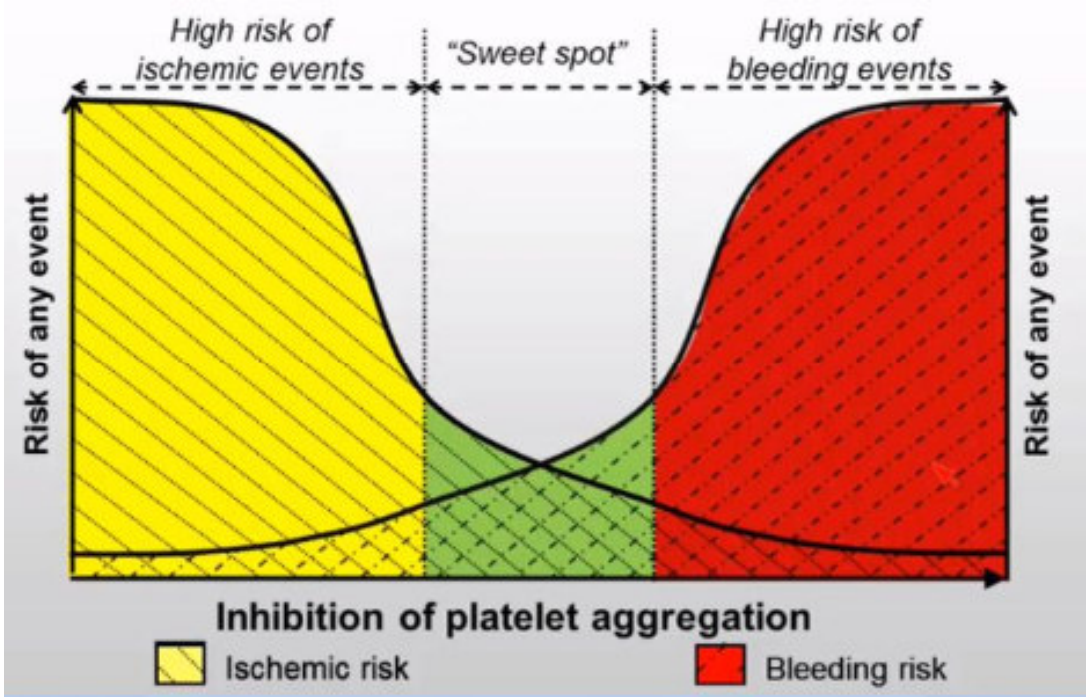
SEGURIDAD Y EFICACIA DE LAS PAUTAS CORTAS DE DOBLE ANTIAGREGACIÓN EN EL SÍNDROME CORONARIO AGUDO TRATADO CON STENT FARMACOACTIVO.

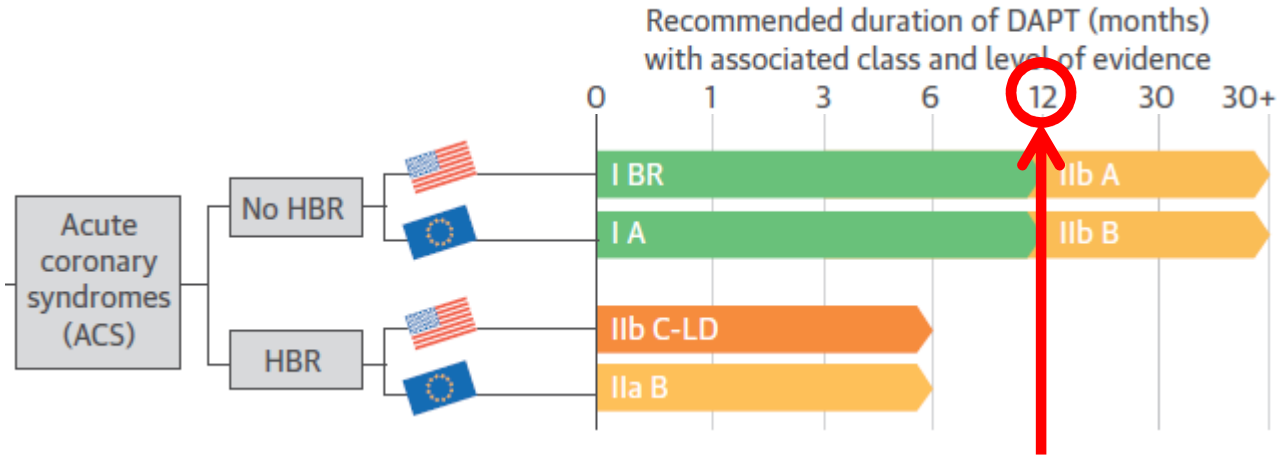
Julio García Tejada
Hospital Universitario
12 de Octubre

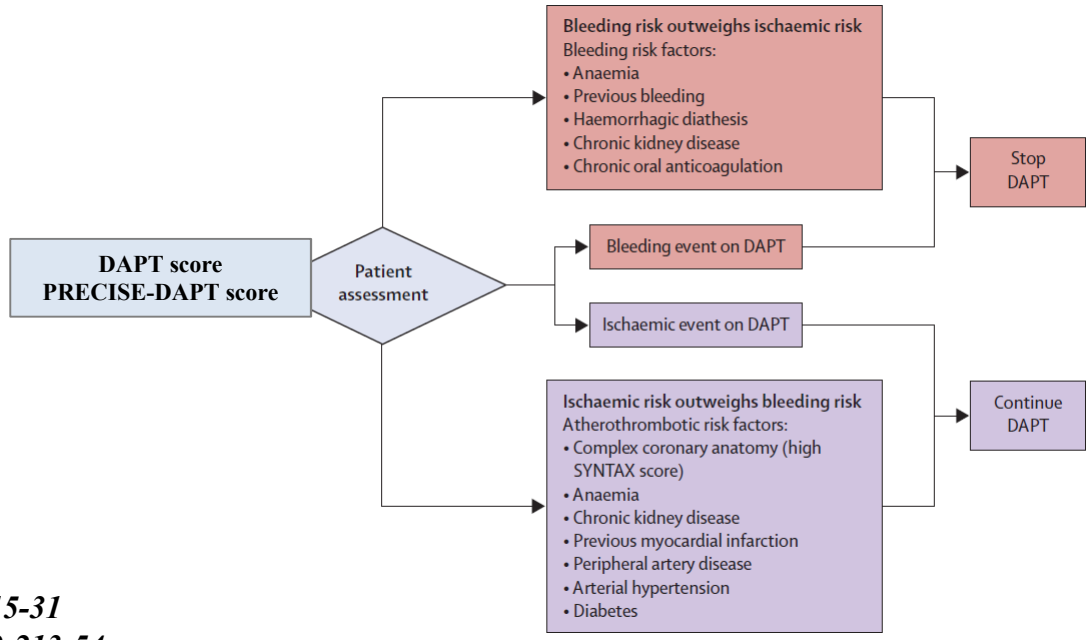
Introducción



Ferreiro JL et. al Thromb Haemost 2010:103:1-8

Introducción





Capodanno D et al. JACC 2018:72;2915-31
Valgimigli L et al. Eur Heart J 2018:39:213-54

Razones para acortar

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1. **ESTUDIOS: eficacia y seguridad**

2. **Equilibrio riesgo isquémico *vs* sangrado**

factores clínicos

factores técnicos

Estudios

Pautas cortas:

	SCA	DES 2ªgen	Duración meses	Objetivo 1º	No inferior	Sangrado Mayor
I LOVE IT2 (2016)	82%	100%	**6** vs 12	Muerte + IAM + TLR	+	=
REDUCE (2017)	100%	100%	**3** vs 12	Muerte + IAM + TLR + TS + ictus + Sangrado M	+	=
DAPT-STEMI (2017)	100%	100%	**6** vs 12	Muerte + IAM + TLR + ictus + Sangrado M	+	=
SMART-DATE (2017)	100%	100%	**6** vs 12	Muerte + IAM + ictus	+	=

Estudios

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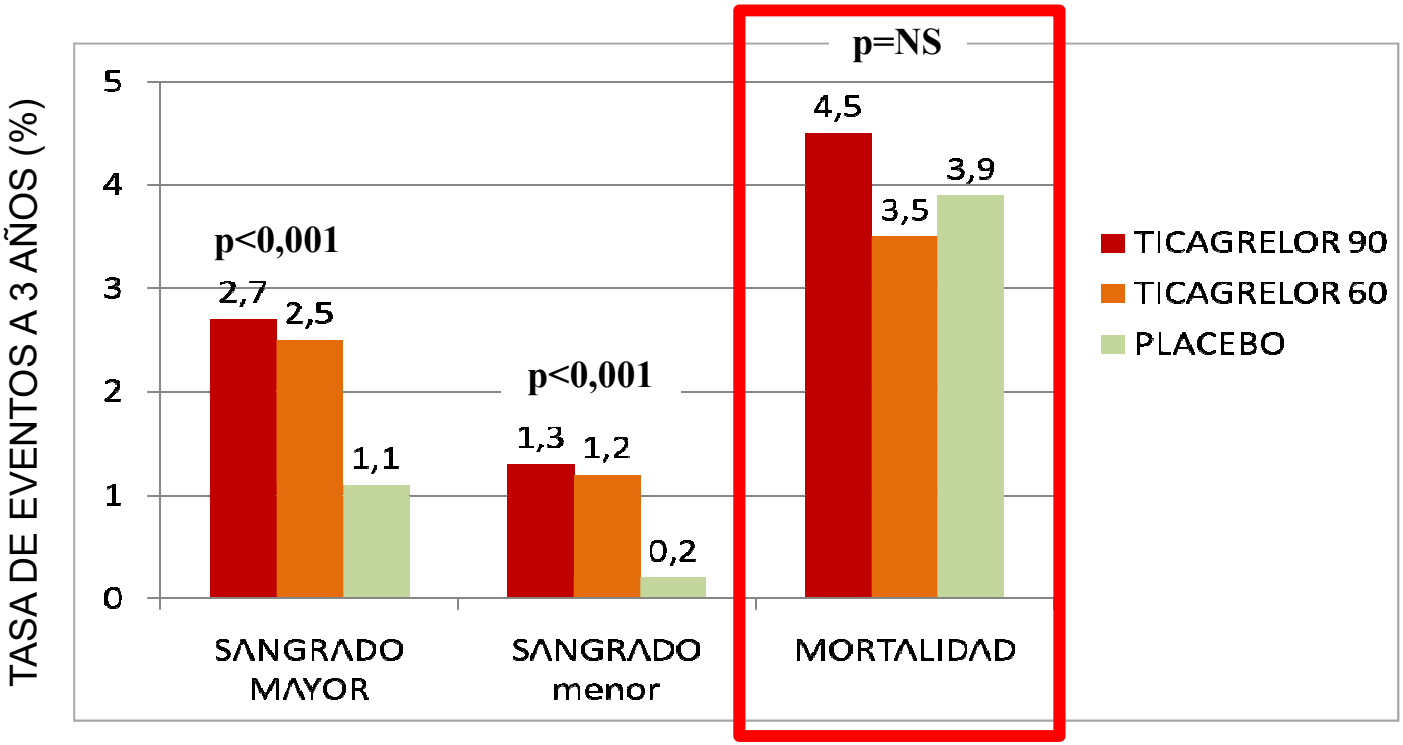
Pautas prolongadas:

	SCA	DES 2ªgen	Duración meses	Objetivo 1º		Sangrado Mayor
PRODIGY (2012)	75%	50%	6 vs **24**	Muerte + IAM + ictus	-	↑
DES-LATE (2014)	61%	64%	12 vs **36**	Muerte + IAM + ictus	-	↑
DAPT (2014)	43%	60%	12 vs **30**	Muerte + IAM + ictus + trombosis stent	+	↑
PEGASUS (2015)	100%	?	12 vs **30**	Muerte + IAM + ictus	+	↑

~~MORTALIDAD~~

Estudios

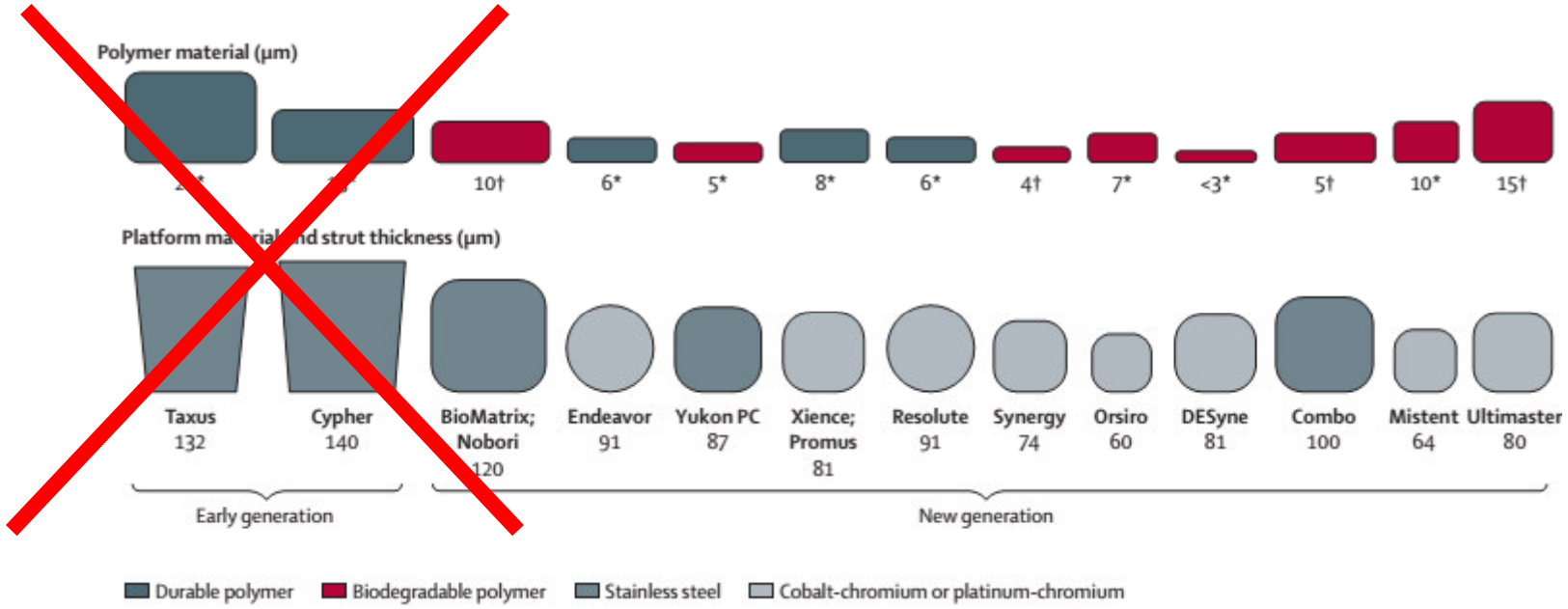
Estudio PEGASUS. *Seguridad y tolerancia*



	Ticagrelor, 90 mg (N=6988)	Ticagrelor, 60 mg (N=6958)	Placebo (N=6996)	Ticagrelor, 90 mg vs. Placebo	
Dyspnea	1205 (18.93)	98[illegible] (15.84)	383 (6.38)	3.55 (3.16–3.98)	<0.001
Event leading to study-drug discontinuation	430 (6.50)	297 (4.55)	51 (0.79)	8.89 (6.65–11.88)	<0.001
Serious adverse event	22 (0.41)	23 (0.45)	9 (0.15)	2.68 (1.24–5.83)	0.01
Renal event	166 (3.30)	173 (3.43)	161 (2.89)	1.17 (0.94–1.46)	0.15
Bradyarrhythmia	107 (2.04)	121 (2.32)	106 (1.98)	1.15 (0.88–1.50)	0.31
Gout	115 (2.28)	101 (1.97)	74 (1.51)	1.77 (1.32–2.37)	<0.001

Bonaca MP et al. NEJM 2015:372;1791-1800

Estudios


Polymer material (µm)
10†
6*
5*
8*
6*
4†
7*
<3*
5†
10*
15†
Platform material and strut thickness (µm)
Taxus
132
Cypher
140
BioMatrix; Nobori
120
Endeavor
91
Yukon PC
87
Xience; Promus
81
Resolute
91
Synergy
74
Orsiro
60
DESyne
81
Combo
100
Mistent
64
Ultimaster
80
Early generation
New generation
Durable polymer
Biodegradable polymer
Stainless steel
Cobalt-chromium or platinum-chromium

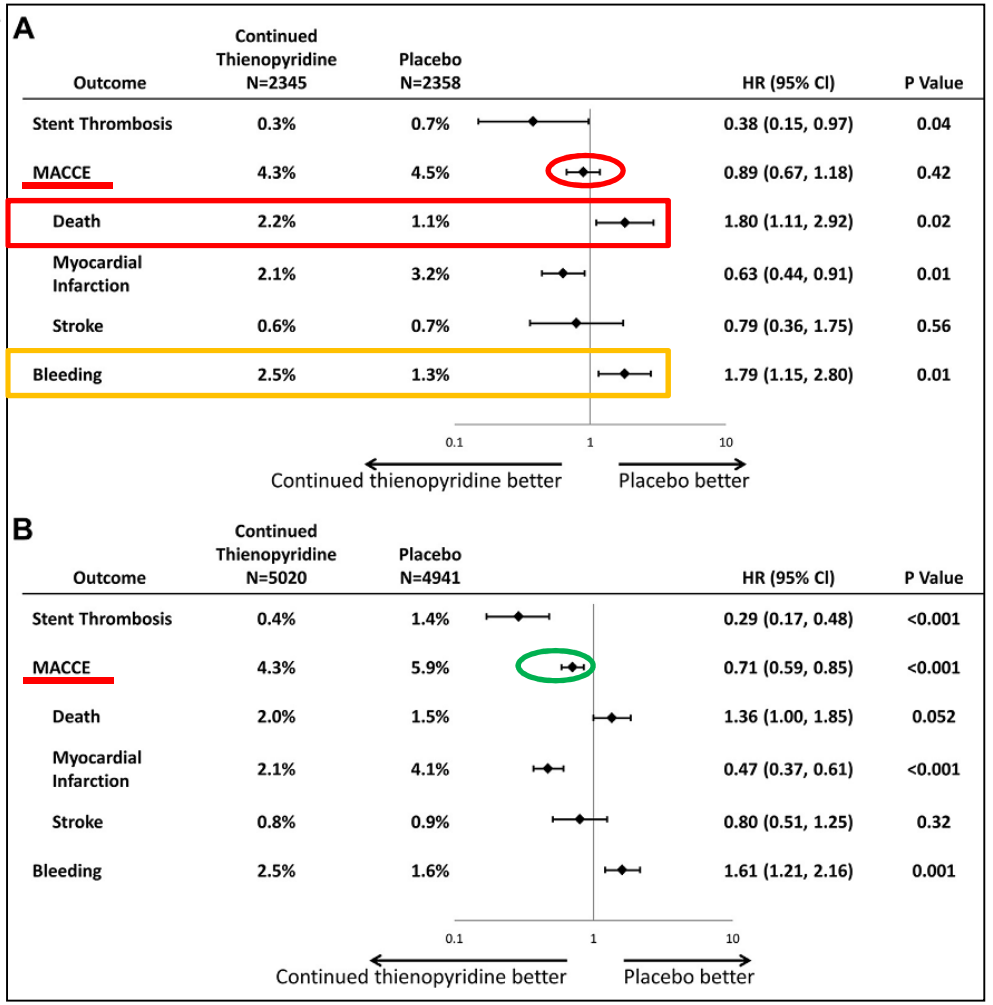
Estudios

Benefits and Risks of Extended Dual Antiplatelet Therapy After Everolimus-Eluting Stents

James B. Hermiller, MD,* Mitchell W. Krucoff, MD,† Dean J. Kereiakes, MD,‡ Stephan Windecker, MD,§
P. Gabriel Steg, MD,‖¶ Robert W. Yeh, MD, MSc,#**†† David J. Cohen, MD, MSc,‡‡ Donald E.
Joseph M. Massaro, PhD,††‖‖ Wen-Hua Hsieh, PhD,†† Laura Mauri, MD, MSc,**††¶¶
on behalf of the DAPT Study Investigators

Estudio DAPT. *JACC Intv 2016:9;138-47*

DES 2ª generación (EES)
(60% de los pacientes)



DES 1ª + 2ª generación
(Total de los pacientes)

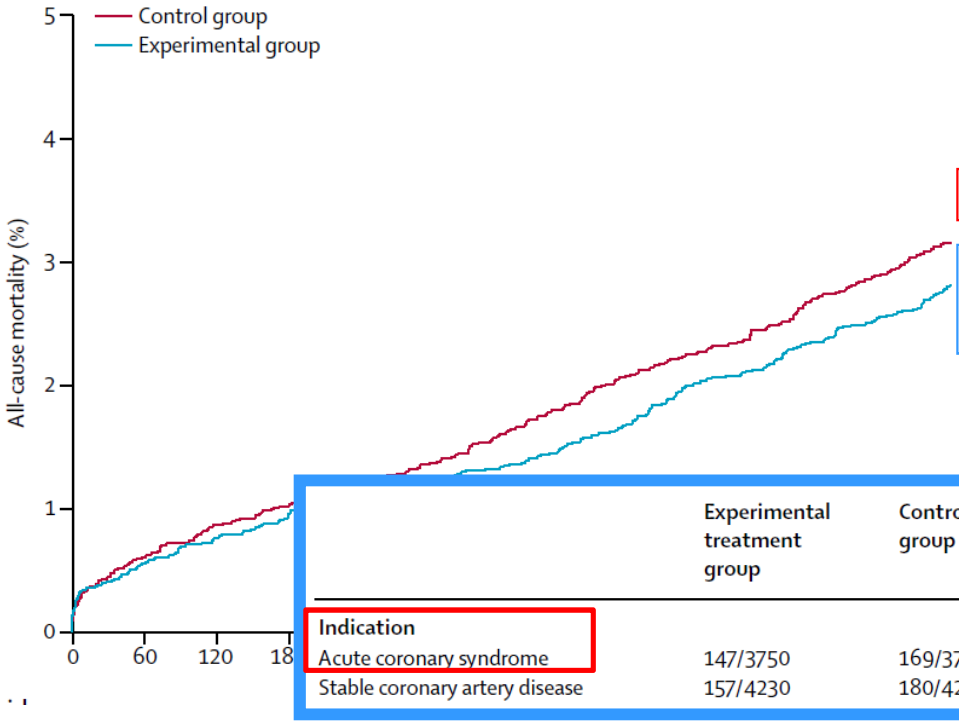
Estudios

Ticagrelor plus aspirin for 1 month, followed by ticagrelor monotherapy for 23 months *vs* aspirin plus clopidogrel or ticagrelor for 12 months, followed by aspirin monotherapy for 12 months after implantation of a drug-eluting stent: a multicentre, open-label, randomised superiority trial

Pascal Vranckx, Marco Valgimigli*, Peter Jüni*, Christian Hamm, Philippe Gabriel Steg, Dik Heg, Gerrit Anne van Es, Eugene P McFadden, Yoshinobu Onuma, Cokky van Meijeren, Ply Chichareon, Edouard Benit, Helge Möllmann, Luc Janssens, Maurizio Ferrario, Aris Moschovitis, Aleksander Zurakowski, Marcello Dominici, Robert Jan Van Geuns, Kurt Huber, Ton Slagboom, Patrick W Serruys, Stephan Windecker, on behalf of*

the GLOBAL LEADERS Investigators

Lancet 2018; 392: 940–49



AAS+TICAGRELOR 12meses……AAS monoterapia 12 meses

AAS+TICAGRELOR 1mes……TICAGRELOR monoterapia 23 meses

MONOTERAPIA CON TICAGRELOR TRAS 1 MES DAPT

	Experimental treatment group	Control group	Rate ratio (95% CI)	p value
Indication				
Acute coronary syndrome	147/3750	169/3737	0·86 (0·69–1·08)	0·19
Stable coronary artery disease	157/4230	180/4251	0·87 (0·71–1·08)	0·22

0·25 0·5 1·0 2·0 4·0

Estudios

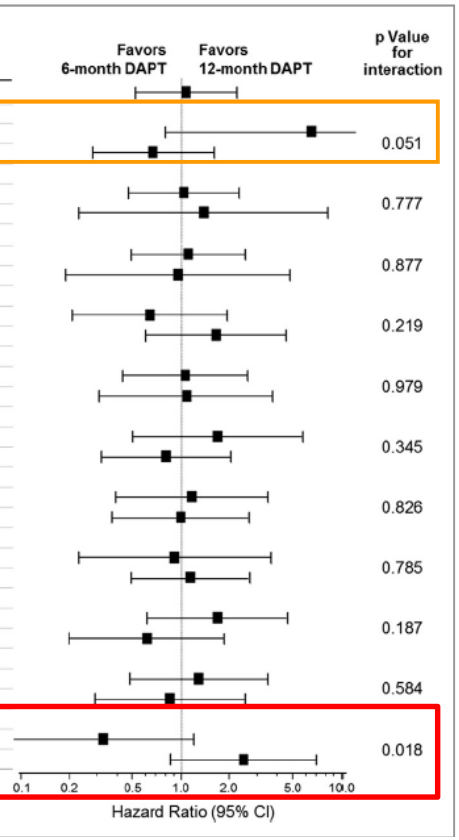
6-Month Versus 12-Month Dual-Antiplatelet Therapy Following Long Everolimus-Eluting Stent Implantation

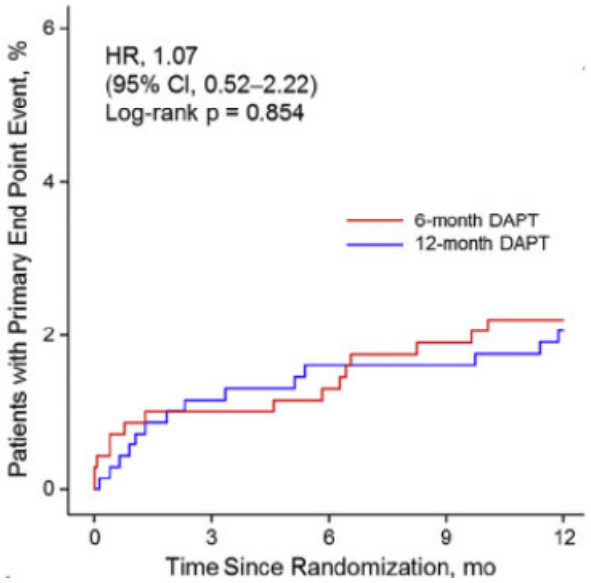
The IVUS-XPL Randomized Clinical Trial

Sung-Jin Hong, MD,[a,b] Dong-Ho Shin, MD, MPH,[b] Jung-Sun Kim, MD,[b] Byeong-Keuk Kim, MD,[b] Young-Guk Ko, MD,[b] Donghoon Choi, MD,[b] Ae-Young Her, MD,[c] Yong Hoon Kim, MD,[c] Yangsoo Jang, MD,[b,d,e] Myeong-Ki Hong, MD,[b,d,e] for the IVUS-XPL Investigators

JACC Intv 2016:9;1438-46

Subgroup	6-month DAPT No. of events	6-month DAPT No. of patients	12-month DAPT No. of events	12-month DAPT No. of patients	Hazard Ratio (95% CI)	p Value for interaction
All patients	15	699	14	701	1.07 (0.52 – 2.22)	
Age, y						
≤65	7	392	1	358	6.50 (0.80 – 52.81)	0.051
>65	8	307	13	343	0.67 (0.28 – 1.62)	
Sex						
Male	12	470	12	494	1.04 (0.47 – 2.31)	0.777
Female	3	229	2	207	1.38 (0.23 – 8.23)	
Hypertension						
Yes	12	443	11	455	1.11 (0.49 – 2.52)	0.877
No	3	256	3	246	0.96 (0.19 – 4.77)	
Diabetes mellitus						
Yes	5	249	8	257	0.64 (0.21 – 1.95)	0.219
No	10	450	6	444	1.65 (0.60 – 4.53)	
Dyslipidemia						
Yes	10	473	9	456	1.06 (0.43 – 2.62)	0.979
No	5	226	5	245	1.08 (0.31 – 3.74)	
Current smoker						
Yes	7	171	4	165	1.69 (0.50 – 5.78)	0.345
No	8	528	10	536	0.81 (0.32 – 2.04)	
Clinical presentation						
Stable angina	7	356	6	358	1.17 (0.39 – 3.49)	0.826
Acute coronary syndrome	8	343	8	343	1.00 (0.37 – 2.66)	
No. of diseased vessels						
One	4	229	4	211	0.91 (0.23 – 3.65)	0.785
Two or three	11	470	10	480	1.15 (0.49 – 2.70)	
Coronary arteries						
LAD	10	432	6	442	1.69 (0.61 – 4.64)	0.187
LCX or RCA	5	267	8	259	0.61 (0.20 – 1.87)	
Reference vessel diameter, mm						
<3.00	9	433	7	435	1.29 (0.48 – 3.46)	0.584
≥3.00	6	266	7	266	0.85 (0.29 – 2.54)	
Use of intravascular ultrasound						
Yes	3	355	9	353	0.33 (0.09 – 1.21)	0.018
No	12	344	5	348	2.45 (0.86 – 6.96)	



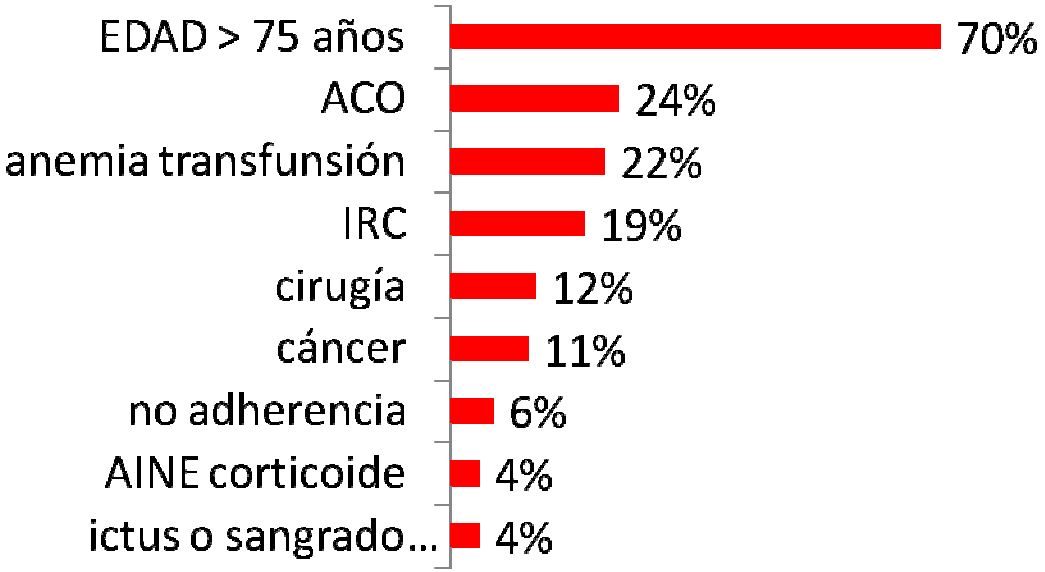


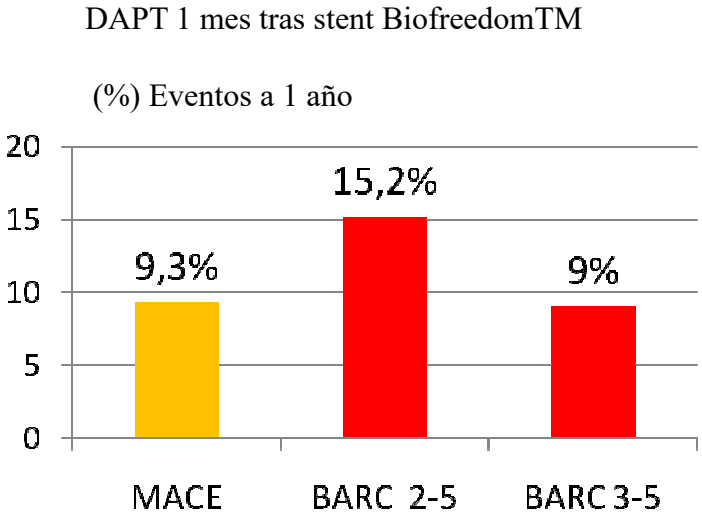
Estudios

Biolimus-A9 polymer-free coated stent in high bleeding risk patients with acute coronary syndrome: a *Leaders Free ACS* sub-study

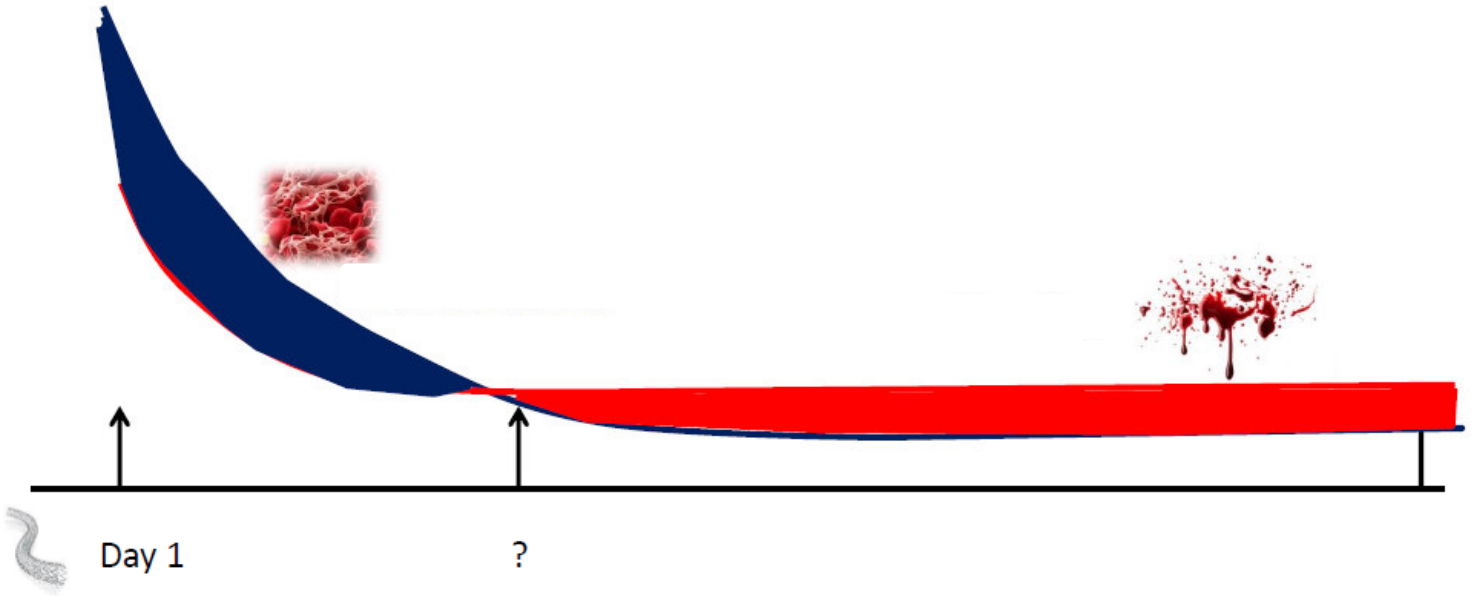
Christoph K. Naber[1]*, Philip Urban[2], Paul J. Ong[3], Mariano Valdes-Chavarri[4], Alexandre A. Abizaid[5], Stuart J. Pocock[6], Franco Fabbiocchi[7], Christophe Dubois[8], Samuel Copt[9], Samantha Greene[9], and Marie-Claude Morice[10], for the LEADERS FREE Investigators

European Heart Journal (2017) **38**, 961–969



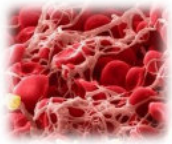


Riesgo isquémico *vs* sangrado

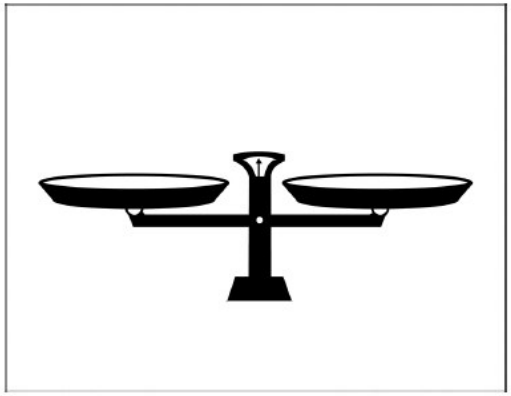


Thrombotic risk > bleeding risk

Bleeding risk > thrombotic risk

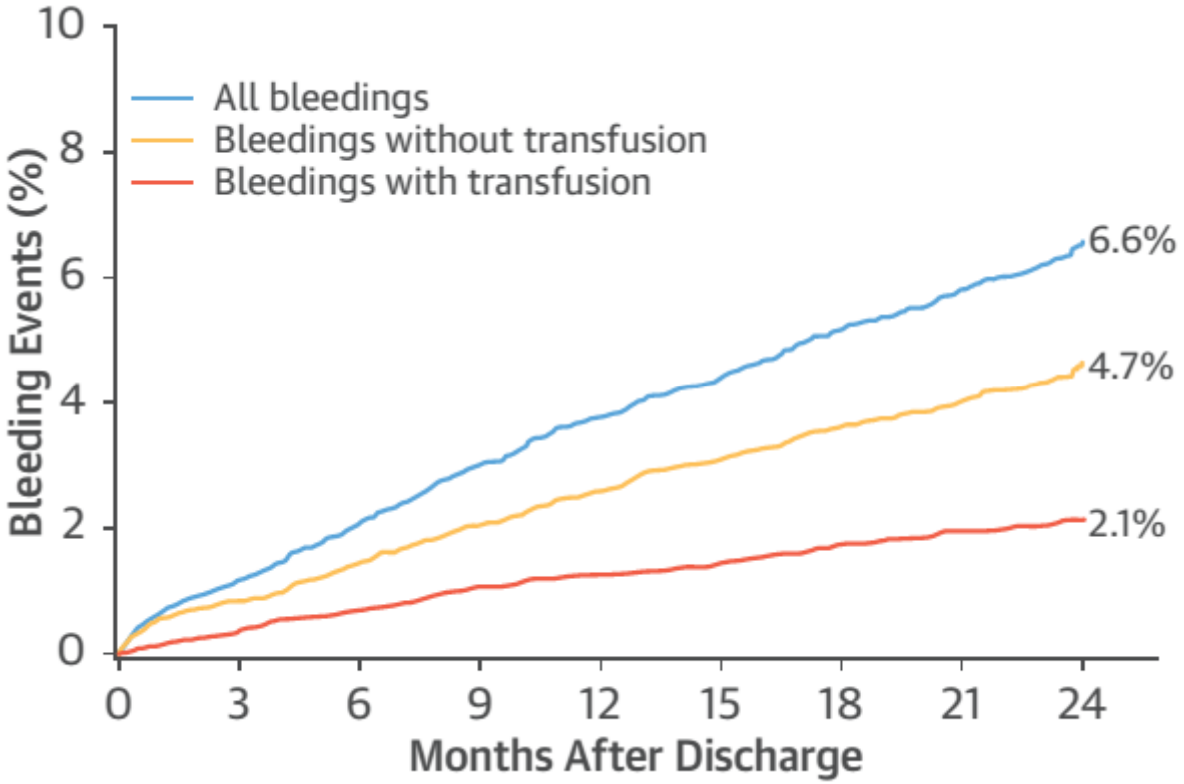


Ischemic Risk



Bleeding Risk

Riesgo isquémico *vs* sangrado



Genereux P et. al JACC 2015;66:1036-45

Riesgo isquémico *vs* sangrado

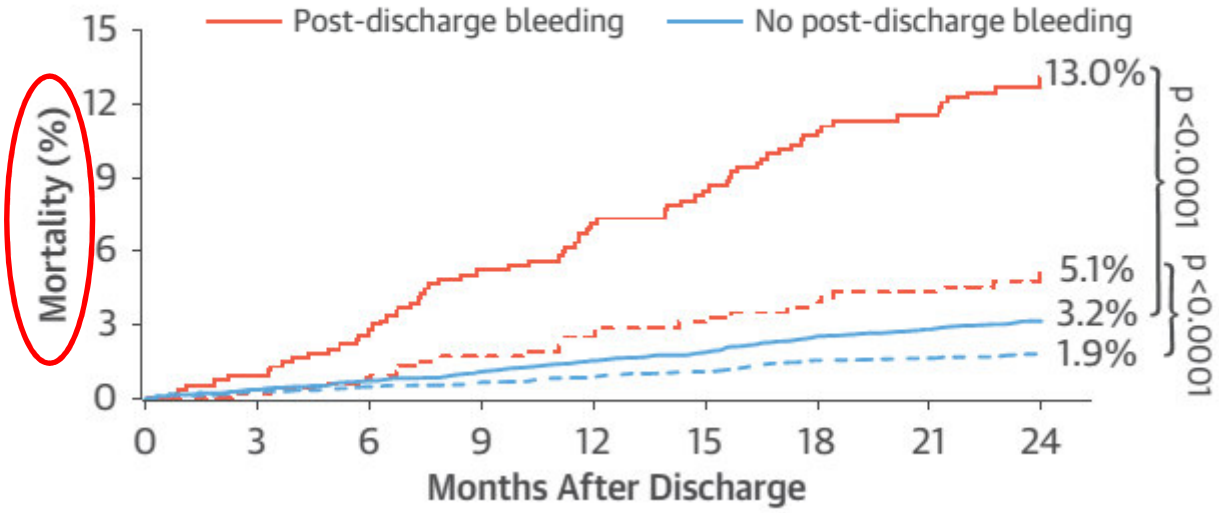
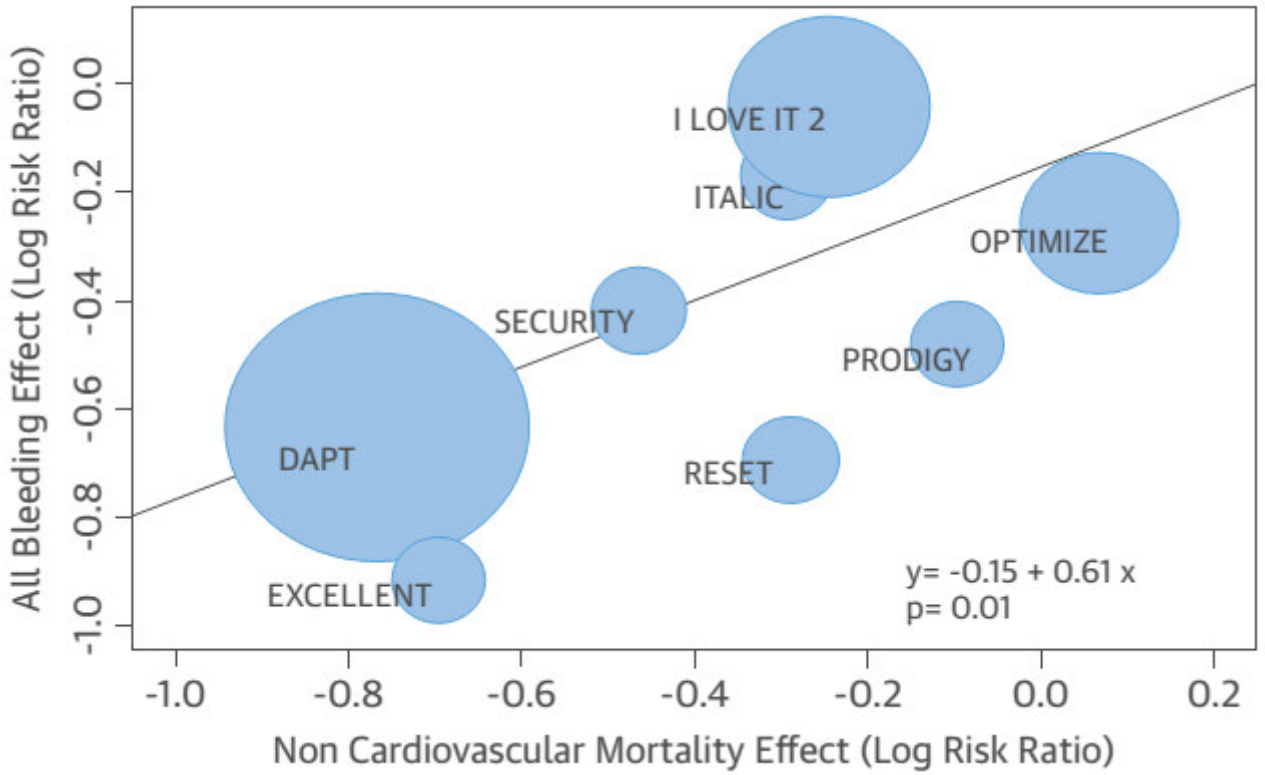


TABLE 4 Independent Predictors of All-Cause Mortality at 2 Years

Variable*	Adjusted HR (95% CI)	p Value
PDB†	5.03 (3.29–7.66)	<0.0001
With transfusion	4.71 (2.76–8.03)	<0.0001
Without transfusion	5.27 (3.32–8.35)	<0.0001
Post-discharge MI†	1.92 (1.18–3.12)	0.009

Genereux P et. al JACC 2015;66:1036-45

Riesgo isquémico *vs* sangrado



Capodanno D et. al JACC 2015;66:1633-40

Riesgo isquémico *vs* sangrado

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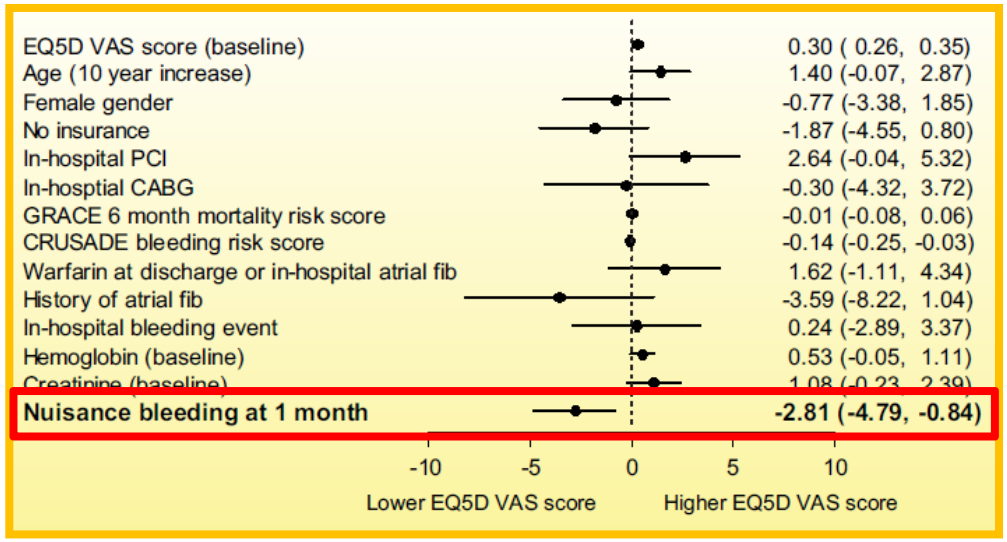
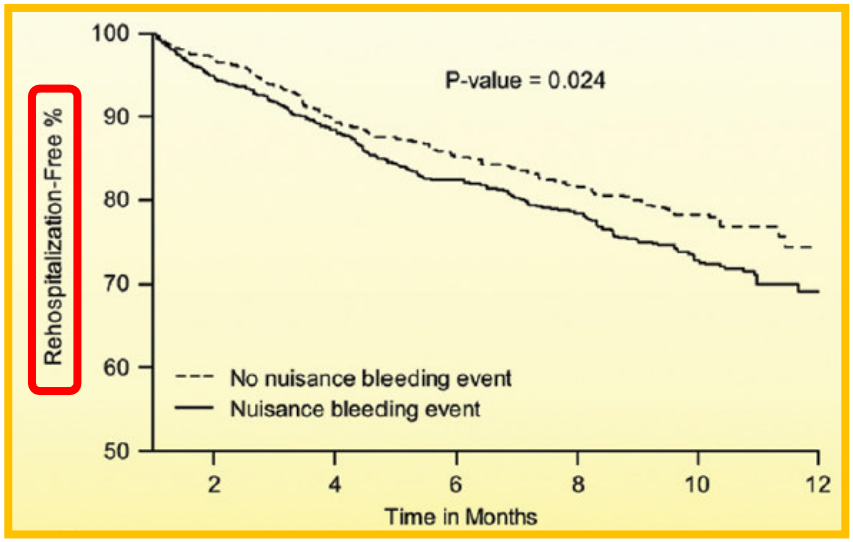
Nuisance Bleeding With Prolonged Dual Antiplatelet Therapy After Acute Myocardial Infarction and its Impact on Health Status

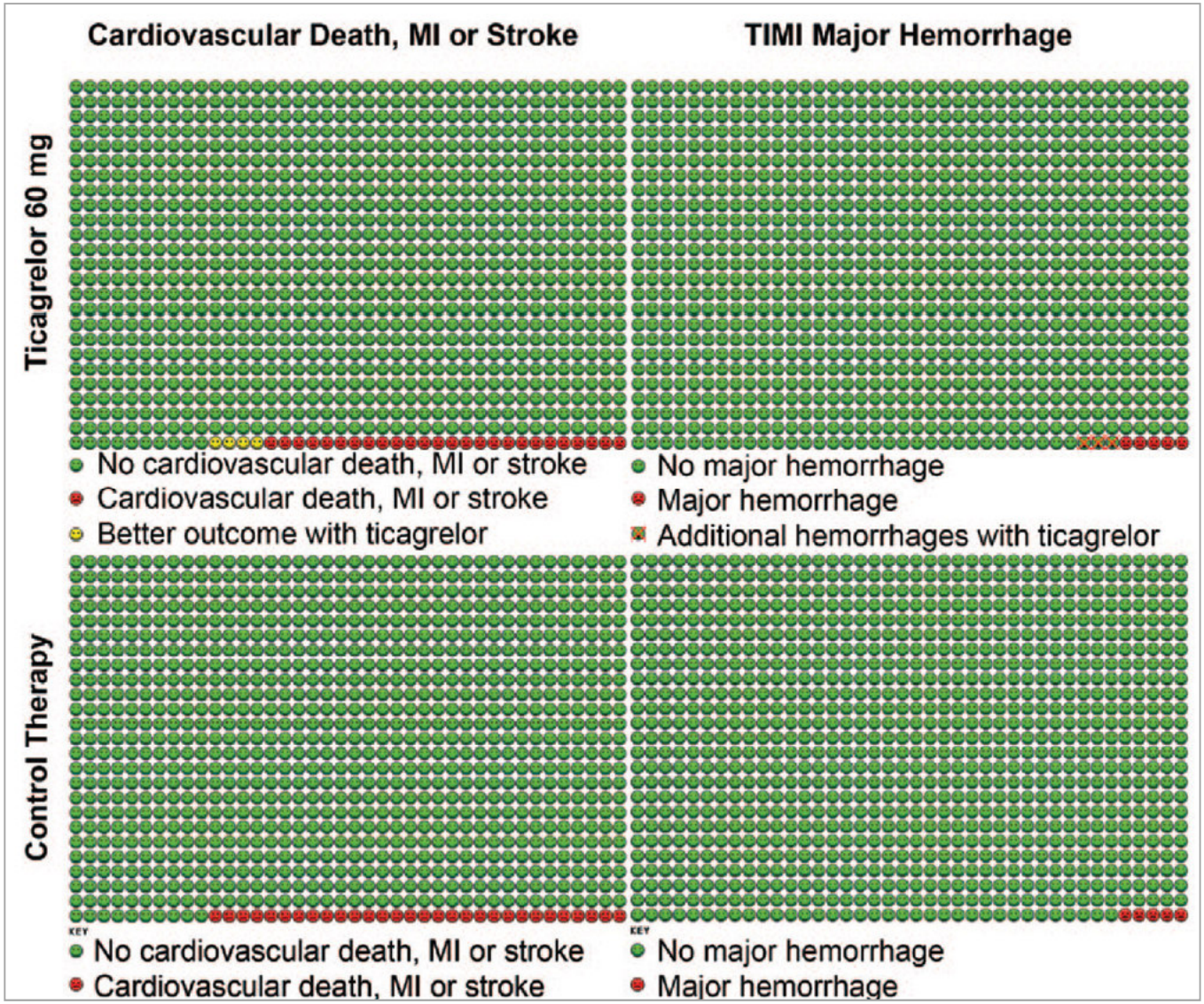
Amit P. Amin, MD, MSc,*† Alok Bachuwar, MD,*† Kimberly J. Reid, MS,‡
Adnan K. Chhatriwalla, MD,‡§ Adam C. Salisbury, MD, MSc,‡§ Robert W. Yeh, MD, MSc,‖
Mikhail Kosiborod, MD,‡§ Tracy Y. Wang, MD, MHS,¶ Karen P. Alexander, MD,¶
Kensey Gosch, MS,‡ David J. Cohen, MD, MSc,‡§ John A. Spertus, MD, MPH,‡§
Richard G. Bach, MD*†

JACC 2013:61;2131-38





Riesgo isquémico *vs* sangrado



Estudio PEGASUS *Bittl JA et al. JACC 2016;68:1116-39*

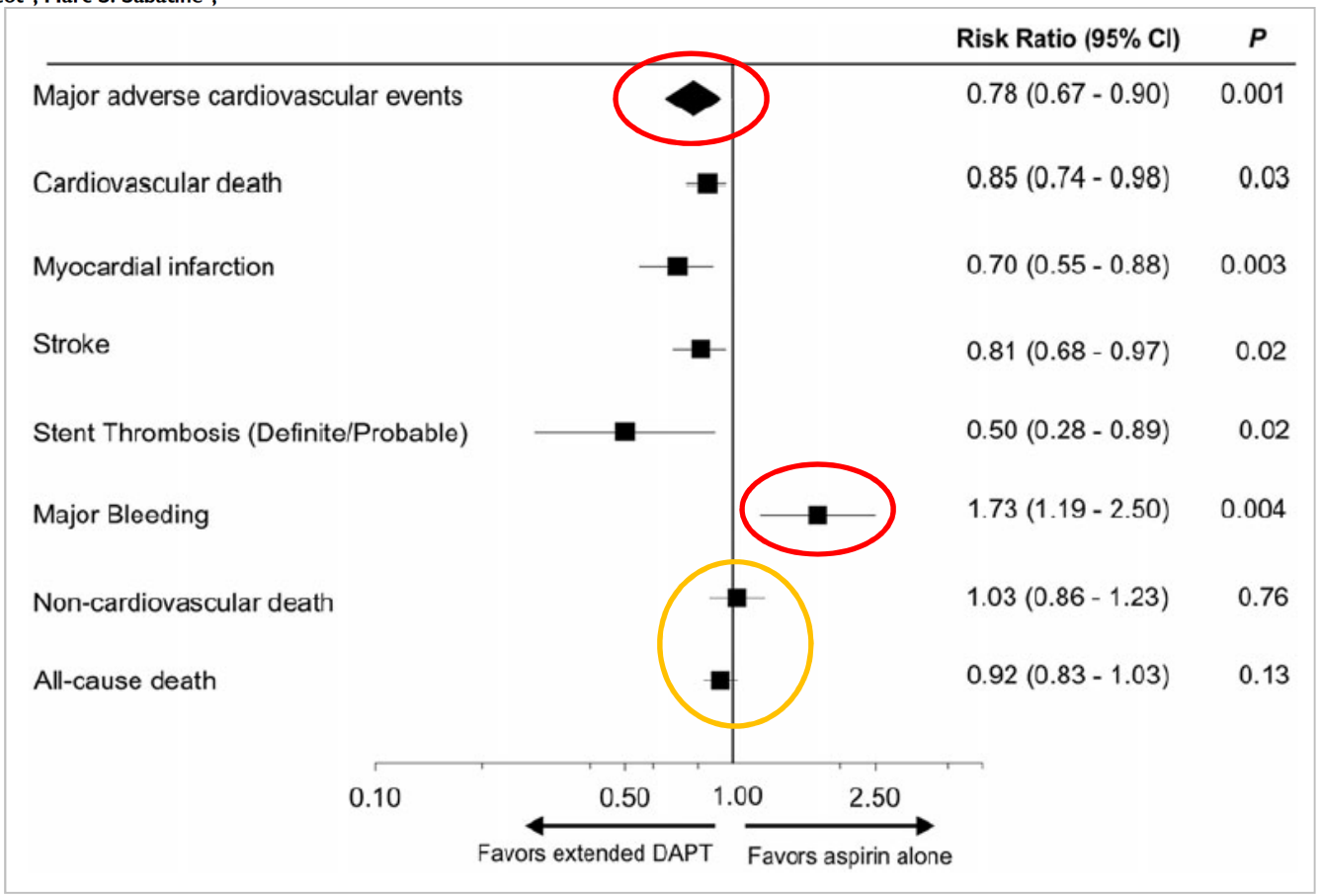
Riesgo isquémico *vs* sangrado

Hospital Universitario 12 de Octubre

Long-term dual antiplatelet therapy for secondary prevention of cardiovascular events in the subgroup of patients with previous myocardial infarction: a collaborative meta-analysis of randomized trials

Jacob A. Udell[1,2*], Marc P. Bonaca[3], Jean-Philippe Collet[4], A. Michael Lincoff[5], Dean J. Kereiakes[6], Francesco Costa[7], Cheol Whan Lee[8], Laura Mauri[9], Marco Valgimigli[7,10], Seung-Jung Park[8], Gilles Montalescot[4], Marc S. Sabatine[3], Eugene Braunwald[3], and Deepak L. Bhatt[3*]

European Heart Journal (2016) **37**, 390–399



Conclusiones

1. **Las pautas cortas de doble antiagregación son seguras y eficaces. No son inferiores a la pauta estándar en cuanto a incidencia de eventos isquémicos, asociándose a tasas similares o menores de sangrado.**

2. **Las pautas prolongadas de doble antiagregación se asocian a mayores tasas de sangrado, sin beneficios en la mortalidad.**

3. **La utilización de stents de última generación y la optimización del resultado de la angioplastia con ecografía intracoronaria favorece la utilización de pautas cortas, especialmente en pacientes con alto riesgo de sangrado.**

4. **El riesgo de sangrado se relaciona con la duración de la doble terapia antiagregante, es continuo en el tiempo y se asocia a mayor mortalidad, equilibrando el beneficio isquémico de las pautas prolongadas.**