial (OPTIMIZE)

This study is currently recruiting participants.
Verified June 2011 by Cardiovascular Research Center, Brazil

Respuesta al tto





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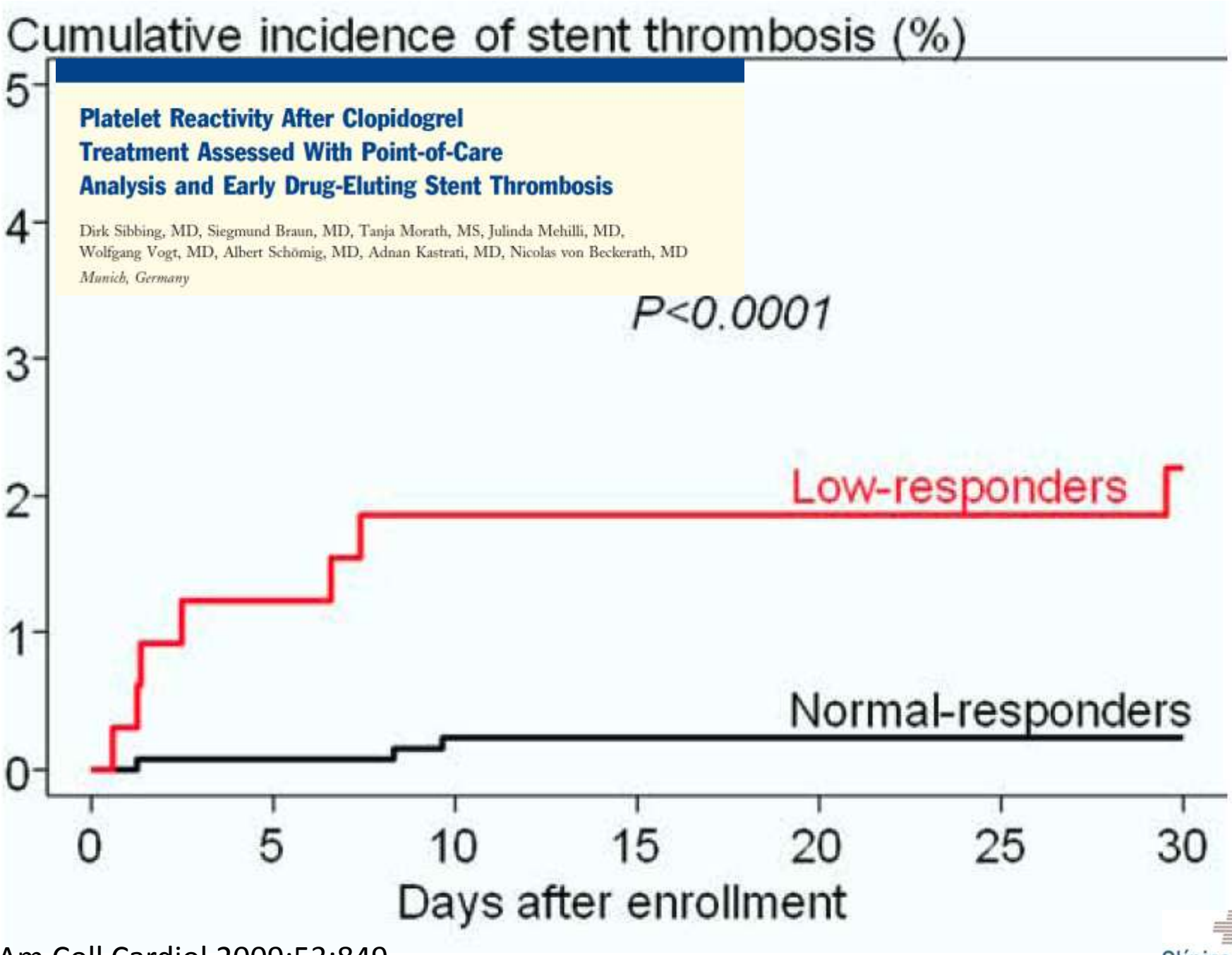

J Am Coll Cardiol 2009;53:849

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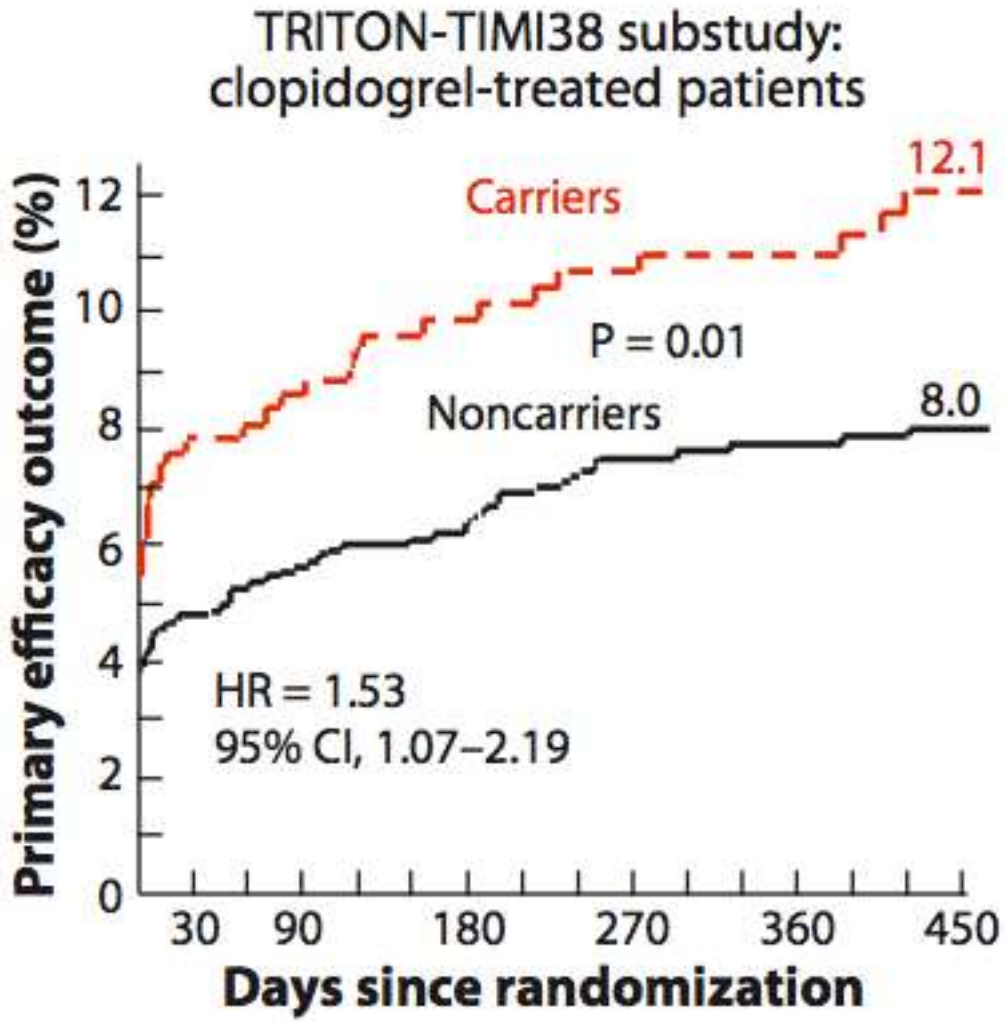
Portadores CYP2C19*2



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Reactividad plaquetar

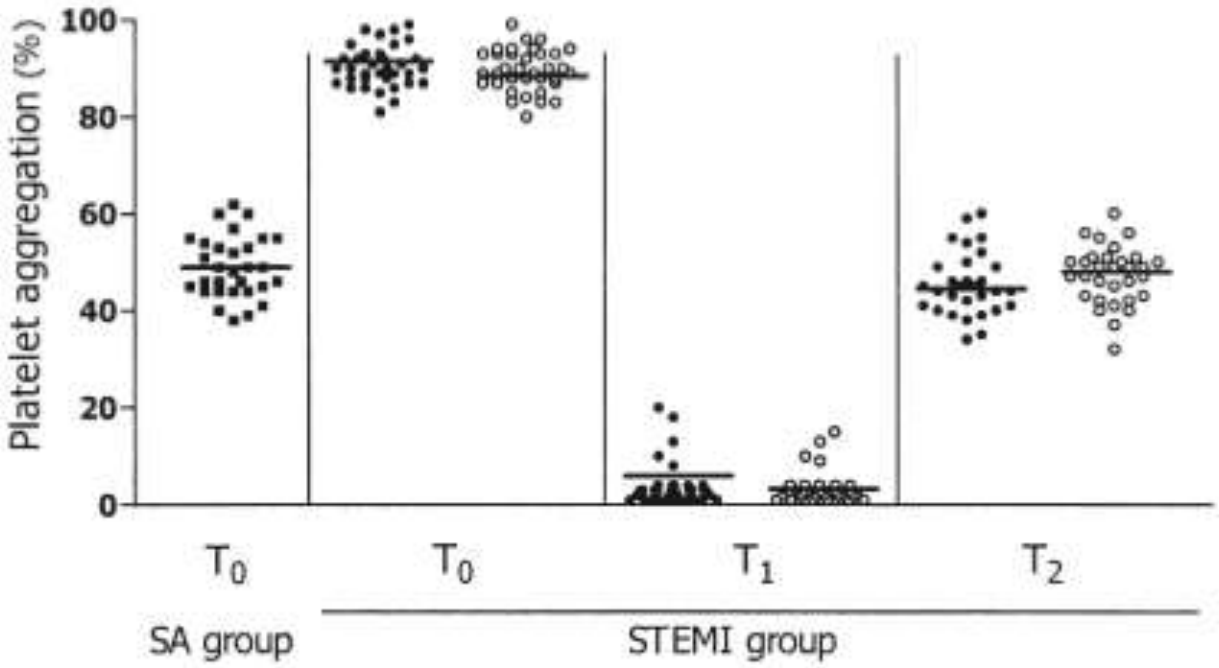
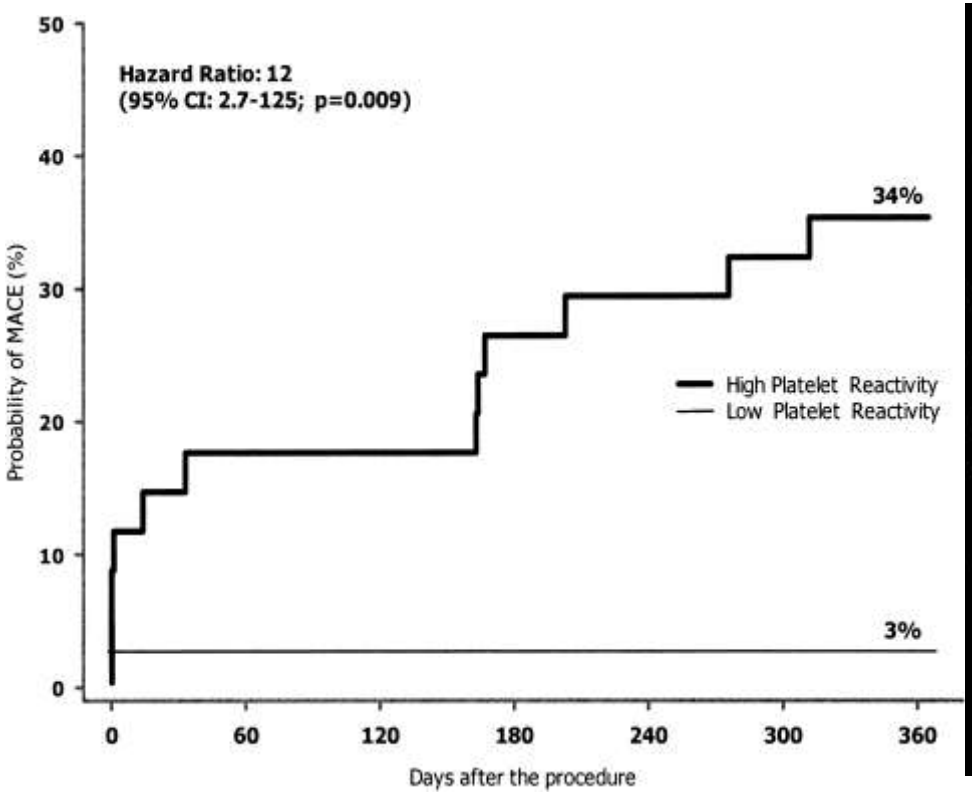
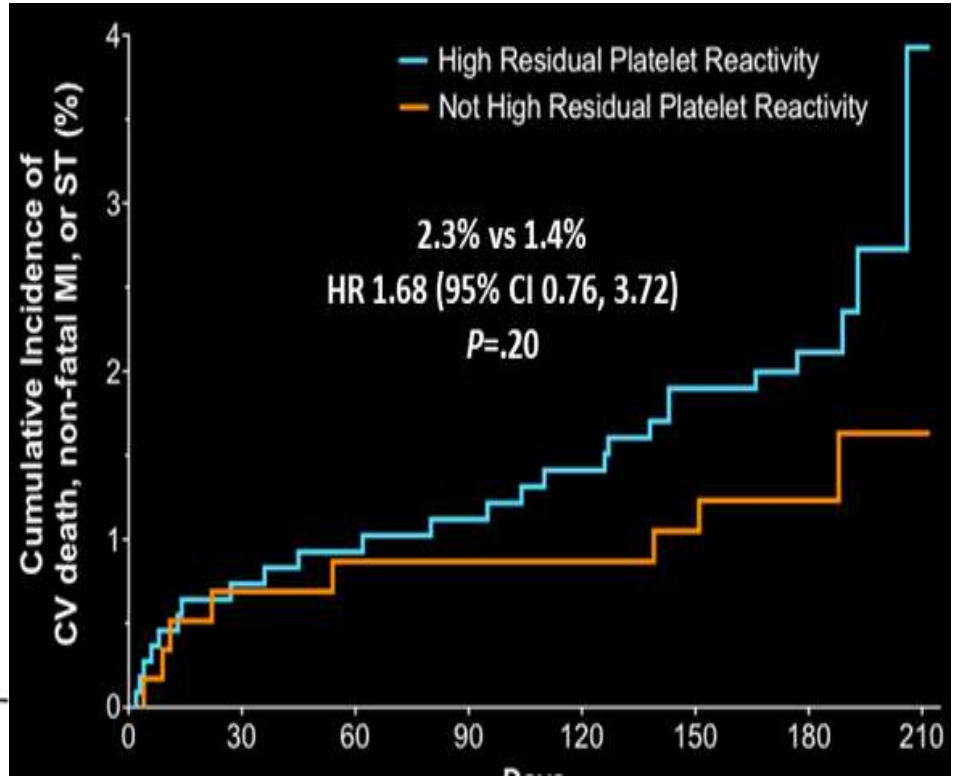


Figure 1. Platelet reactivity assays. **Solid squares** = patients with stable angina (SA); **open squares** = patients with ST-segment elevation myocardial infarction (STEMI); **solid circles** = abciximab subgroup; **open circles** = single high-dose bolus (SHDB) tirofiban subgroup. CADP = cartridge adenosine diphosphate closure time; T_0 = baseline; T_1 = 10 min after glycoprotein IIb/IIIa bolus; T_2 = discharge.

Probability of major adverse cardiac events (MACE) in patients stratified according to Platelet Reactivity at Admission. Campo, G. et al. J Am Coll Cardiol 2006;48:2178

Reactividad plaquetar





Campo, G. et al. J Am Coll Cardiol 2006;48:2178-2185
JAMA, GRAVITAS. 2011

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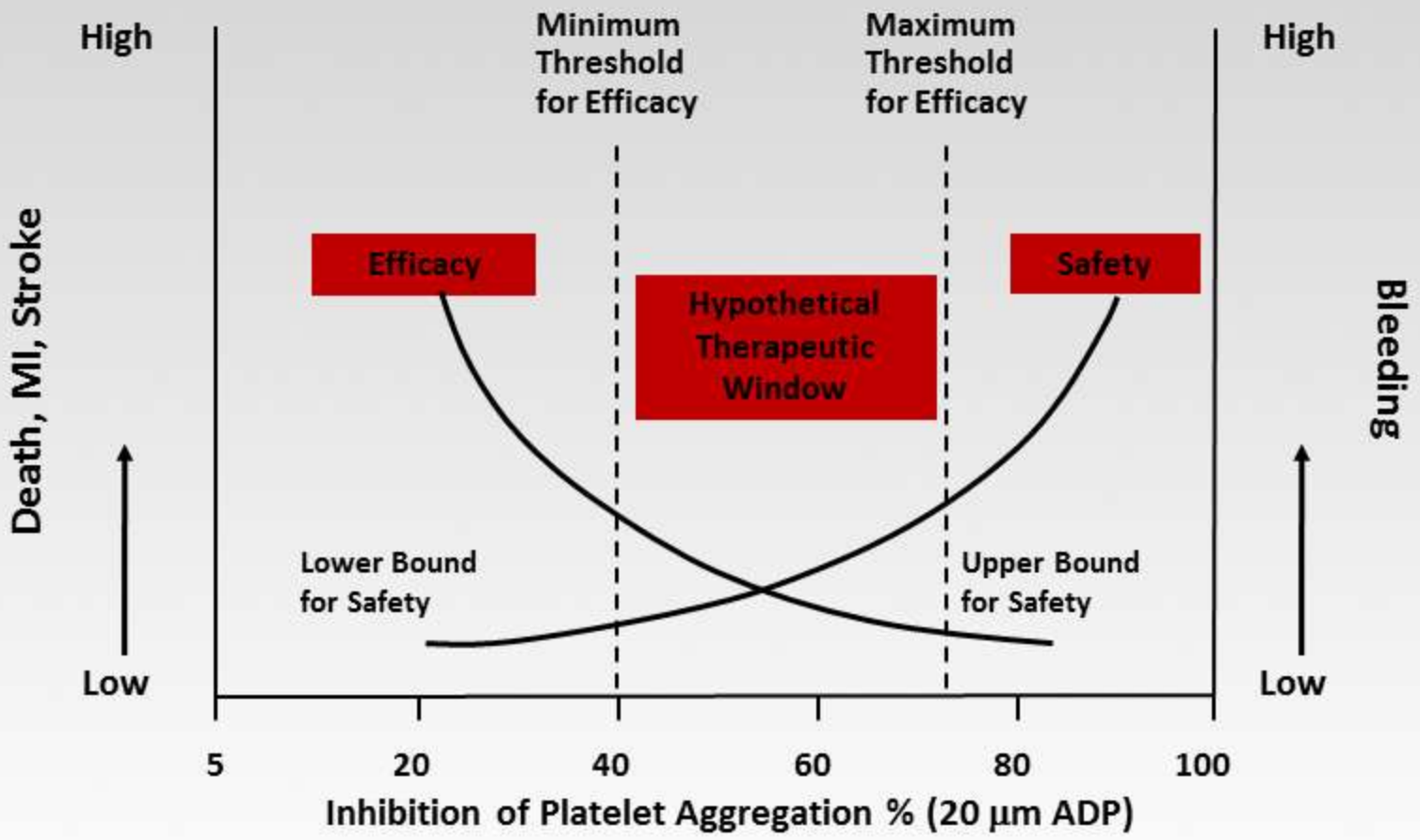
Consensus and Future Directions on the Definition of High On-Treatment Platelet Reactivity to Adenosine Diphosphate

Laurent Bonello, MD,* Udaya S. Tantry, PHD,§§ Rossella Marcucci, MD, PHD,‖ Ruediger Blindt, MD,# Dominick J. Angiolillo, MD, PHD,‖‖ Richard Becker, MD,¶¶ Deepak L. Bhatt, MD, MPH,## Marco Cattaneo, MD,¶ Jean Philippe Collet, MD, PHD,‡ Thomas Cuisset, MD,† Christian Gachet, MD, PHD,§ Gilles Montalescot, MD, PHD,‡ Lisa K. Jennings, PHD,*** Dean Kereiakes, MD,††† Dirk Sibbing, MD,** Dietmar Trenk, PHD,†† Jochem W. Van Werkum, MD, PHD,‡‡ Franck Paganelli, MD,* Matthew J. Price, MD,‡‡‡ Ron Waksman, MD,§§§ Paul A. Gurbel, MD,§§ for the Working Group on High On-Treatment Platelet Reactivity

Beneficio clinico neto



From Becker RC. Pharmacogenetics and safety parameters for platelet P2Y12 receptor antagonists. *J Thromb Thrombolysis*. 2009;28:513-514. Republished with permission.

Artículo especial

Prevención de complicaciones hemorrágicas en el síndrome coronario agudo

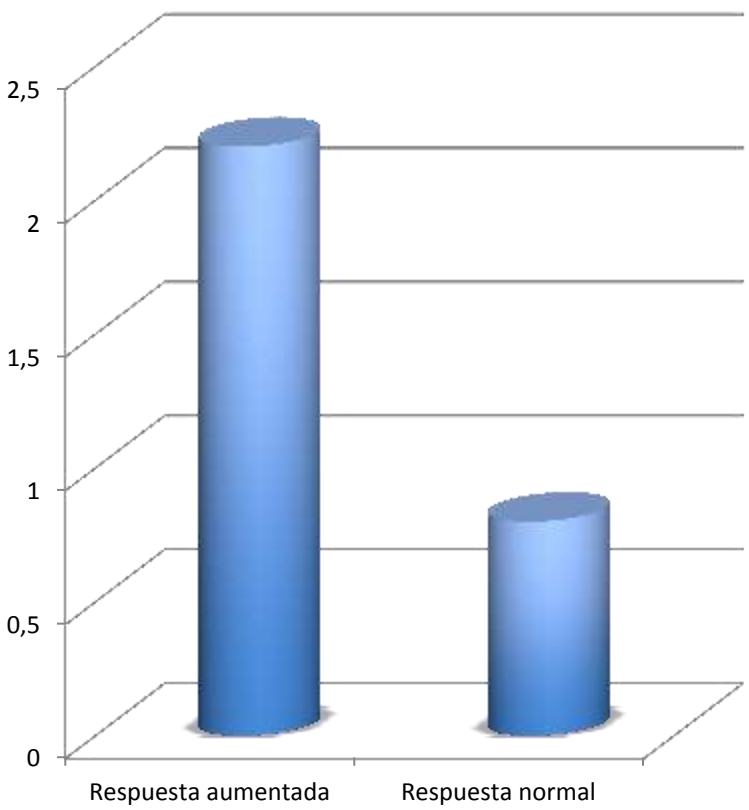
Reduction of haemorrhagic risk in acute coronary syndromes

ÁlvaroA. Merino [a,*], Inmaculada Roldán [b], Francisco Marín [c] y Fernando Worner [d], en representación del núcleo del Grupo de Trabajo de Trombosis Cardiovascular de la Sociedad Española de Cardiología (addĕndum)

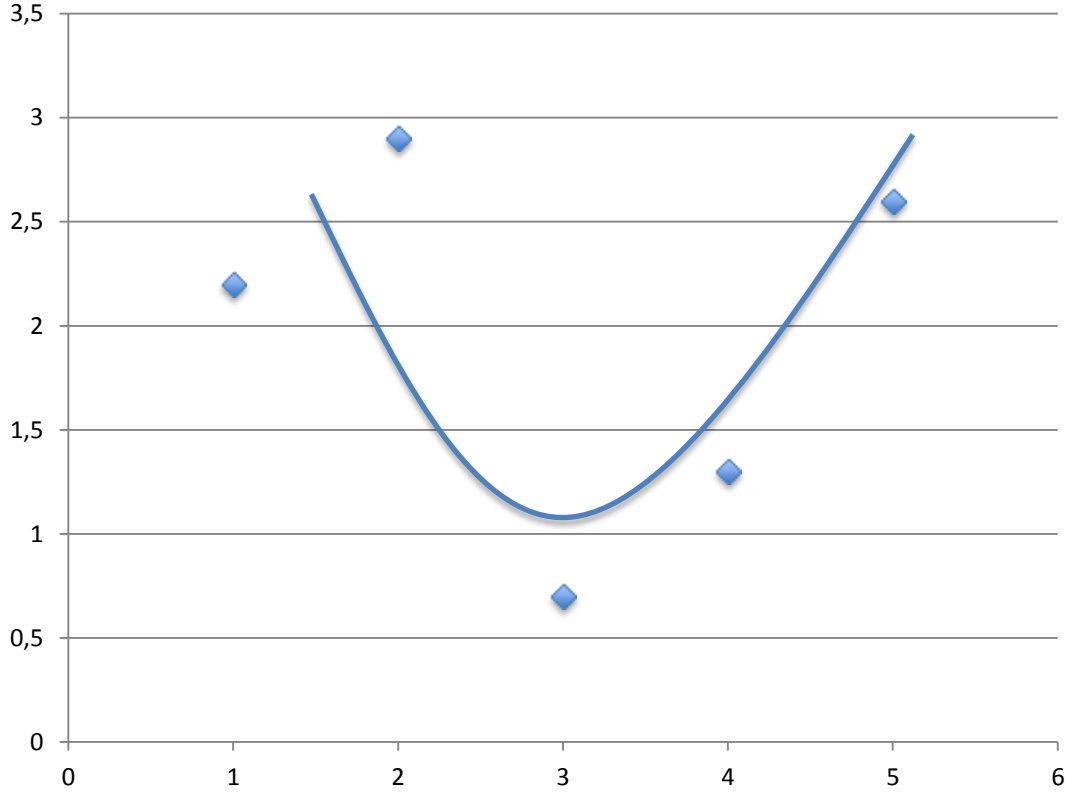
Estudio	Eventos trombóticos		Hemorragias mayores		Beneficio clínico
CURE[42]					
	Clopidogrel	Placebo	Clopidogrel	Placebo	Clopidogrel vs Placebo
	9,3%	11,4%	3,7%	2,7%	1,1%
TRITON-TIMI 38[29]					
	Prasugrel	Clopidogrel	Prasugrel	Clopidigrel	Prasugrel vs Clopidogrel
	9,9%	12,1%	2,4%	1,8%	1,6%
CHAMPION PCI[35]					
	Cangrelor	Clopidogrel	Cangrelor	Clopidogrel	Cangrelor vs Clopidogrel
	7,5%	7,1%	3,6%	2,9%	- 1,1%
CHAMPION PLATFORM[36]					
	Cangrelor	Placebo	Cangrelor	Placebo	Cangrelor vs Placebo
	7,0%	8,0%	5,5	3,5%	- 1,0%
PLATO[37]					
	Ticagrelor	Clopidogrel	Ticagrelor	Clopidogrel	Ticagrelor vs Clopidogrel
	9,8%	11,7%	4,5%	3,8%	1,2%

A. Merino Med Cli 2011 y Rev Esp Cardiol 2011

Beneficio clínico clopidogrel Post-stenting



Hemorragias mayores



Hemorragias mayores + trombosis stent

Sibbing JTH 2010

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Catheterization and Cardiovascular Interventions 79:255–262 (2012)

Editorial

"Conversations in Cardiology": How Do You Pick the Best Antiplatelet Drug—Clopidogrel, Prasugrel, Ticagrelor for Your PCI Patient?

Morton J. Kern,* MD, FSCAI, FAHA, FACC

Preguntas:

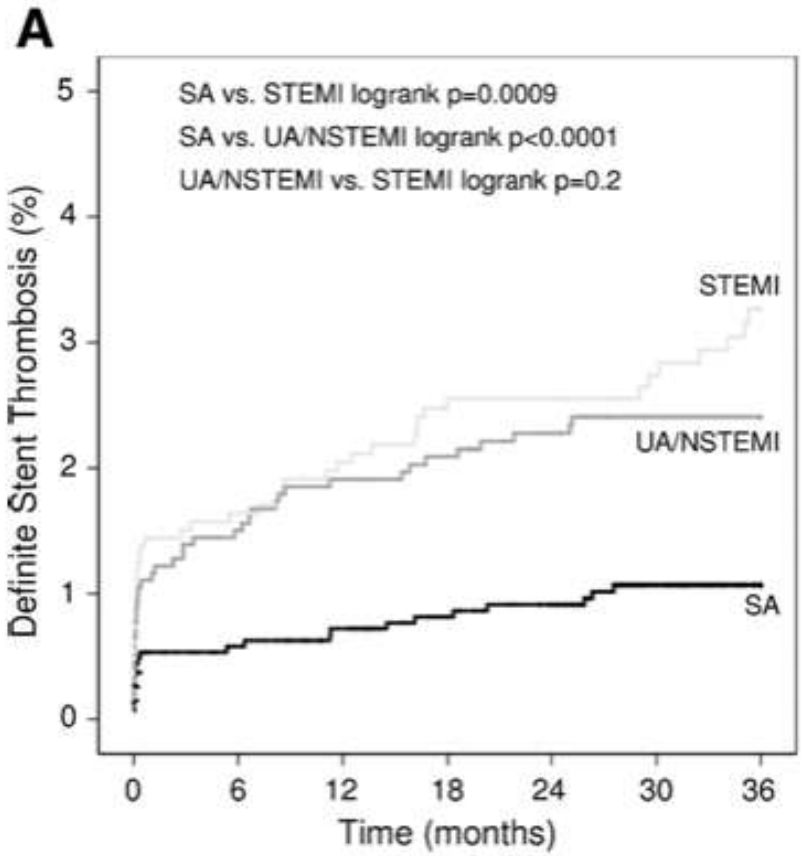
1. ¿Tengo que tener clopidogrel, prasugrel y ticagrelor en el hospital?
2. ¿qué ventajas/inconvenientes hay en usar prasugrel vs ticagrelor?
3. ¿prasugrel y ticagrelor sólo en ptes de alto riesgo de trombosis

Posibles respuestas:

1. Seguir con clopidogrel por precio y por facilidad de admin (1 c/24 h)
2. Mantener los tres y administrar prasugral y ticagrelor sólo a los de alto riesgo
3. Cambiar a ticagrelor porque reduce la mortalidad
4. Prasugrel y ticagrelor en el hospital y clopidogrel pasado un mes
5. Preocupación por el riesgo de sangrado con prasugrel/ticagrelor (alto riesgo)

Table 3. Independent Predictors of Stent Thrombosis

Variables	Hazard Ratio (95% Confidence Interval)	*P* Value
Subacute stent thrombosis		
Premature antiplatelet therapy discontinuation	161.17 (26.03-997.94)	<.001
Renal failure	10.06 (3.13-32.35)	<.001
Bifurcation lesion	5.96 (1.90-18.68)	.002
Diabetes	5.84 (1.74-19.55)	.004
Left ventricular ejection fraction per 10% decrease	1.12 (1.06-1.19)	<.001
Stent length, per 1-mm increase	1.03 (1.00-1.05)	.01
Late stent thrombosis		
Premature antiplatelet therapy discontinuation	57.13 (14.84-219.96)	<.001
Bifurcation lesion	8.11 (2.50-26.26)	.001
Left ventricular ejection fraction per 10% decrease	1.06 (1.01-1.12)	.03
Cumulative stent thrombosis		
Premature antiplatelet therapy discontinuation	89.78 (29.90-269.60)	<.001
Renal failure	6.49 (2.60-16.15)	<.001
Bifurcation lesion	6.42 (2.93-14.07)	<.001
Diabetes	3.71 (1.74-7.89)	.001
Left ventricular ejection fraction per 10% decrease	1.09 (1.05-1.13)	<.001



JAMA. 2005;293(17):2126-2130. doi:10.1001/jama.293.17.2126
JACC Int 2009

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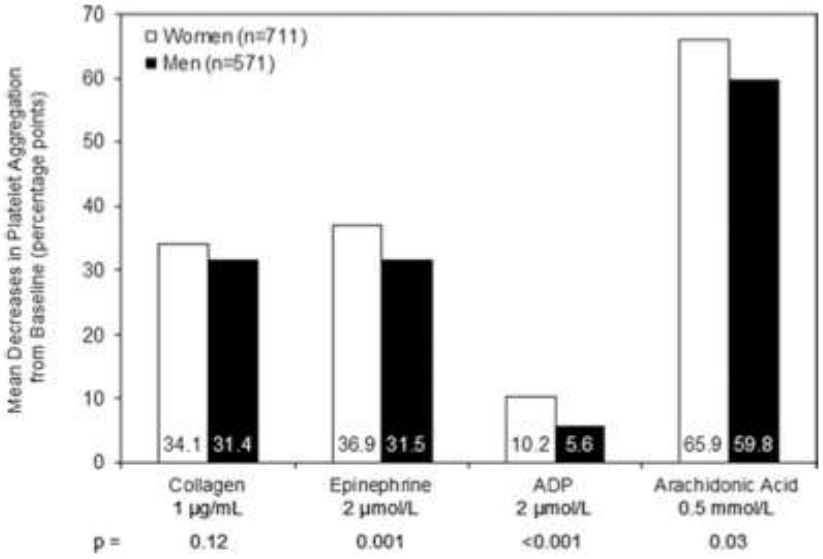
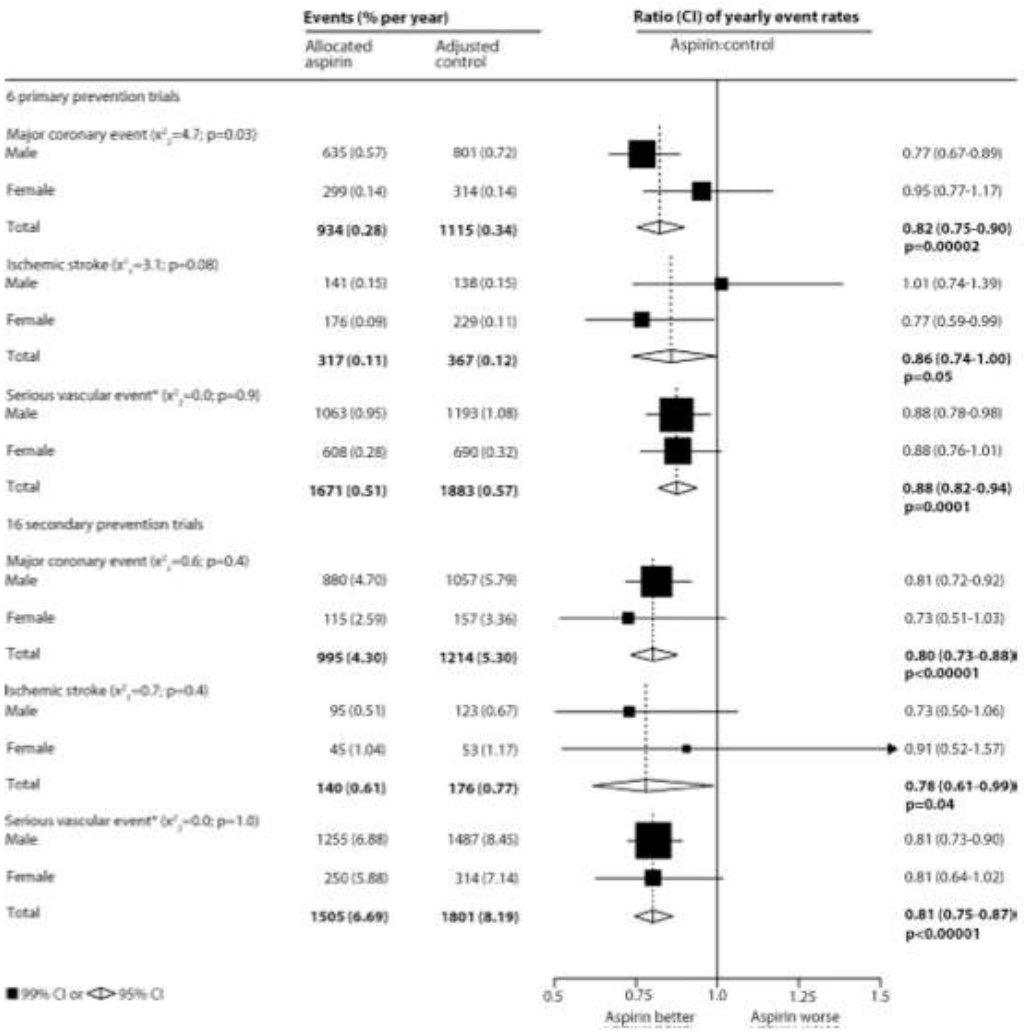
STATE-OF-THE-ART PAPER

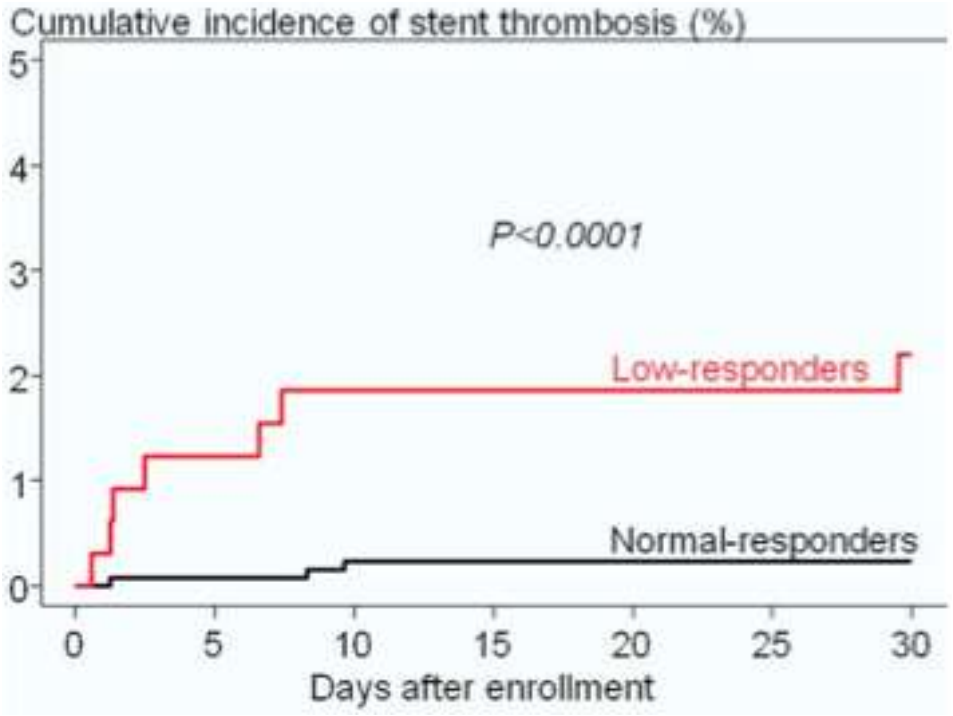
Platelet Biology and Response to Antiplatelet Therapy in Women

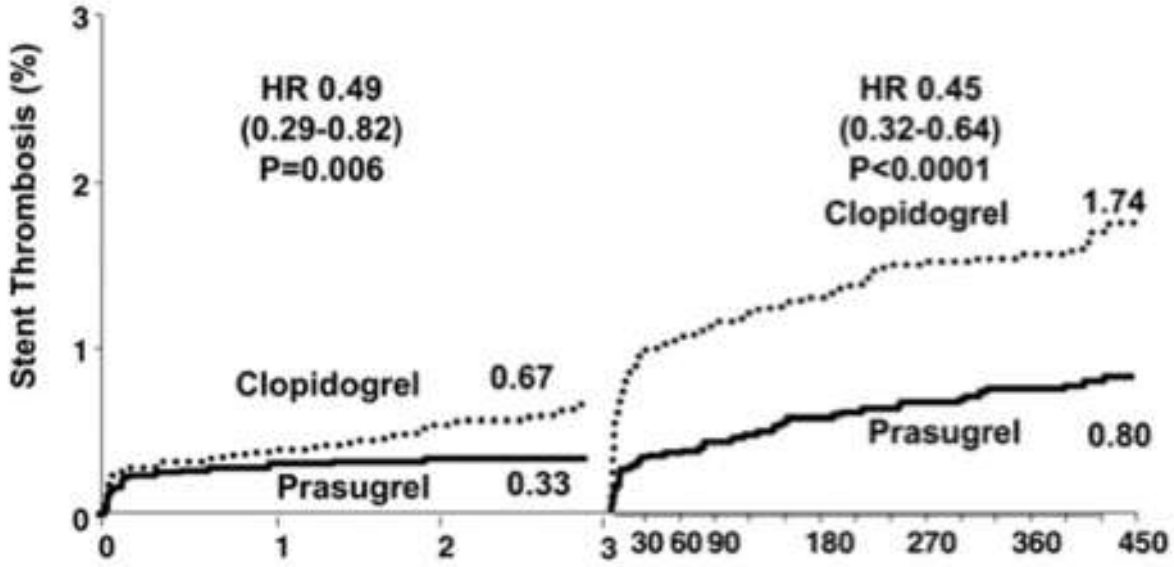
Implications for the Development and Use of Antiplatelet Pharmacotherapies for Cardiovascular Disease

Tracy Y. Wang, MD, MHS, MSc,* Dominick J. Angiolillo, MD, PhD,† Mary Cushman, MD, MSc,‡ Marc S. Sabatine, MD, MPH,§ Paul F. Bray, PhD,‖ Susan S. Smyth, MD, PhD,¶ Harold L. Dauerman, MD,‡ Patricia A. French, BS,# Richard C. Becker, MD*









Adjusted indirect comparison meta-analysis of prasugrel vs ticagrelor for patients with acute coronary syndromes

Biondi-Zoccai G, Lotrionte M, Agostoni P, Abbate A, Romagnoli E, Sangiorgi G, et al.

Int J Cardiol. 2011;159:325.

12-month results: Prasugrel or ticagrelor vs clopidogrel

Outcome	OR (95% CI)	p
Death/MI/stroke	0.83 (0.77–0.89)	<0.001
Death	0.83 (0.74–0.93)	0.001
Nonfatal MI	0.79 (0.73–0.86)	0.001
Nonfatal stroke	1.12 (0.91–1.38)	0.28
Stent thrombosis	0.61 (0.51–0.74)	<0.001
Major bleeding	1.09 (0.99–1.21)	0.08
Drug discontinuation	1.12 (1.05–1.19)	<0.001

12-month results: Prasugrel vs ticagrelor

Outcome	OR (95% CI)	p
Death/MI/stroke	0.99 (0.86–1.13)	0.86
Death	1.22 (0.96–1.55)	0.11
Nonfatal MI	0.89 (0.75–1.06)	0.20
Nonfatal stroke	0.86 (0.55–1.33)	0.49
Stent thrombosis	0.64 (0.43–0.93)	0.02
Major bleeding	1.43 (1.10–1.85)	0.007
Drug discontinuation	1.03 (0.88–1.19)	0.73