

# ***NOVEDADES EN EL TRATAMIENTO DE LA CARDIOPATIA ISQUEMICA***

**Congreso SEC 2011  
Maspalomas**

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Unidad Coronaria.  
Hospital Virgen Macarena. Sevilla

# Declaración de potenciales conflictos de intereses

## *NOVEDADES EN EL TRATAMIENTO DE LA CARDIOPATIA ISQUEMICA*

Relativas a esta presentación no existen conflictos de intereses

Rafael Hidalgo Urbano  
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# NOVEDAD

- 1. Cualidad de nuevo.
- 2. Cosa nueva.
- 3. Cambio producido en algo.
- 4. Suceso reciente, noticia.
- 5. Innovar en algo lo que ya estaba en práctica

# NOVEDADES EN EL TRATAMIENTO DE LA CARDIOPATIA ISQUEMICA

- **Fármacos**
  - Antianginosos
  - Antiagregantes, Anticoagulantes
- **Revascularización**
  - Intervencionismo coronario
  - Cirugía coronaria
- **Prevención**

**ANTIANGINOSOS**

# Cardiopatía isquémica estable

- **IVABRADINA**

**Safety of *Ivabradine* in Patients With Coronary Artery Disease and Left Ventricular Systolic Dysfunction (from the BEAUTIFUL Holter Substudy)**

Michal Tendera, MD<sup>a,\*</sup>, Mario Talajic, MD<sup>b</sup>, Michele Robertson, BSc<sup>c</sup>, Jean-Claude Tardif, MD<sup>b</sup>, Roberto Ferrari, MD<sup>d</sup>, Ian Ford, PhD<sup>c</sup>, P. Gabriel Steg, MD<sup>e</sup>, and Kim Fox, MD<sup>f</sup>, on Behalf of the BEAUTIFUL Investigators

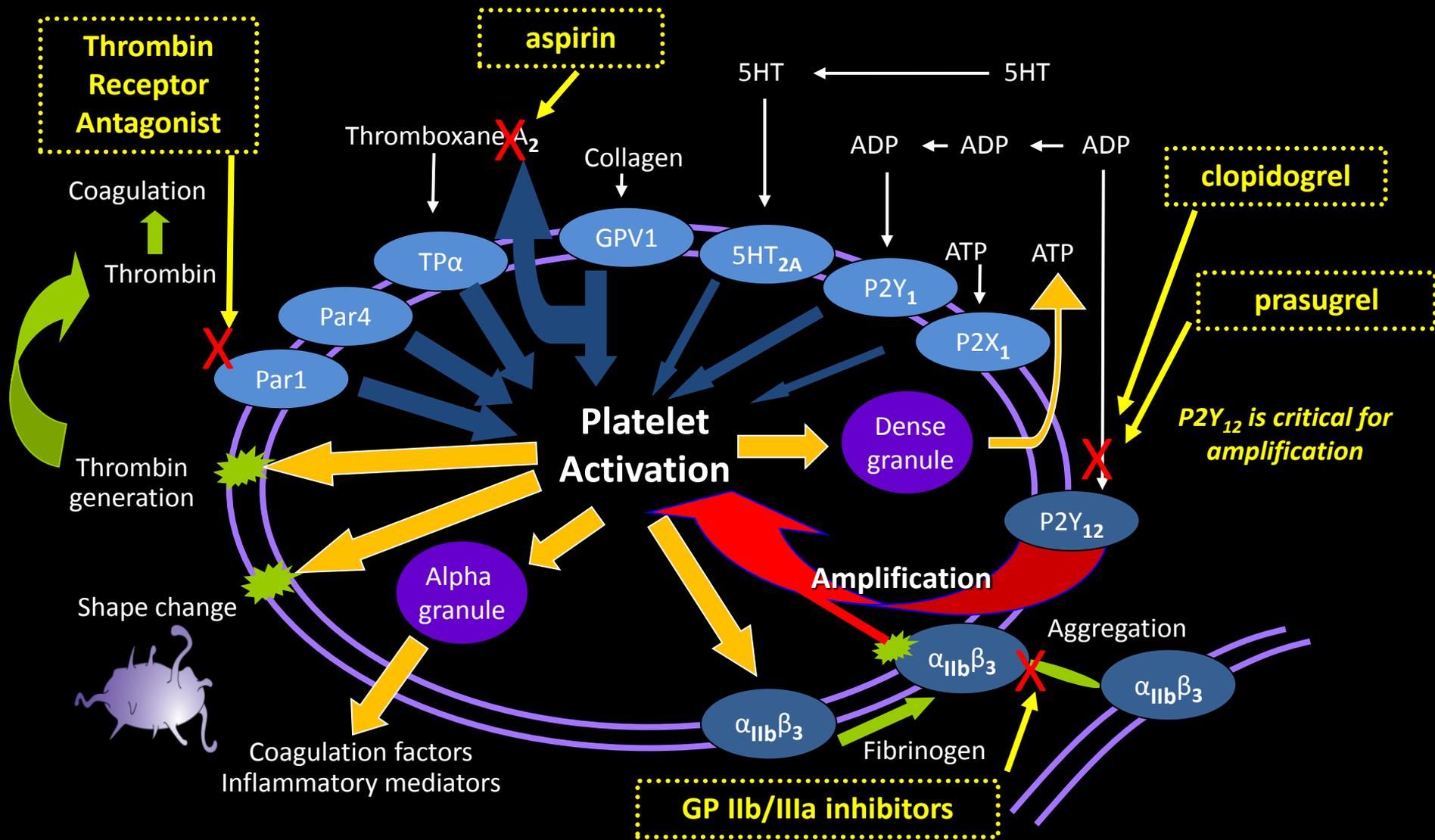
Am J Cardiol 2011;107:805– 811

- Seguridad uso asociado a betabloqueantes

- **RANOLAZINA**

**ANTIAGREGANTES**

# Vías de activación plaquetaria



5HT=5-hidroxitriptamina; ADP=Adenosín difosfato; GP=Glicoproteína; PAR=receptor activado por proteasas; TP=receptor de tromboxano A $_2$ .

Adaptado a partir de Storey RF et al. *Curr Pharm Des* 2006;12:1255-1259

# Clopidogrel Response Variability

## Genetic Factors

- Polymorphisms of CYP
- Polymorphisms of GPIa
- Polymorphisms of P2Y<sub>12</sub>
- Polymorphisms of GPIIb/IIIa

## Clinical Factors

- Failure to prescribe/poor compliance
- Under-dosing
- Poor absorption
- Drug-drug interactions CYP3A4/CYP2C19
- Acute coronary syndrome
- Diabetes mellitus/insulin resistance
- Elevated body mass index

## Cellular Factors

- Accelerated platelet turnover
- Reduced CYP3A metabolic activity
- Increased ADP exposure
- Up-regulation of the P2Y<sub>12</sub> pathway
- Up-regulation of the P2Y<sub>1</sub> pathway
- Up-regulation of P2Y-independent pathways (collagen, epinephrine, TXA<sub>2</sub>, thrombin)

# HIPORRESPONDADORES

- ¿Hay que hacer test de función plaquetaria?
- ¿Hay que hacer test genéticos?
- ¿Hay que recurrir a la triple antiagregación?
- ¿Usamos aas más nuevos antiagregantes?
- ¿Usamos aas y doble dosis de clopidogrel?

¿Test de agregación  
plaquetaria?

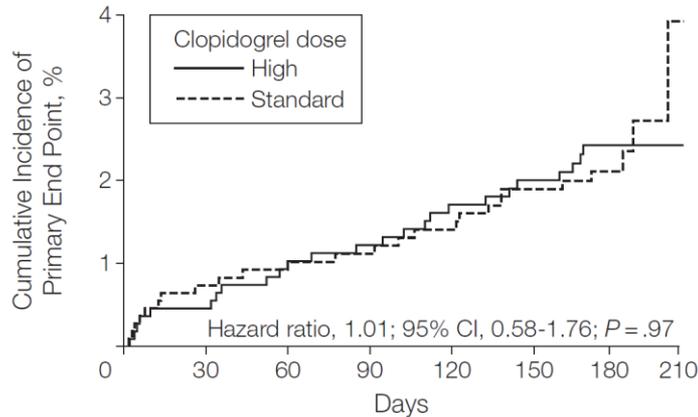
# GRAVITAS Study Design

Elective or Urgent PCI with DES\*

VerifyNow P2Y12 Test 12-24 hours post-PCI

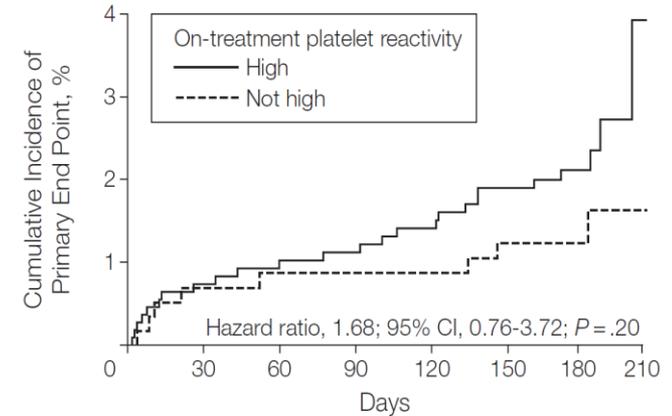
PRU  $\geq$  230

Patients with high on-treatment platelet reactivity receiving high- or standard-dose clopidogrel



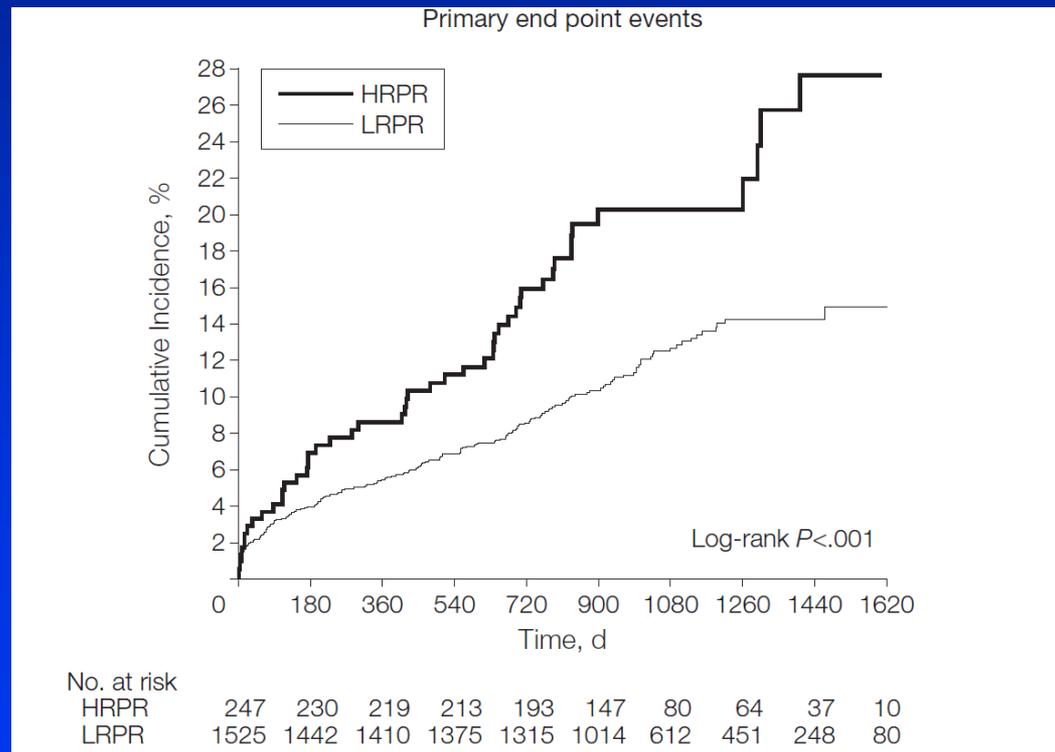
No. at risk	0	30	60	90	120	150	180	210
High-dose clopidogrel	1109	1056	1029	1017	1007	998	747	54
Standard-dose clopidogrel	1105	1057	1028	1020	1015	1005	773	53

Patients with and without high on-treatment platelet reactivity receiving standard-dose clopidogrel



No. at risk	0	30	60	90	120	150	180	210
High on-treatment reactivity	1105	1057	1028	1020	1015	1005	773	53
Not high on-treatment reactivity	586	565	552	551	549	546	415	19

# High Residual Platelet Reactivity After Clopidogrel Loading and Long-term Cardiovascular Events Among Patients With Acute Coronary Syndromes Undergoing PCI



# POPULAR Study

## Comparison of Platelet Function Tests in Predicting Clinical Outcome in Patients Undergoing Coronary Stent Implantation

- El estudio POPULAR analizó la utilidad de los tests de función plaquetaria en 1069 ptes con stent
- El agregómetro de transmisión de luz, el VerifyNow y el Plateworks proporcionaron un moderado Valor Predictivo para eventos CVs al año
- Las mediciones con PFA-100 o IMPACT-R no tuvieron valor pronóstico alguno
- Ninguno predijo el riesgo de sangrado

¿Test genéticos?

## Drugs

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[Home](#) > [Drugs](#) > [Drug Safety and Availability](#) > [Postmarket Drug Safety Information for Patients and Providers](#)

### Drug Safety and Availability

#### Postmarket Drug Safety Information for Patients and Providers

[Index to Drug-Specific Information](#)

[Approved Risk Evaluation and Mitigation Strategies \(REMS\)](#)

[Postmarketing Safety Evaluation of New Molecular Entities: Final Report](#)

[Drug Safety Information for Healthcare Professionals](#)

## FDA Drug Safety Communication: Reduced effectiveness of Plavix (clopidogrel) in patients who are poor metabolizers of the drug

### Safety Announcement

#### Additional Information for Patients

#### Additional Information for Healthcare Professionals

#### Data Summary

### Safety Announcement

[03-12-2010] The U.S. Food and Drug Administration (FDA) has added a *Boxed Warning* to the label for Plavix, the anti-blood clotting medication. The *Boxed Warning* is about patients who do not effectively metabolize the drug (i.e. "poor metabolizers") and therefore may not receive the full benefits of the drug.

The *Boxed Warning* in the drug label will include information to:

- Warn about reduced effectiveness in patients who are poor metabolizers of Plavix. Poor metabolizers do not effectively convert Plavix to its active form in the body.
- Inform healthcare professionals that tests are available to identify genetic differences in CYP2C19 function.
- Advise healthcare professionals to consider use of other anti-platelet medications or alternative dosing strategies for Plavix in patients identified as poor metabolizers.

Plavix is given to reduce the risk of heart attack, unstable angina, stroke, and cardiovascular death in patients with cardiovascular disease. Plavix works by decreasing the activity of blood cells called platelets, making platelets less likely to form blood clots.

For Plavix to work, enzymes in the liver (particularly CYP2C19) must convert (metabolize) the drug to its active form. Patients who are poor metabolizers of the drug, do not effectively convert Plavix to its active form. In these patients, Plavix has less effect on platelets, and therefore less ability to prevent heart attack, stroke, and cardiovascular death. It is estimated that 2 to 14% of the population are poor metabolizers; the rate varies based on racial

2% Blancos  
4% Negros  
14% asiáticos

14% asiáticos

¿Triple antiagregación?

## A Randomized, Double-Blind, Multicenter Comparison Study of Triple Antiplatelet Therapy With Dual Antiplatelet Therapy to Reduce Restenosis After Drug-Eluting Stent Implantation in Long Coronary Lesions

Results From the DECLARE-LONG II (Drug-Eluting Stenting Followed by Cilostazol Treatment Reduces Late Restenosis in Patients with Long Coronary Lesions) Trial

Variable	Triple (n = 250)	Dual (n = 249)	p Value
Death	6 (2.4%)	3 (1.2%)	0.51
Cardiac	4 (1.6%)	1 (0.4%)	
Noncardiac	2 (0.8%)	2 (0.8%)	
MI	4 (1.6%)	4 (1.6%)	0.99
Q-wave	2 (0.8%)	1 (0.4%)	
Non-Q-wave	2 (0.8%)	3 (1.2%)	
Ischemic-driven TLR	13 (5.2%)	25 (10.0%)	0.04
Cutting balloon	6 (2.4%)	12 (4.8%)	
Drug-eluting stent	6 (2.4%)	12 (4.8%)	
Bypass surgery	1 (0.4%)	1 (0.4%)	
Stent thrombosis	4 (1.6%)	1 (0.4%)	0.18
Acute	1 (0.4%)	0	
Subacute	2 (0.8%)	1 (0.4%)	
Late	1 (0.4%)	0	
Ischemic-driven TVR	13 (5.2%)	26 (10.4%)	0.03
Death/MI/ischemic-driven TVR	18 (7.2%)	31 (12.4%)	0.05
MACE (death/MI/ischemic-driven TLR)	18 (7.2%)	30 (12.0%)	0.07

Variable	Triple (n = 250)	Dual (n = 249)	p Value
Bleeding complications	18 (7.2%)	17 (6.8%)	0.87
Major bleeding	6 (2.4%)	2 (0.8%)	0.16
Minor bleeding	1 (0.4%)	1 (0.4%)	0.99
Minimal bleeding	11 (4.4%)	14 (5.6%)	0.53
Headache	11 (4.4%)	2 (0.8%)	0.01
Palpitation	4 (1.6%)	1 (0.4%)	0.18
Rash	8 (3.2%)	7 (2.8%)	0.80
Gastrointestinal trouble	6 (2.4%)	2 (0.8%)	0.16
Thrombocytopenia	1 (0.4%)	0	0.99
Neutropenia	1 (0.4%)	0	0.99
Hepatic dysfunction	0	4 (1.6%)	0.06
Drug discontinuation	47 (18.8%)	28 (11.2%)	0.02

¿Subir dosis de  
Clopidogrel?

# Study Design, Flow and Compliance

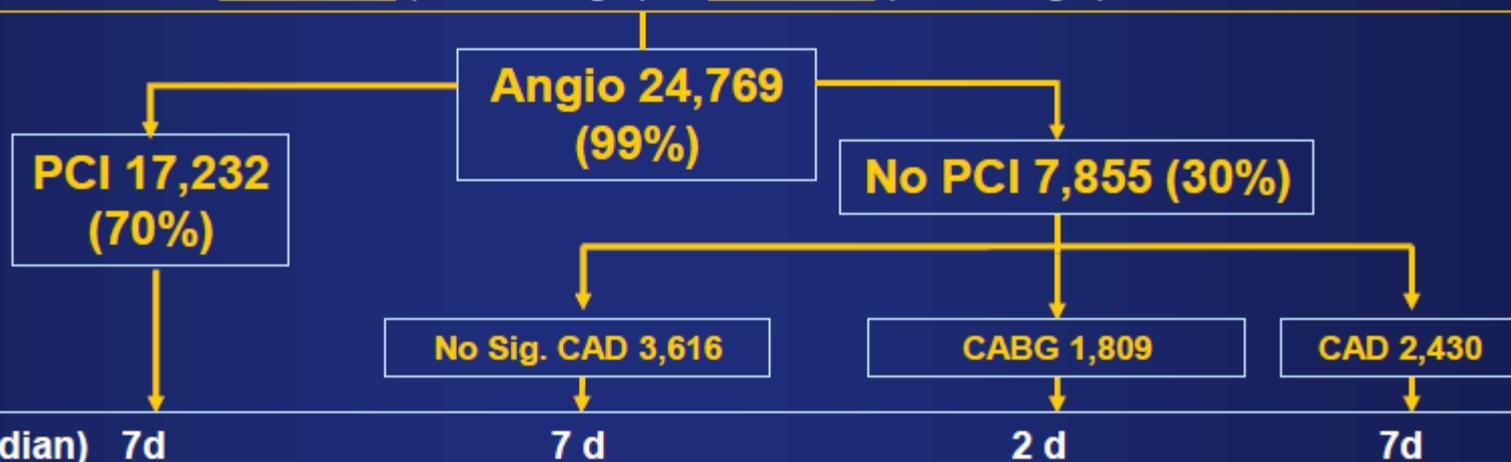
**25,087 ACS Patients (UA/NSTEMI 70.8%, STEMI 29.2%)**

- ✓ Planned Early (<24 h) Invasive Management with **intended PCI**
- ✓ Ischemic ECG Δ (80.8%) or ↑cardiac biomarker (42%)

Randomized to receive (2 X 2 factorial):

**CLOPIDOGREL: Double-dose (600 mg then 150 mg/d x 7d then 75 mg/d) vs Standard dose (300 mg then 75 mg/d)**

**ASA: High Dose (300-325 mg/d) vs Low dose (75-100 mg/d)**



**Efficacy Outcomes:** CV Death, MI or stroke at day 30  
Stent Thrombosis at day 30

**Safety Outcomes:** Bleeding (CURRENT defined Major/Severe and TIMI Major)

**Key Subgroup:** PCI v No PCI

**Complete  
Followup  
99.8%**

## Conclusions

### Clopidogrel Dose Comparison

1. Double-dose clopidogrel significantly reduced stent thrombosis and major CV events (composite of CV death, MI or stroke) in PCI.
2. In patients not undergoing PCI, double dose clopidogrel was not significantly different from standard dose (70% had no significant CAD or stopped study drug early for CABG).
3. There was a modest excess in CURRENT-defined major bleeds but no difference in TIMI major bleeds, ICH, fatal bleeds or CABG-related bleeds.

# Nuevos Antiagregantes

# TRITON-TIMI 38

TIMI group, Daiichi Sankyo, Eli Lilly

707 HOSPITALES, 30 PAÍSES (Nov 04 - Enero 07)

SCA (STEMI or UA/NSTEMI) y PCI Planeada

Aspirina

N= 13,608 10074 scasest y  
3534 Scacest

Doble ciego

CLOPIDOGREL  
300 mg DC / 75 mg DM

PRASUGREL  
60 mg DC/ 10 mg DM

Duración tratamiento: 6-15 meses:14.5 meses

Seguimiento: al alta, a los 30 y 90 días y cada 3 meses; 14 pérdidas de seguimiento

1º endpoint: Muerte CV, IAM no fatal, AVC no fatal

2º endpoint: EP 1º a los 30 y 90 días.

Muerte CV, IAM no fatal o UTVR a los 30 y 90 d

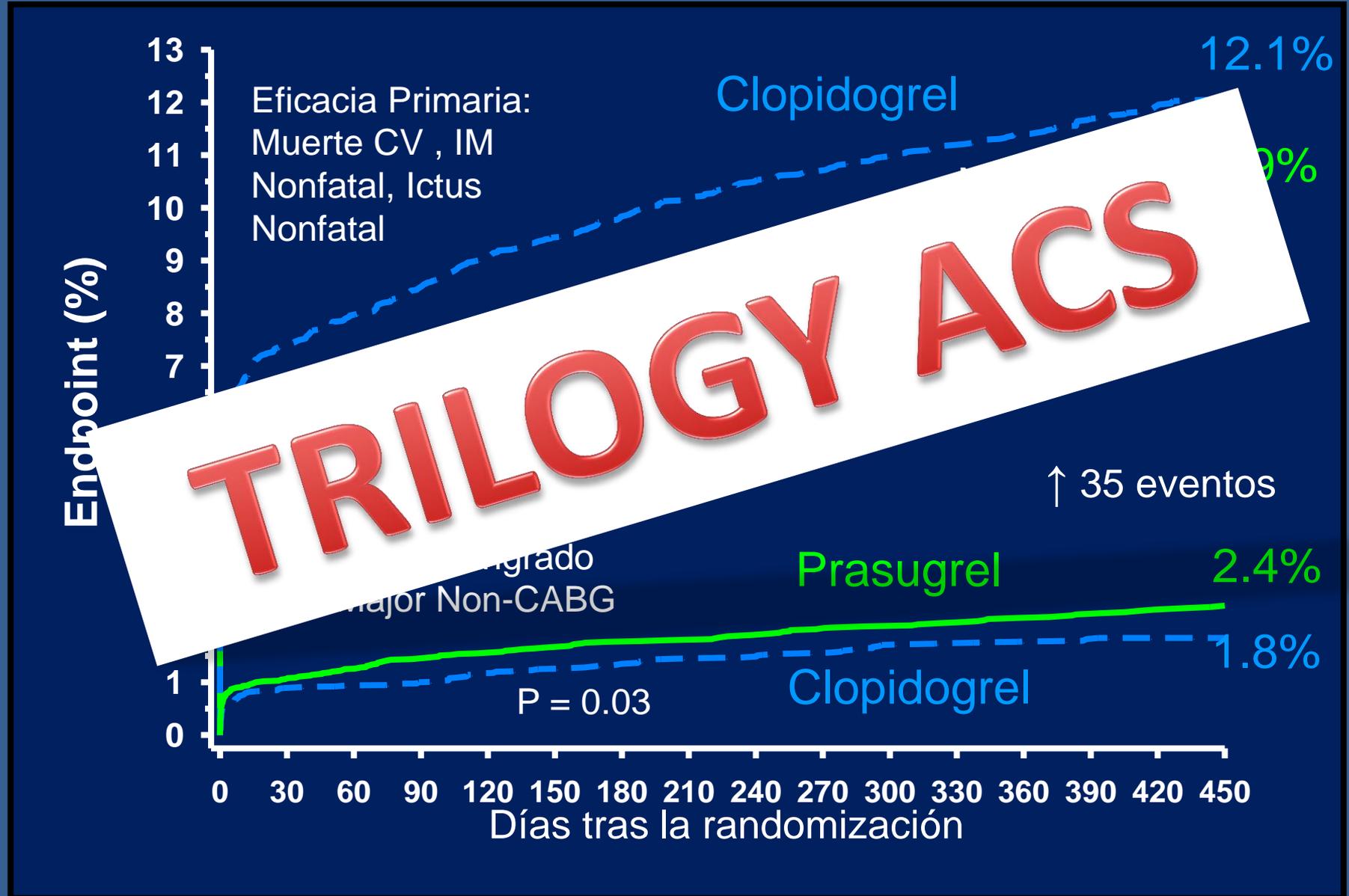
Trombosis de stent (probable o definitiva según ARC).

Muerte CV, IAM no fatal, AVC no fatal o rehospitalización por evento isquémico card.

Análisis preespecificado adicional: End point primario 0-3 días y  $\geq 3$  días

Endpoint de seguridad: TIMI major bleeds non CABG, Life-threatening bleeds, TIMI mayor o menor bleeds

# TRITON-TIMI38: EFICACIA Y SEGURIDAD EN LA POBLACION TOTAL



# PLATO study design



NSTE-ACS (moderate-to-high risk) STEMI (if primary PCI)  
Clopidogrel-treated or -naive;  
randomised within 24 hours of index event  
(N=18,624)

**Clopidogrel**  
If pre-treated, no additional loading dose;  
if naive, standard 300 mg loading dose,  
then 75 mg qd maintenance;  
(additional 300 mg allowed pre PCI)

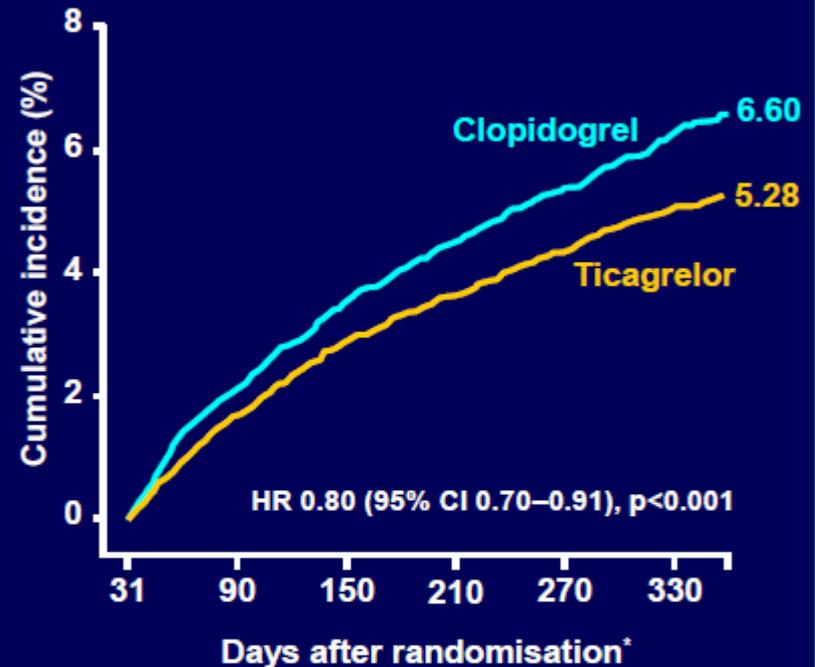
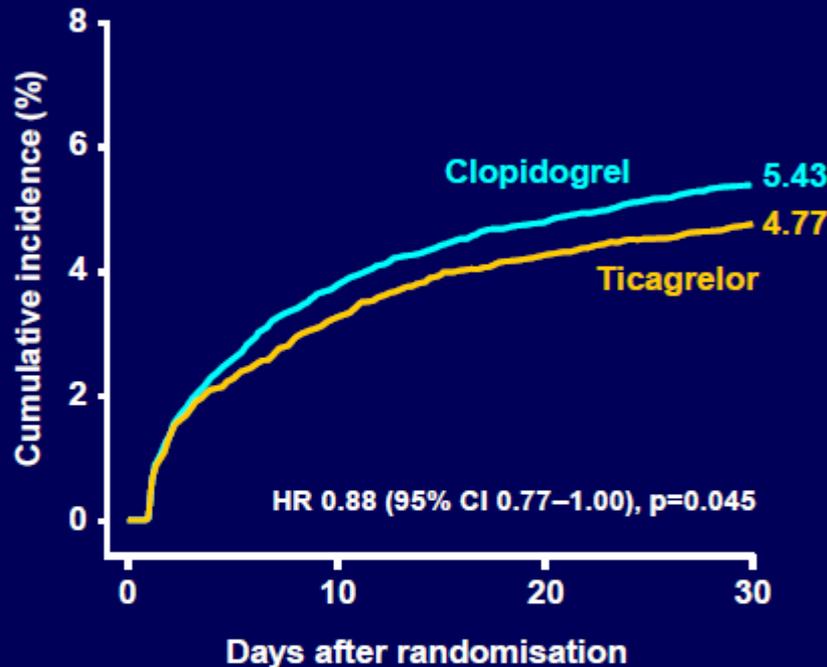
**Ticagrelor**  
180 mg loading dose, then  
90 mg bid maintenance;  
(additional 90 mg pre-PCI)

**6–12-month exposure**

Primary endpoint: CV death + MI + Stroke  
Primary safety endpoint: Total major bleeding

PCI = percutaneous coronary intervention; ASA = acetylsalicylic acid;  
CV = cardiovascular; TIA = transient ischaemic attack

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



No. at risk

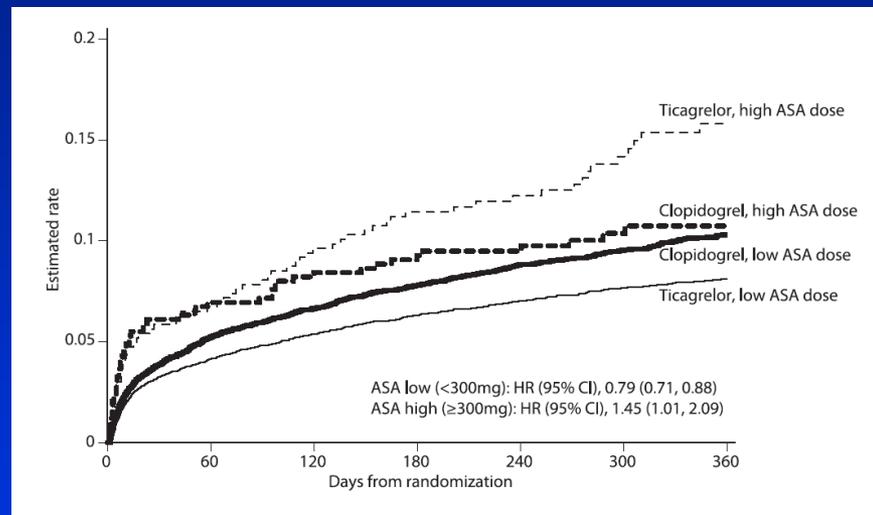
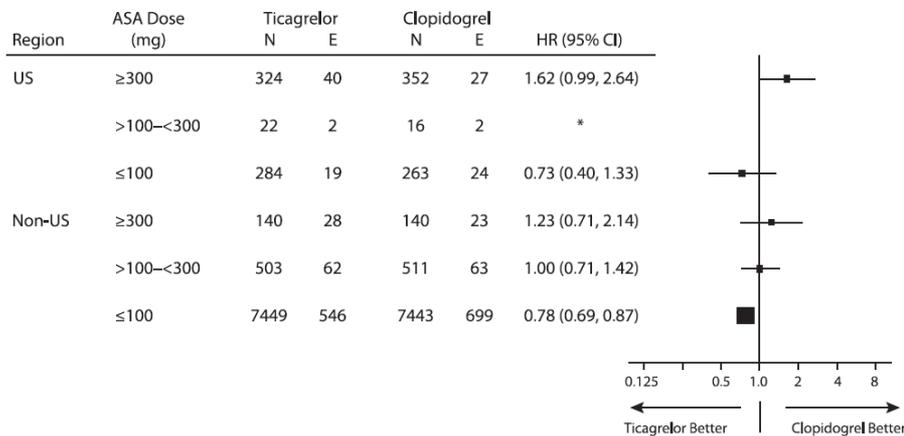
Ticagrelor	9,333	8,942	8,827	8,763
Clopidogrel	9,291	8,875	8,763	8,688

	8,673	8,543	8,397	7,028	6,480	4,822
	8,688	8,437	8,286	6,945	6,379	4,751

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

# Ticagrelor Compared With Clopidogrel by Geographic Region in the Platelet Inhibition and Patient Outcomes (PLATO) Trial

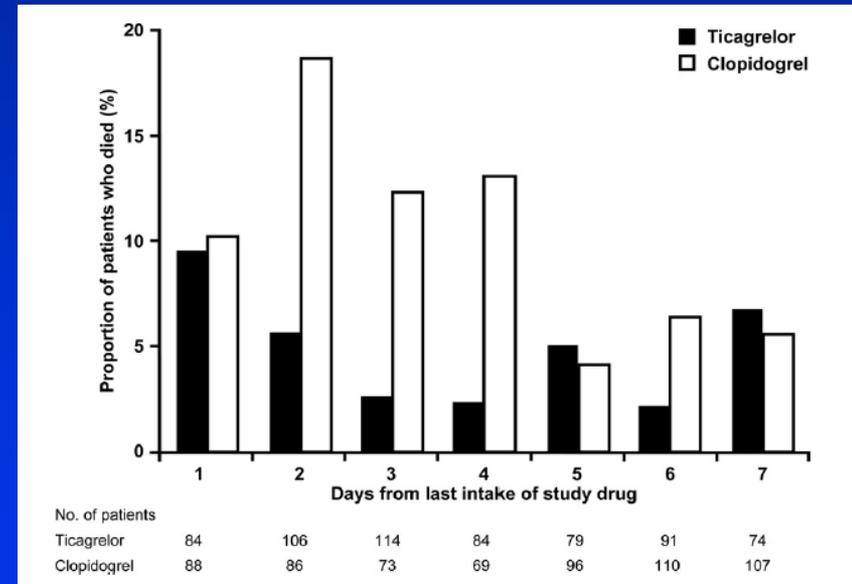
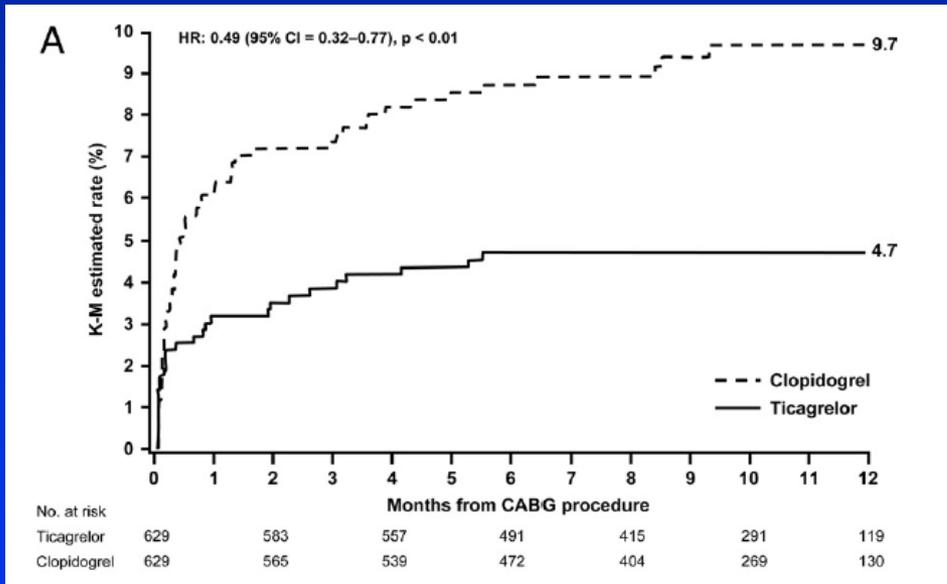
Kenneth W. Mahaffey, MD; Daniel M. Wojdyla, MS; Kevin Carroll, MS; Richard C. Becker, MD; Robert F. Storey, MD, DM; Dominick J. Angiolillo, MD, PhD; Claes Held, MD, PhD; Christopher P. Cannon, MD; Stefan James, MD, PhD; Karen S. Pieper, MS; Jay Horrow, MD; Robert A. Harrington, MD; Lars Wallentin, MD, PhD; on behalf of the PLATO Investigators



**Conclusions**—The regional interaction could arise from chance alone. Results of 2 independently performed analyses identified an underlying statistical interaction with aspirin maintenance dose as a possible explanation for the regional difference. The lowest risk of cardiovascular death, myocardial infarction, or stroke with ticagrelor compared with clopidogrel is associated with a low maintenance dose of concomitant aspirin.

# Ticagrelor Versus Clopidogrel in Patients With Acute Coronary Syndromes Undergoing Coronary Artery Bypass Surgery

Results From the PLATO (Platelet Inhibition and Patient Outcomes) Trial



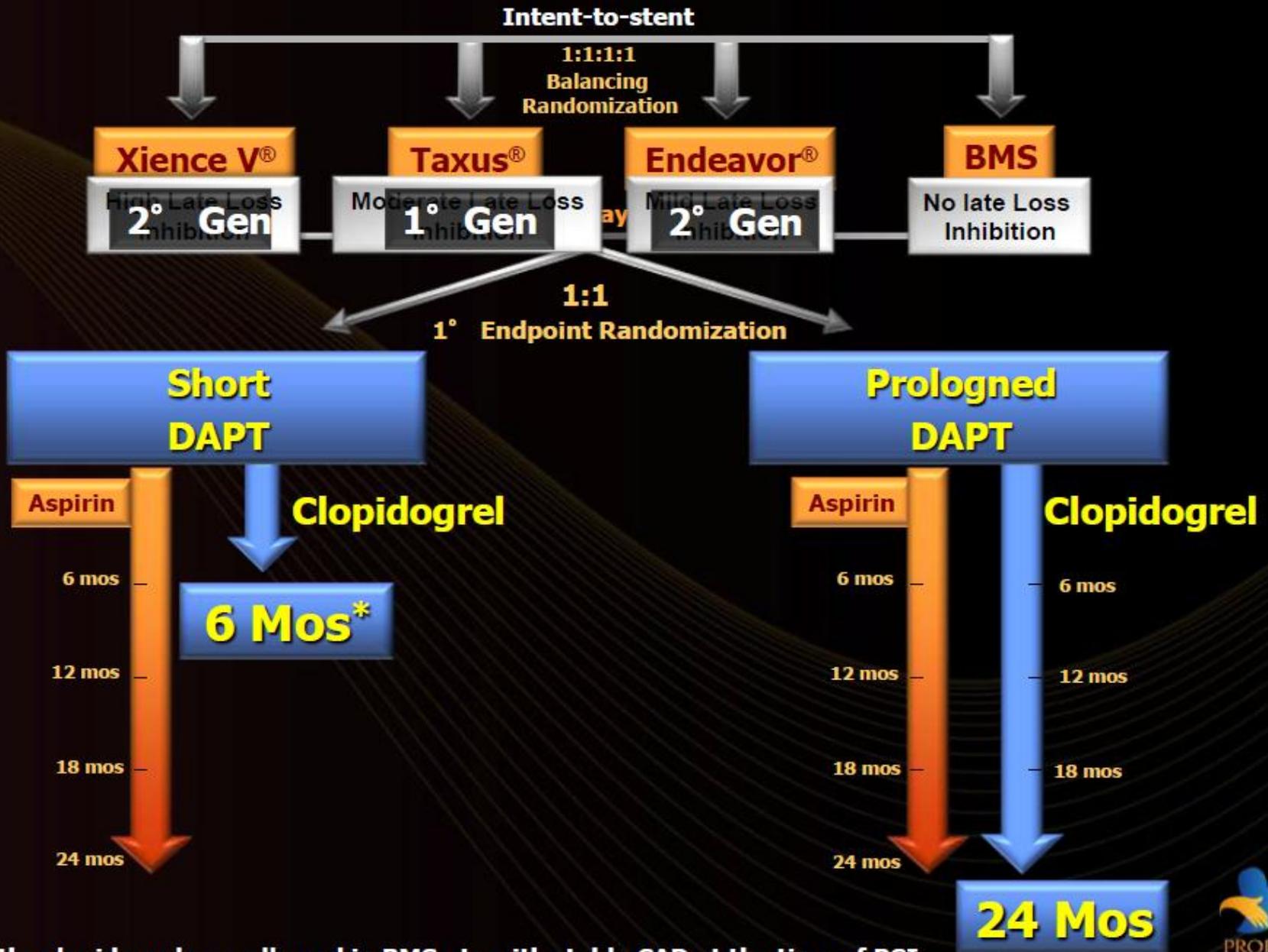
ESC, Hotline III, Paris, August, 30, 2011



**PROlonging Dual  
antiplatelet treatment after  
Gradings stent-induced  
Intimal hyperplasia studY**

**M. Valgimigli, MD, PhD  
University of Ferrara, *ITALY*  
On behalf of the PRODIGY  
Investigators**

# PRODIGY Study Flow Chart

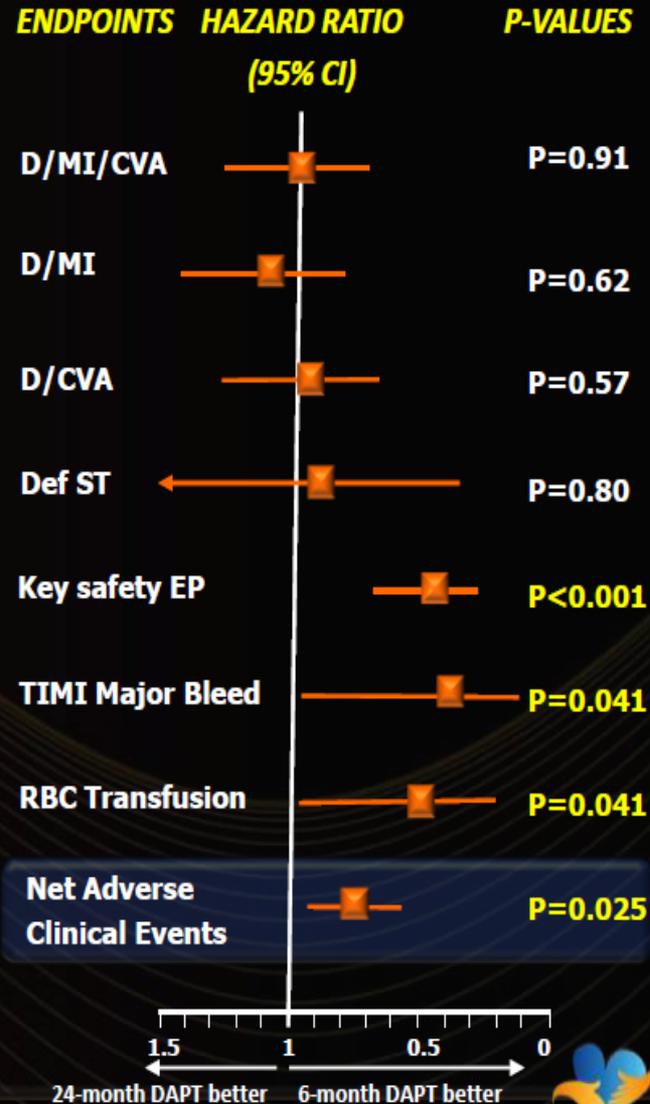


\*: <6 months clopidogrel was allowed in BMS pts with stable CAD at the time of PCI

# Summary

Our study failed to show that prolonging DAPT for 24 months is superior to 6 month duration of Tx in pts receiving 1 or 2 gen DES or at least 1 month after BMS

While we cannot rule out the possibility that a smaller than previously anticipated benefit may exist, the clear increase in bleeding, transfusion and net adverse clinical events, suggests that current recommendations may have overemphasized the benefit over the risk of long-term treatment with aspirin and clopidogrel





# ***Bern-Rotterdam Cohort Study***



***Newer generation everolimus-eluting stents  
eliminate the risk of very late stent  
thrombosis compared with early generation  
sirolimus-eluting and paclitaxel-eluting stents***

**Lorenz Räber, Michael Magro, Giulio G. Stefanini,  
Bindu Kalesan, Ron T. van Domburg, Yoshinobu Onuma,  
Peter Wenaweser, Joost Daemen, Bernhard Meier, Peter Jüni,  
Patrick W. Serruys, Stephan Windecker**

***Department of Cardiology***

***Swiss Cardiovascular Center and Clinical Trials Unit Bern***

***Bern University Hospital, Switzerland***

***Thoraxcenter, Erasmus Medical Center, Rotterdam, The Netherlands***

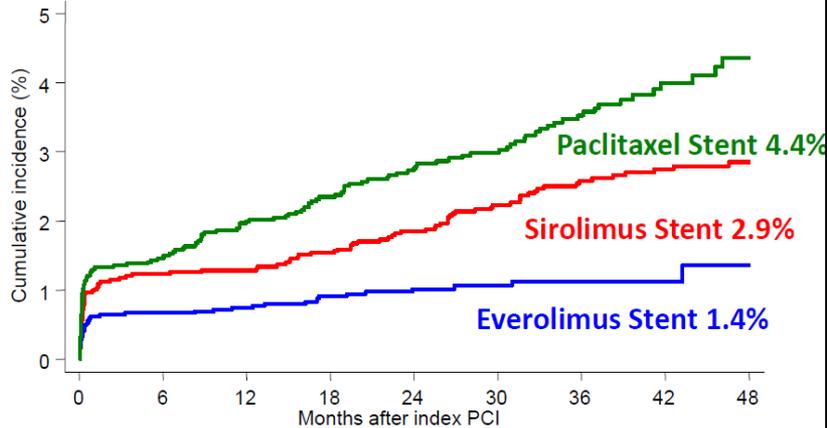
# BR Cohort Study - Patient Flow

12339 Patients Undergoing PCI

## Primary Endpoint ARC Definite ST @ 4 Years

EES vs. SES Hazard Ratio\* = 0.41, 95% CI 0.27–0.62, P<0.0001

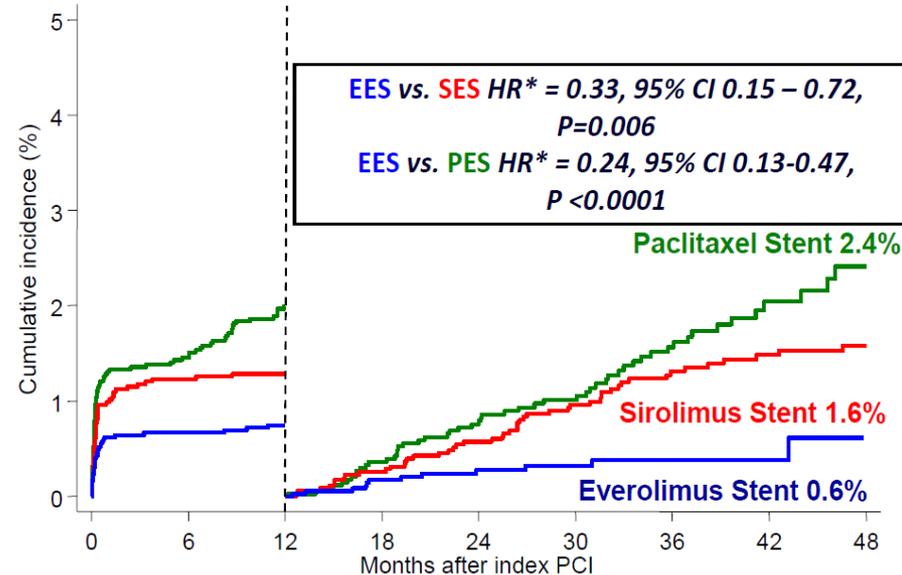
EES vs. PES Hazard Ratio\* = 0.33, 95% CI 0.23–0.48, P<0.0001



No. at risk		0	6	12	18	24	30	36	42	48
PES	4214	3916	3797	3176	2905	2344	1880	1077	686	
SES	3784	3617	3569	3499	3404	3080	2521	2118	1734	
EES	4135	3913	3793	3284	2604	1856	1041	514	208	

\*from Cox proportional hazards model

## Very Late ST (1-4yrs)



EES vs. SES HR\* = 0.33, 95% CI 0.15 – 0.72, P=0.006

EES vs. PES HR\* = 0.24, 95% CI 0.13–0.47, P<0.0001

\*from Cox proportional hazards model

\*F/U rate at the time of latest follow-up

# MANTENANCE OF PLATELET INHIBITION WITH CANGLELOR (BRIDGE)

**This study has been completed.**

First Received on October 6, 2008. Last Updated on September 12, 2011 [History of Changes](#)

Sponsor:	The Medicines Company
Information provided by (Responsible Party):	The Medicines Company
ClinicalTrials.gov Identifier:	NCT00767507

## ► Purpose

The purpose of this study is to demonstrate that patients receiving cangrelor infusion before coronary artery bypass grafting have an acceptable safety profile and can undergo surgery without excessive bleeding peri-operatively.

Condition	Intervention	Phase
Acute Coronary Syndrome	Procedure: Coronary Artery Bypass Graft Surgery	Phase II

Enrollment: 210  
 Study Start Date: October 2008  
 Study Completion Date: July 2011  
 Primary Completion Date: June 2011 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Cangrelor: Active Comparator Intervention: Procedure: Coronary Artery Bypass Graft Surgery	Procedure: Coronary Artery Bypass Graft Surgery Coronary Artery Bypass Graft Surgery
Placebo: Placebo Comparator Intervention: Procedure: Coronary Artery Bypass Graft Surgery	Procedure: Coronary Artery Bypass Graft Surgery Coronary Artery Bypass Graft Surgery

## ► Eligibility

Ages Eligible for Study: 18 Years to 90 Years  
 Genders Eligible for Study: Both  
 Accepts Healthy Volunteers: No

### Criteria

#### Inclusion Criteria:

- Written informed consent 18 Years of Age non emergent coronary bypass graft surgery Received a thienopyridine within 48 hours prior to enrollment

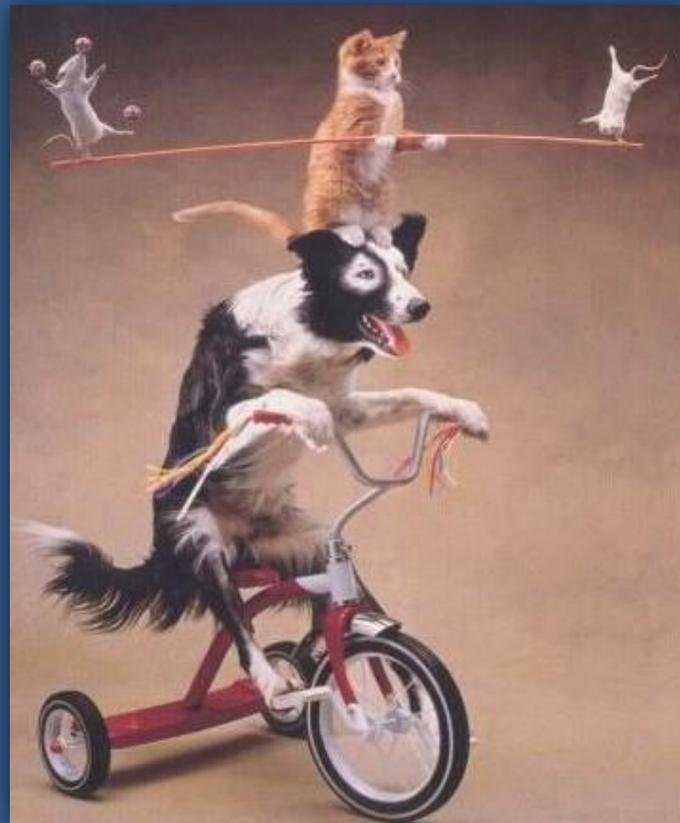
#### Exclusion Criteria:

- Confirmed or suspected pregnancy Cerebrovascular accident within one yar Intracranial neoplasm History of bleeding diathesis Thrombocytopenia

# GUIAS DE PRACTICA CLINICA

# Tratamiento del SCA: balance de riesgos

- Beneficio clínico (eficacia antiisquémica)
- Complicaciones hemorrágicas



# Valoración riesgo hemorrágico

CRUSADE Bleeding Score Nomogram

Predictor	Range	Score
<b>Baseline hematocrit (%)</b>	<31	9
	31-33.9	7
	34-36.9	3
	37-39.9	2
	≥40	0
<b>Creatinine clearance (mL/min)</b> (Note: Cockcroft-Gault is truncated at >90 mL/min)	≤15	39
	>15-30	35
	>30-60	28
	>60-90	17
	>90-120	7
<b>Heart rate (bpm)</b> (Note: heart rate is truncated at	>120	0
	≤70	0
	71-80	1
	81-90	3
	91-100	6
	101-110	8
<b>Sex</b>	111-120	10
	≥121	11
<b>Signs of CHF at presentation</b>	Male	0
	Female	8
<b>Prior vasular disease</b> (defined as prior PAD or stroke)	No	0
	Yes	6
<b>Diabetes mellitus</b>	No	0
	Yes	6
<b>Systolic blood pressure</b> (mm Hg)	≤90	10
	91-100	8
	101-120	5
	121-180	1
	181-200	3
	≥201	5

## Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association  
Learn and Live<sup>SM</sup>

Baseline Risk of Major Bleeding in Non ST-Segment Elevation Myocardial Infarction: The CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines) Bleeding Score

Sumeet Subherwal, Richard G. Bach, Anita Y. Chen, Brian F. Gage, Sunil V. Rao, L. Kristin Newby, Tracy Y. Wang, W. Brian Gibler, E. Magnus Ohman, Matthew T. Roe, Charles V. Pollack, Jr, Eric D. Peterson and Karen P. Alexander  
*Circulation* 2009;119:1873-1882; originally published online Mar 30, 2009;  
DOI: 10.1161/CIRCULATIONAHA.108.828511

### Patient Risk Score and Corresponding Rate of Major Bleeding:

Very Low risk	Low risk	Moderate risk	High risk	Very high risk
≤20	21-30	31-40	41-50	>50
3.1%	5.5%	8.6%	11.9%	19.5%

Perfil del sangrador: Mujer anciana con I.Renal



## Guidelines on myocardial revascularization

### The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)<sup>†</sup>

**Authors/Task Force Members:** William Wijns (Chairperson) (Belgium)\*, Philippe Kolh (Chairperson) (Belgium)\*, Nicolas Danchin (France), Carlo Di Mario (UK), Volkmar Falk (Switzerland), Thierry Folliguet (France), Scot Garg (The Netherlands), Kurt Huber (Austria), Stefan James (Sweden), Juhani Knuuti (Finland), Jose Lopez-Sendon (Spain), Jean Marco (France), Lorenzo Menicanti (Italy), Miodrag Ostojic (Serbia), Massimo F. Piepoli (Italy), Charles Pirlet (Belgium), Jose L. Pomar (Spain), Nicolaus Reifart (Germany), Flavio L. Ribichini (Italy), Martin J. Schalij (The Netherlands), Paul Sergeant (Belgium), Patrick W. Serruys (The Netherlands), Sigmund Silber (Germany), Miguel Sousa Uva (Portugal), David Taggart (UK)

NSTE-ACS				
<b>Antiplatelet therapy</b>				
	ASA	I	C	—
	Clopidogrel (with 600 mg loading dose as soon as possible)	I	C	—
	Clopidogrel (for 9–12 months after PCI)	I	B	55
	Prasugrel <sup>d</sup>	IIa	B	246,247
	Ticagrelor <sup>d</sup>	I	B	248
	+ GPIIb–IIIa antagonists (in patients with evidence of high intracoronary thrombus burden)			
	Abciximab (with DAPT)	I	B	249
	Tirofiban, Eptifibatide	IIa	B	55
	Upstream GPIIb–IIIa antagonists	III	B	65
<b>Anticoagulation</b>				
Very high-risk of ischaemia <sup>e</sup>	UFH (+GPIIb–IIIa antagonists) or	I	C	—
	Bivalirudin (monotherapy)	I	B	251
Medium-to-high-risk of ischaemia <sup>e</sup>	UFH	I	C	—
	Bivalirudin	I	B	251
	Fondaparinux	I	B	250
	Enoxaparin	IIa	B	55, 60
Low-risk of ischaemia <sup>e</sup>	Fondaparinux	I	B	250
	Enoxaparin	IIa	B	55, 60
STEMI				
<b>Antiplatelet therapy</b>				
	ASA	I	B	55, 94
	Clopidogrel <sup>f</sup> (with 600 mg loading dose as soon as possible)	I	C	—
	Prasugrel <sup>d</sup>	I	B	246,252
	Ticagrelor <sup>d</sup>	I	B	248,253
	+ GPIIb–IIIa antagonists (in patients with evidence of high intracoronary thrombus burden)			
	Abciximab	IIa	A	55, 94
	Eptifibatide	IIa	B	259, 260
	Tirofiban	IIb	B	55, 94
	Upstream GPIIb–IIIa antagonists	III	B	86
<b>Anticoagulation</b>				
	Bivalirudin (monotherapy)	I	B	255
	UFH	I	C	—
	Fondaparinux	III	B	256

# POSICIONAMIENTO EN GUÍAS DE PRÁCTICA CLÍNICA

## GUIAS NICE 2009(National Institute for health and Clinical Excellence)

Prasugrel en combinación con aspirina se recomienda en pacientes con SCA-ICP en las tres siguientes circunstancias clínicas:

- ICP primaria/inmediata en pacientes con STEMI
- Pacientes STEMI/NSTEMI que han padecido trombosis del stent, estando bajo el tratamiento con clopidogrel.
- Pacientes con diabetes mellitus. (STEMI y no-STEMI)

# Guías Americanas de SCACEST 2009

- II b-IIIa durante APTC 1<sup>a</sup> en pacientes seleccionados ( IIa)
- Se introduce Prasugrel ( IB) en APTC 1<sup>a</sup> y en STEMI no primaria, manteniendo Clopidogrel 300-600 mg (IC)
- Mantener Clopidogrel o Prasugrel al menos 1 año en STEMI y stent
- Se añade bivalirudina como anticoagulante en STEMI 1<sup>a</sup> ( I )
- Es razonable el uso de trombectomía en APTC 1<sup>a</sup> ( IIa)
- Stent DES como alternativa a convencionales en APTC 1<sup>a</sup> ( II a)
- Creación de redes comunitarias de atención al STEMI
- Traslado de pacientes FB a centros con hemodinámica( IIa y IIb)
- Elimina la recomendación de normalizar la glucemia con insulina iv

# Guías Europeas 2011 SCASEST

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Aspirin should be given to all patients without contraindications at an initial loading dose of 150–300 mg, and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A
A P2Y <sub>12</sub> inhibitor should be added to aspirin as soon as possible and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding.	I	A
A proton pump inhibitor (preferably not omeprazole) in combination with DAPT is recommended in patients with a history of gastrointestinal haemorrhage or peptic ulcer, and appropriate for patients with multiple other risk factors ( <i>H. elicobacter pylori</i> infection, age ≥65 years, concurrent use of anticoagulants or steroids).	I	A
Prolonged or permanent withdrawal of P2Y <sub>12</sub> inhibitors within 12 months after the index event is discouraged unless clinically indicated.	I	C
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).	I	B
Prasugrel (60-mg loading dose, 10-mg daily dose) is recommended for P2Y <sub>12</sub> -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. <sup>d</sup>	I	B
Clopidogrel (300-mg loading dose, 75-mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel.	I	A
A 600-mg loading dose of clopidogrel (or a supplementary 300-mg dose at PCI following an initial 300-mg loading dose) is recommended for patients scheduled for an invasive strategy when ticagrelor or prasugrel is not an option.	I	B

# **CLOPIDOGREL Y PROTECCION GÁSTRICA**

# Clopidogrel e IBP

EMA  
17 Marzo  
2010



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

17 March 2010  
EMA/174948/2010

## Public statement

### Interaction between clopidogrel and proton-pump inhibitors

CHMP updates warning for clopidogrel-containing medicines

Taking all of the currently available data into account, the CHMP and its Pharmacovigilance Working Party have concluded that **there are no solid grounds to extend the warning to other PPIs.** The class warning for all PPIs has been replaced with a warning stating that **only the concomitant use of clopidogrel and omeprazole or esomeprazole should be discouraged.** The Committee also recommended that a **description of the results of the two recent studies that show the interaction between clopidogrel and omeprazole be added to the product information.**

Xavier Luria  
Head of Sector, Safety and Efficacy of Medicines

AEMPS  
27 Abril 2010



agencia española de  
medicamentos y  
productos sanitarios

SUBDIRECCIÓN GENERAL  
DE MEDICAMENTOS  
DE USO HUMANO

## COMUNICACIÓN SOBRE RIESGOS DE MEDICAMENTOS PARA PROFESIONALES SANITARIOS

Ref: 2010/04  
26 de abril de 2010

Corrección de 27 de abril de 2010

### NOTA INFORMATIVA

INTERACCIÓN DE CLOPIDOGREL CON LOS INHIBIDORES DE  
LA BOMBA DE PROTONES: ACTUALIZACIÓN DE LA  
INFORMACIÓN Y RECOMENDACIONES DE USO

Se desaconseja el uso concomitante de clopidogrel con omeprazol o esomeprazol o con otros inhibidores de CYP2C19, excepto **cuando** se considere estrictamente necesario.

Estas recomendaciones no se aplican al resto de IBP diferentes a omeprazol o esomeprazol, ya que, aunque no puede descartarse completamente esta interacción, la evidencia actualmente disponible no apoya esta precaución.

# Clopidogrel e IBP

# Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart  
Association®   
*Learn and Live*™

**ACCF/ACG/AHA 2010 Expert Consensus Document on the Concomitant Use of Proton Pump Inhibitors and Thienopyridines: A Focused Update of the ACCF/ACG/AHA 2008 Expert Consensus Document on Reducing the Gastrointestinal Risks of Antiplatelet Therapy and NSAID Use: A Report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents**

Writing Committee Members, Neena S. Abraham, Mark A. Hlatky, Elliott M. Antman, Deepak L. Bhatt, David J. Bjorkman, Craig B. Clark, Curt D. Furberg, David A. Johnson, Charles J. Kahi, Loren Laine, Kenneth W. Mahaffey, Eamonn M. Quigley, James Scheiman, Laurence S. Sperling and Gordon F. Tomaselli  
*Circulation* 2010;122:2619-2633; originally published online Nov 8, 2010;

ANTIPLATELET THERAPY

## **Clopidogrel–PPI interaction, an ongoing controversy**

Paul A. Gurbel and Udaya S. Tantry

*Nat. Rev. Cardiol.* 8, 7–8 (2011)

**SPICE** Evaluation of the Influence of Statins and Proton Pump Inhibitors on Clopidogrel Antiplatelet Effects

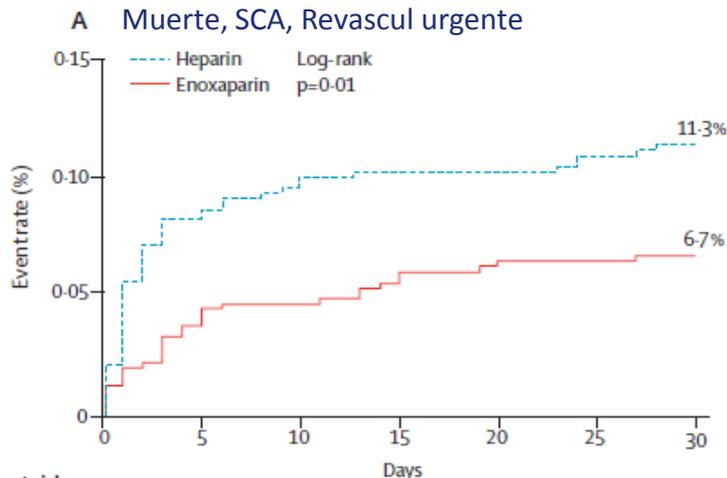
**ANTICOAGULANTES**

# NUEVOS ANTICOAGULANTES en SCA

- **Inhibidores factor Xa**
  - Apixaban (APPRAISE-2): suspensión prematura por aumentos del sangrado con eficacia similar
  - Rivaroxaban (ATLAS ACS2-TIMI 51): Eficacia clínica superior con mayor sangrado (beneficio clínico neto?)
  - Doroxaban (RUBI-1): Fase II. Mayor sangrado sin beneficio clínico. Suspensión investigación
- **Inhibidores PAR-1**
  - Voropaxar (TRACER): Análisis interino seguridad

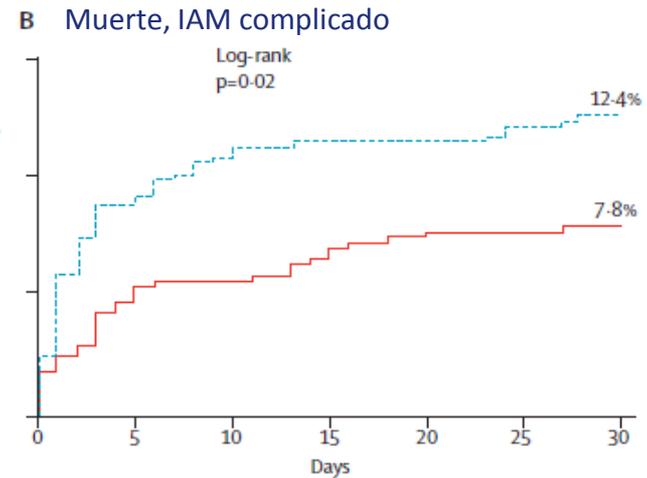
# Intravenous enoxaparin or unfractionated heparin in primary percutaneous coronary intervention for

ST-segment elevation myocardial infarction



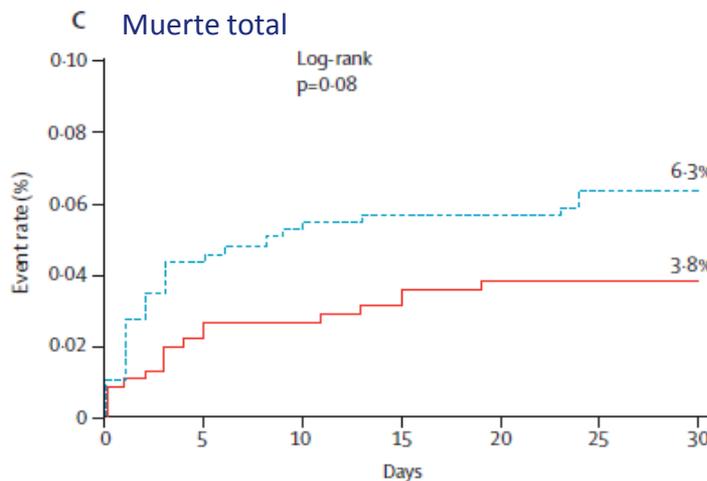
Patients at risk

	0	5	10	15	20	25	30
Heparin	460	417	406	403	403	400	
Enoxaparin	450	426	421	417	414	413	



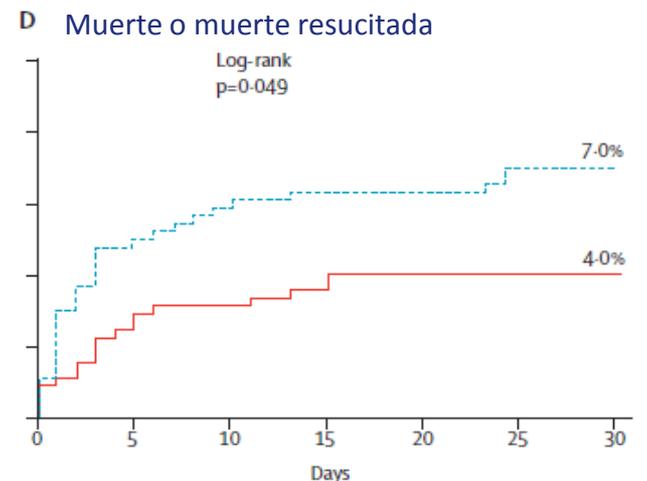
Patients at risk

	0	5	10	15	20	25	30
Heparin	460	415	401	398	398	395	
Enoxaparin	450	422	417	413	409	408	



Patients at risk

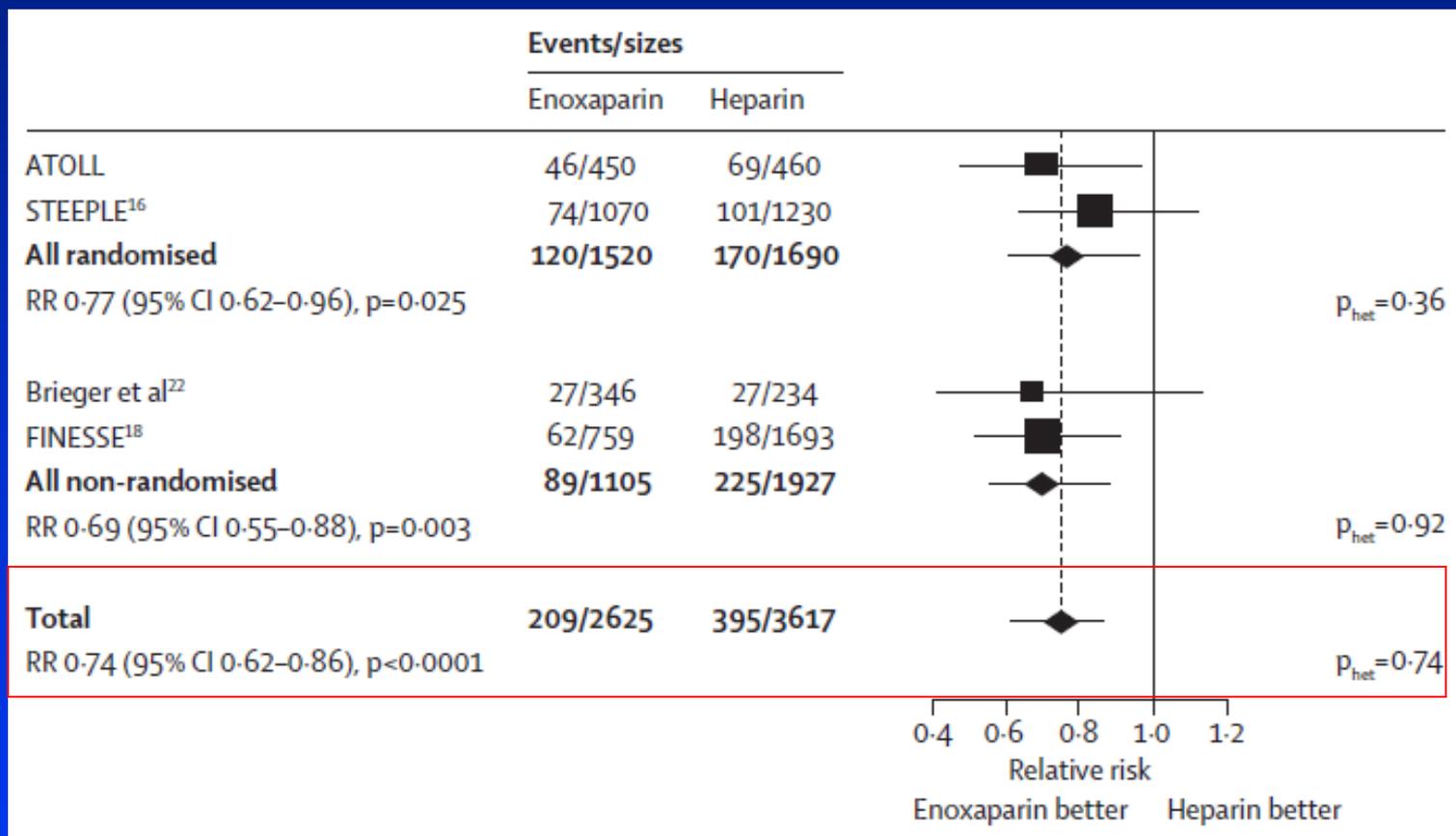
	0	5	10	15	20	25	30
Heparin	460	435	426	424	424	421	
Enoxaparin	450	433	430	428	425	425	



Patients at risk

	0	5	10	15	20	25	30
Heparin	460	433	423	421	421	418	
Enoxaparin	450	432	428	426	424	424	

# Intravenous enoxaparin or unfractionated heparin in primary percutaneous coronary intervention for ST-elevation myocardial infarction: the international randomised open-label ATOLL trial



**Qué hacer en los pacientes  
anticoagulados que requieren  
doble antiagregación?**

**Table 11** Antithrombotic strategies following coronary artery stenting in patients with AF at moderate to high thrombo-embolic risk (in whom oral anticoagulation therapy is required)

Haemorrhagic risk	Clinical setting	Stent implanted	Anticoagulation regimen
Low or intermediate (e.g. HAS-BLED score 0–2)	Elective	Bare-metal	<u>1 month</u> : triple therapy of VKA (INR 2.0–2.5) + aspirin $\leq$ 100 mg/day + clopidogrel 75 mg/day <u>Up to 12th month</u> : combination of VKA (INR 2.0–2.5) + clopidogrel 75 mg/day <sup>b</sup> (or aspirin 100 mg/day) <u>Lifelong</u> : VKA (INR 2.0–3.0) alone
	Elective	Drug-eluting	<u>3 (-olimus<sup>a</sup> group) to 6 (paclitaxel) months</u> : triple therapy of VKA (INR 2.0–2.5) + aspirin $\leq$ 100 mg/day + clopidogrel 75 mg/day <u>Up to 12th month</u> : combination of VKA (INR 2.0–2.5) + clopidogrel 75 mg/day <sup>b</sup> (or aspirin 100 mg/day) <u>Lifelong</u> : VKA (INR 2.0–3.0) alone
	ACS	Bare-metal/ drug-eluting	<u>6 months</u> : triple therapy of VKA (INR 2.0–2.5) + aspirin $\leq$ 100 mg/day + clopidogrel 75 mg/day <u>Up to 12th month</u> : combination of VKA (INR 2.0–2.5) + clopidogrel 75 mg/day <sup>b</sup> (or aspirin 100 mg/day) <u>Lifelong</u> : VKA (INR 2.0–3.0) alone
High (e.g. HAS-BLED score $\geq$ 3)	Elective	Bare-metal <sup>c</sup>	<u>2–4 weeks</u> : triple therapy of VKA (INR 2.0–2.5) + aspirin $\leq$ 100 mg/day + clopidogrel 75 mg/day <u>Lifelong</u> : VKA (INR 2.0–3.0) alone
	ACS	Bare-metal <sup>c</sup>	<u>4 weeks</u> : triple therapy of VKA (INR 2.0–2.5) + aspirin $\leq$ 100 mg/day + clopidogrel 75 mg/day <u>Up to 12th month</u> : combination of VKA (INR 2.0–2.5) + clopidogrel 75 mg/day <sup>b</sup> (or aspirin 100 mg/day) <u>Lifelong</u> : VKA (INR 2.0–3.0) alone

ACS = acute coronary syndrome; AF = atrial fibrillation; INR = international normalized ratio; VKA = vitamin K antagonist

Gastric protection with a proton pump inhibitor (PPI) should be considered where necessary.

<sup>a</sup>Sirolimus, everolimus, and tacrolimus.

<sup>b</sup>Combination of VKA (INR 2.0–3.0)+aspirin  $\leq$ 100 mg/day (with PPI, if indicated) may be considered as an alternative.

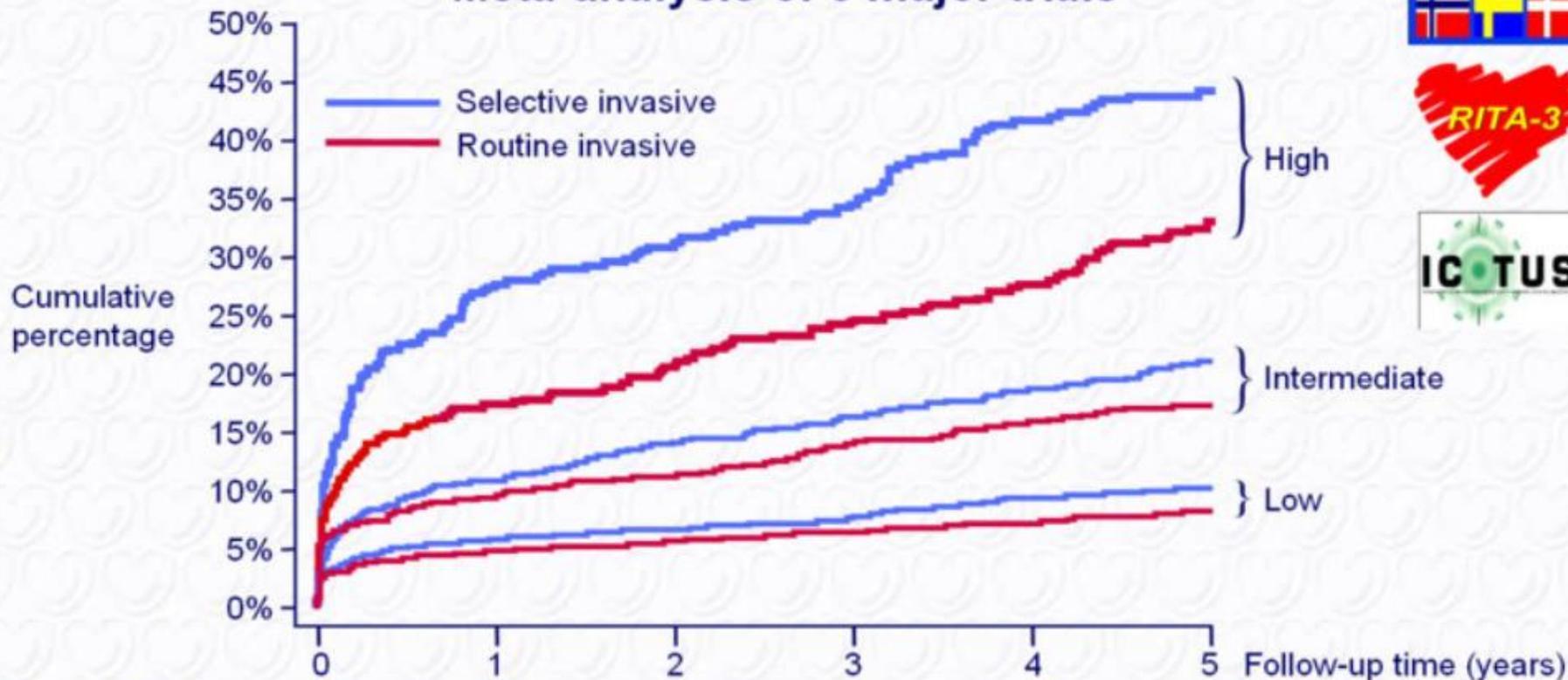
<sup>c</sup>Drug-eluting stents should be avoided as far as possible, but, if used, consideration of more prolonged (3–6 months) triple antithrombotic therapy is necessary.

Adapted from Lip et al.<sup>61</sup>

# REVASCULARIZACION

# Intended Early Invasive vs. Conservative Strategy

Long term outcome by initial Risk Score  
Meta-analysis of 3 major trials



Selective invasive	2746	2452	2351	2178	2077	2005
Routine invasive	2721	2485	2410	2235	2166	2079

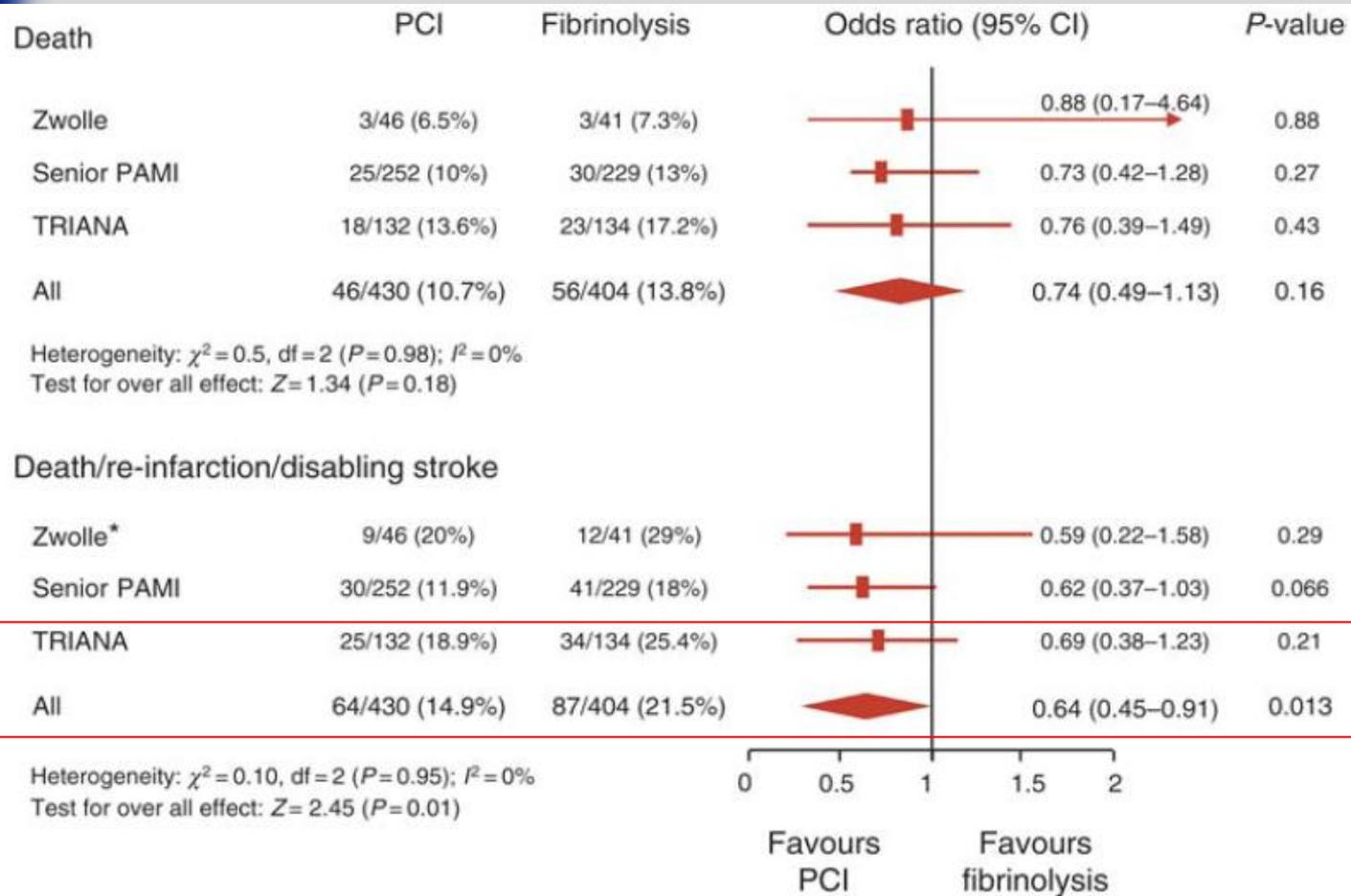
Fox KA et al. JACC 2010;55(22):2435-45



# Primary angioplasty vs. fibrinolysis in very old patients with acute myocardial infarction: TRIANA (TRatamiento del Infarto Agudo de miocardio en Ancianos) randomized trial

A

Cummulative survival free of death, re-infarction, or disabling stroke

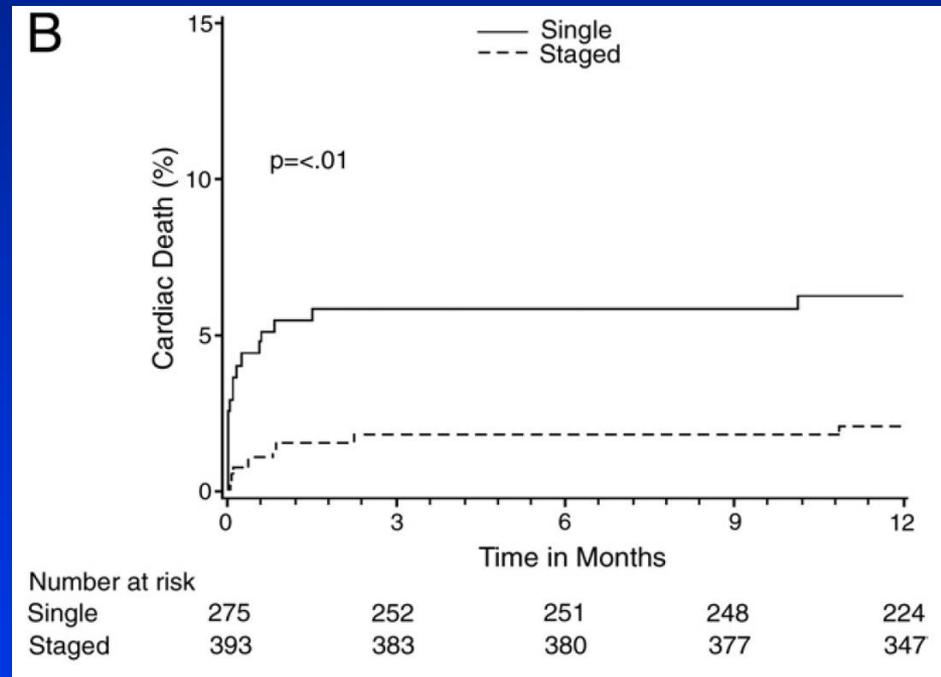
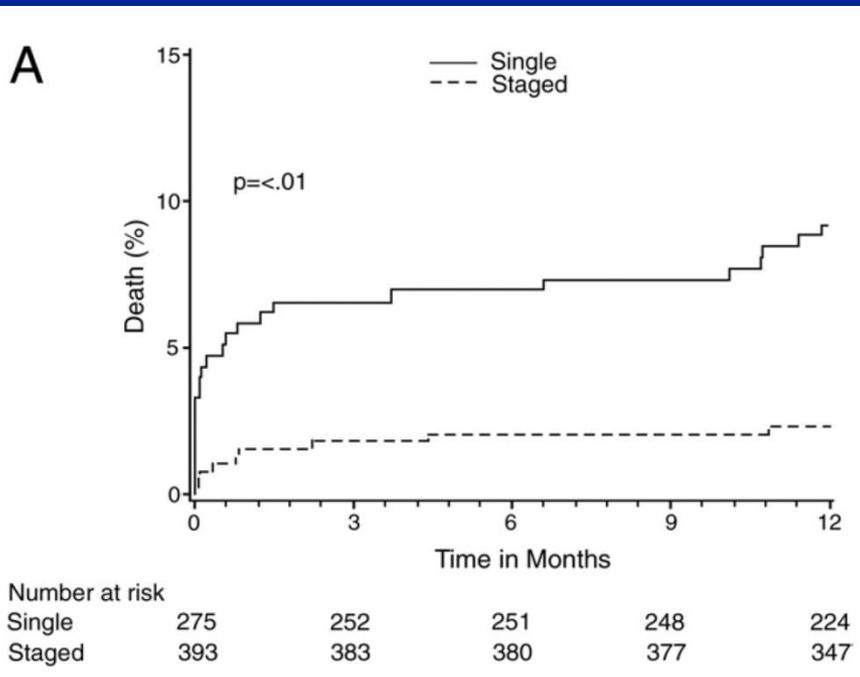


Patients at risk  
Primary PCI  
Fibrinolysis

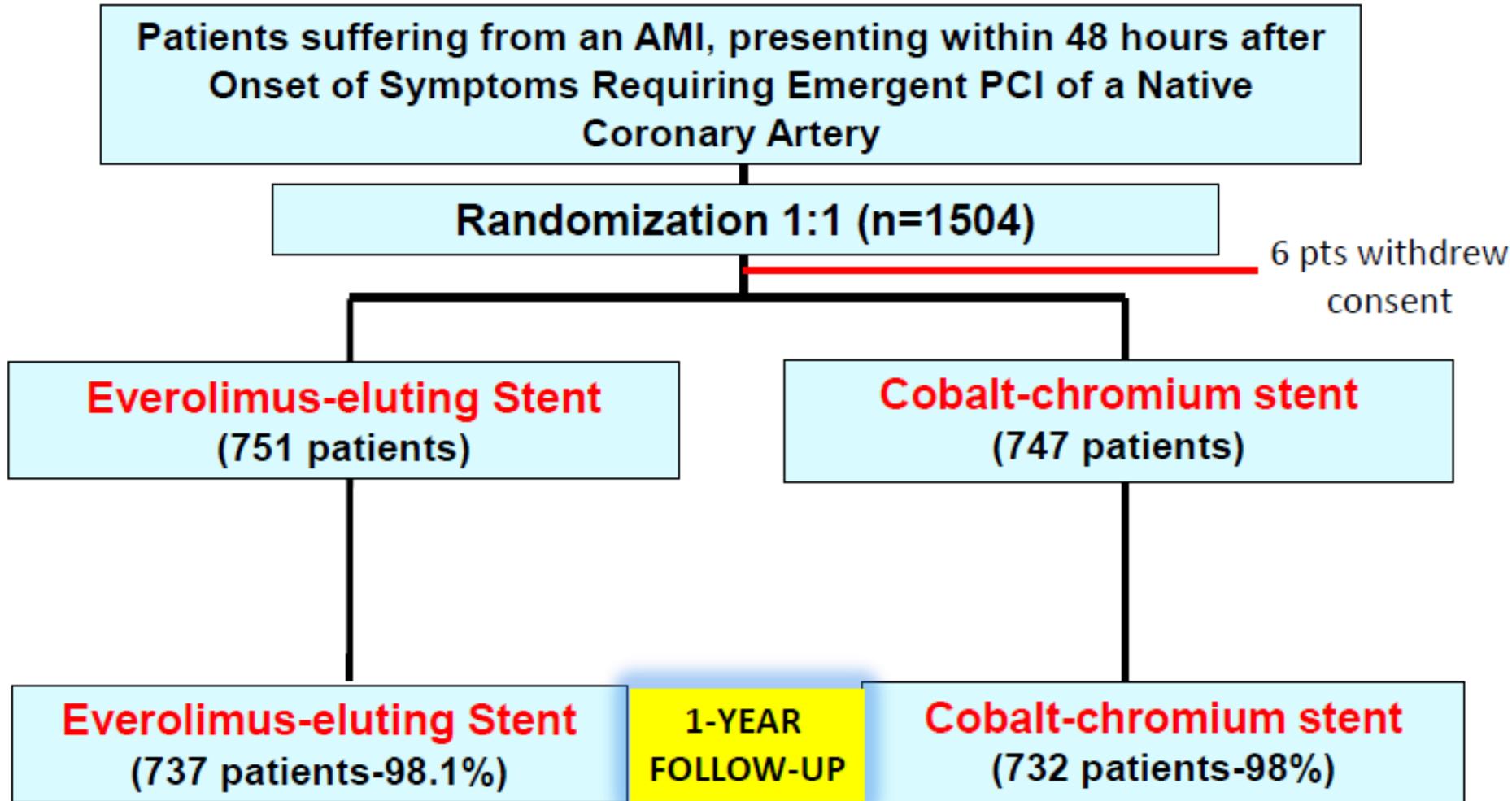
\*Total strokes

# Prognostic Impact of Staged Versus “One-Time” Multivessel Percutaneous Intervention in Acute Myocardial Infarction

Analysis From the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) Trial

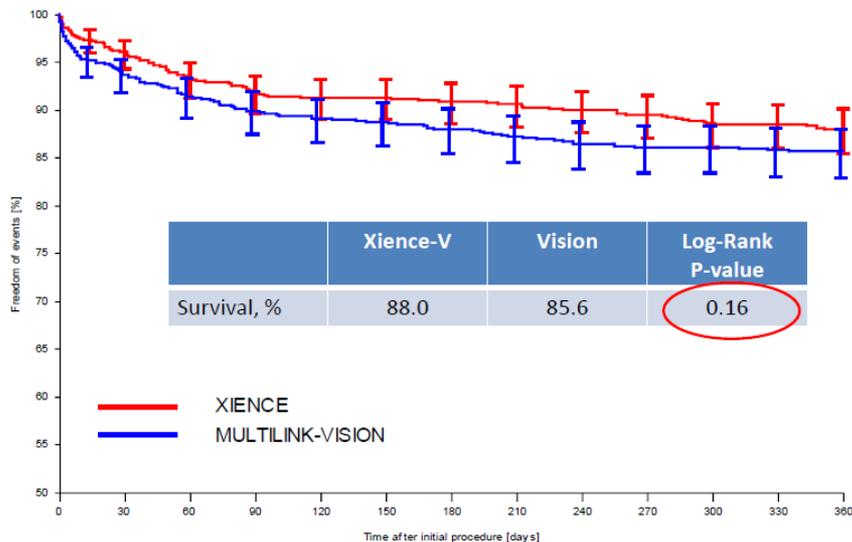


# Study Design = All-comer RCT



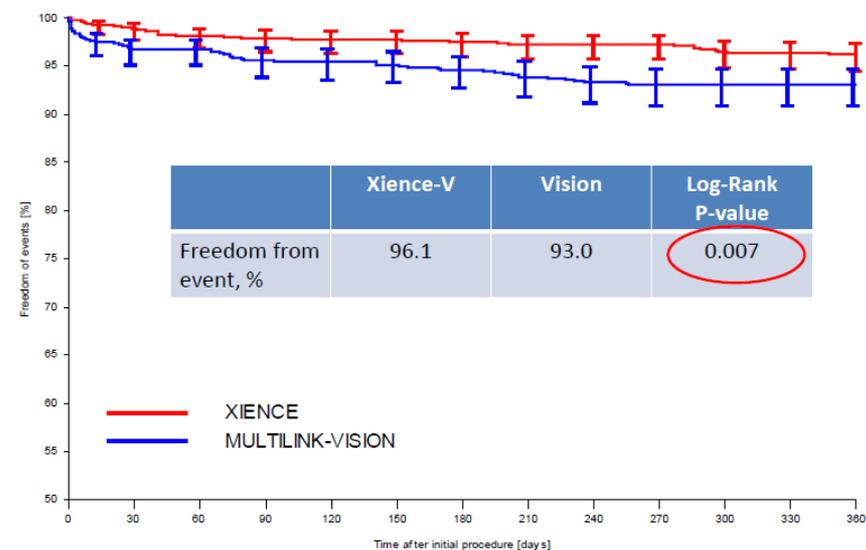
## Primary Endpoint:

Composite of all-cause death, any MI or any revascularization



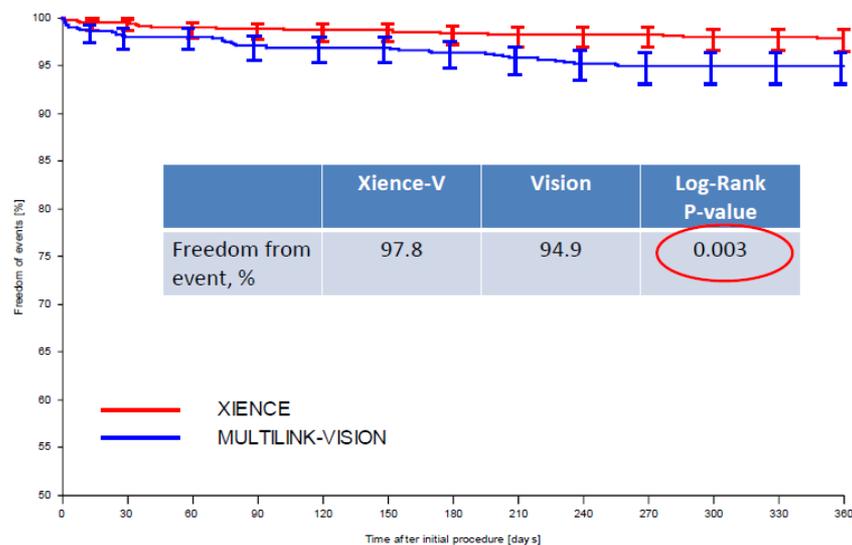
## Secondary Endpoints:

Target Vessel Revascularization



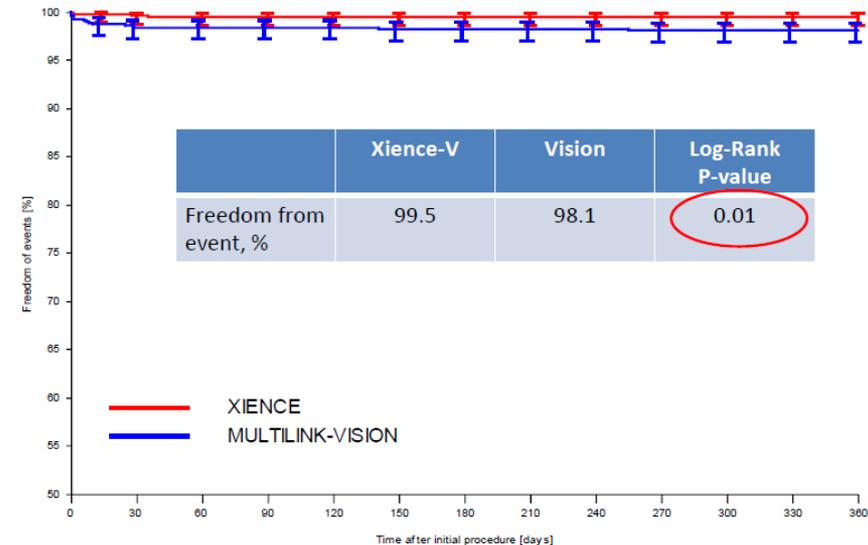
## Secondary Endpoints:

Target Lesion Revascularization

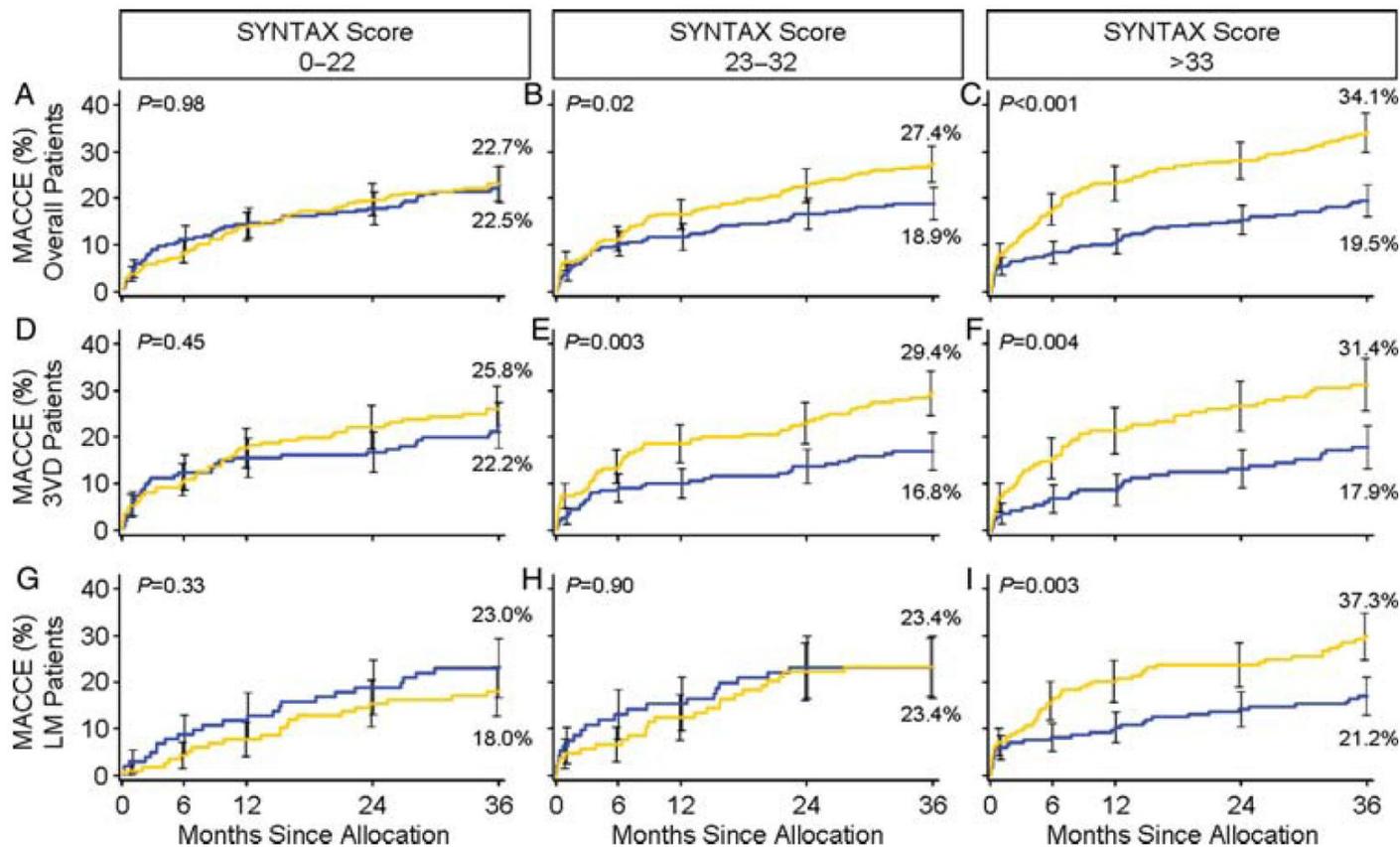


## Secondary Endpoints:

Definite Stent Thrombosis



## Comparison of coronary bypass surgery with drug-eluting stenting for the treatment of left main and/or three-vessel disease: 3-year follow-up of the SYNTAX trial



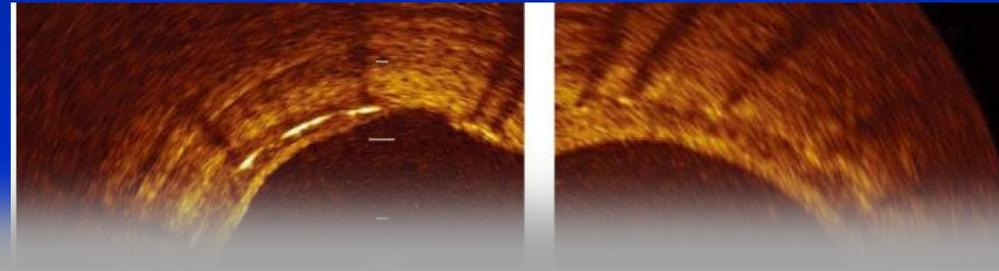


## STELLIUM 1: First-In-Man Follow-up Evaluation of Bioabsorbable Polymer-Coated Paclitaxel-Eluting Stent

Amane Kozuki, MD; Junya Shite, MD; Toshiro Shinke, MD; Naoki Miyoshi, MD; Takahiro Sawada, MD; Farrel Hellig, MD; Mark Abelson, MD; Basil Brown, MD; Sajidah Khan, MD; Martin Mpe, MD; Mpiko Ntsekhe, MD; Damian Conway; Ken-ichi Hirata, MD

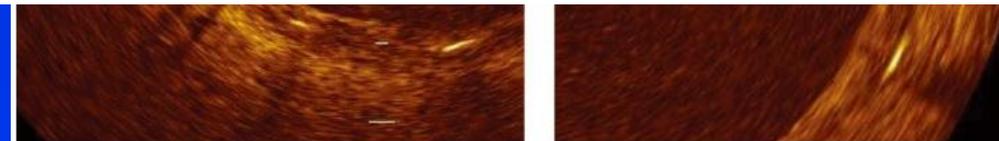
**Table 1. Baseline Clinical Characteristics**

Patients	37
Age (years)	57±9
Male (%)	69
Hypertension (%)	65

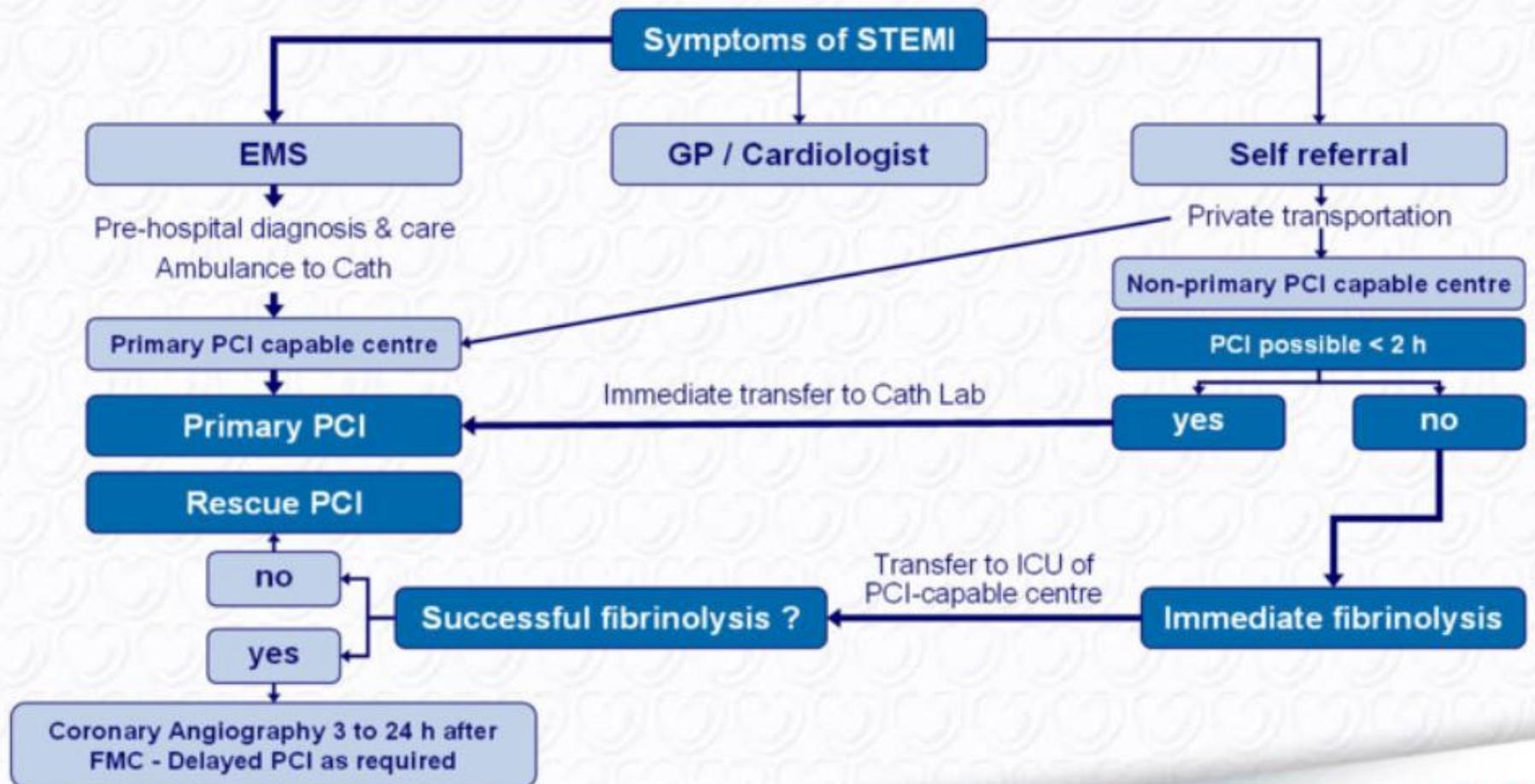


**Conclusions:** This first-in-man study of the Stellium™ stent shows the promising possibility of bioabsorbable polymeric surface coating paclitaxel-eluting stents out to 6 months. The low rate of peri-strut low intensity suggests low cellular toxicity of the Stellium™ stent compared with the first-generation DES. (*Circ J* 2010; 74: 2089–2096)

Prior PCI (%)	9
---------------	---



# Organisation of STEMI patient disposal describing pre- and in-hospital management, and reperfusion strategies within 12 h of First Medical Contact (FMC)



# PROYECTO COMÚN DE MIOCARDIO

## PROYECTO COMÚN PARA LA ATENCIÓN DEL INFARTO AGUDO DE MIOCARDIO CON ELEVACION DE ST EN LA PROVINCIA DE SEVILLA

# INFARTO AGUDO PROVINCIA DE

Dr. Jose M. Cruz Fernandez y Dr. Angel Sánchez González

en representación del Grupo de Trabajo para el tratamiento del Infarto agudo de  
Miocardio en Sevilla.

Sevilla, 15 de Diciembre de 2010

Dr. Jo

nzález

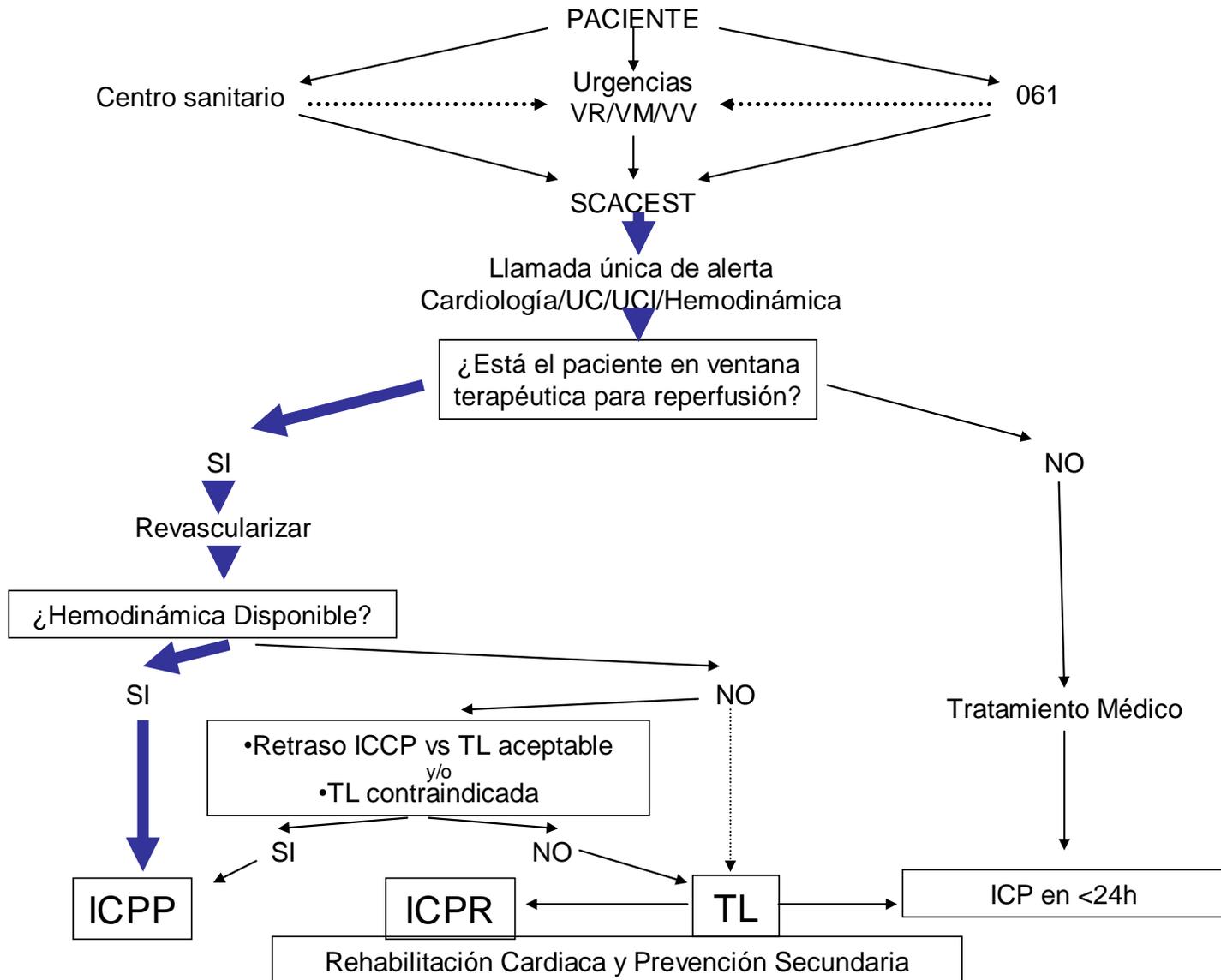
en represen

to del Infarto

Como resultado de las deliberaciones comunes del Grupo de Trabajo, y de las tres comisiones en las que se dividió el Grupo para un abordaje focalizado de distintas áreas de interés, se ha redactado un documento en donde se recogen los consensos y puntos de vista particulares que se llevaron a cabo en Sevilla entre los días 4 y 5 de Octubre de 2010

# PROYECTO DE ACTUACION ANTE EL SCACEST EN SEVILLA

## Protocolo de actuación



# PROYECTO DE ACTUACION ANTE EL SCACEST EN SEVILLA

## Protocolo de actuación

- **Llamada única:**

- **Objetivos:**

- **Comprobar la POSIBILIDAD de ICPP**
      - Con un retraso vs la TL ASUMIBLE, en función de la gravedad del paciente.
      - Si el paciente está en SHOCK CARDIOGENICO o bien si la TROMBOLISIS ESTA CONTRAINDICADA, se indicará ICPP aunque ello suponga una mayor demora en su aplicación
      - Inicialmente en el HcH de referencia y, en su defecto, en cualquiera de los otros dos HcH.
    - **Activar en el HcH todos los recursos necesarios para garantizar el tratamiento completo del paciente incluyendo tanto su acceso directo al laboratorio de Hemodinámica como su posterior traslado a la Unidad Coronaria.**

- **Números:**

- » HVR.- 750856 / 697.950.856 HEMODINAMICA
    - » HVM.- 749242 / 670.949.242 URGENCIAS/CARDIOLOGIA
    - » HVV.- 698428 / 671 598.428 CUIDADOS INTENSIVOS

**PREVENCION**

ORIGINAL ARTICLE

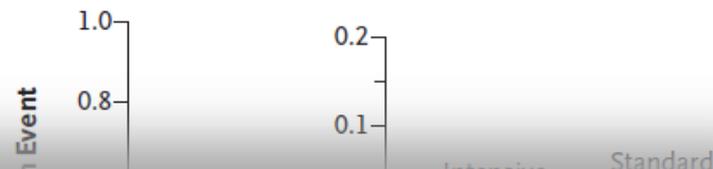
# Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

The ACCORD Study Group\*

**A Primary Outcome**



**B Nonfatal Stroke**



**CONCLUSIONS**

In patients with type 2 diabetes at high risk for cardiovascular events, targeting a systolic blood pressure of less than 120 mm Hg, as compared with less than 140 mm Hg, did not reduce the rate of a composite outcome of fatal and nonfatal major cardiovascular events. (ClinicalTrials.gov number, NCT00000620.)

**No. at Risk**

Intensive	2362	2273	2182	2117	1770	1080	298	175	80
Standard	2371	2274	2196	2120	1793	1127	358	195	108

**No. at Risk**

Intensive	2362	2291	2223	2174	1841	1128	313	186	88
Standard	2371	2287	2235	2186	1879	1196	382	215	114

# Effects of Varespladib Methyl on Biomarkers and Major Cardiovascular Events in Acute Coronary Syndrome Patients

Robert S. Rosenson, MD,\* Colin Hislop, MD,† Michael Elliott, MA,† Yuri Stasiv, PhD,† Michael Goulder, BSc,‡ David Waters, MD§

*New York, New York; Hayward and San Francisco, California; Nottingham, United Kingdom*

## Conclusions

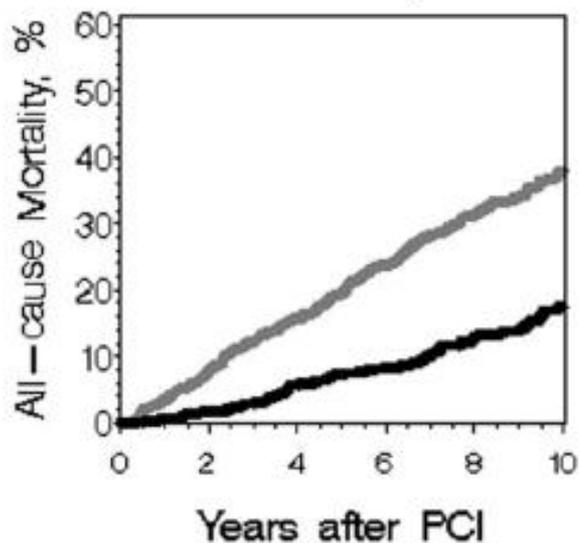
The FRANCIS study demonstrates that treatment with varespladib reduces concentration of LDL-C, hsCRP, and sPLA<sub>2</sub> in ACS patients treated with evidence-based therapies inclusive of high-dose atorvastatin. Elevated levels of these biomarkers have been shown to identify CHD patients who remain at high risk for recurrent cardiovascular events; however, in this study, there were no treatment differences in clinical cardiovascular event. A large, prospective, double-blind, placebo-controlled trial in ACS patients will be required to explore the future role of varespladib treatment in cardiovascular event reduction.

# VISTA-16

## Impact of Cardiac Rehabilitation on Mortality and Cardiovascular Events After Percutaneous Coronary Intervention in the Community

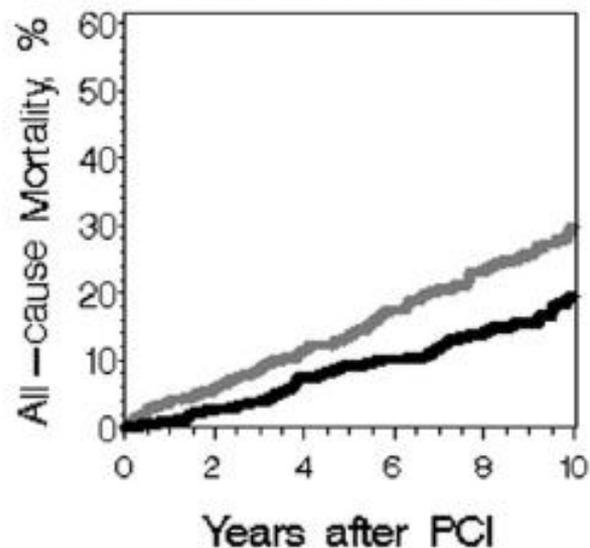
Kashish Goel, Ryan J. Lennon, R. Thomas Tilbury, Ray W. Squires and Randal J. Thomas

Landmark comparison



No Rehab	1224	992	701	479	321	202
Cardiac Rehab	785	630	527	377	250	131

Matched pairs comparison



No Rehab	719	576	433	304	194	115
Cardiac Rehab	719	591	477	336	225	125

**Muchas Gracias**