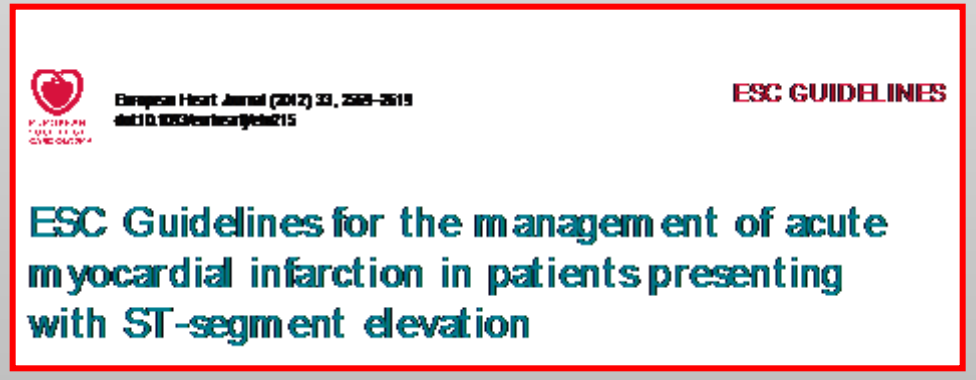
Seminario 2: Nuevos Antiagregantes

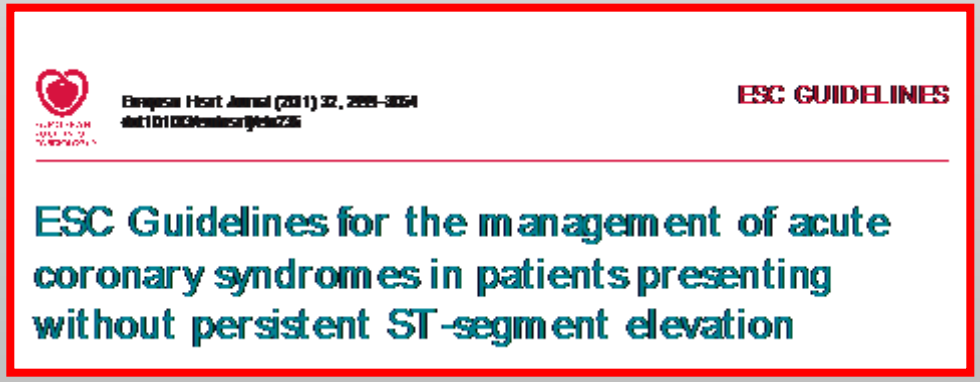
Pablo Avanzas y José Luis Ferreiro

AVANCES EN SCA

- Los nuevos fármacos antiagregantes (ticagrelor y prasugrel) han supuesto un avance importante en el tratamiento del SCA.
- Las actuales guías de practica clínica de la Sociedad Europea de Cardiología recomiendan su uso sobre clopidogrel.



G. Steg. European Heart Journal. 2012; 33, 2569–2619



CW. Hamm. Eur Heart J. (2011) 32, 2999–3054

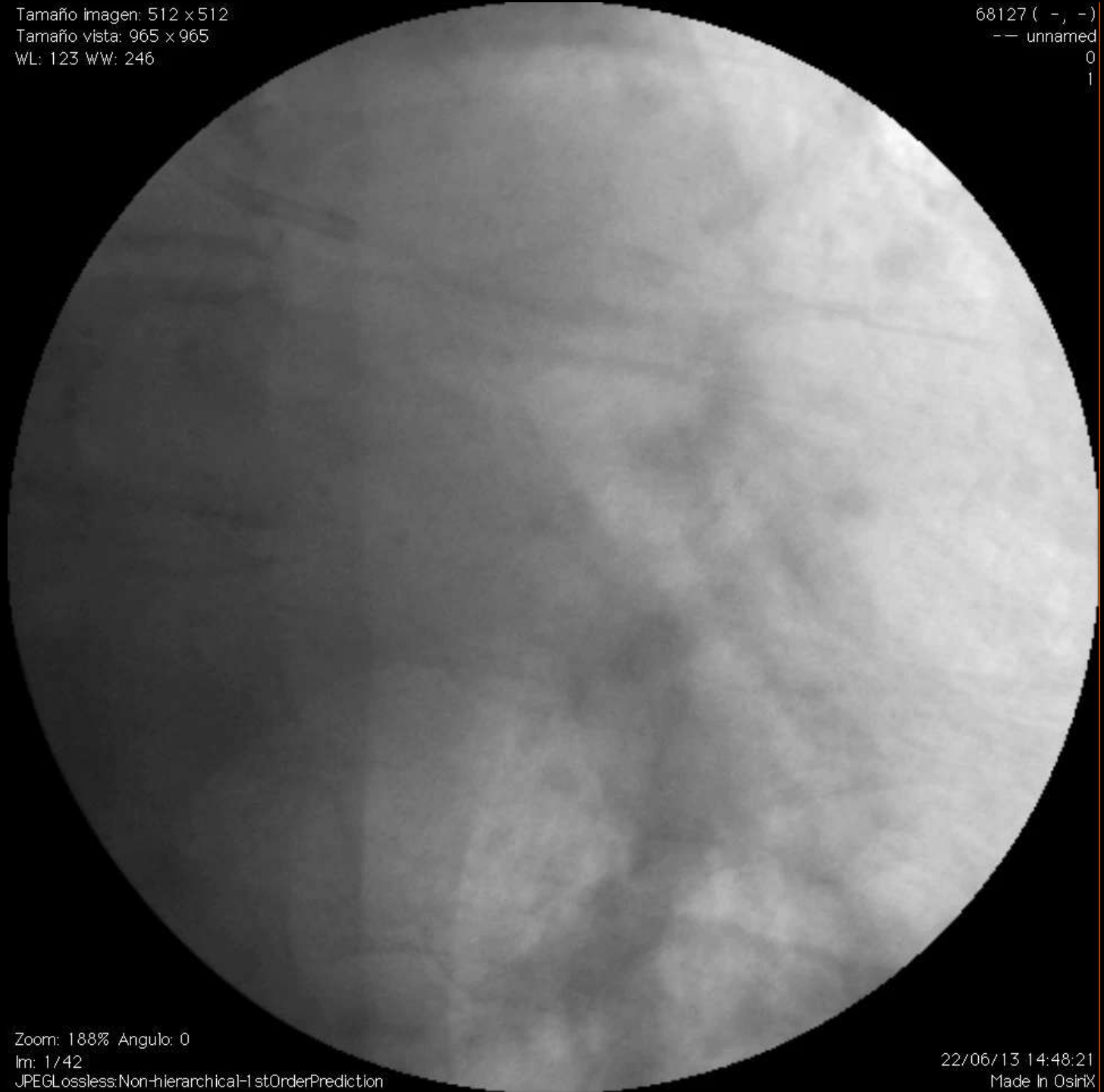
AVANCES EN SCA

- El objetivo del seminario es revisar en distintos escenarios clínicos las posibilidades terapéuticas en cuanto al tratamiento antiagregante.
- Formato:

1. Presentación del caso.
2. Planteamiento de diferentes opciones.
3. Votación (resultado según Guías).
4. Discusión de las posibilidades de tratamiento antiagregante.

CASO CLINICO 1

- Varón de 70 años.
- FRCV: HTA, fumador.
- Antecedentes personales: Sin interés.
- Acude a urgencias por dolor torácico.
- Diagnóstico: **SCACEST lateral**.
- Tratamiento en urgencias: Aspirina, heparina sódica.
- ACTP primaria.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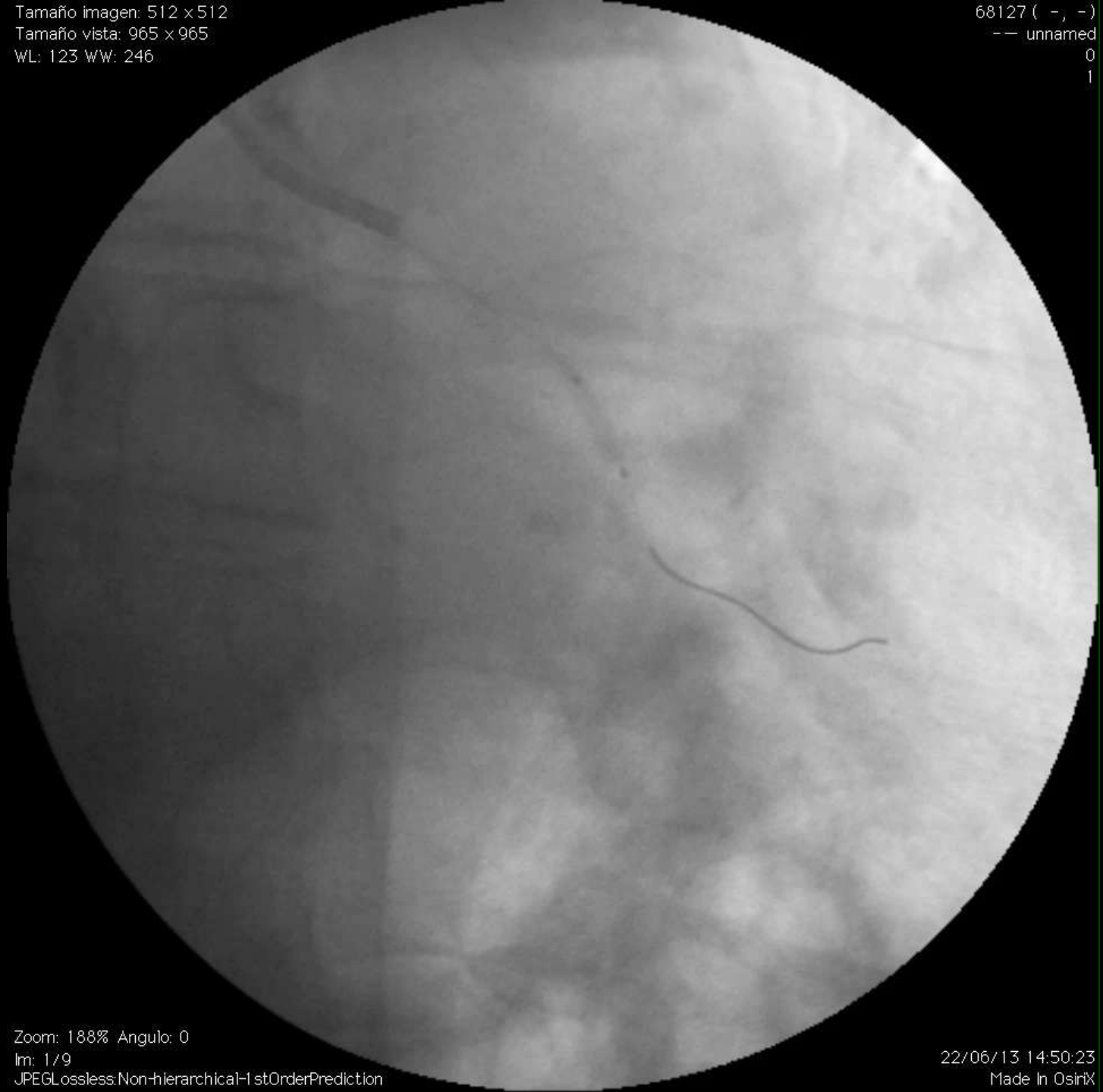
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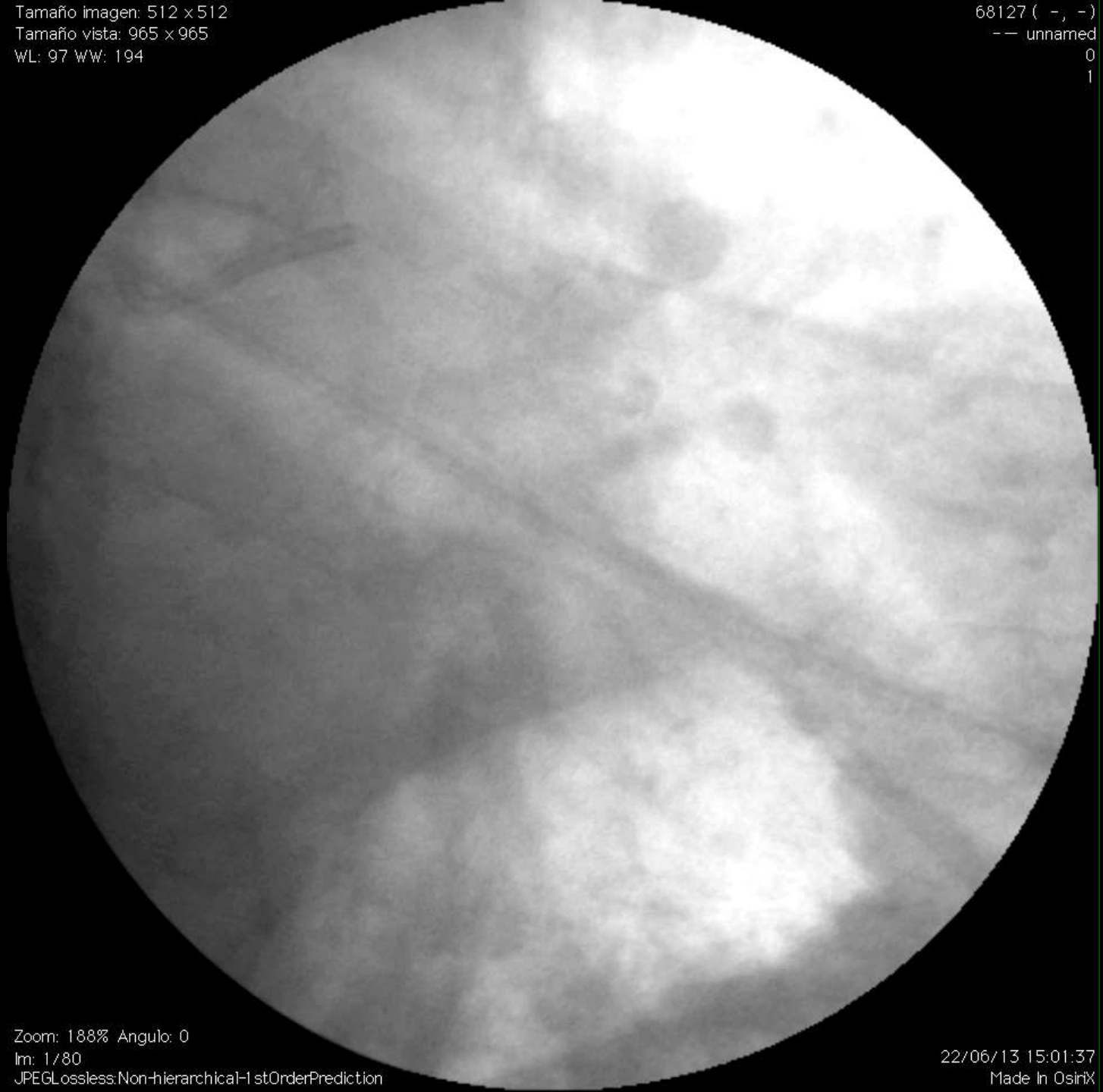
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Si en su hospital tiene disponibles todos los antiagregantes

¿Qué tratamiento antiagregante administraría?

1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Las respuestas 3 y 4 son correctas.

Si en su hospital tiene disponibles todos los antiagregantes

¿Qué tratamiento antiagregante administraría?

1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Las respuestas 3 y 4 son correctas.

ANTIAGREGACIÓN EN EL SCACEST

European Heart Journal (2012) 33, 2569–2619
doi:10.1093/eurheartj/ehs215

ESC GUIDELINES

ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC)

Authors/Task Force Members: Ph. Gabriel Steg (Chairperson) (France)*, Stefan K. James (Chairperson) (Sweden)*, Dan Atar (Norway), Luigi P. Badano (Italy), Carina Blömstrom-Lundqvist (Sweden), Michael A. Borger (Germany), Carlo Di Mario (United Kingdom), Kenneth Dickstein (Norway), Gregory Ducrocq (France), Francisco Fernandez-Aviles (Spain), Anthony H. Gershlick (United Kingdom), Pantaleo Giannuzzi (Italy), Sigrun Halvorsen (Norway), Kurt Huber (Austria), Peter Juni (Switzerland), Adnan Kastrati (Germany), Juhani Knuuti (Finland), Mattie J. Lenzen (Netherlands), Kenneth W. Mahaffey (USA), Marco Valgimigli (Italy), Arnoud van 't Hof (Netherlands), Petr Widimsky (Czech Republic), Doron Zahger (Israel)

ESC Committee for Practice Guidelines (CPG): Jeroen J. Bax (Chairman) (Netherlands), Helmut Baumgartner (Germany), Claudio Ceconi (Italy), Veronica Dean (France), Christi Deaton (UK), Robert Fagard (Belgium), Christian Funck-Brentano (France), David Hasdai (Israel), Arno Hoes (Netherlands), PaulusKirchhof (Germany/UK), Juhani Knuuti (Finland), Philippe Kolh (Belgium), Theresa McDonagh (UK), Cyril Moulin (France), Bogdan A. Popescu (Romania), Željko Reiner (Croatia), Udo Sechtem (Germany), Per Anton Sirnes (Norway), Michal Tendera (Poland), Adam Torbicki (Poland), Alec Vahanian (France), Stephan Windecker (Switzerland).

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ANTIAGREGACIÓN EN EL SCACEST

RECOMIENDAN TICAGRELOR/PRASUGREL SOBRE CLOPIDOGREL

G. Steg. Rev Esp Cardiol. 2013;66(1):53.e1-e46

ANTIAGREGACIÓN EN EL SCACEST

The NEW ENGLAND JOURNAL of MEDICINE

Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes

Stephen D. Wiviott, M.D., Eugene Braunwald, M.D., Carolyn H. McCabe, B.S., Gilles Montalescot, M.D., Ph.D., Witold Ruzyllo, M.D., Shmuel Gottlieb, M.D., Franz-Joseph Neumann, M.D., Diego Ardissino, M.D., Stefano De Servi, M.D., Sabina A. Murphy, M.P.H., Jeffrey Riesmeyer, M.D., Govinda Weerakkody, Ph.D., C. Michael Gibson, M.D., and Elliott M. Antman, M.D., for the TRITON–TIMI 38 Investigators*

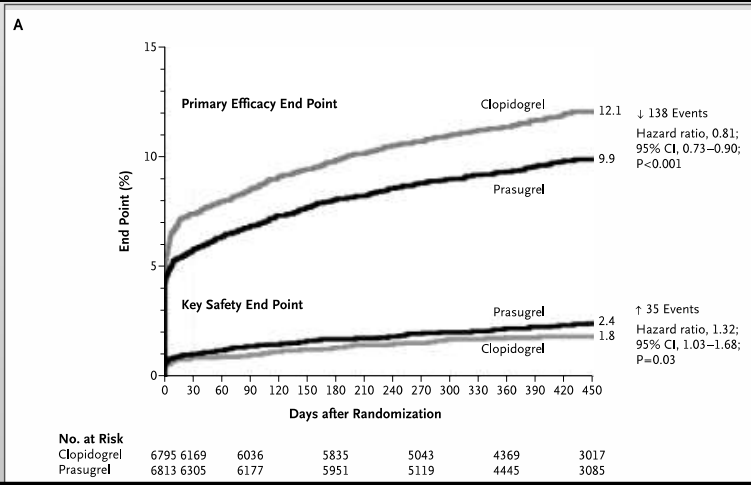


Figure 1. Cumulative Kaplan–Meier Estimates of the Rates of Key Study End Points during the Follow-up Period.

Panel A shows data for the primary efficacy end point (death from cardiovascular causes, nonfatal myocardial infarction [MI], or nonfatal stroke) (top) and for the key safety end point (Thrombolysis in Myocardial Infarction [TIMI] major bleeding not related to coronary-artery bypass grafting) (bottom) during the full follow-up period. The hazard ratio for prasugrel, as compared with clopidogrel, for the primary efficacy end point at 30 days was 0.77 (95% confidence interval [CI], 0.67 to 0.88; P<0.001) and at 90 days was 0.80 (95% CI, 0.71 to 0.90; P<0.001). Data for the primary efficacy end point are also shown from the time of randomization to day 3 (Panel B) and from 3 days to 15 months, with all end points occurring before day 3 censored (Panel C). In Panel C, the number at risk includes all patients who were alive (regardless of whether a nonfatal event had occurred during the first 3 days after randomization) and had not withdrawn consent for follow-up. The P values in Panel A for the primary efficacy end point were calculated with the use of the Gehan–Wilcoxon test; all other P values were calculated with the use of the log-rank test.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 10, 2009 VOL. 361 NO. 11

Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes

Lars Wallentin, M.D., Ph.D., Richard C. Becker, M.D., Andrzej Budaj, M.D., Ph.D., Christopher P. Cannon, M.D., Håkan Emanuelsson, M.D., Ph.D., Claes Held, M.D., Ph.D., Jay Horrow, M.D., Steen Husted, M.D., D.Sc., Stefan James, M.D., Ph.D., Hugo Katus, M.D., Kenneth W. Mahaffey, M.D., Benjamin M. Scirica, M.D., M.P.H., Allan Skene, Ph.D., Philippe Gabriel Steg, M.D., Robert F. Storey, M.D., D.M., and Robert A. Harrington, M.D., for the PLATO Investigators*

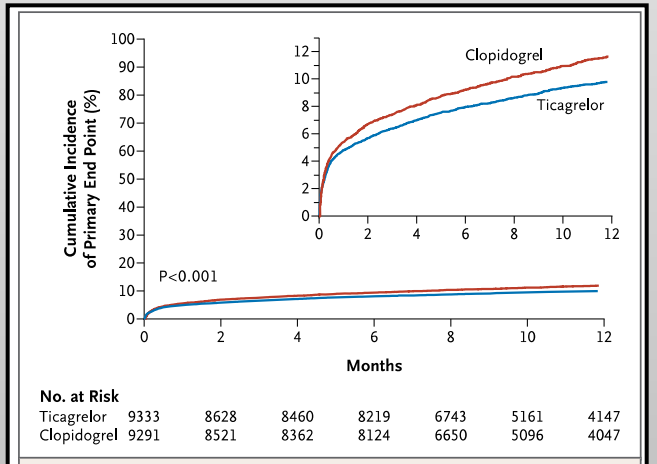
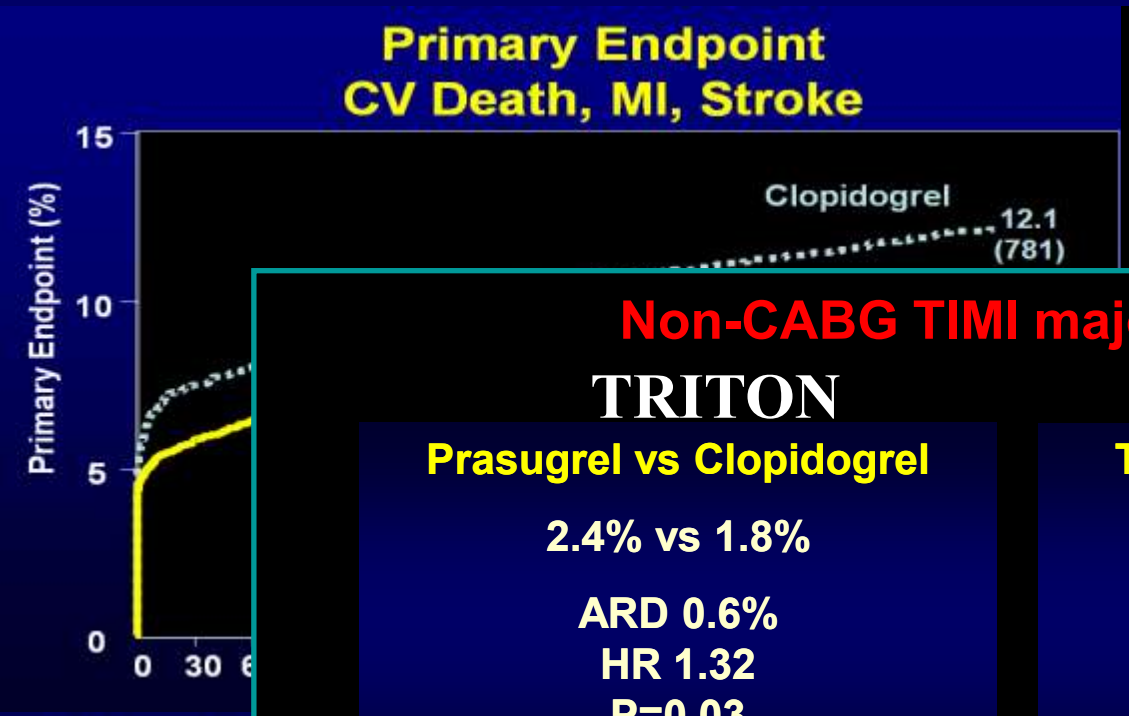


Figure 1. Cumulative Kaplan–Meier Estimates of the Time to the First Adjudicated Occurrence of the Primary Efficacy End Point.

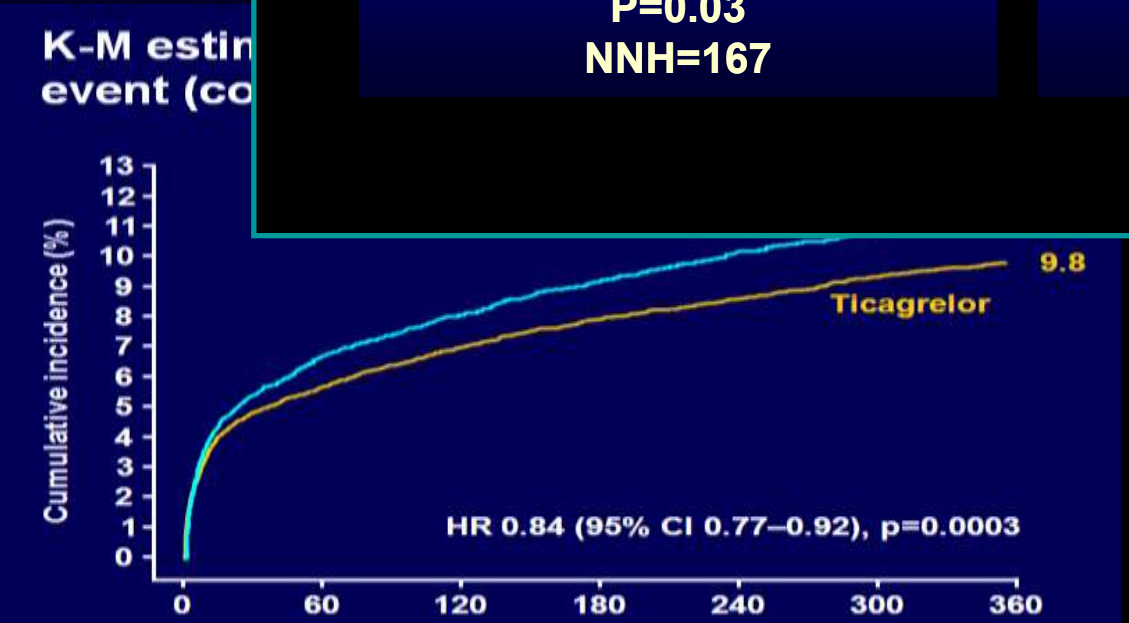
The primary end point — a composite of death from vascular causes, myocardial infarction, or stroke — occurred significantly less often in the ticagrelor group than in the clopidogrel group (9.8% vs. 11.7% at 12 months; hazard ratio, 0.84; 95% confidence interval, 0.77 to 0.92; P<0.001).

SCA: PRASUGREL Y TICAGRELOR vs. CLOPIDOGREL



Non-CABG TIMI major bleeding

TRITON	PLATO
Prasugrel vs Clopidogrel	Ticagrelor vs Clopidogrel
2.4% vs 1.8%	2.8% vs 2.2%
ARD 0.6%	ARD 0.6%
HR 1.32	HR 1.25
P=0.03	P=0.03
NNH=167	NNH=167



TRITON TIMI 38
ogrel)

PLATO
(ticagrelor vs clopidogrel)

Prasugrel compared with clopidogrel in patients undergoing percutaneous coronary intervention for ST-elevation myocardial infarction (TRITON-TIMI 38): double-blind, randomised controlled trial

Gilles Montalescot, Stephen D Wiviott, Eugene Braunwald, Sabina A Murphy, C Michael Gibson, Carolyn H McCabe, Elliott M Antman, for the TRITON-TIMI 38 investigators

Summary

Background Mechanical reperfusion with stenting for ST-elevation myocardial infarction (STEMI) is supported by dual antiplatelet treatment with aspirin and clopidogrel. Prasugrel, a potent and rapid-acting thienopyridine, is a potential alternative to clopidogrel. We aimed to assess prasugrel versus clopidogrel in patients undergoing percutaneous coronary intervention (PCI) for STEMI.

Methods We undertook a double-blind, randomised controlled trial in 707 sites in 30 countries. 3534 participants presenting with STEMI were randomly assigned by interactive voice response system either prasugrel (60 mg loading, 10 mg maintenance [n=1769]) or clopidogrel (300 mg loading, 75 mg maintenance [n=1765]) and were unaware of the allocation. The primary endpoint was cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke. Efficacy analyses were by intention to treat. Follow-up was to 15 months, with secondary analyses at 30 days. This trial is registered with ClinicalTrials.gov, number NCT00097591.

Findings At 30 days, 115 (6·5%) individuals assigned prasugrel had met the primary endpoint compared with 166 (9·5%) allocated clopidogrel (hazard ratio 0·68 [95% CI 0·54–0·87]; p=0·0017). This effect continued to 15 months (174 [10·0%] *vs* 216 [12·4%]; 0·79 [0·65–0·97]; p=0·0221). The key secondary endpoint of cardiovascular death, myocardial infarction, or urgent target vessel revascularisation was also significantly reduced with prasugrel at 30 days (0·75 [0·59–0·96]; p=0·0205) and 15 months (0·79 [0·65–0·97]; p=0·0250), as was stent thrombosis. Treatments did not differ with respect to thrombolysis in myocardial infarction (TIMI) major bleeding unrelated to coronary-artery bypass graft (CABG) surgery at 30 days (p=0·3359) and 15 months (p=0·6451). TIMI life-threatening bleeding and TIMI major or minor bleeding were also similar with the two treatments, and only TIMI major bleeding after CABG surgery was significantly increased with prasugrel (p=0·0033).

Interpretation In patients with STEMI undergoing PCI, prasugrel is more effective than clopidogrel for prevention of ischaemic events, without an apparent excess in bleeding.

Funding Daiichi Sankyo and Eli Lilly.

Lancet 2009; 373: 723–31

See Comment page 695

Institute of Cardiology, INSERM U856, Université Paris 6, Pitié-Salpêtrière Hospital (AP-HP), Paris, France (Prof G Montalescot MD); **and TIMI Study Group, Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA** (S D Wiviott MD, E Braunwald MD, S A Murphy MPH, C M Gibson MD, C H McCabe BS, E M Antman MD)

Correspondence to: Prof Gilles Montalescot, Bureau 236, Institute of Cardiology, INSERM U856, Pitié-Salpêtrière Hospital (AP-HP), 47 Boul de l'Hôpital, 75013 Paris, France
gilles.montalescot@psl.aphp.fr

Introduction

Major innovations in catheter-based management of ST-segment elevation myocardial infarction (STEMI) include use of bare metal and drug-eluting stents and platelet glycoprotein IIb/IIIa inhibitors. Use of drug-eluting stents has significantly lowered restenosis but has had little effect on ischaemic events such as death, reinfarction, or stent thrombosis.[1–3] Conversely, glycoprotein IIb/IIIa inhibitors have had no effect on restenosis but have been associated with a reduction in major ischaemic events associated with percutaneous coronary intervention (PCI) in patients with STEMI.[4]

As use of stents has grown, thienopyridines—especially clopidogrel—have become increasingly important for treatment of STEMI.[5–10] However, up to now, no randomised controlled trials have been undertaken to compare clopidogrel (or the first-generation thienopyridine, ticlopidine) with placebo in patients undergoing PCI for STEMI. The effectiveness of clopidogrel in this setting has been presumed on the basis of results of studies of scheduled PCI.[11–13]

Prasugrel is a novel third-generation thienopyridine and a more potent blocker of the platelet $P2Y_{12}$ receptor than clopidogrel, producing consistent platelet inhibition.[14] The TRial to assess Improvement in Therapeutic Outcomes by optimizing platelet inhibitioN with prasugrel–Thrombolysis In Myocardial Infarction (TRITON-TIMI) 38 was designed to compare clopidogrel with prasugrel. In a previous report, prasugrel was superior to clopidogrel in reduction of ischaemic events in patients undergoing PCI for the entire spectrum of acute coronary syndrome, albeit with increased bleeding.[15] We report here results for the STEMI population, which represents the first large experience for prasugrel in mechanical reperfusion of STEMI.

Ticagrelor Versus Clopidogrel in Patients With ST-Elevation Acute Coronary Syndromes Intended for Reperfusion With Primary Percutaneous Coronary Intervention

A Platelet Inhibition and Patient Outcomes (PLATO) Trial Subgroup Analysis

Philippe Gabriel Steg, MD; Stefan James, MD, PhD; Robert A. Harrington, MD; Diego Ardissino, MD; Richard C. Becker, MD; Christopher P. Cannon, MD; Håkan Emanuelsson, MD, PhD; Ariel Finkelstein, MD; Steen Husted, MD, DSc; Hugo Katus, MD; Jan Kilhamn, MD, PhD; Sylvia Olofsson, BSc; Robert F. Storey, MD, DM; W. Douglas Weaver, MD; Lars Wallentin, MD, PhD; for the PLATO Study Group

Background—Aspirin and clopidogrel are recommended for patients with acute coronary syndromes (ACS) or undergoing coronary stenting. Ticagrelor, a reversible oral P2Y12-receptor antagonist, provides faster, greater, and more consistent platelet inhibition than clopidogrel and may be useful for patients with acute ST-segment elevation (STE) ACS and planned primary percutaneous coronary intervention.

Methods and Result—Platelet Inhibition and Patient Outcomes (PLATO), a randomized, double-blind trial, compared ticagrelor with clopidogrel for the prevention of vascular events in 18 624 ACS patients. This report concerns the 7544 ACS patients with STE or left bundle-branch block allocated to either ticagrelor 180-mg loading dose followed by 90 mg twice daily or clopidogrel 300-mg loading dose (with provision for 300 mg clopidogrel at percutaneous coronary intervention) followed by 75 mg daily for 6 to 12 months. The reduction of the primary end point (myocardial infarction, stroke, or cardiovascular death) with ticagrelor versus clopidogrel (10.8% versus 9.4%; hazard ratio [HR], 0.87; 95% confidence interval, 0.75 to 1.01; $P=0.07$) was consistent with the overall PLATO results. There was no interaction between presentation with STE/left bundle-branch block and randomized treatment (interaction $P=0.29$). Ticagrelor reduced several secondary end points, including myocardial infarction alone (HR, 0.80; $P=0.03$), total mortality (HR, 0.82; $P=0.05$), and definite stent thrombosis (HR, 0.66; $P=0.03$). The risk of stroke, low in both groups, was higher with ticagrelor (1.7% versus 1.0%; HR,1.63; 95% confidence interval, 1.07 to 2.48; $P=0.02$). Ticagrelor did not affect major bleeding (HR, 0.98; $P=0.76$).

Conclusion—In patients with STE-ACS and planned primary percutaneous coronary intervention, the effects of ticagrelor were consistent with those observed in the overall PLATO trial.

Clinical Trial Registration—URL: http://www.ClinicalTrials.gov. Unique identifier: NCT00391872.

(*Circulation*. 2010;122:2131-2141.)

Key Words: acute coronary syndrome ■ hemorrhage ■ myocardial infarction ■ platelets ■ thrombosis

Rapid, consistent, and pronounced P2Y12 inhibition is important for treatment of patients with acute coronary syndrome (ACS), particularly in ST-segment elevation ACS (STE-ACS), and in patients treated with intracoronary stent and is recommended in these patients for up to 1 year after the index episode.[1,2] Clopidogrel yields moderate and variable inhibition of platelet aggregation with a fairly slow onset, even with the currently recommended double loading dose.[3] These variations have been shown to affect clinical outcomes in ACS,[4–8] particularly in patients undergoing primary percutaneous coronary intervention (PCI) for STE-ACS.[9] Furthermore, the addition of clopidogrel to aspirin is associated

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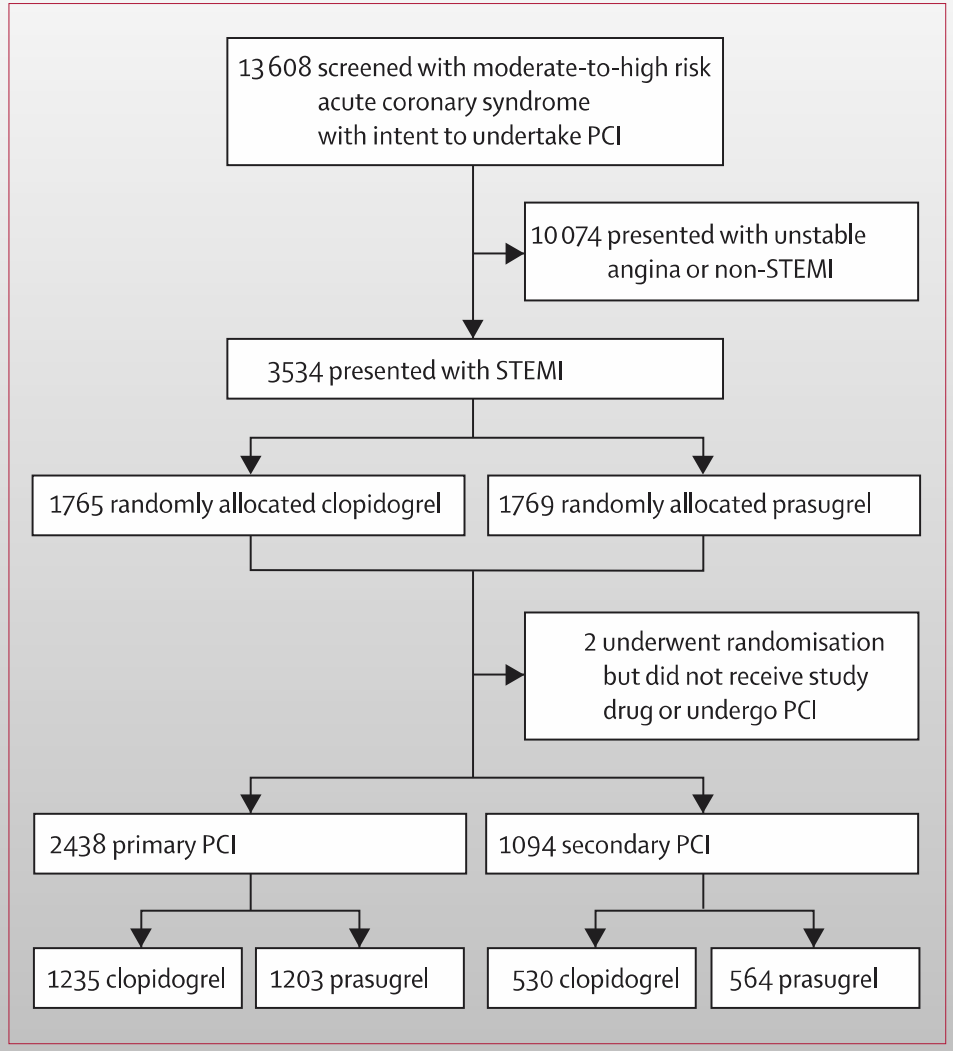
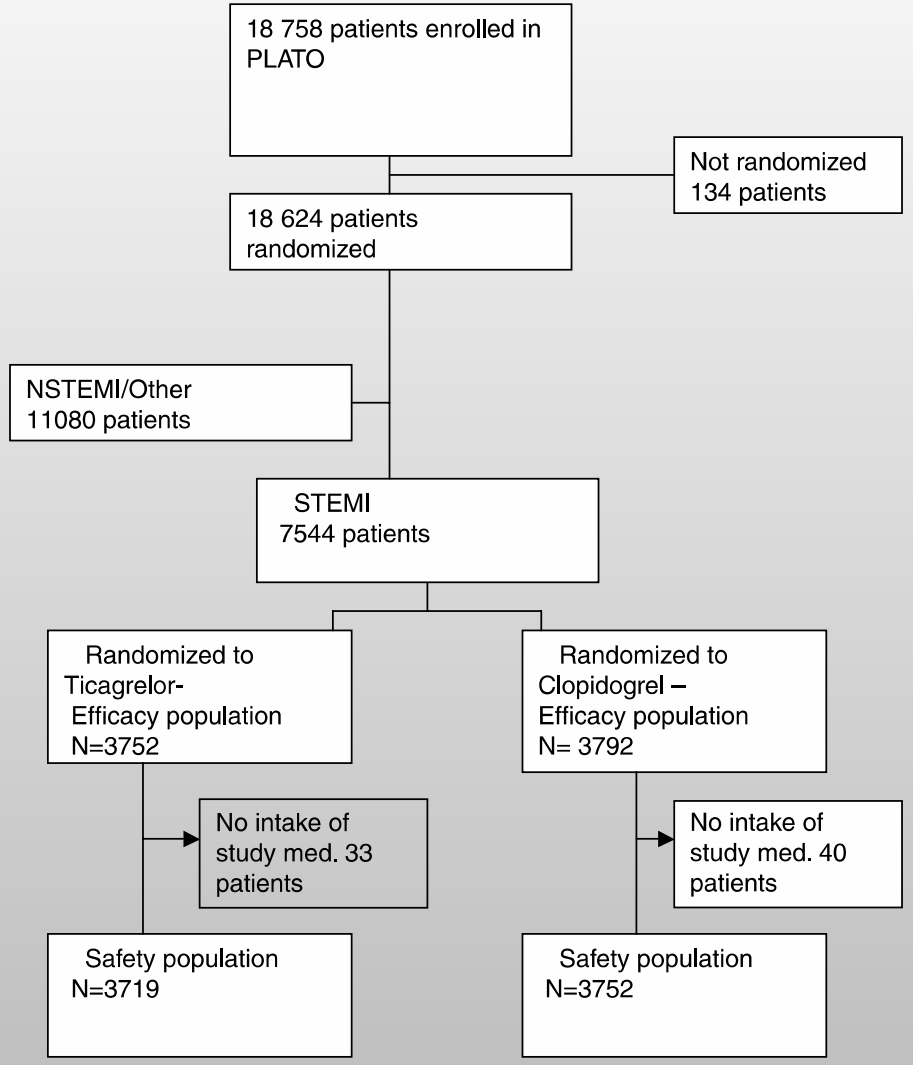
***Circulation* is available at http://circ.ahajournals.org** **DOI: 10.1161/CIRCULATIONAHA.109.927582**

ANTIAGREGACIÓN EN EL SCACEST



TRITON trial

ANTIAGREGACIÓN EN EL SCACEST

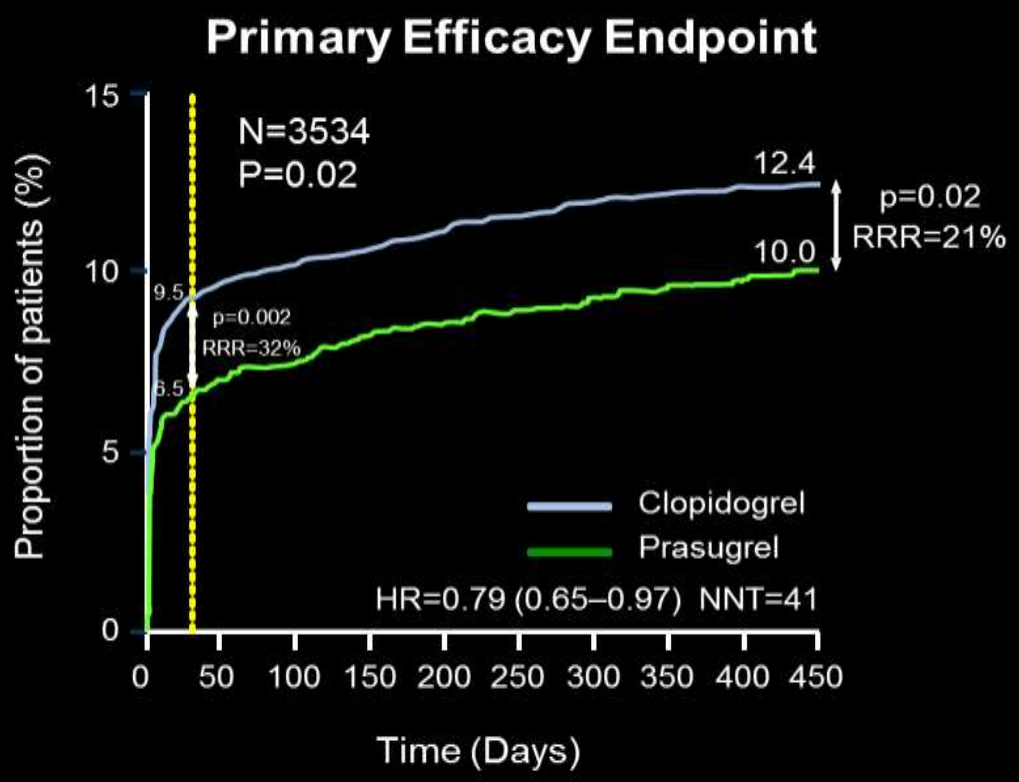


PLATO trial

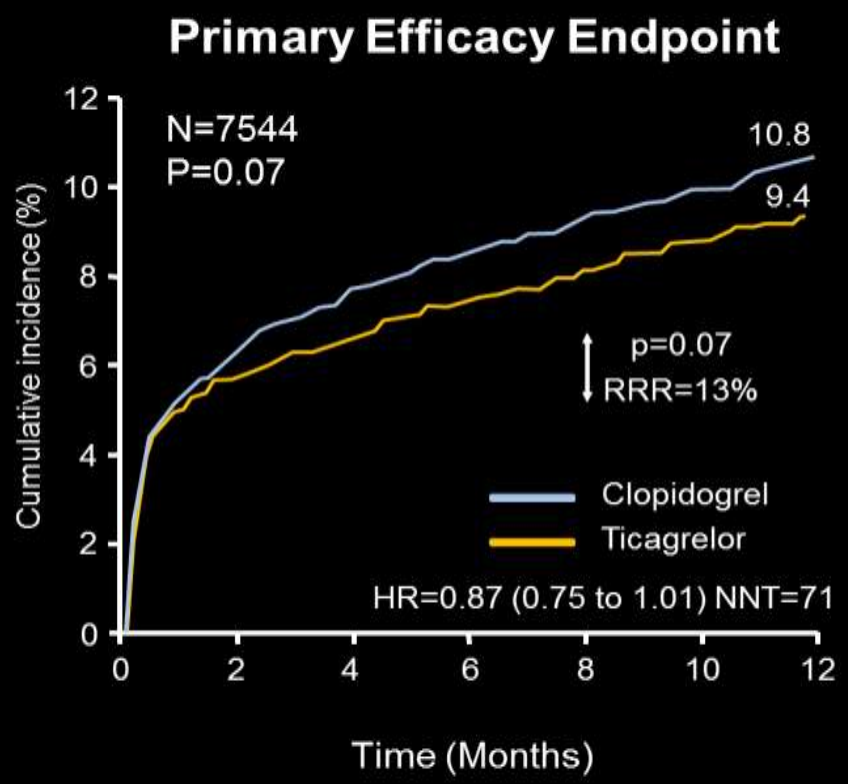
STEMI: PRASUGREL AND TICAGRELOR

Pretreatment allowed

TRITON



PLATO



No differences in bleeding

Montalescot G et al. Lancet 2009;373:723-731
Steg PG et al. Circulation 2010;122:2131-2141

Si el paciente tuviese antecedente de ictus,

¿Qué tratamiento antiagregante administraría?

1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Las respuestas 3 y 4 son correctas.

Si el paciente tuviese antecedente de ictus,

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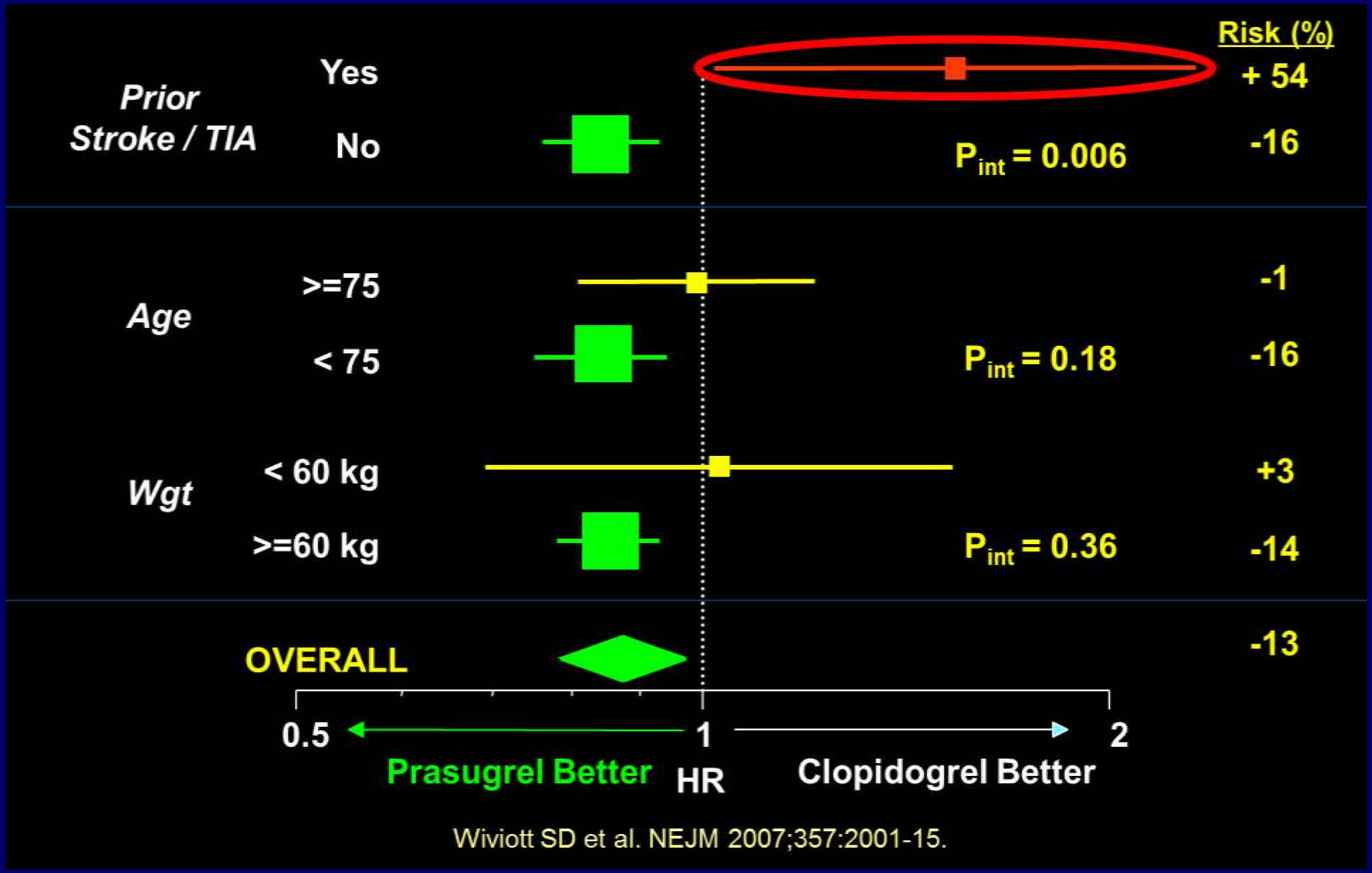
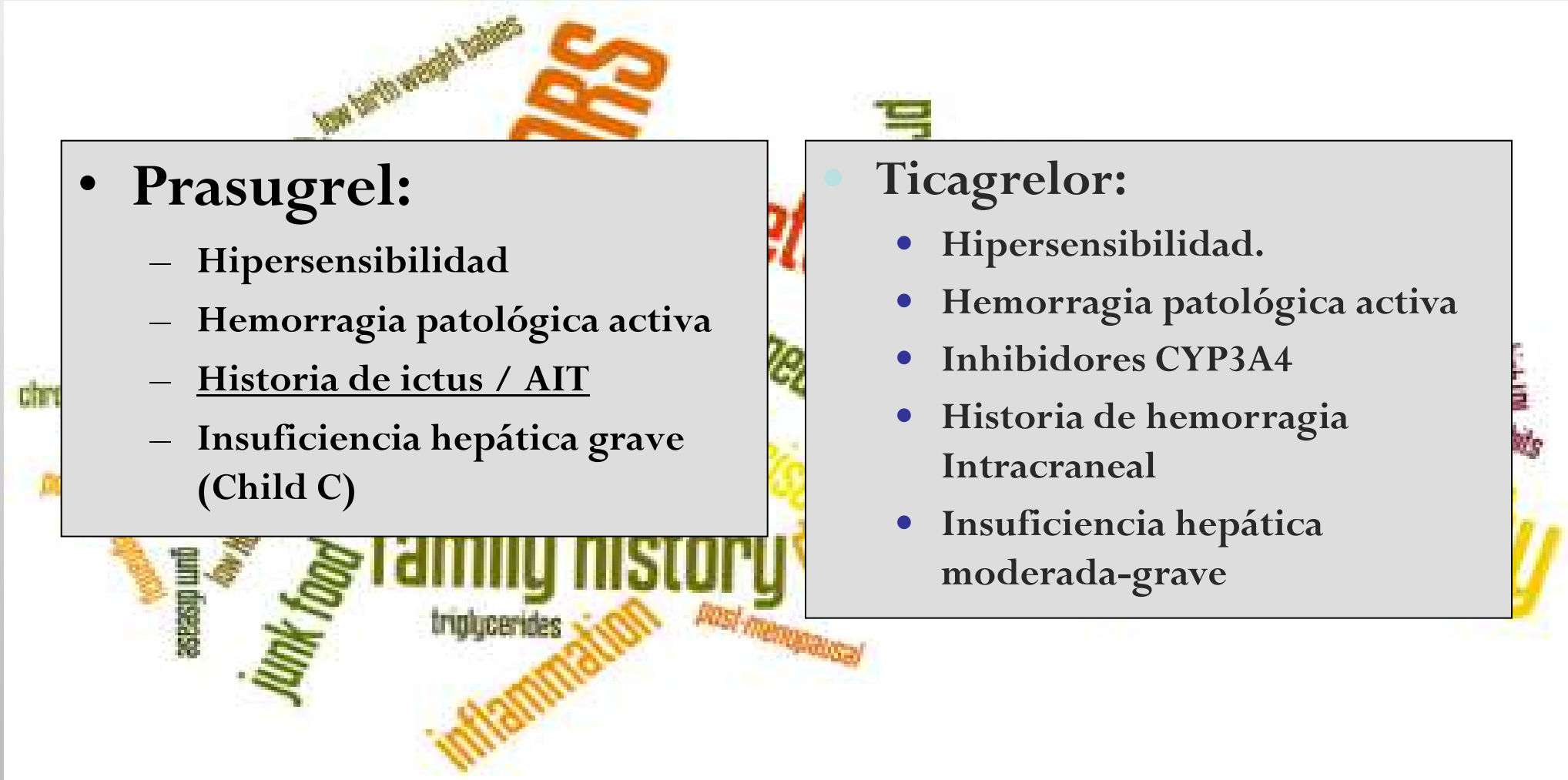
PRASUGREL: VULNERABLE SUBGROUPS



Wiviott SD et al. NEJM 2007;357:2001-15.

CONTRAINDICACIONES



- **Prasugrel:**
  - **Hipersensibilidad**
  - **Hemorragia patológica activa**
  - **Historia de ictus / AIT**
  - **Insuficiencia hepática grave (Child C)**

- **Ticagrelor:**
  - **Hipersensibilidad.**
  - **Hemorragia patológica activa**
  - **Inhibidores CYP3A4**
  - **Historia de hemorragia Intracraneal**
  - **Insuficiencia hepática moderada-grave**

ANTIAGREGACIÓN EN EL SCACEST

Stroke

Ticagrelor Versus Clopidogrel in Patients With Acute Coronary Syndromes and a History of Stroke or Transient Ischemic Attack

Stefan K. James, MD, PhD; Robert F. Storey, MD, DM; Nardev S. Khurmi, MD; Steen Husted, MD, DSc; Matyas Keltai, MD, PhD; Kenneth W. Mahaffey, MD; Juan Maya, MD, MS; Joao Morais, MD; Renato D. Lopes, MD, PhD; Jose C. Nicolau, MD, PhD; Prem Pais, MD; Dimitar Raev, MD, ScD; Jose L. Lopez-Sendon, MD, PhD; Susanna R. Stevens, MS; Richard C. Becker, MD; for the PLATO Study Group

***Background*—**Patients with acute coronary syndromes and history of stroke or transient ischemic attack (TIA) have an increased rate of recurrent cardiac events and intracranial hemorrhages.

***Methods and Results*—**We evaluated treatment effects of ticagrelor versus clopidogrel in patients with acute coronary syndrome with and without a history of prior stroke or TIA in the PLATelet inhibition and patient Outcomes (PLATO) trial. Of the 18 624 randomized patients, 1152 (6.2%) had a history of stroke or TIA. Such patients had higher rates of myocardial infarction (11.5% versus 6.0%), death (10.5% versus 4.9%), stroke (3.4% versus 1.2%), and intracranial bleeding (0.8% versus 0.2%) than patients without prior stroke or TIA. Among patients with a history of stroke or TIA, the reduction of the primary composite outcome and total mortality at 1 year with ticagrelor versus clopidogrel was consistent with the overall trial results: 19.0% versus 20.8% (hazard ratio, 0.87; 95% confidence interval, 0.66–1.13; interaction $P=0.84$) and 7.9% versus 13.0% (hazard ratio, 0.62; 95% confidence interval, 0.42–0.91). The overall PLATO-defined bleeding rates were similar: 14.6% versus 14.9% (hazard ratio, 0.99; 95% confidence interval, 0.71–1.37), and intracranial bleeding occurred infrequently (4 versus 4 cases, respectively).

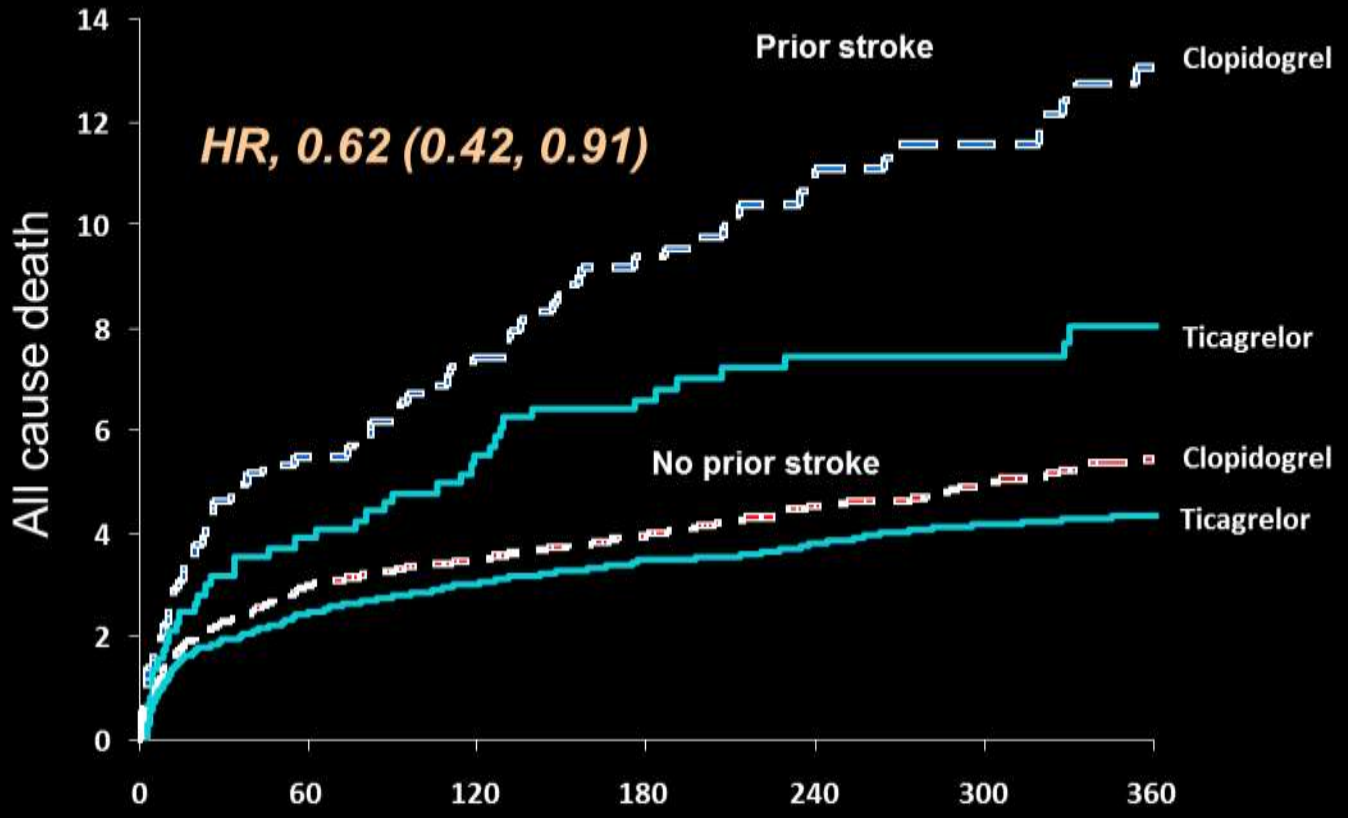
***Conclusions*—**Patients with acute coronary syndrome with a prior history of ischemic stroke or TIA had higher rates of clinical outcomes than patients without prior stroke or TIA. However, the efficacy and bleeding results of ticagrelor in these high-risk patients were consistent with the overall trial population, with a favorable clinical net benefit and associated impact on mortality.

***Clinical Trial Registration*—**URL: http://www.clinicatrials.gov. Unique identifier: NCT00391872.

(*Circulation*. 2012;125:2914-2921.)

Key Words: acute coronary syndrome ■ antiplatelet drugs ■ cardiovascular diseases ■ stroke ■ ticagrelor

TICAGRELOR: PRIOR STROKE OR TIA



Patient at risk

Prior stroke	Clopidogrel	588	542	530	507	397	314	246
	Ticagrelor	564	534	525	511	411	332	254
No prior stroke	Clopidogrel	8699	8318	8245	8078	6679	5124	4115
	Ticagrelor	8761	8382	8289	8107	6701	5143	4162

James S et al. Circulation 2012.

Si se le hubiese administrado clopidogrel en urgencias,

¿Qué tratamiento antiagregante administraría?

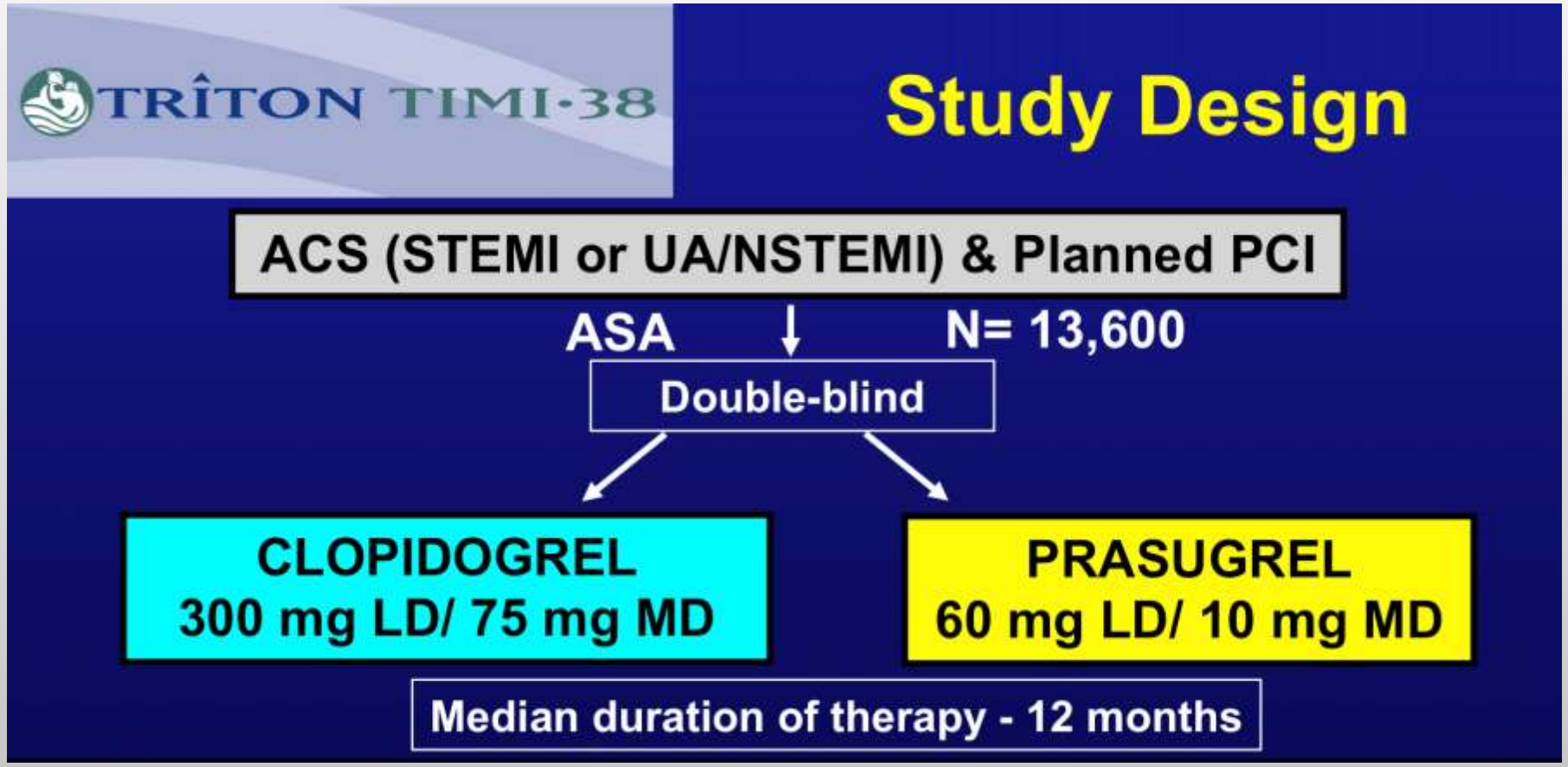
1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Las respuestas 3 y 4 son correctas.

Si se le hubiese administrado clopidogrel en urgencias,

¿Qué tratamiento antiagregante administraría?

1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Las respuestas 3 y 4 son correctas.

ANTIAGREGACIÓN EN EL SCACEST



TRITON: No contempla clopidogrel previo

Datos indirectos TRILOGY-ACS y TRIPLET de seguridad

Si le hemos puesto un stent recubierto,

¿Durante cuanto tiempo mantenemos la doble antiagregación?

1. 1 mes.
2. 3 meses.
3. 6 meses.
4. 9 meses.
5. 1 año.

Si le hemos puesto un stent recubierto,

¿Durante cuanto tiempo mantenemos la doble antiagregación?

1. 1 mes.
2. 3 meses.
3. 6 meses.
4. 9 meses.
5. 1 año.

Y si el stent es no recubierto,

¿Durante cuanto tiempo mantenemos la doble antiagregación?

1. 1 mes.
2. 3 meses.
3. 6 meses.
4. 9 meses.
5. 1 año.

Y si el stent es no recubierto,

¿Durante cuanto tiempo mantenemos la doble antiagregación?

1. 1 mes.
2. 3 meses.
3. 6 meses.
4. 9 meses.
5. 1 año.

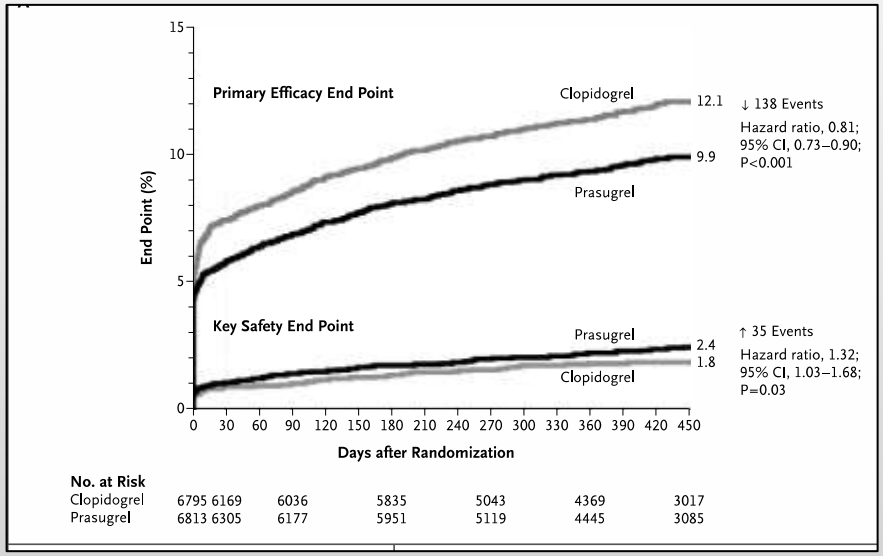
¿Durante cuanto tiempo mantenemos la doble antiagregación?

Tabla 22
Tratamientos de rutina en las fases aguda, subaguda y a largo plazo del infarto de miocardio con elevación del segmento ST

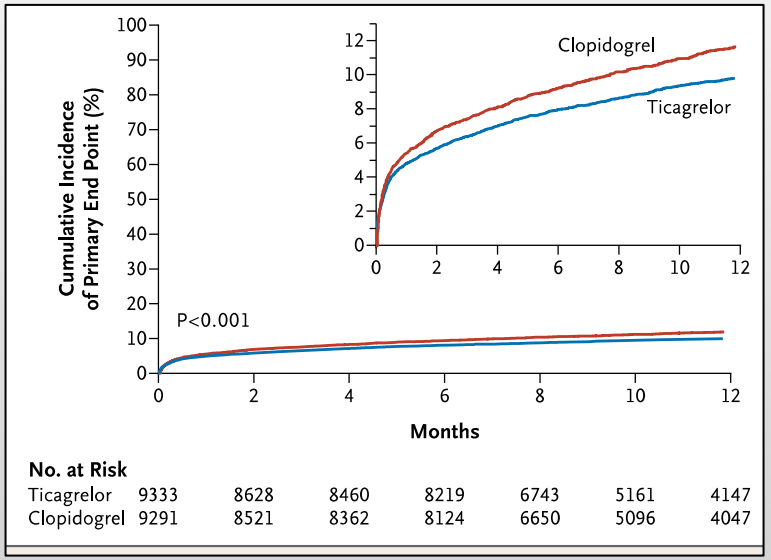
Recomendaciones	Clase[a]	Nivel[b]	Referencias
Los fumadores activos con IAMCEST deben recibir asesoramiento y derivarse a un programa para dejar de fumar	I	B	225
Todos los hospitales que participen en la atención de pacientes con IAMCEST deben tener un protocolo para dejar de fumar	I	C	–
Se recomienda una rehabilitación basada en el ejercicio	I	B	232, 233
Está indicado el tratamiento antiplaquetario indefinido con dosis bajas de aspirina (75-100 mg) en todos los pacientes con IAMCEST	I	A	237
En pacientes intolerantes a la aspirina, el clopidogrel está indicado como alternativa	I	B	243
Se recomienda la doble antiagregación plaquetaria con una combinación de aspirina y prasugrel o aspirina y ticagrelor (más que aspirina y clopidogrel) en pacientes tratados con ICP	I	A	109, 110
La doble antiagregación plaquetaria con aspirina y un inhibidor oral del receptor de ADP debe prolongarse hasta 12 meses después del IAMCEST, con un mínimo estricto de:	I	C	245-247, 283
• 1 mes para pacientes portadores de un *stent* convencional	I	C	
• 6 meses para pacientes portadores de un *stent* farmacoactivo	IIb	B	
En pacientes con un trombo ventricular izquierdo se debe usar anticoagulación durante un mínimo de 3 meses	IIa	B	344-346

G. Steg. Rev Esp Cardiol. 2013;66(1):53.e1-e46

¿Durante cuanto tiempo mantenemos la doble antiagregación?



TRITON



PLATO

Beneficio continuado de prasugrel y ticagrelor

STENT-SPECIFIC ISSUES

	Cypher sirolimus-eluting sent	Taxus paclitaxel-eluting stent	BioMatrix biolimus-eluting stent	Xience V everolimus-eluting stent	Resolute zotarolimus-eluting stent
TLR at 2 years	7·1%	5·9%	6·3%	5·1%	5·7%
Definite stent thrombosis at 2 years	2·5%	2·7%	2·2%	0·5%	1·3%

Stent-related efficacy and safety of early and new generation drug-eluting stents from randomised trials in unrestricted populations at 2 years

Stent	Strut Thickness		Polymer Thickness	Drug Load
Cypher	140 µm	2.5	12.6 µm	~10 ug/mm
Taxus Express	132 µm	2.7	16 µm	1 ug/mm2
Biomatrix	137 µm	2.2		15.6 µg/mm
Endeavor	91 µm	1.3	5.3 µm	10 ug/mm
Xience V	81 µm	0.5	7.8 µm	~6 ug/mm

ANTIAGREGACIÓN EN EL SCACEST: RESUMEN

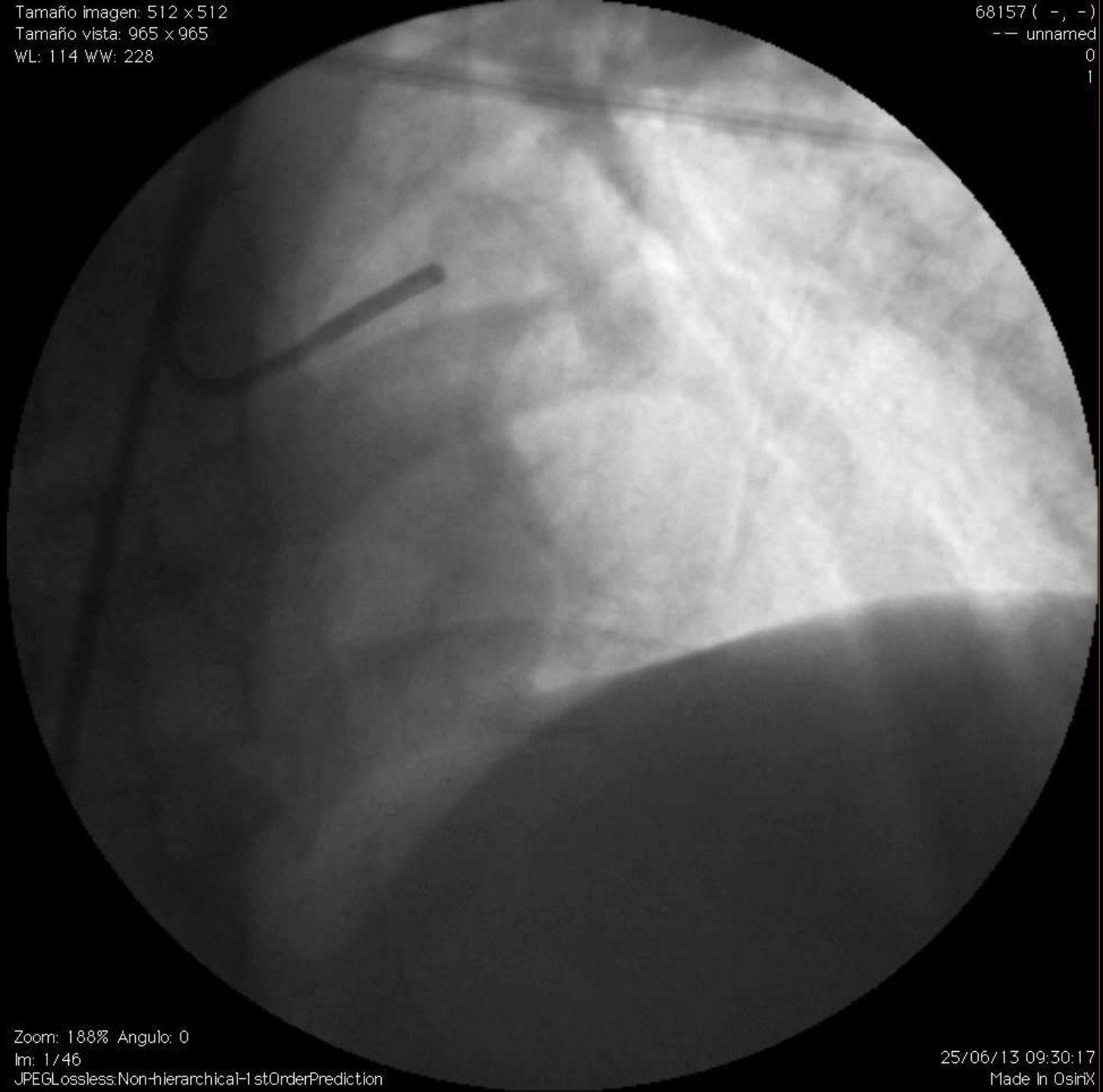
Tabla 12
Medicación antitrombótica periprocedimiento en la angioplastia primaria

Recomendaciones	Clase[a]	Nivel[b]	Referencias
Tratamiento antiplaquetario			
Se recomienda aspirina por vía oral o i.v. (si no se puede deglutir)	I	B	133, 134
Se recomienda un inhibidor del receptor de ADP además de la aspirina. Las opciones son:	I	A	135, 136
• Prasugrel en pacientes que no han tomado clopidogrel, si no hay historia previa de accidente cerebrovascular/AIT, edad < 75 años	I	B	109
• Ticagrelor	I	B	110
• Clopidogrel, preferiblemente cuando el prasugrel o ticagrelor no estén disponibles o estén contraindicados	I	C	–

G. Steg. Rev Esp Cardiol. 2013;66(1):53.e1-e46

CASO CLINICO 2

- Mujer de 60 años.
- FRCV: HTA, hipercolesterolemia.
- Antecedentes personales: Sin interés.
- Avisa al 061 por dolor torácico.
- Diagnóstico: **SCASEST anterior**.
- Tratamiento en urgencias: Aspirina, clopidogrel y enoxaparina.
- Se programa para cateterismo en 24 horas.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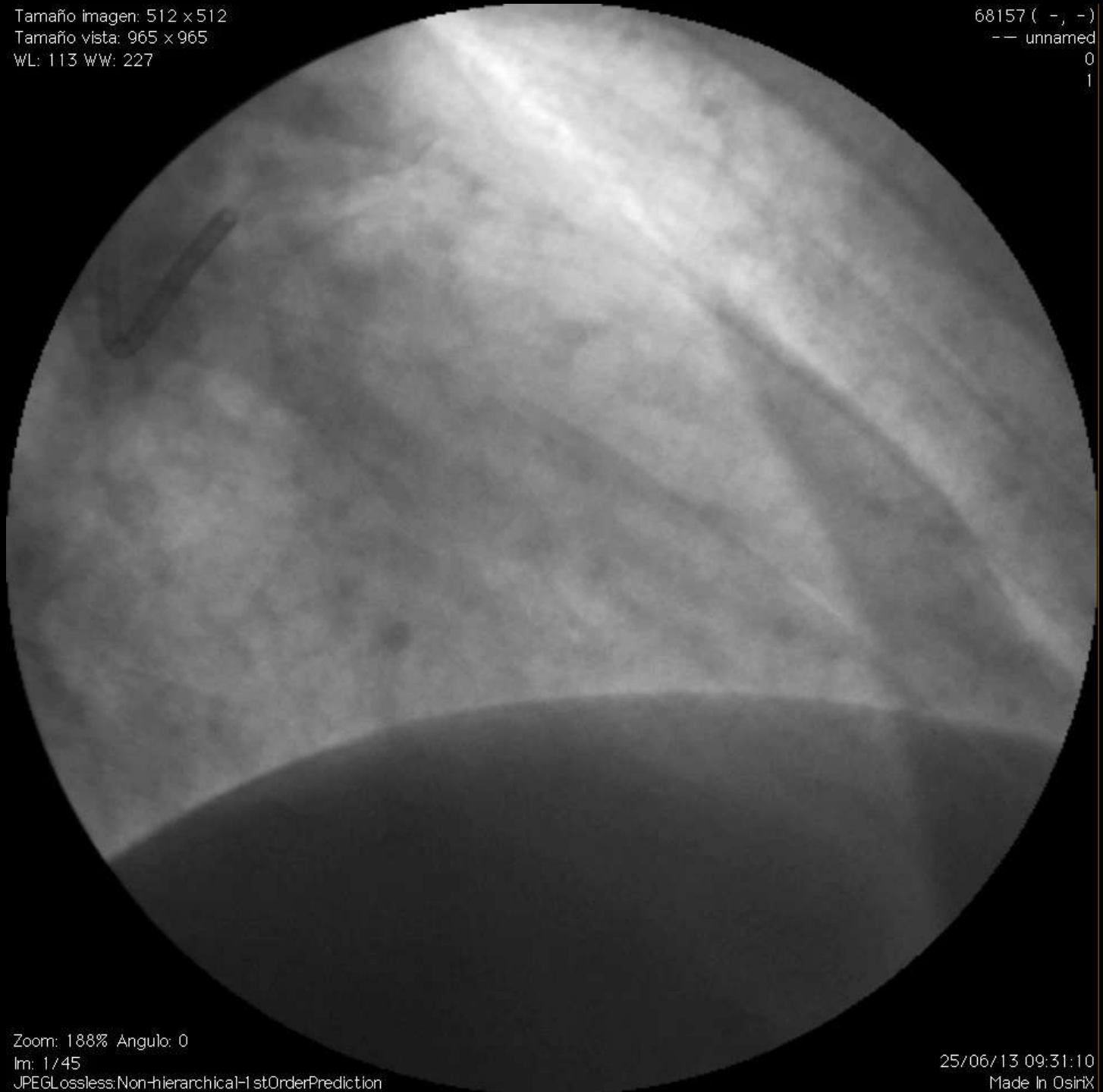
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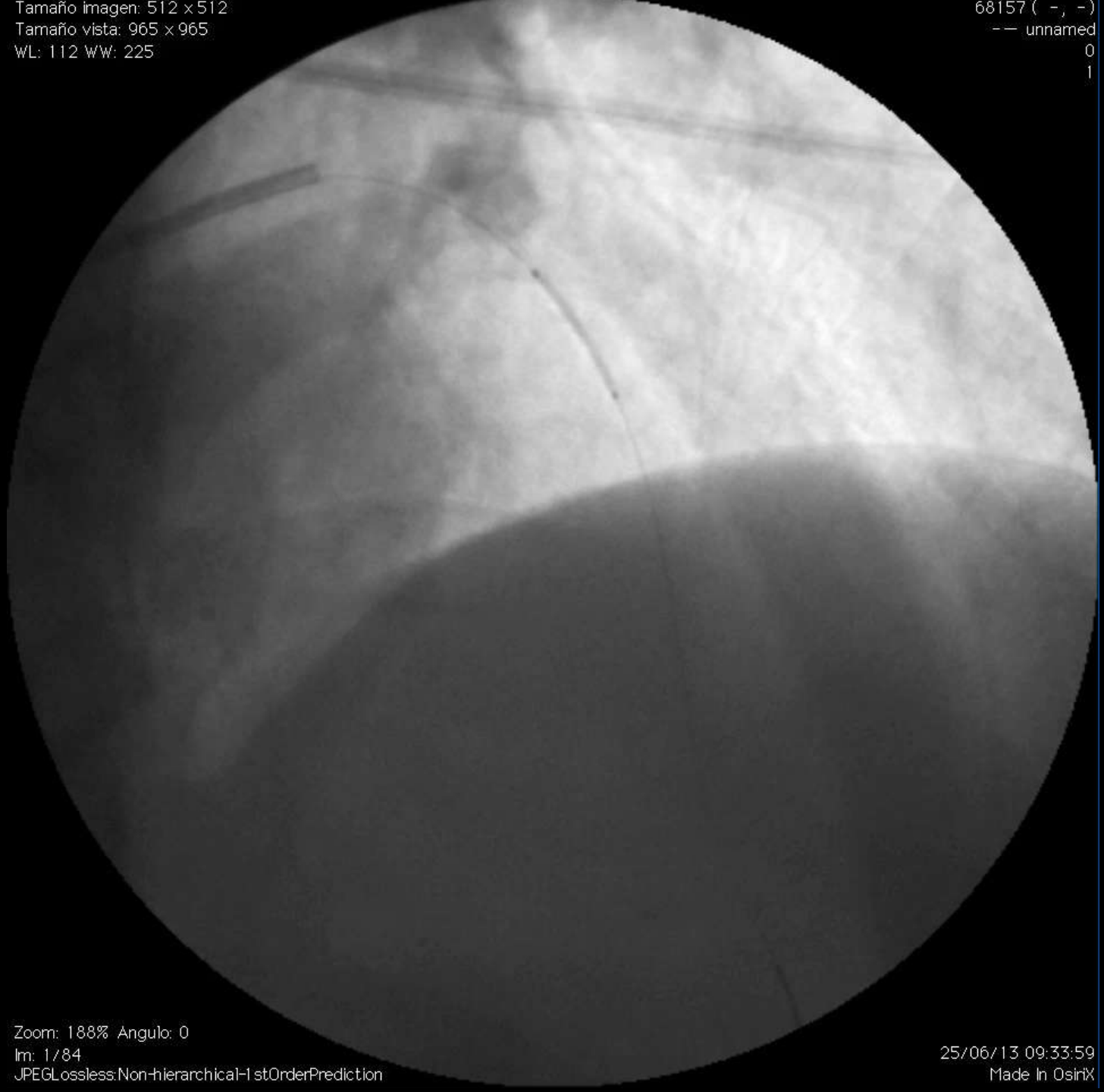
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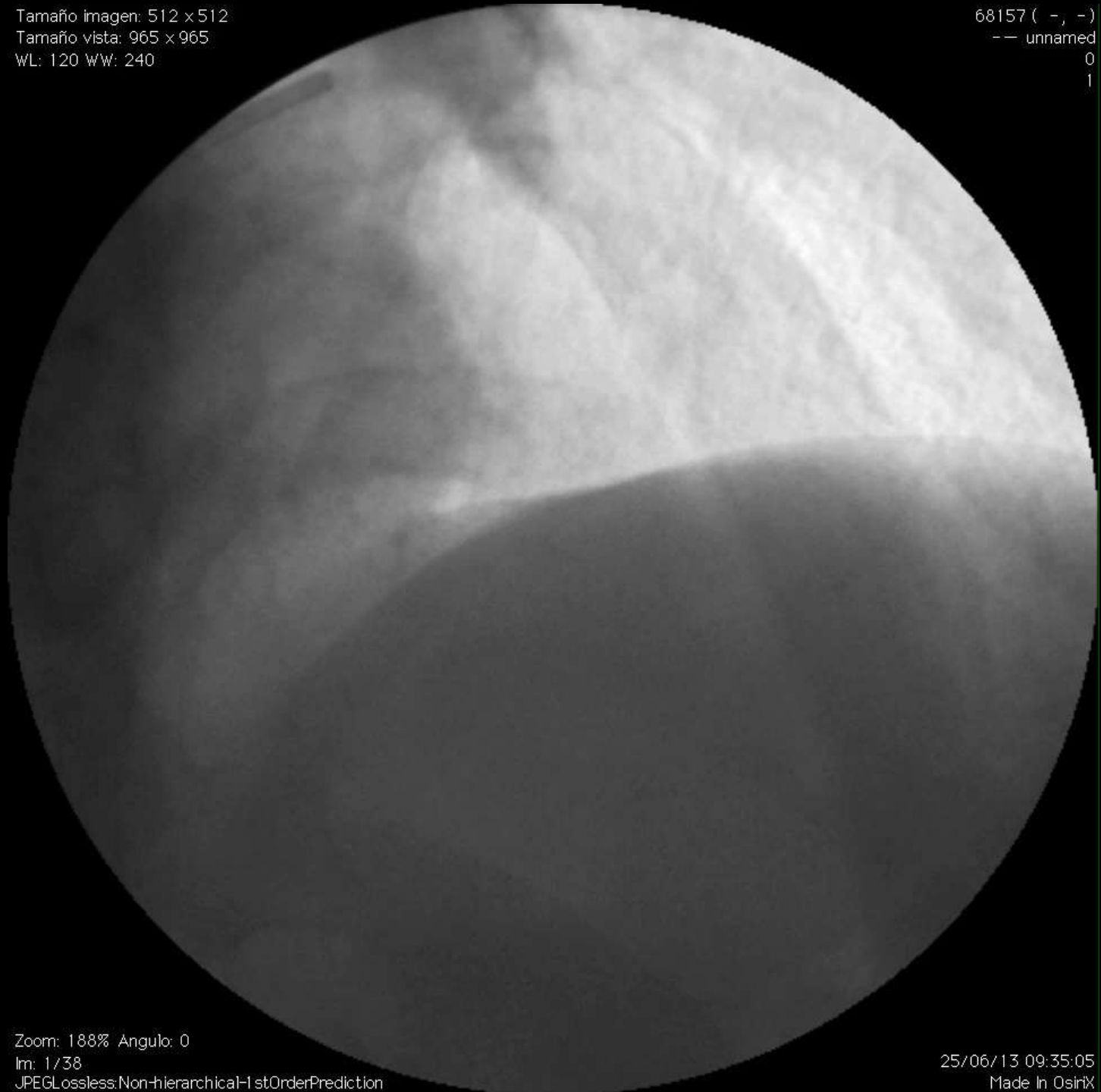
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Si en su hospital tiene disponibles todos los antiagregantes

¿Qué tratamiento antiagregante administraría?

1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Se podría utilizar cualquiera de las anteriores pautas.

Si en su hospital tiene disponibles todos los antiagregantes

¿Qué tratamiento antiagregante administraría?

1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Se podría utilizar cualquiera de las anteriores pautas.

ANTIAGREGACIÓN EN EL SCASEST

¿Qué nos dicen las guías?

Recomendaciones para los fármacos antiplaquetarios orales

Recomendaciones	Clase[a]	Nivel[b]	Ref.[c]
Se debe administrar AAS a todos los pacientes que no tengan contraindicaciones para una dosis de carga inicial de 150-300 mg y una dosis de mantenimiento de 75-100 mg diarios a largo plazo independientemente de la estrategia de tratamiento	I	A	107, 108
Se debe añadir un inhibidor $P2Y_{12}$ al AAS lo antes posible y mantenerlo durante 12 meses, excepto cuando haya contraindicaciones, como riesgo excesivo de sangrado	I	A	110, 130, 132
Se recomienda un inhibidor de la bomba de protones (preferiblemente no omeprazol) en combinación con la antiagregación plaquetaria doble para pacientes con historia de hemorragia gastrointestinal o úlcera péptica, y es adecuado en pacientes con múltiples factores de riesgo adicionales (infección por *Helicobacter pylori*, edad ≥ 65 años, uso concomitante de anticoagulantes o esteroides)	I	A	125-127
Se desaconseja la interrupción prolongada o permanente de inhibidores $P2Y_{12}$ en los 12 meses siguientes al episodio principal, excepto cuando esté clínicamente indicado	I	C	—

CW. Hamm. Rev Esp Cardiol. 2012;65(2):173.e1-e55

SCASEST: ANTIAGREGACION

Ticagrelor

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)

Class	Level
I	B

INDICACION "ALL COMERS"

CW. Hamm. European Heart Journal (2011) 32, 2999–3054

SCASEST: ANTIAGREGACION

Prasugrel

Prasugrel (60-mg loading dose, 10-mg daily dose) is recommended for $P2Y_{12}$-inhibitor-naïve patients (especially diabetics) in whom coronary anatomy is known and who are proceeding to PCI unless there is a high risk of lifethreatening bleeding or other contraindications

Class	Level
I	B

INDICACION MÁS «RESTRINGIDA»

CW. Hamm. European Heart Journal (2011) 32, 2999–3054

CASO 2

Si no se hubiese administrado clopidogrel y la paciente fuese diabética...

¿Qué tratamiento antiagregante administraría?

1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Las respuestas 3 y 4 son correctas.

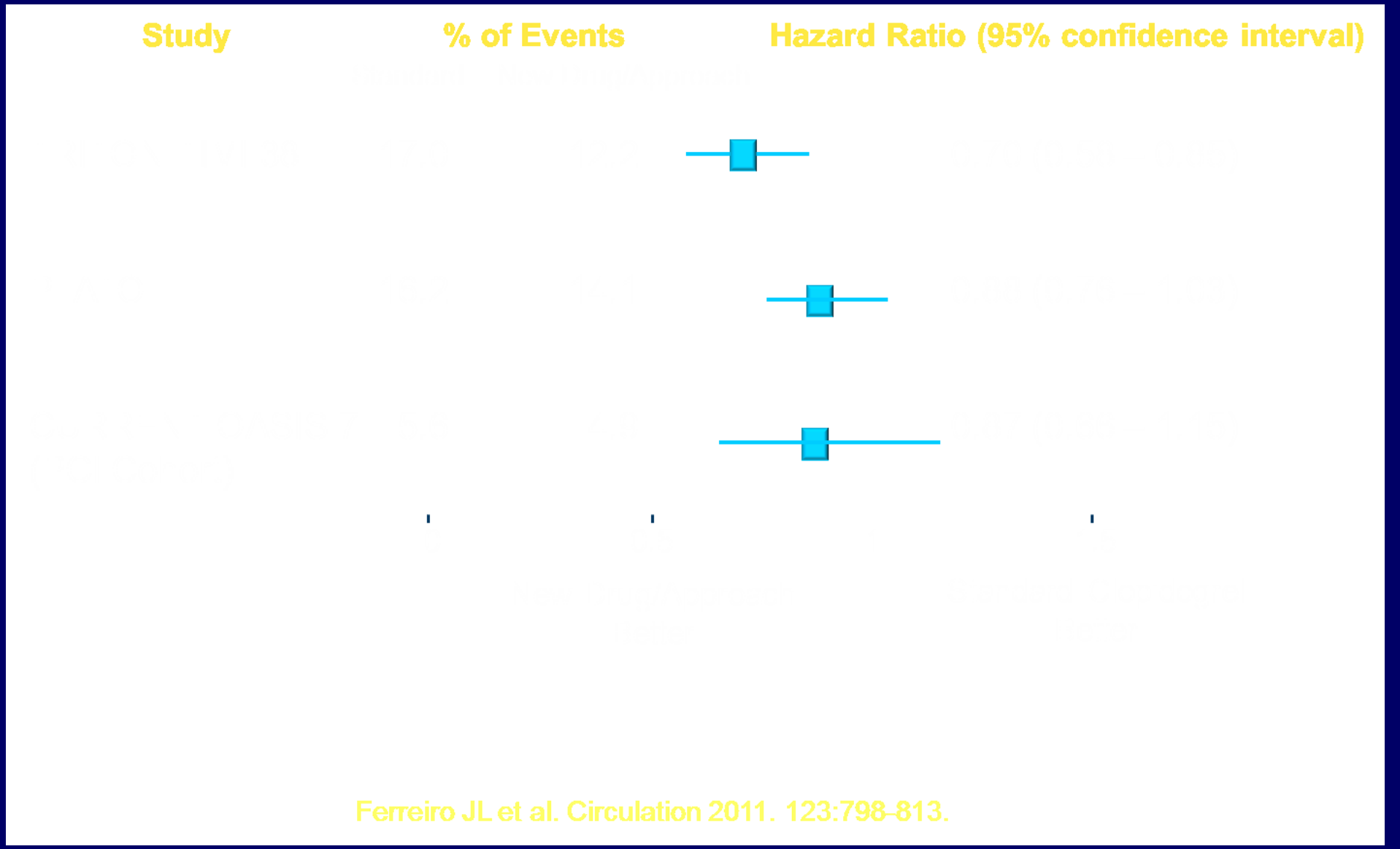
CASO 2

Si no se hubiese administrado clopidogrel y la paciente fuese diabética...

¿Qué tratamiento antiagregante administraría?

1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Las respuestas 3 y 4 son correctas.

ACS IN DM PATIENTS



Ferreiro JL et al. Circulation 2011. 123:798-813.

CASO 2

Si no se hubiese administrado clopidogrel y la paciente tuviese insuficiencia renal...

¿Qué tratamiento antiagregante administraría?

1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Las respuestas 3 y 4 son correctas.

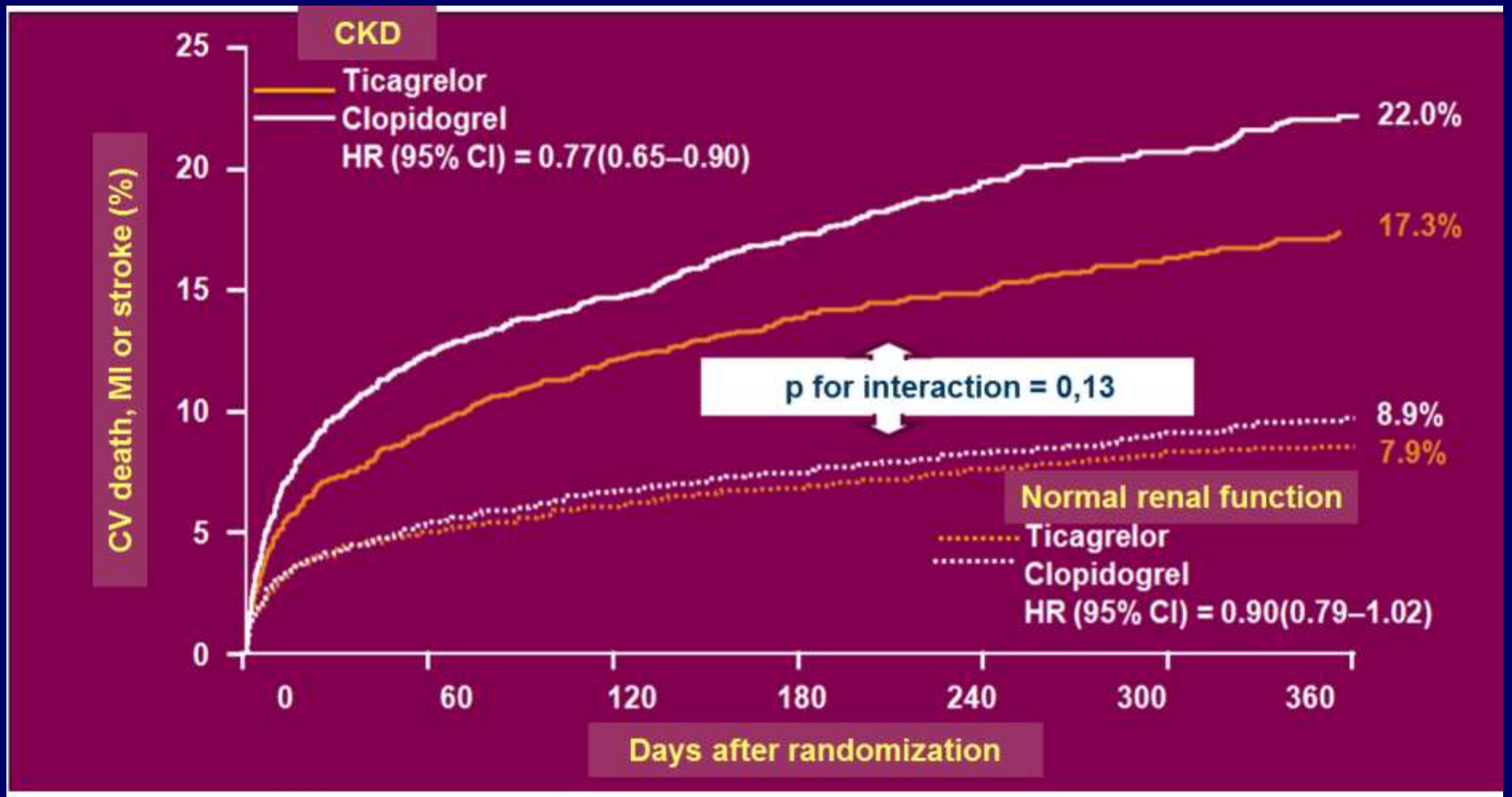
CASO 2

Si no se hubiese administrado clopidogrel y la paciente tuviese insuficiencia renal...

¿Qué tratamiento antiagregante administraría?

1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Las respuestas 3 y 4 son correctas.

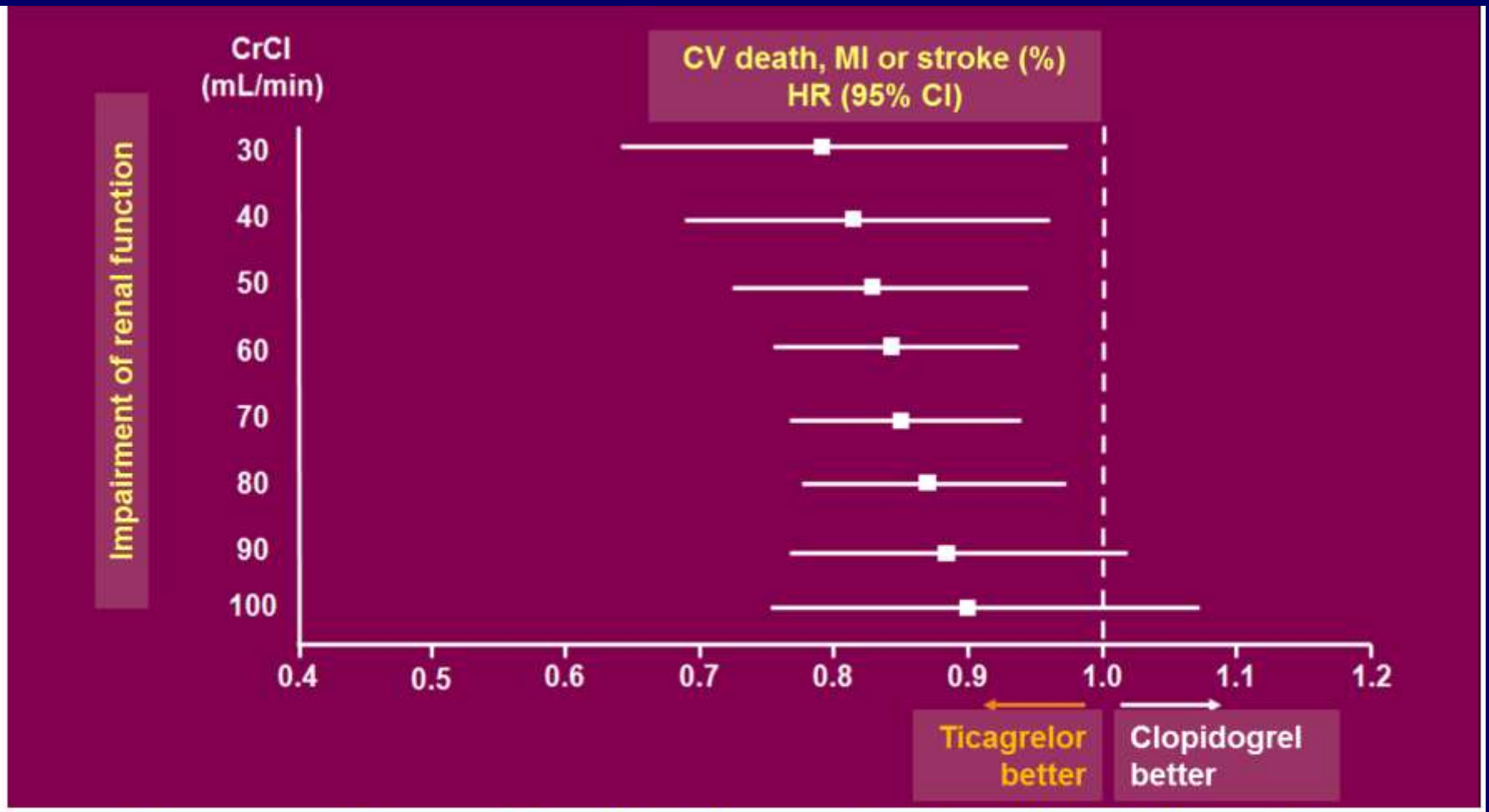
TICAGRELOR: CKD



Renal function analytic control 1 month after initiating therapy

James S et al. Circulation. 2010;122:1056–1067.

TICAGRELOR: CKD



The worse the renal function, the greater benefit with ticagrelor

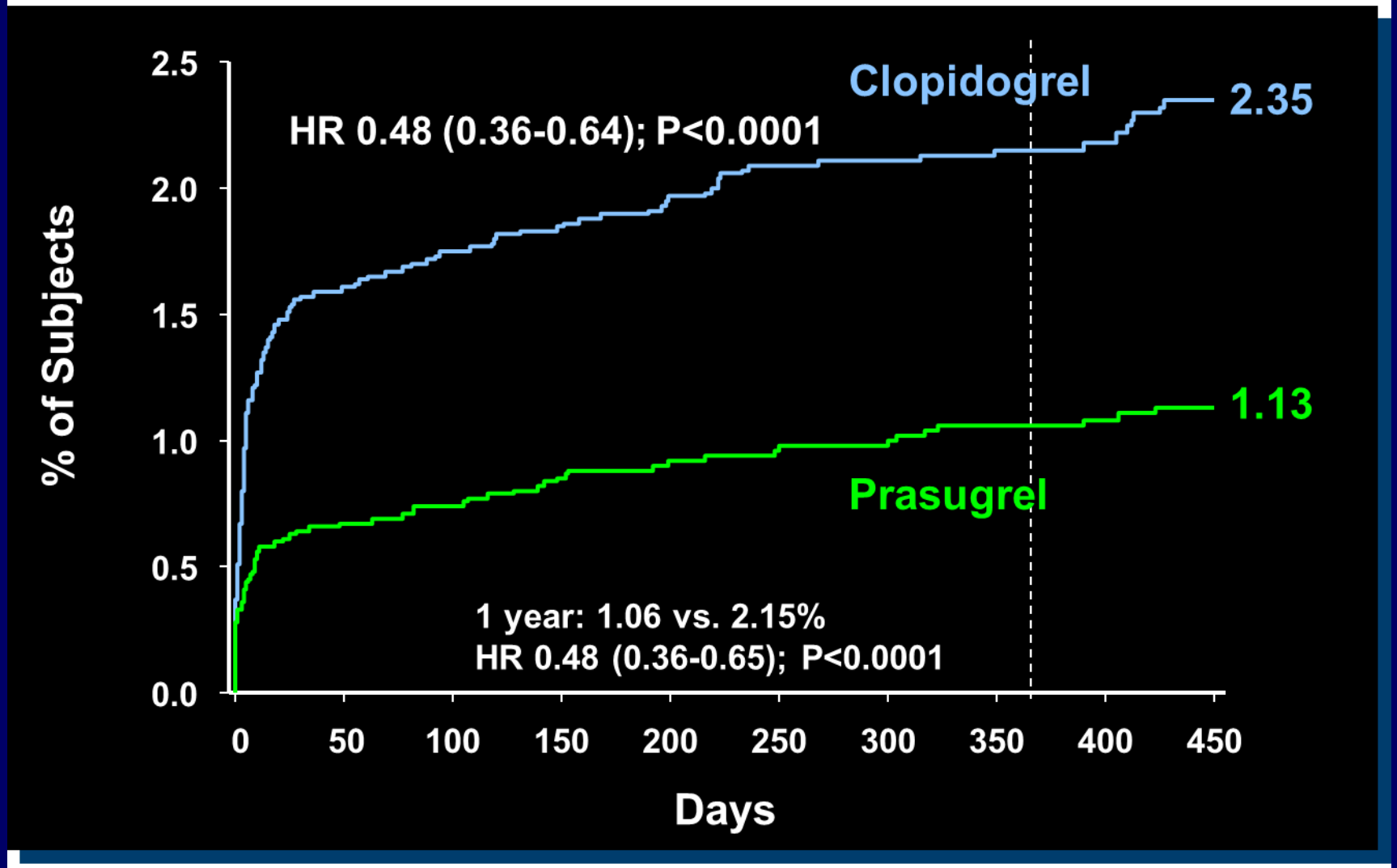
James S et al. Circulation. 2010;122:1056–1067.

Y si el stent hubiera quedado mal apuesto y hubiese alto riesgo de trombosis del stent...

¿Qué tratamiento antiagregante administraría?

1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Las respuestas 3 y 4 son correctas.

PRASUGREL: STENT THROMBOSIS



Wiviott SD JL et al. NEJM 2007;357:2001-15.

TICAGRELOR: STENT THROMBOSIS

	Ticagrelor (n=5,640)	Clopidogrel (n=5,649)	HR (95% CI)	*P* value
Stent thrombosis, n (%)				
Definite	71 (1.3)	106 (1.9)	0.67 (0.50–0.91)	0.009
Probable or definite	118 (2.1)	158 (2.8)	0.75 (0.59–0.95)	0.02
Possible, probable, definite	155 (2.8)	202 (3.6)	0.77 (0.62–0.95)	0.01

Wallentin L et al. NEJM 2009;361:1045-57.

Y si la paciente precisara ACO (FA permanente)...

¿Qué tratamiento antiagregante (+ACO) administraría?

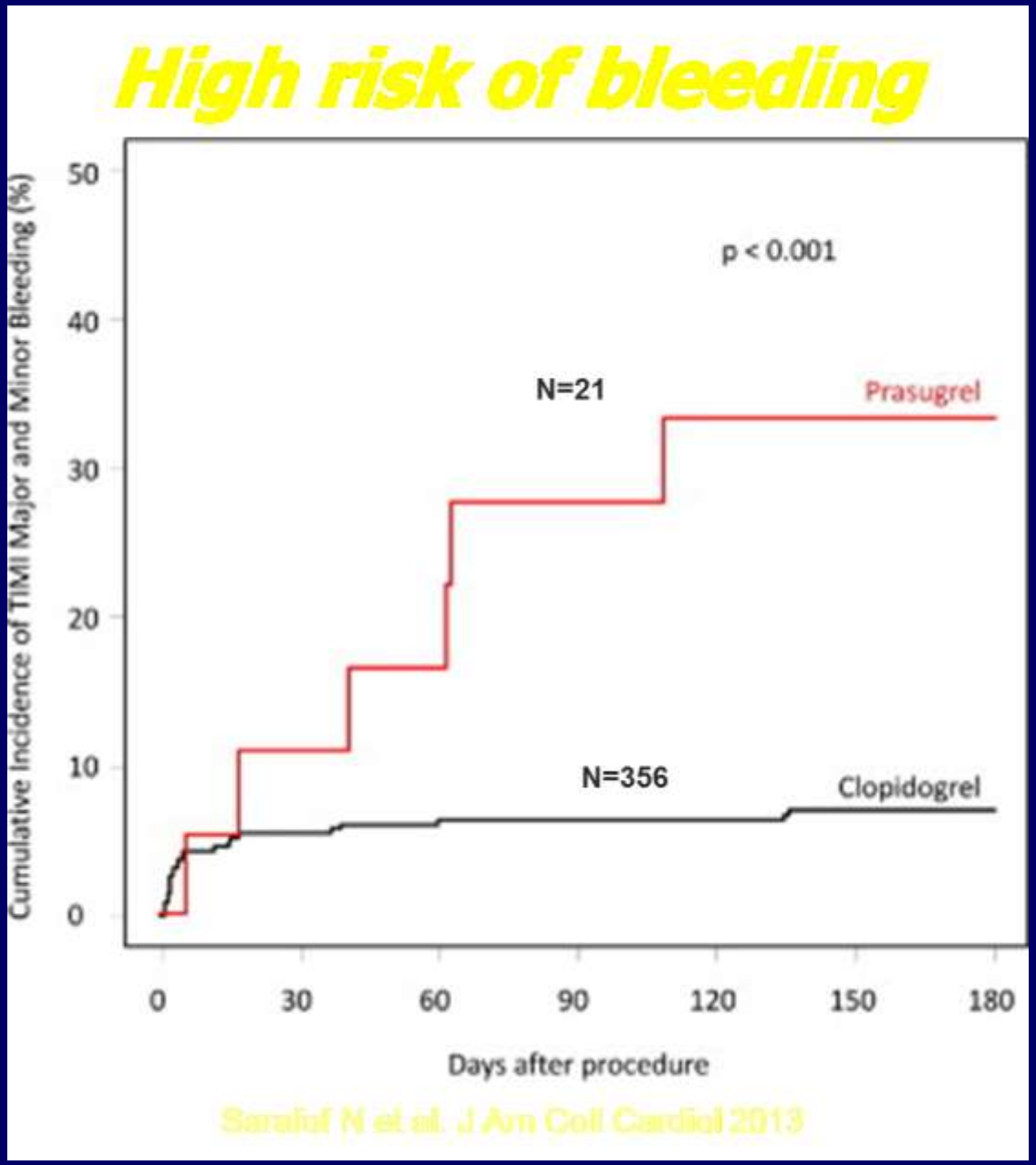
1. Solo clopidogrel.
2. Aspirina y clopidogrel.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Las respuestas 3 y 4 son correctas.

Y si la paciente precisara ACO (FA permanente)...

¿Qué tratamiento antiagregante (+ACO) administraría?

1. Solo clopidogrel.
2. Aspirina y clopidogrel.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Las respuestas 3 y 4 son correctas.

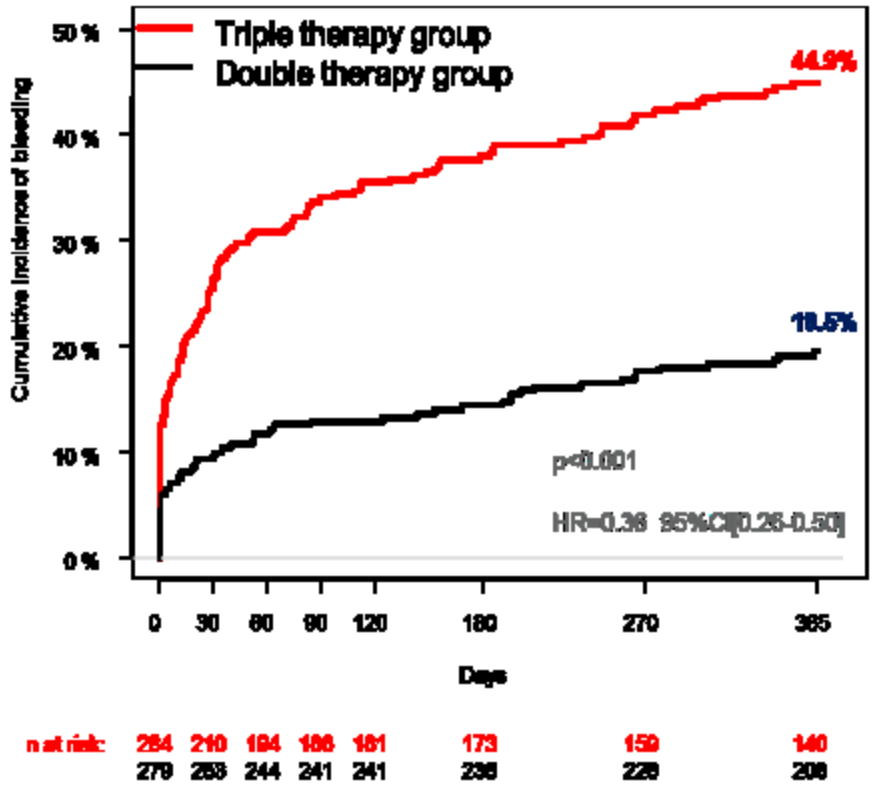
TRIPLE THERAPY



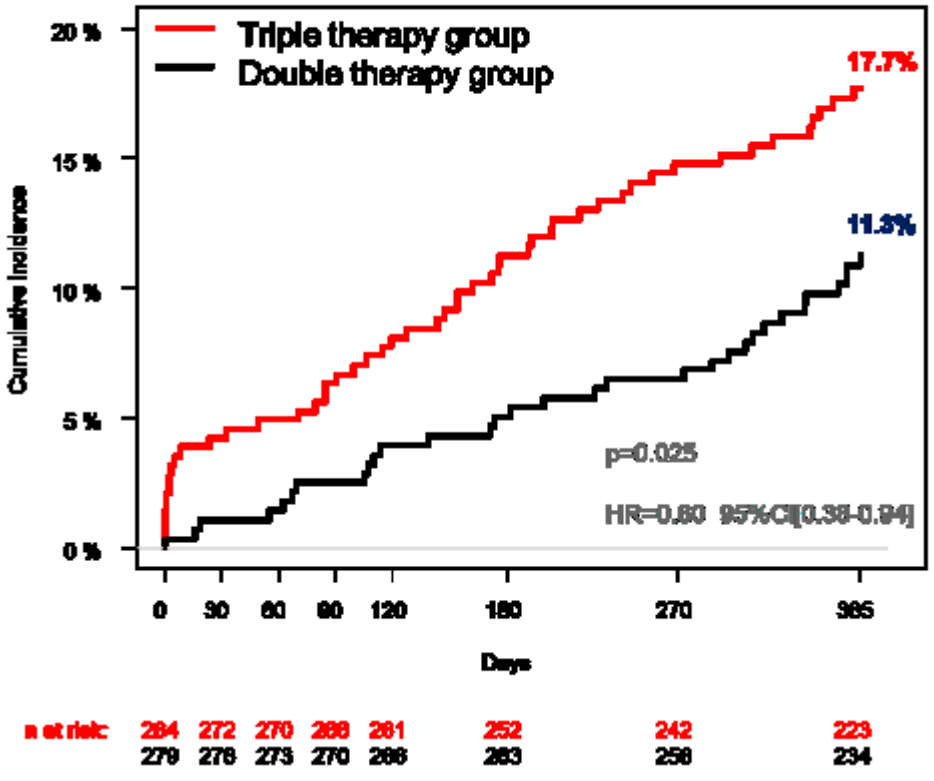
DOUBLE VS. TRIPLE THERAPY

WOEST trial

Primary Endpoint: Total number of TIMI bleeding events



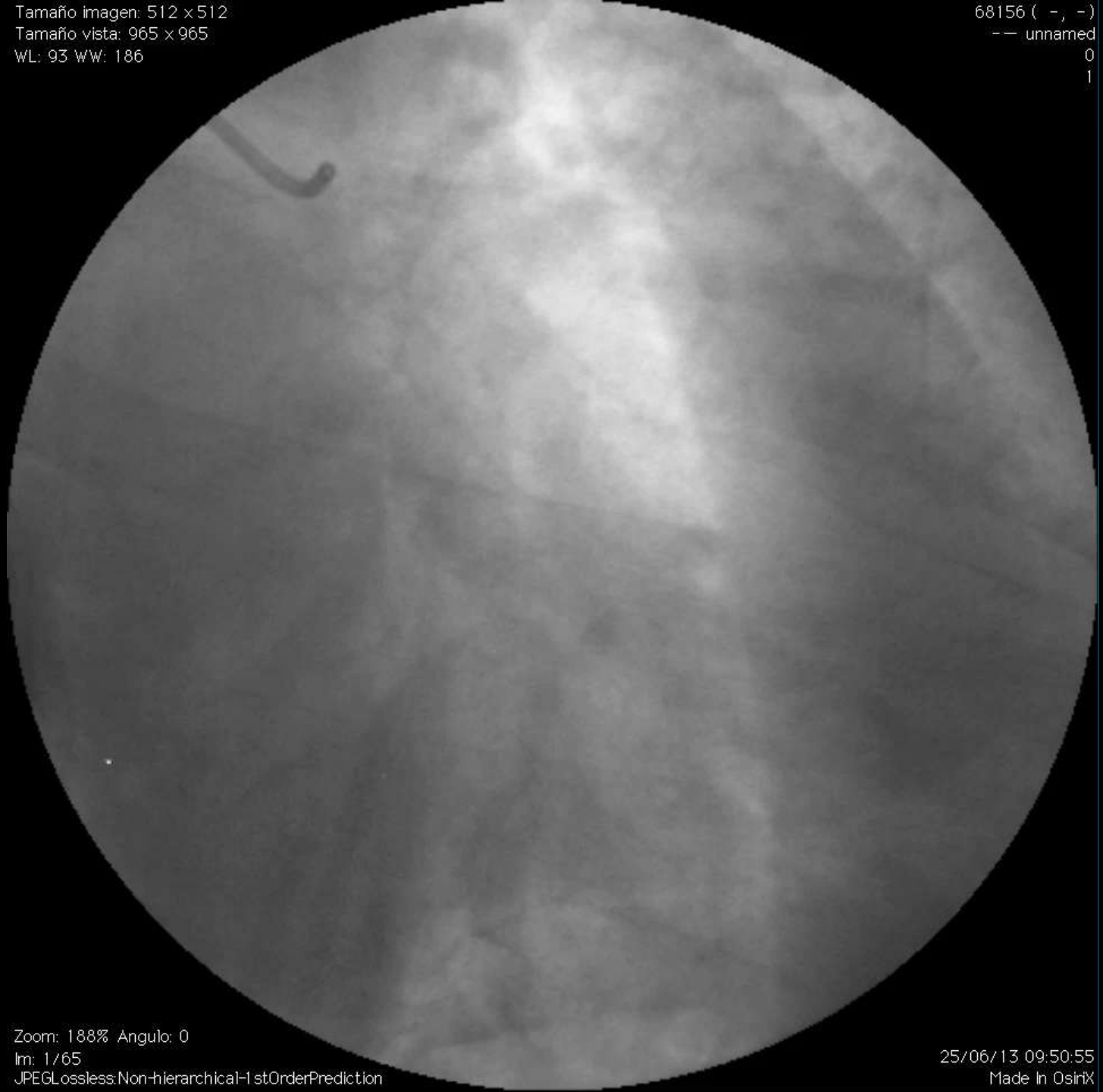
Secondary Endpoint (Death, MI,TVR, Stroke, ST)



Dewilde WJ et al. Lancet 2013;381:1107-15

CASO CLINICO 3

- Mujer de 70 años.
- FRCV: HTA, fumadora.
- Antecedentes personales: SCASEST lateral, stent (3 años antes).
- Acude a urgencias por dolor torácico.
- Diagnóstico: **SCASEST lateral**, de alto riesgo.
- Tratamiento en urgencias: Aspirina, clopidogrel y enoxaparina.
- Se programa para cateterismo en 24 horas.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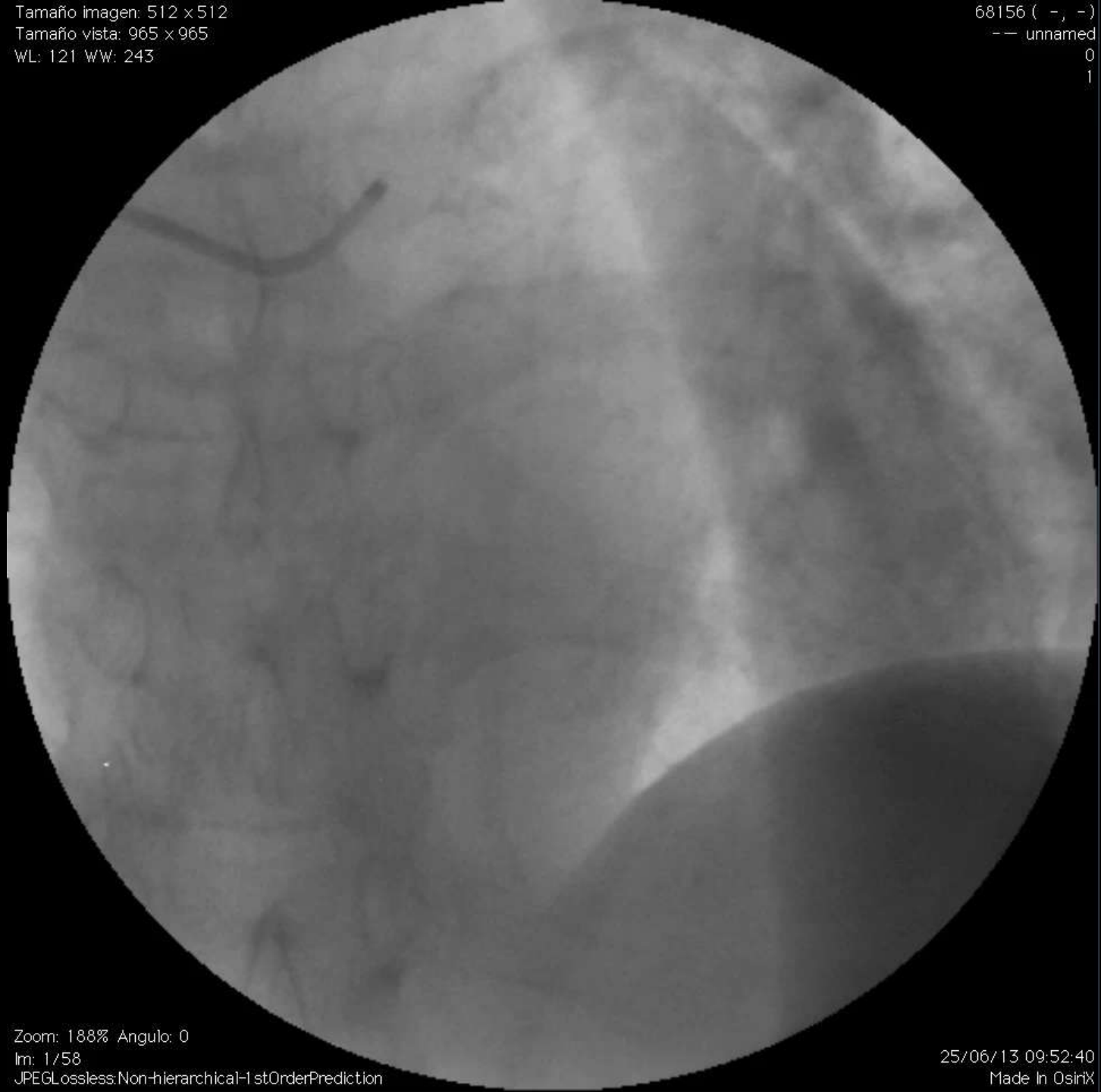
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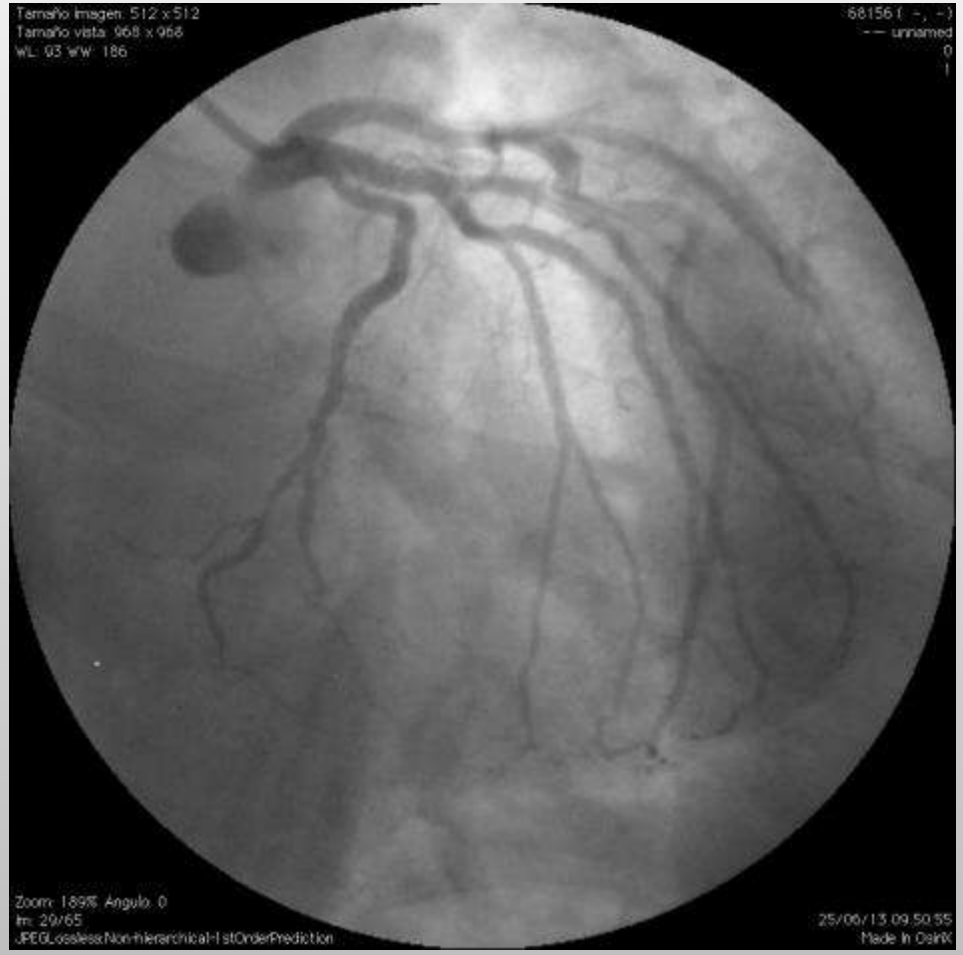
Se decide tratamiento médico, mal lecho distal



Si en su hospital tiene disponibles todos los antiagregantes

¿Qué tratamiento antiagregante administraría?

1. Solo aspirina.
2. Aspirina y clopidogrel, 75 mg diarios.
3. Aspirina y prasugrel.
4. Aspirina y ticagrelor.
5. Se podría utilizar cualquiera de las anteriores pautas.

Si en su hospital tiene disponibles todos los antiagregantes

¿Qué tratamiento antiagregante administraría?

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3. Aspirina y prasugrel.
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5. Se podría utilizar cualquiera de las anteriores pautas.

ANTIAGREGACIÓN EN EL SCASEST

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prasugrel versus Clopidogrel for Acute Coronary Syndromes without Revascularization

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ANTIAGREGACIÓN EN EL SCASEST

ABSTRACT

BACKGROUND

The effect of intensified platelet inhibition for patients with unstable angina or myocardial infarction without ST-segment elevation who do not undergo revascularization has not been delineated.

METHODS

In this double-blind, randomized trial, in a primary analysis involving 7243 patients under the age of 75 years receiving aspirin, we evaluated up to 30 months of treatment with prasugrel (10 mg daily) versus clopidogrel (75 mg daily). In a secondary analysis involving 2083 patients 75 years of age or older, we evaluated 5 mg of prasugrel versus 75 mg of clopidogrel.

RESULTS

At a median follow-up of 17 months, the primary end point of death from cardiovascular causes, myocardial infarction, or stroke among patients under the age of 75 years occurred in 13.9% of the prasugrel group and 16.0% of the clopidogrel group (hazard ratio in the prasugrel group, 0.91; 95% confidence interval [CI], 0.79 to 1.05; P=0.21). Similar results were observed in the overall population. The prespecified analysis of multiple recurrent ischemic events (all components of the primary end point) suggested a lower risk for prasugrel among patients under the age of 75 years (hazard ratio, 0.85; 95% CI, 0.72 to 1.00; P=0.04). Rates of severe and intracranial bleeding were similar in the two groups in all age groups. There was no significant between-group difference in the frequency of nonhemorrhagic serious adverse events, except for a higher frequency of heart failure in the clopidogrel group.

CONCLUSIONS

Among patients with unstable angina or myocardial infarction without ST-segment elevation, prasugrel did not significantly reduce the frequency of the primary end point, as compared with clopidogrel, and similar risks of bleeding were observed. (Funded by Eli Lilly and Daiichi Sankyo; TRILOGY ACS ClinicalTrials.gov number, NCT00699998.)

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*The Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes (TRILOGY ACS) investigators are listed in the Supplementary Appendix, available at NEJM.org.

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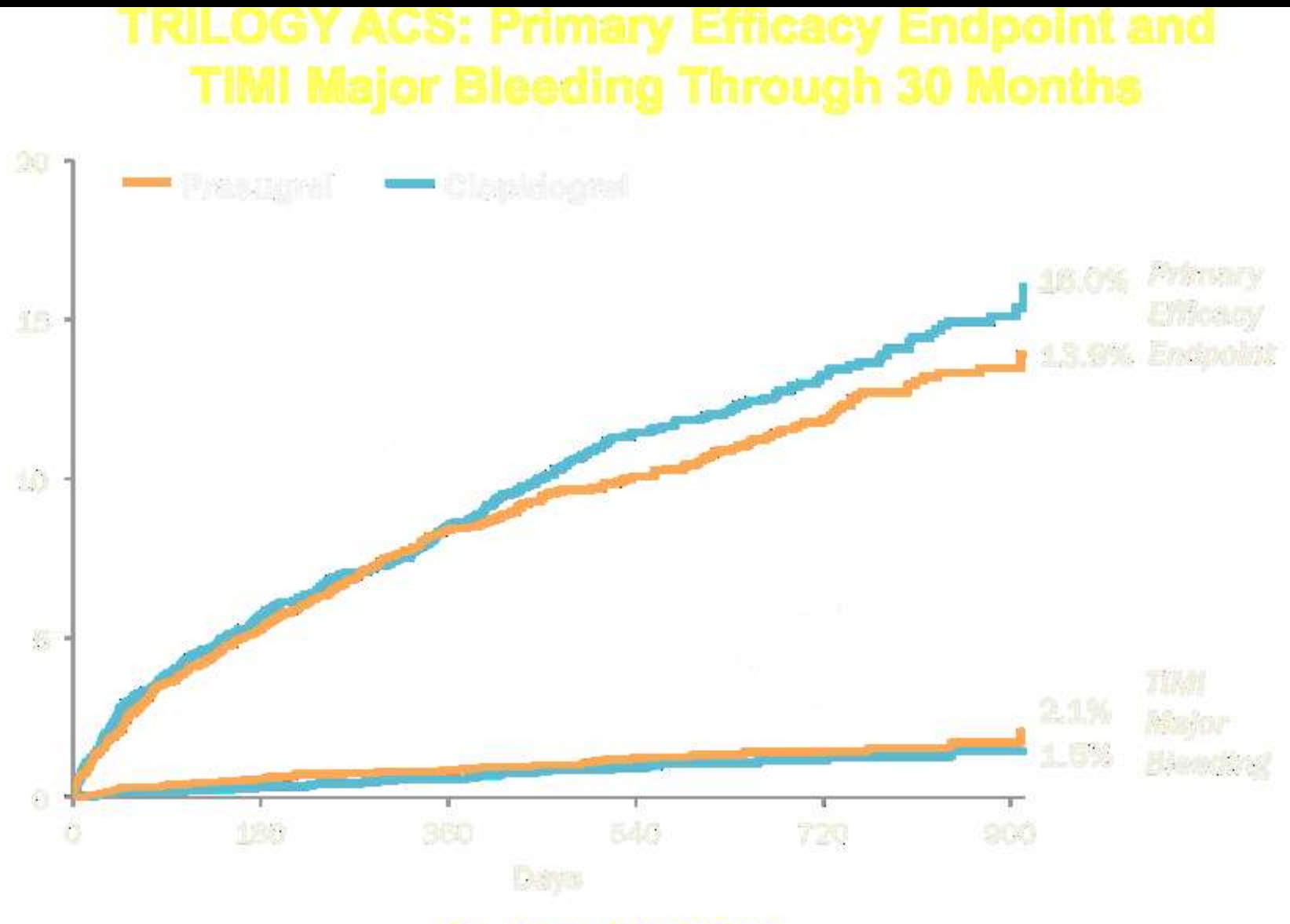
NON-INVASIVE STRATEGY: PRASUGREL



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RESEARCH

Ticagrelor versus clopidogrel in patients with acute coronary syndromes intended for non-invasive management: substudy from prospective randomised PLATelet inhibition and patient Outcomes (PLATO) trial

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ANTIAGREGACIÓN EN EL SCASEST

Abstract

Objective To evaluate efficacy and safety outcomes in patients in the PLATelet inhibition and patient Outcomes (PLATO) trial who at randomisation were planned for a non-invasive treatment strategy.

Design Pre-specified analysis of pre-randomisation defined subgroup of prospective randomised clinical trial.

Setting 862 centres in 43 countries.

Participants 5216 (28%) of 18 624 patients admitted to hospital for acute coronary syndrome who were specified as planned for non-invasive management.

Interventions Randomised treatment with ticagrelor (n=2601) versus clopidogrel (2615).

Main outcome measurements Primary composite end point of cardiovascular death, myocardial infarction, and stroke; their individual components; and PLATO defined major bleeding during one year.

Results 2183 (41.9%) patients had coronary angiography during their initial hospital admission, 1065 (20.4%) had percutaneous coronary intervention, and 208 (4.0%) had coronary artery bypass surgery. Cumulatively, 3143 (60.3%) patients had been managed non-invasively by the end of follow-up. The incidence of the primary end point was lower with ticagrelor than with clopidogrel (12.0% (n=295) *v* 14.3% (346); hazard ratio 0.85, 95% confidence interval 0.73 to 1.00; P=0.04). Overall mortality was also lower (6.1% (147) *v* 8.2% (195); 0.75, 0.61 to 0.93; P=0.01). The incidence of total major bleeding (11.9% (272) *v* 10.3% (238); 1.17, 0.98 to 1.39; P=0.08) and non-coronary artery bypass grafting related major bleeding (4.0% (90) *v* 3.1% (71); 1.30, 0.95 to 1.77; P=0.10) was numerically higher with ticagrelor than with clopidogrel.

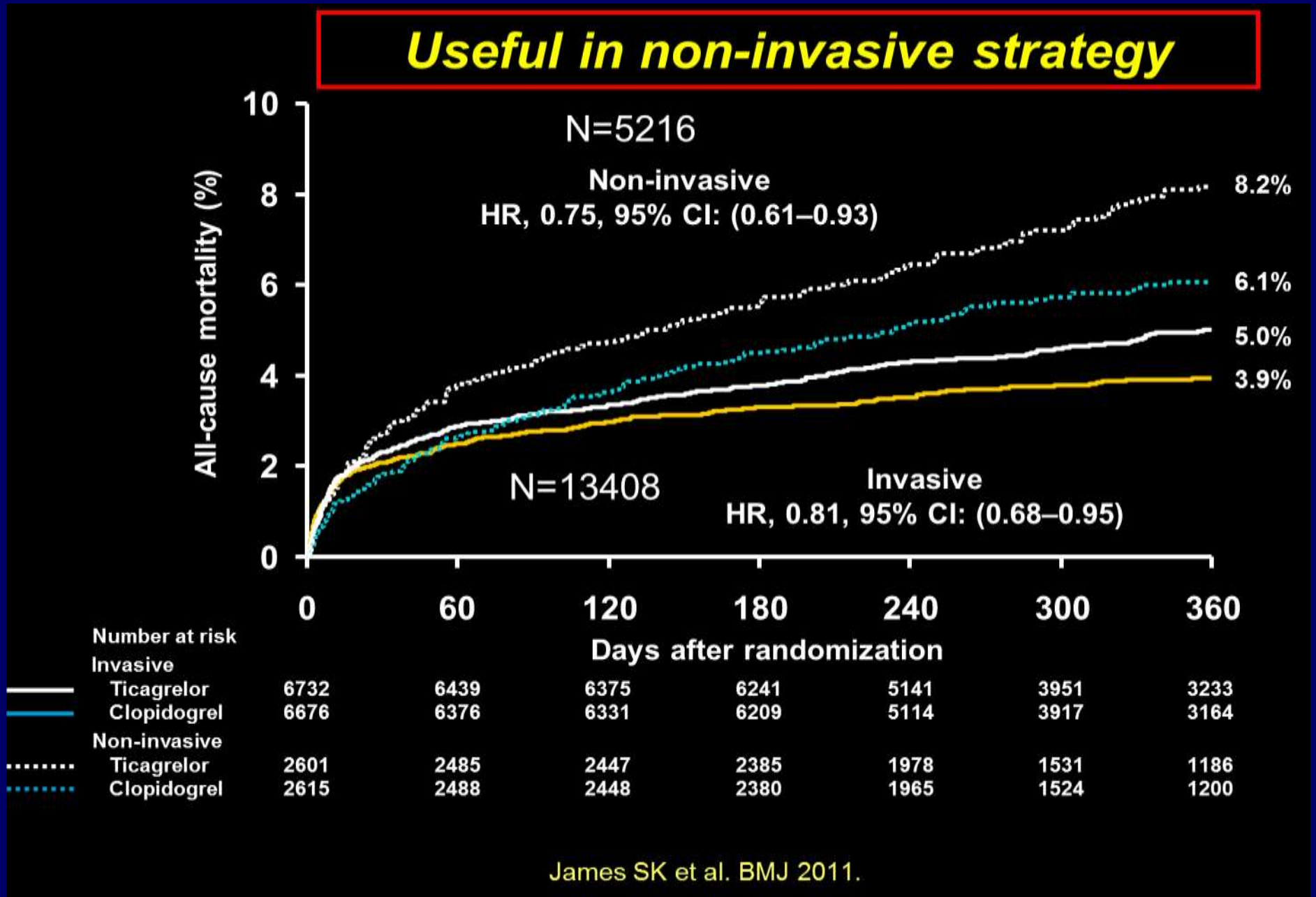
Conclusions In patients with acute coronary syndrome initially intended for non-invasive management, the benefits of ticagrelor over clopidogrel were consistent with those from the overall PLATO results, indicating the broad benefits of P2Y12 inhibition with ticagrelor regardless of intended management strategy.

Trial registration Clinical trials NCT00391872.

Introduction

In patients with non-ST elevation acute coronary syndrome with moderate to high risk characteristics, current guidelines recommend an invasive strategy with angiography followed by percutaneous coronary intervention or coronary artery bypass grafting if appropriate.[1 2] However, the Invasive versus Conservative Treatment in Unstable Coronary Syndromes (ICTUS) trial supports a conservative, non-invasive strategy with intensive medical treatment and invasive procedures only in case of signs or symptoms of ischaemia,[3] and this is

NON-INVASIVE STRATEGY: TICAGRELOR



James SK et al. BMJ 2011.

GRACIAS POR SU ATENCIÓN

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