SINDROME CORONARIO AGUDO

Dr. Jose Antonio Diarte De Miguel
Hospital Universitario Miguel Servet.
Zaragoza

Epidemiologia SCA

MORTALIDAD POR ENFERMEDAD CORONARIA EN ESPAÑA

- En España, las tasas de mortalidad por EC han disminuido de manera continuada durante los últimos 40 años (fig. 1A).
- Sin embargo, el numero absoluto de muertes por EC aumentó de 1980 a 2000 y se ha reducido de manera constante desde entonces (fig. 1B).
- La EC sigue siendo la más frecuente causa individual de muerte para los varones y la segunda para las mujeres.

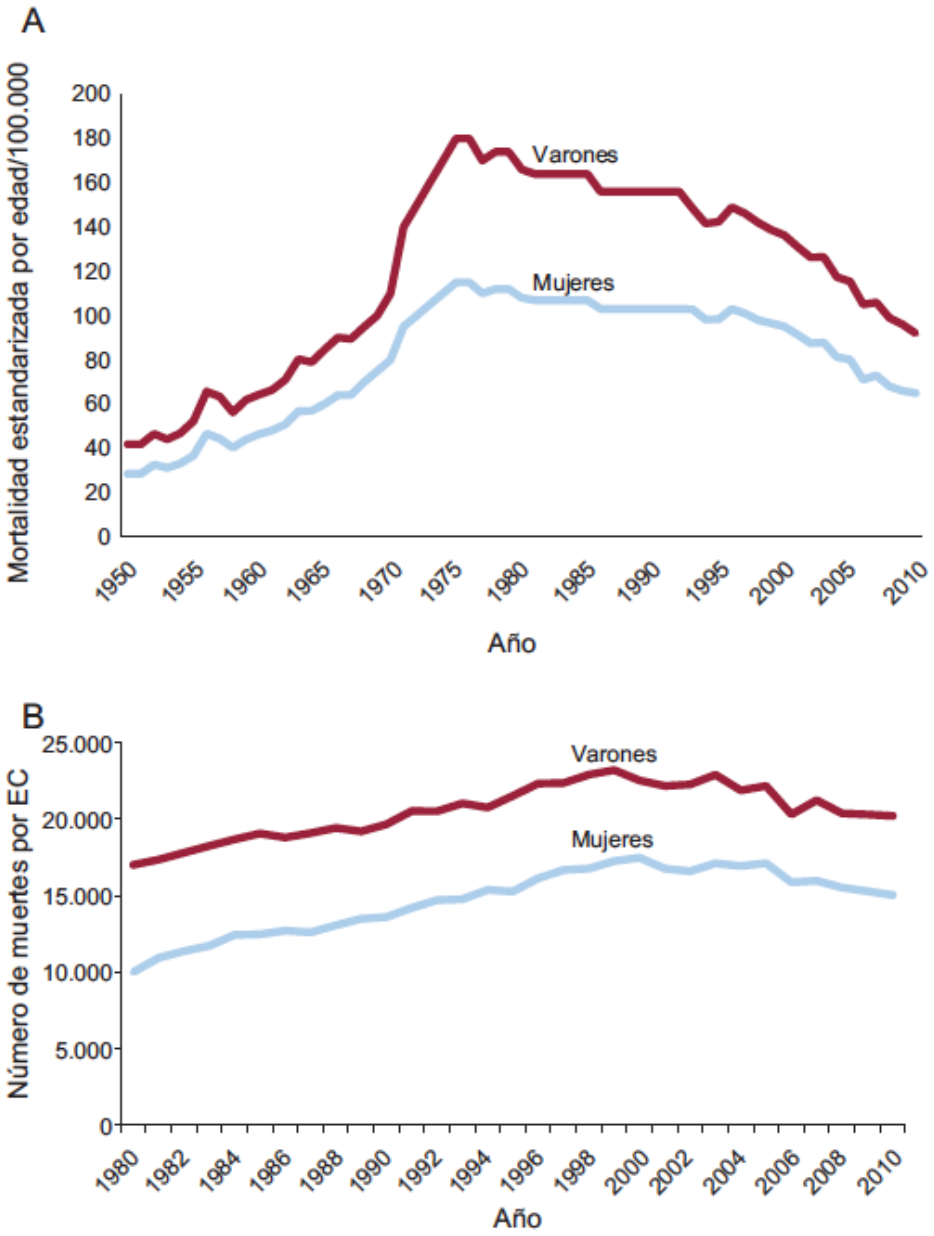
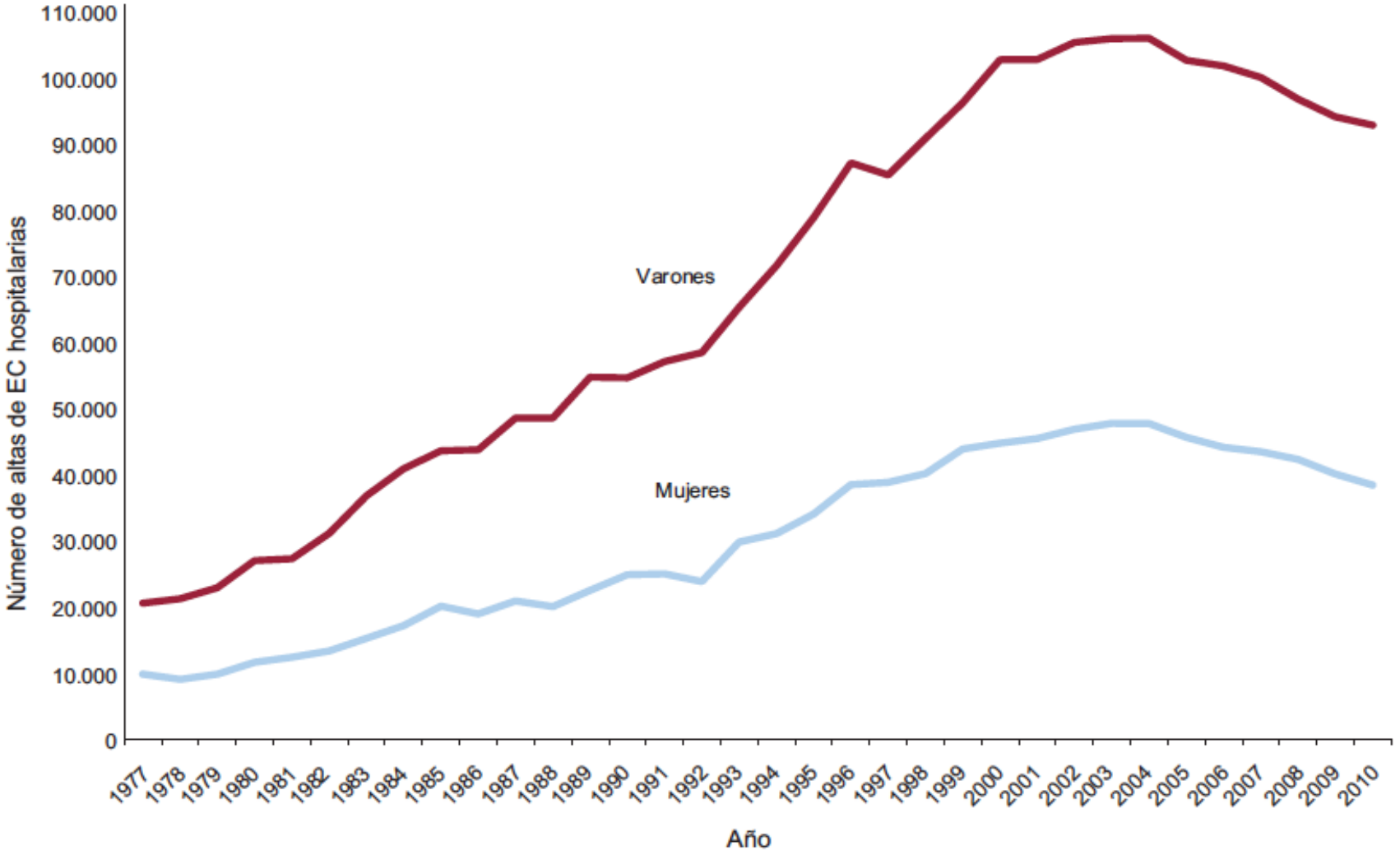


Figura 1. Tendencia de la mortalidad por enfermedad coronaria en España. A: tasas estandarizadas de mortalidad por enfermedad coronaria en 1950-2010 según el sexo. B: número de muertes anuales por enfermedad coronaria en 1980-2010 según el sexo. EC: enfermedad coronaria.

I.R. Degano et al / Rev Esp Cardiol. 2013;66(6):472–481

Morbilidad: Nº de casos de enfermedad coronaria hospitalizados en 1977-2010 por sexo, según el NE



I.R. Degano et al / Rev Esp Cardiol. 2013;66(6):472–481

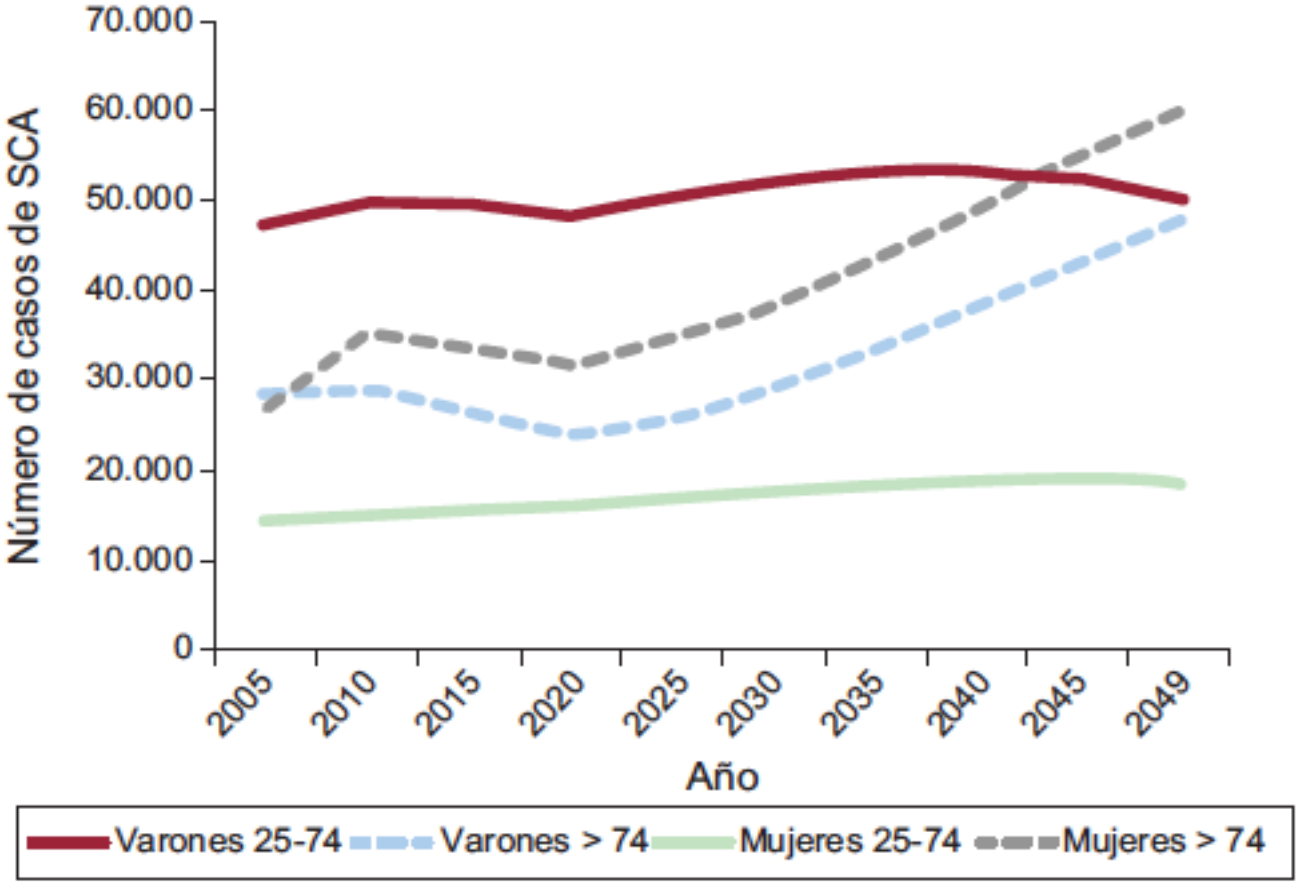
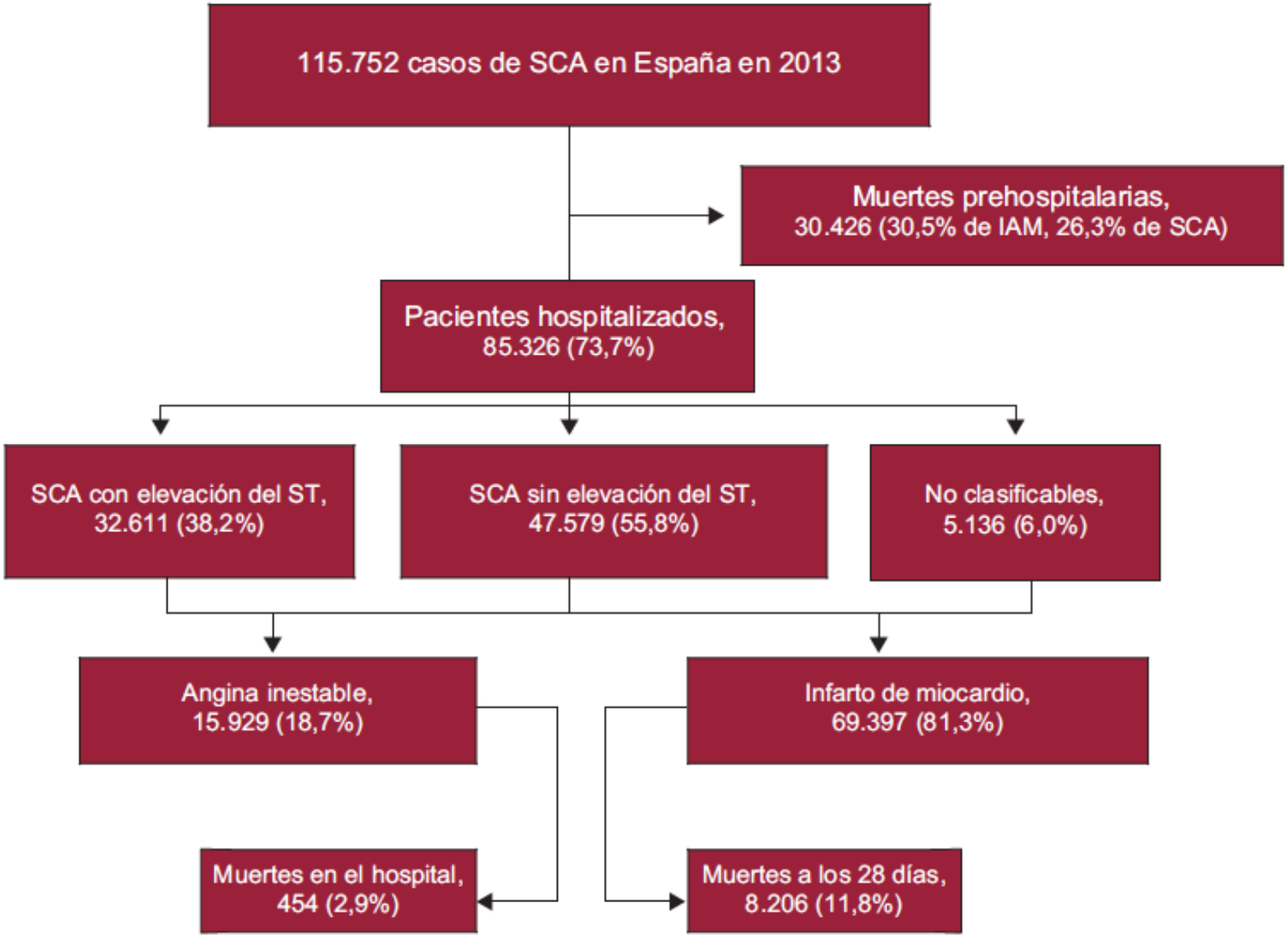


Figura 6. Estimación del número de síndromes coronarios agudos esperables desde 2005 a 2049 según sexo y grupo etario en la población española. Reproducido con permiso de Dégano et al[15]. SCA: síndrome coronario agudo.

I. Ferreira-Gonzalez / Rev Esp Cardiol. 2014;67(2):139–144 141

Número de casos de sindrome coronario agudo en España 2013



I.R. Degano et al / Rev Esp Cardiol. 2013;66(6):472–481

Letalidad 2013

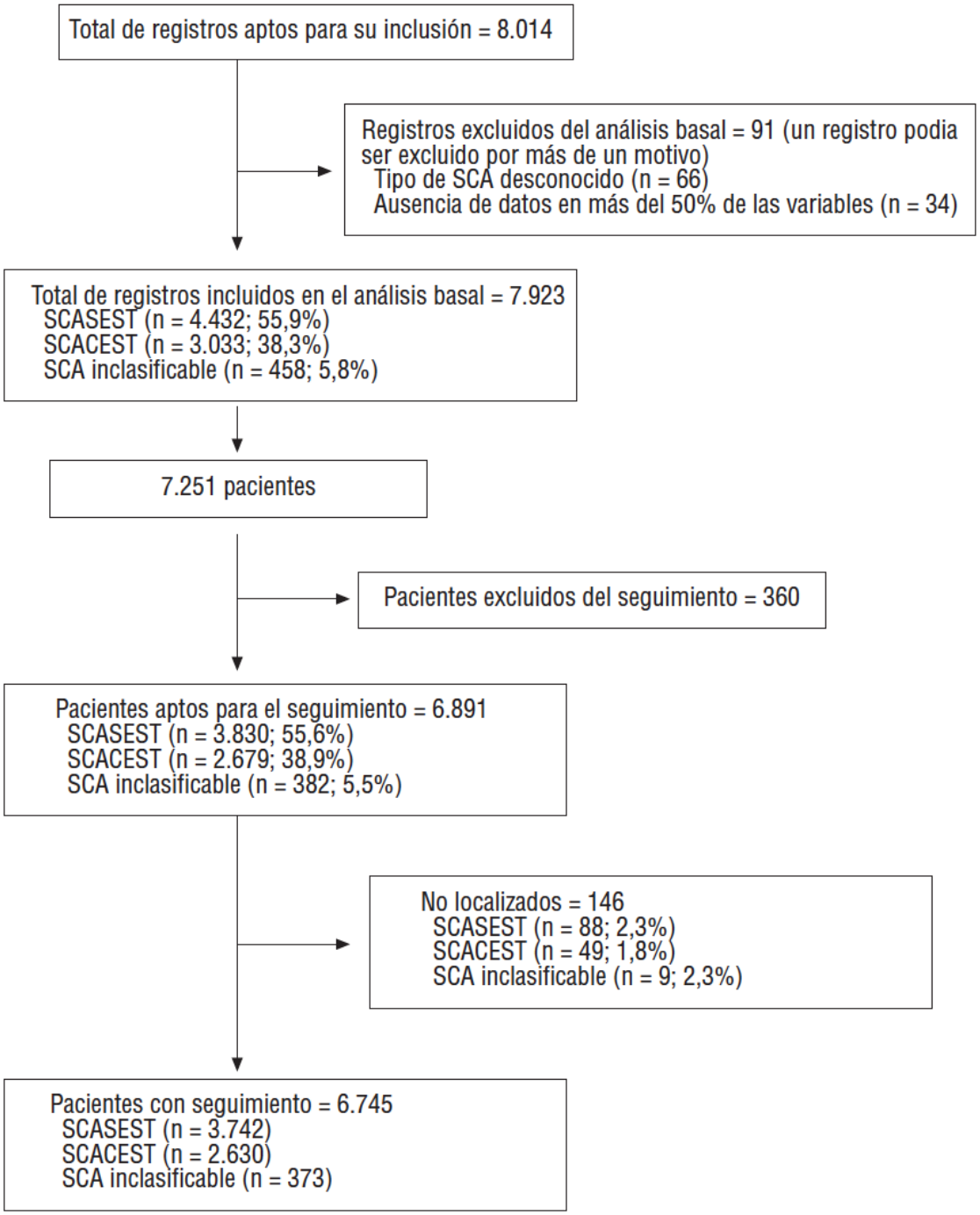
- En 2013, la letalidad del SCA a los 28 días será del 34% en total, de un 10% en los pacientes que lleguen con vida al hospital y de un 26% en las muertes fuera del hospital.
- Estas cifras representan una ligera mejora, en especial en cuanto a los pacientes hospitalizados, respecto a las estimaciones de 2002, que fueron del 38, el 15 y el 27% respectivamente.

SCACST vs SCASST

- En los últimos años, la proporción de pacientes con SCA con elevación del segmento ST (SCACEST) ha disminuido, mientras que la proporción de pacientes con SCASEST ha aumentado.
- Los pacientes con SCASEST tienden a ser de mayor edad y a tener una EC mas extensa. Así pues, teniendo en cuenta el envejecimiento esperado de la población, se prevé un aumento del porcentaje de pacientes con SCASEST en las próximas décadas.

Perfil del SCA en España

Estudio MASCARA (Manejo del Síndrome Coronario Agudo. Registro Actualizado). Resultados globales



Rev Esp Cardiol. 2008;61(8):803-16

Supervivencia a 6 meses.

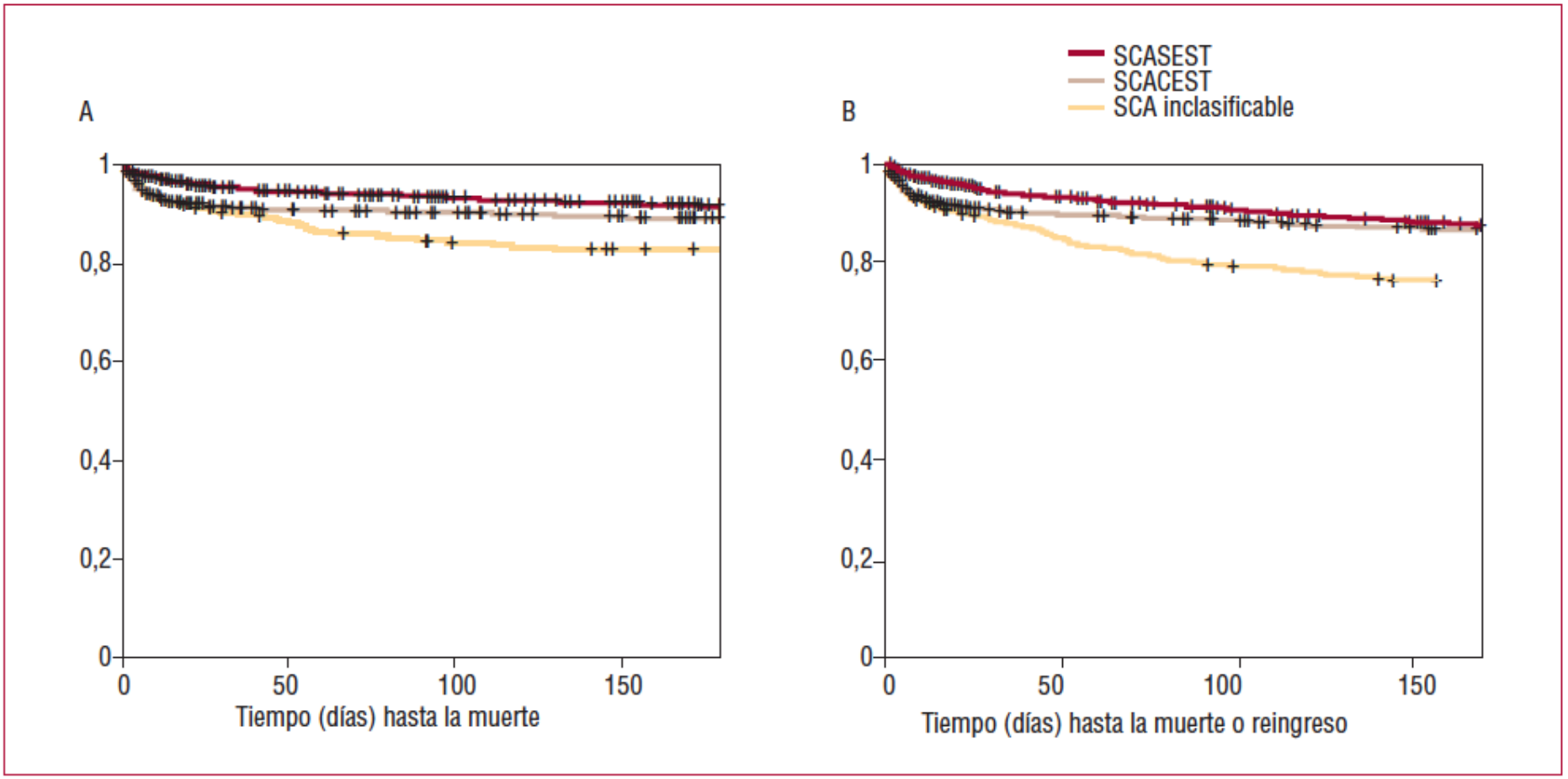


Fig. 3. Curvas de supervivencia a 6 meses del episodio índice según tipo de SCA. A: supervivencia total. B: supervivencia libre de ingreso.

The Second Euro Heart Survey on ACS-II.

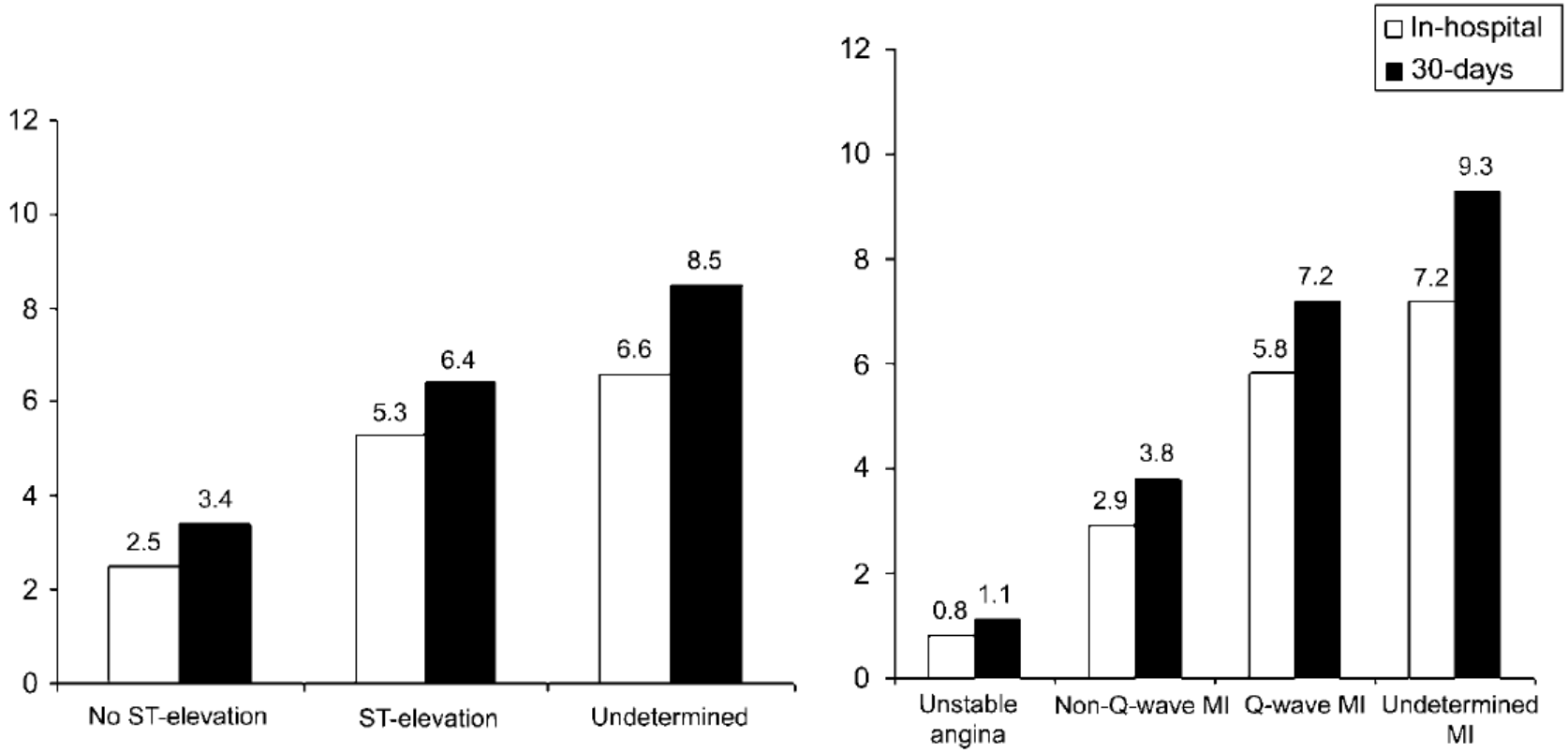
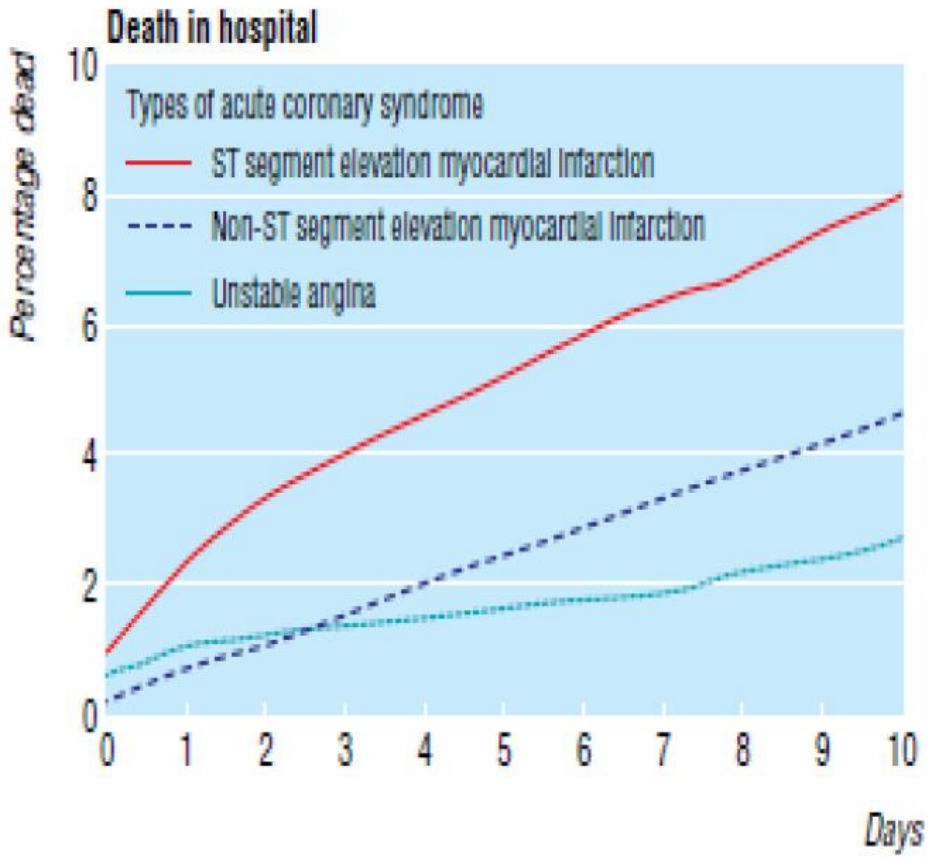
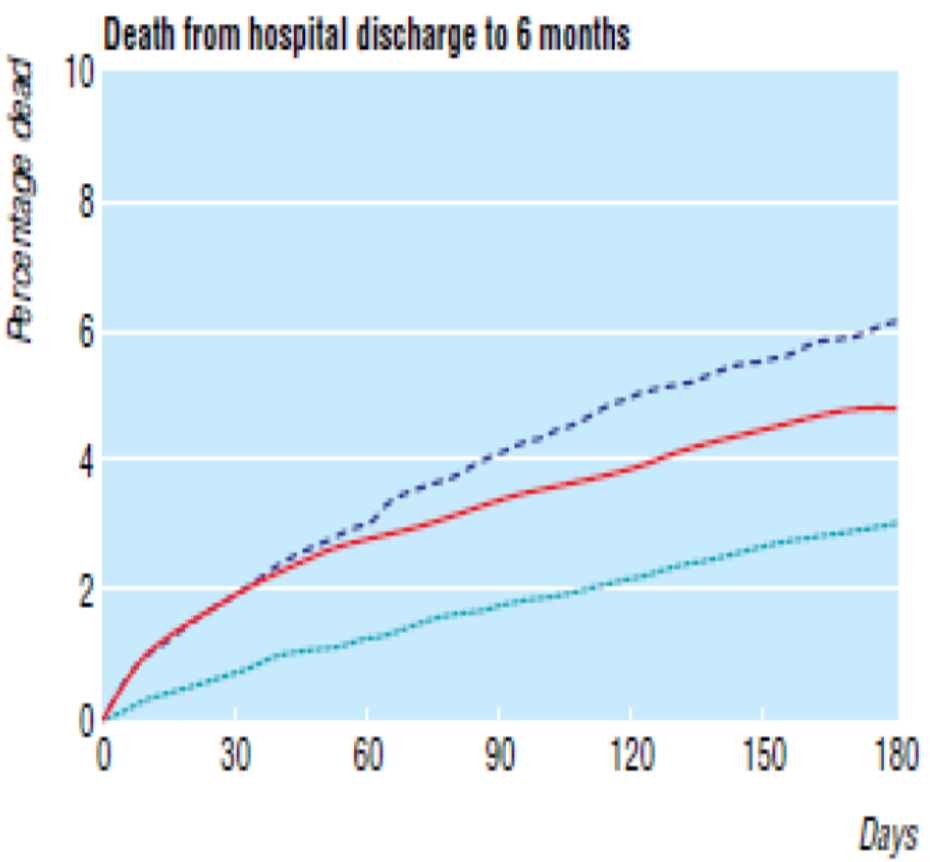


Figure 4 In-hospital and 30-day mortality by initial ECG presentation and final diagnosis (it should be noted that data on 30-day mortality were missing for 283 patients (4.4%).

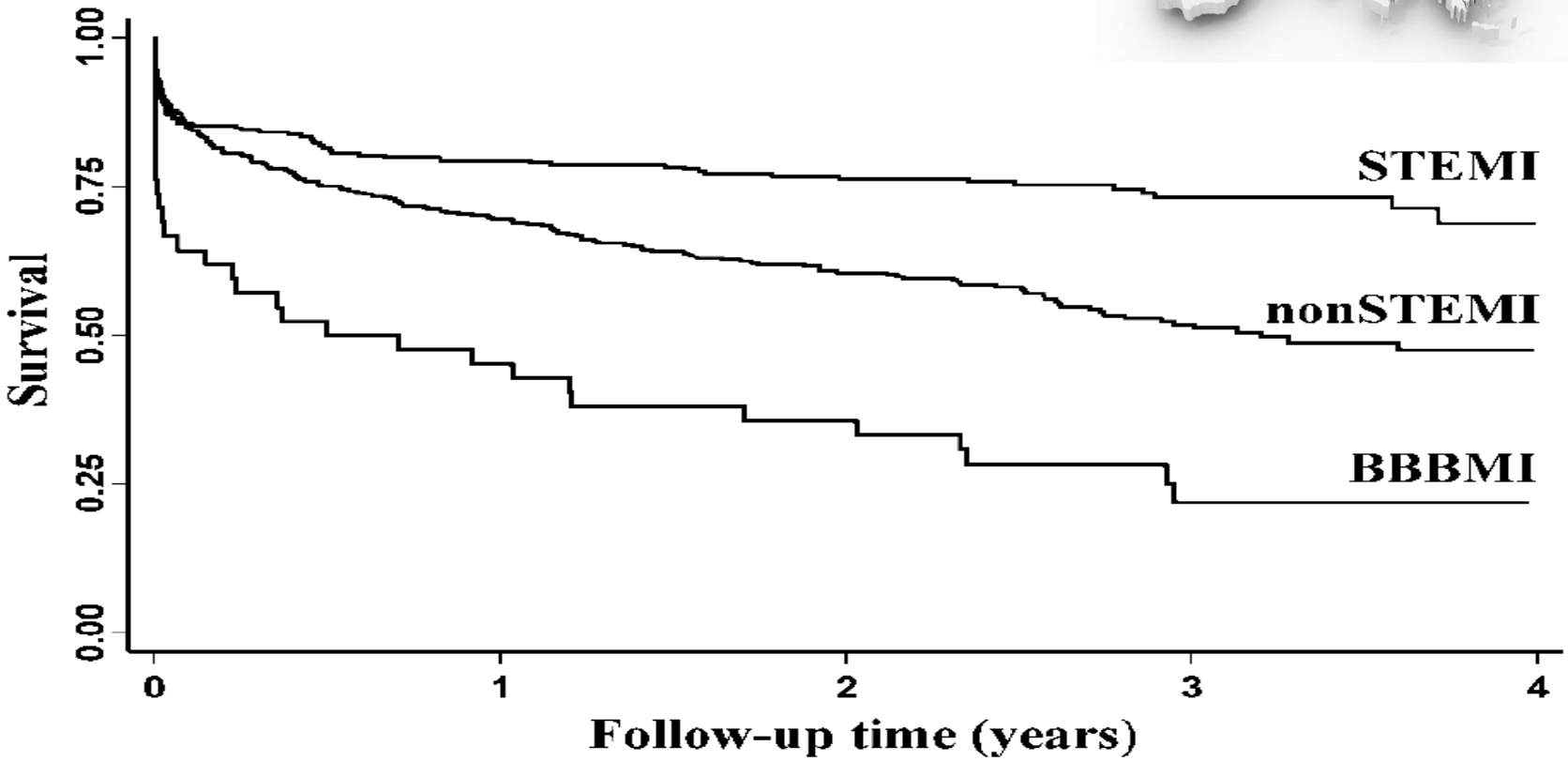
Supervivencia después de un SCA
n: 43810





GRACE, BMJ 2006

SCASEST en Europa

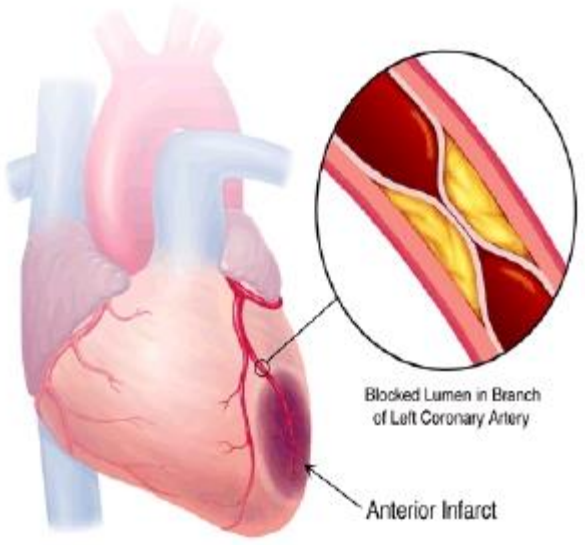


Bassand J-P, et al. Eur Heart J 2007;28:1598-60
Terkelsen, Eur Heart J 2005;26:18-26

CLASIFICACION SINDROME CORONARIO

Myocardial Infarction Type 1

Spontaneous myocardial infarction related to **atherosclerotic plaque** rupture, fissuring, or dissection with resulting intraluminal thrombus in one or more coronary arteries leading to decreased myocardial blood flow with ensuing myocyte necrosis

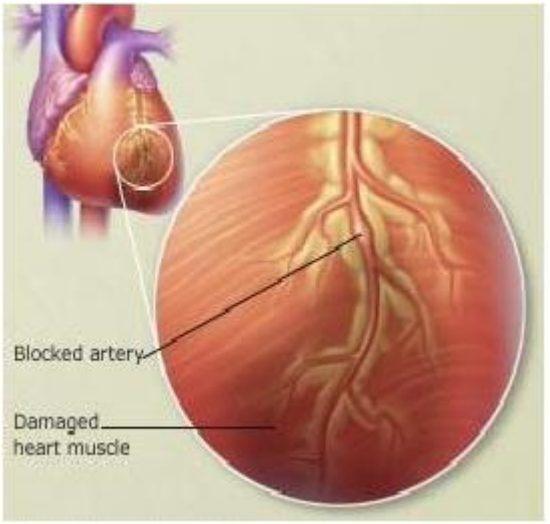


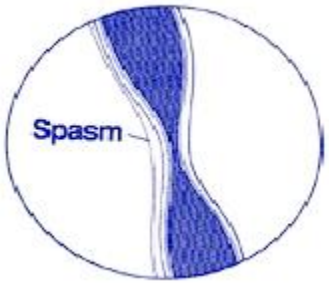
Update

Third Universal Definition of Myocardial Infarction

Myocardial Infarction Type 2

Myocardial infarction where a condition other than CAD contributes to an imbalance between myocardial oxygen supply and/or demand, e.g. coronary artery spasm, tachy-/brady-arrhythmia, anaemia, respiratory failure, hypotension or hypertension





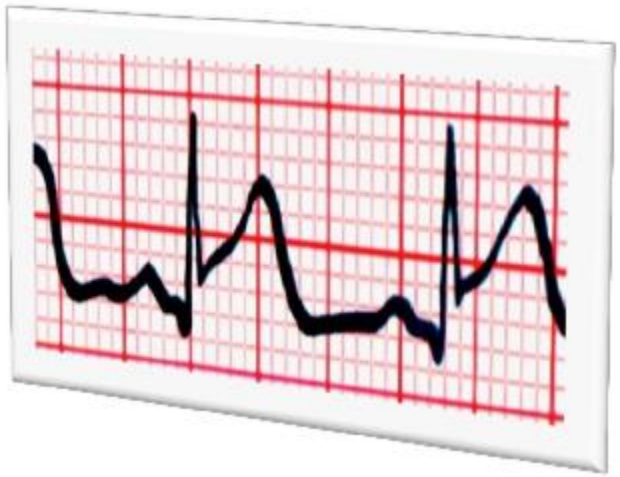
Update

Third Universal Definition of Myocardial Infarction

ST Segment Elevation Criteria

New ST elevation at the J point in 2 contiguous leads with the following cut-points:

- **≥0.1 mV in all leads except leads V_2–V_3 in men and women**
- **In leads V_2-V_3, ≥0.2 mV in men ≥40 years and ≥0.25 mV in men <40 years**
- **In leads V_2-V_3, ≥0.15 mV in women**



Age and gender specific

Update

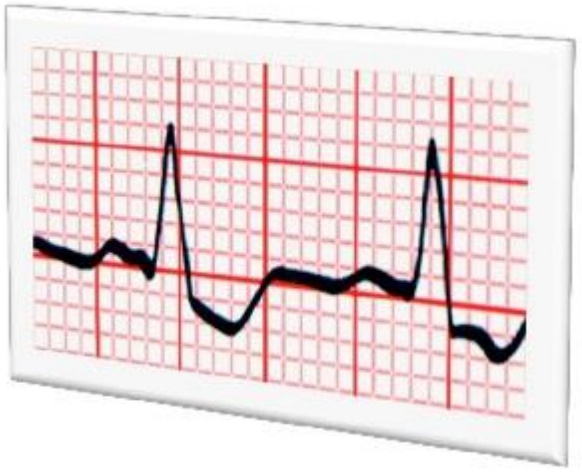
Third Universal Definition of Myocardial Infarction

Non-ST Segment Elevation Criteria

- New horizontal or down-sloping ST segment depression ≥0.05 mV in 2 contiguous leads

OR

- T inversion ≥0.1 mV in 2 contiguous leads with prominent R wave or R/S ratio >1



Unchanged

Third Universal Definition of Myocardial Infarction

ESC SCASEST 2011: Estratificación del riesgo

Recomendaciones para el diagnóstico y la estratificación del riesgo

Recomendaciones	Clase[a]	Nivel[b]	Ref[c]
En pacientes con sospecha de SCASEST, el diagnóstico y la estratificación del riesgo isquémico/hemorrágico a corto plazo se debe basar en la combinación de la historia clínica, síntomas, hallazgos físicos, ECG (monitorización del segmento ST continua o repetida) y biomarcadores	I	A	16, 18, 27, 30, 56-58
Se recomienda el uso de clasificaciones de riesgo establecidas para el pronóstico y el sangrado (p. ej., GRACE, CRUSADE)	I	B	50, 83
y antes del alta hospitalaria			
Se recomiendan otras derivaciones para el ECG (V_{3R}, V_{4R}, V_7-V_9) cuando las derivaciones habituales no son concluyentes	I	C	18
Se debe tomar una muestra de sangre rápidamente para la determinación de troponinas (troponina cardiaca T o I). Los resultados deben estar disponibles en un plazo de 60 min. La prueba debe repetirse a las 6-9 h de la evaluación inicial si la primera determinación no es concluyente. Es aconsejable repetir la determinación después de 12-24 h si el estado clínico sigue indicando SCA	I	A	27, 30
Se recomienda un protocolo rápido de exclusión (0 y 3 h) cuando se disponga de pruebas de alta sensibilidad para determinación de troponinas	I	B	20, 21, 23
Se recomienda un ecocardiograma a todos los pacientes para evaluar la función ventricular izquierda general y regional y para descartar o confirmar un diagnóstico diferencial	I	C	–
La angiografía coronaria está indicada en pacientes en los que se tenga que determinar la extensión de la enfermedad coronaria o de la lesión causal (véase la sección 5.4)	I	C	–
La angiografía coronaria por TC se debe considerar como una alternativa a la angiografía invasiva para excluir un SCA cuando hay una probabilidad baja a intermedia de enfermedad coronaria y cuando las troponinas y el ECG no sean concluyentes	IIa	B	37-41
En pacientes sin dolor recurrente, con ECG normal, troponinas negativas y clasificación de riesgo baja, se recomienda una prueba de estrés no invasiva para inducción de isquemia antes de decidir sobre la estrategia invasiva	I	A	35, 54, 55

CRUSADE: Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines; ECG: electrocardiograma; GRACE: Global Registry of Acute Coronary Events; SCA: síndrome coronario agudo; SCASEST: síndrome coronario agudo sin elevación del segmento ST; TC: tomografía computarizada.

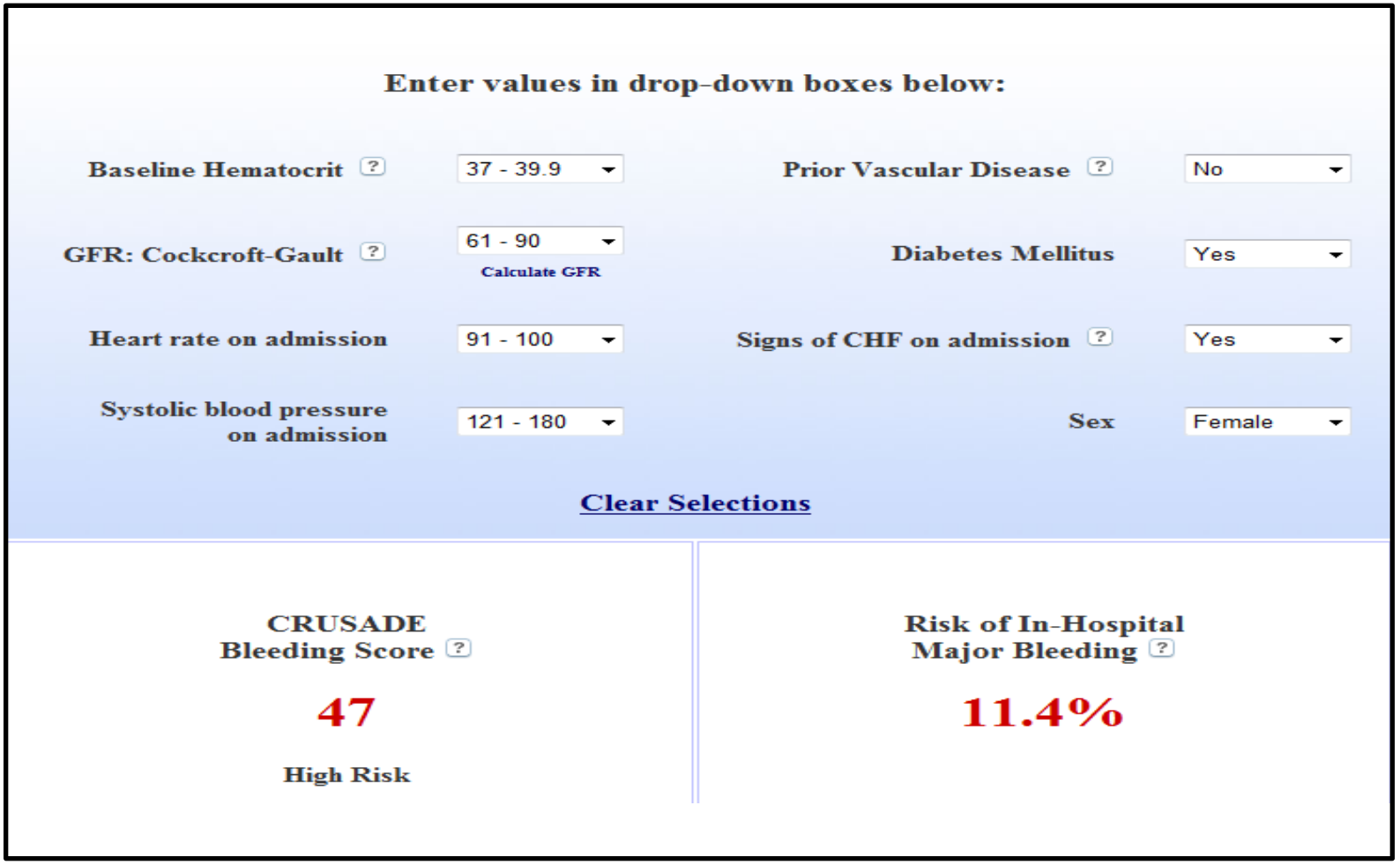
Hamm CW, et al. Rev Esp Cardiol 2012;65(2):173.e1-e55

Escalas de Riesgo

- Riesgo Sangrado: CRUSADE

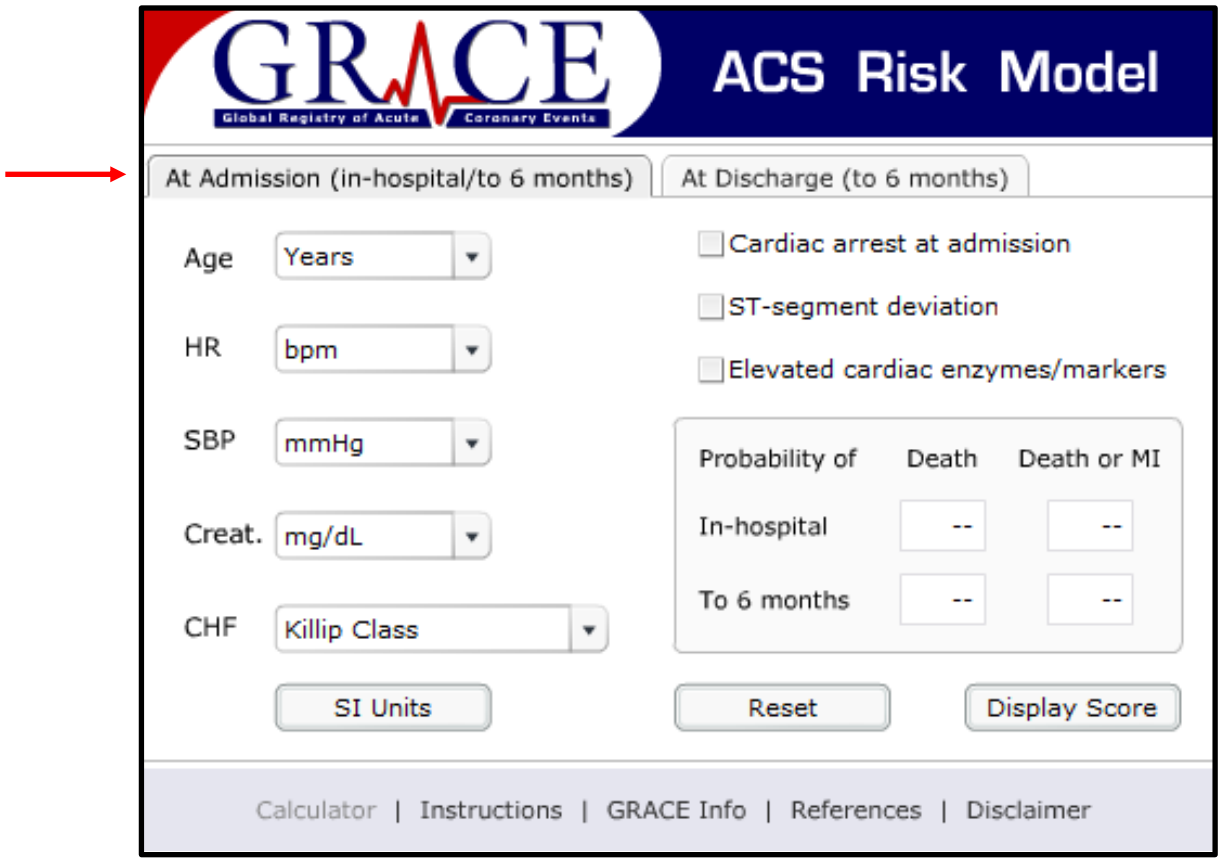
- Riesgo isquémico: GRACE y TIMI

CRUSADE BLEEDING SCORE



www.crusadebleedingscore.org

GRACE RISK SCORE



www.outcomes.org/grace

Fox KA et al. BMJ. 2006;333:1091; Pieper KS et al Am Heart J. 2009. 157:1097-105

GRACE 2.0 Risk Calculator

The GRACE 2.0 ACS Risk Calculator implements the revised GRACE algorithms for predicting death or death/myocardial infarction following an initial acute coronary syndrome (ACS).

WHAT'S NEW IN 2.0?

- "Mini-GRACE" algorithm (for use when serum creatinine and Killip class may not be available)
- New 1- and 3-year calculations
- New calculations provide probabilities directly, bypassing scores
- Population histograms with high-, medium- and low-risk markers

DOWNLOAD THE MOBILE APP

Available on the App Store

USE THE CALCULATOR ONLINE

WEB VERSION

Disclaimer

This risk scoring tool is intended for use by clinicians, in conjunction with individual patient assessment. We assume no responsibility for how you use or interpret the GRACE 2.0 ACS Risk Calculator app or any other information provided on this website. Read more.

TIMI STUDY GROUP
An Academic Research Organization of
Brigham and Women's Hospital and Harvard Medical School

TIMI RISK SCORE

TIMI Risk Score for UA/NSTEMI

Estimates mortality for patients with unstable angina and non-ST elevation MI.

Age ≥ 65 years?	☐ Yes +1
≥ 3 Risk Factors for CAD?	☐ Yes +1
Known CAD (stenosis ≥ 50%)?	☐ Yes +1
ASA Use in Past 7d?	☐ Yes +1
Severe angina (≥ 2 episodes w/in 24 hrs)?	☐ Yes +1
ST changes ≥ 0.5mm?	☐ Yes +1
+ Cardiac Marker?	☐ Yes +1
Patient has none of these	None Present
Score	Click! points

TIMI STUDY GROUP
An Academic Research Organization of
Brigham and Women's Hospital and Harvard Medical School

TIMI RISK SCORE

TIMI RISK SCORE for UA/NSTEMI

HISTORICAL	POINTS
Age ≥ 65	1
≥ 3 CAD risk factors (FHx, HTN, chol, DM, active smoker)	1
Known CAD (stenosis ≥ 50%)	1
ASA use in past 7 days	1
PRESENTATION	
Recent (≤24H) severe angina	1
cardiac markers	1
ST deviation ≥ 0.5 mm	1

RISK SCORE = Total Points (0 - 7)

RISK OF CARDIAC EVENTS (%) BY 14 DAYS IN TIMI 11B*

RISK SCORE	DEATH OR MI	DEATH, MI OR URGENT REVASC
0/1	3	5
2	3	8
3	5	13
4	7	20
5	12	26
6/7	19	41

*Entry criteria:UA or NSTEMII defined as ischemic pain at rest within past 24H, with evidence of CAD (ST segment deviation or +marker)

ANTIAGREGACION

- La identificación del síndrome coronario agudo (SCA) como un proceso aterotrombótico ha dado un papel predominante a las plaquetas en la enfermedad cardiovascular.
- La eficacia de la antiagregación plaquetaria en la prevención y el tratamiento de las enfermedades cardiovasculares es un hecho establecido y comprobado en numerosos estudios

Tabla 1.
CLASIFICACIÓN DE LOS MEDICAMENTOS ANTIPLAQUETARIOS.

Sitio de acción	Fármaco	Ruta de administración
Inhibidor de la ciclo-oxigenasa 1 (COX-1)	Ácido acetil salicílico	Oral / IV / Rectal
Tienopiridinas	Ticlopidina	Oral
	Clopidogrel	Oral
	Prasugrel	Oral
Inhibidores del receptor $P2Y_{12}$ no tienopiridinas	Ticagrelor	Oral
	Cangrelor	IV
	Elinogrel	Oral / IV
Inhibidores Gp IIb/IIIa	Abciximab	IV
	Tirofibán	IV
	Eptifibatide	IV
Inhibidores de la fosfodiesterasa	Dipiridamol	Oral
	Cilostazol	Oral
Inhibidores PAR_1	Varopaxar	Oral
	Atopaxar	Oral

Gp: glicoproteína. IV: intravenoso.

¿Por que buscar nuevos antiagregantes?

- La eficacia del clopidogrel se ve limitada por la lenta y variable transformación del profármaco en metabolito activo
- Una modesta y variable inhibición plaquetaria,
- La irreversibilidad de acción
- El incremento del riesgo de sangrado y el mayor riesgo de trombosis del stent e infarto agudo de miocardio (IAM)
- Un riesgo trombótico residual en los pacientes con respuesta pobre.

TABLA 1. **Nuevas dianas terapéuticas plaquetarias y fármacos antiagregantes en distintas fases de desarrollo en SCA. Estudios en fase 3**

Receptor	Inhibidor	Estudios en fase 3
TXA/PG	Terutrobán (S18886)	Ningún estudio en marcha
PAR1	Vorapaxar (SCH 530348)	TRA-CER y TRA 2P-TIMI 50 en marcha
$P2Y_{12}$	Prasugrel	TRITON-TIMI 38 finalizado, TRILOGY en marcha
	Ticagrelor	PLATO, finalizado
	Cangrelor	CHAMPION PCI y PLATFORM, suspendidos; BRIDGE activo
	Elinogrel	Se va a iniciar estudio en fase 3 tras INNOVATE PCI

ADP: adenosindifosfato; $P2Y_{12}$: principal receptor de ADP en la plaqueta; PAR1: principal receptor plaquetario para la trombina en humanos; SCA: síndrome coronario agudo; TXA/PC: receptor de tromboxano/prostaciclina.

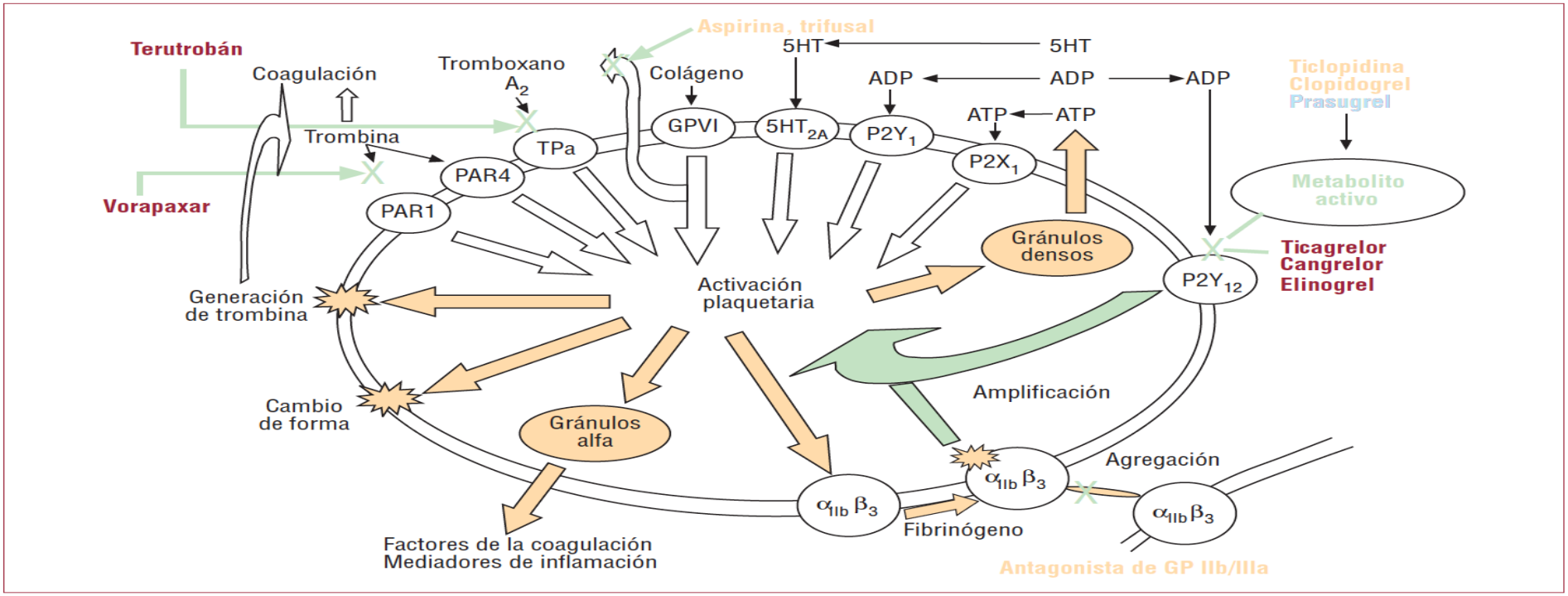


Fig. 1. Receptores plaquetarios y sus inhibidores. Nuevas dianas terapéuticas y fármacos antiplaquetarios. αIIb β3: glucoproteína (GB) IIb/IIIa; $5HT_{2A}$: receptor del 5HT (hidoxitriptófano); ADP: adenosindifosfato; ATP: adenosintrifosfato; GPVI: proteína GVI activada por colágeno; $P2X_1$: receptor de ATP; $P2Y_{12}$, $P2Y_1$: receptores de ADP; PAR1, PAR4: receptores de la trombina. Reproducida con permiso de Storey[4].

Rev Esp Cardiol Supl. 2010;10:12D-22D

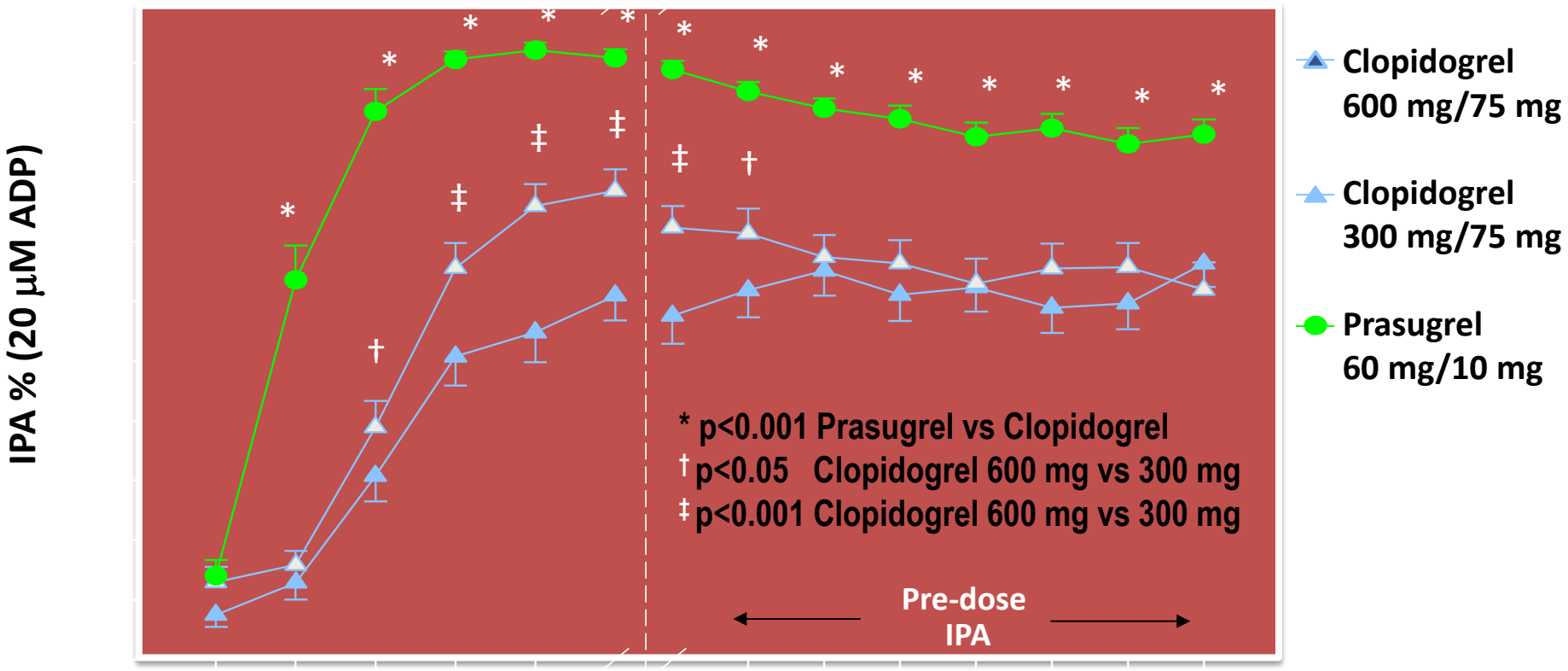
Tabla 2.
CARACTERÍSTICAS FARMACOLÓGICAS DE LOS NUEVOS ANTIAGREGANTES PLAQUETARIOS.

	Clopidogrel	Prasugrel	Ticagrelor	Cangrelor	Elinogrel
Unión al receptor	Irreversible	Irreversible	Reversible	Reversible	Reversible
Dosis					
Dosis de carga	300-600 mg	60 mg	180 mg	30 mg bolo IV	En estudio
Dosis de mantenimiento	75 mg QD	10 mg QD	90 mg BID	4 mcg/kg/min	En estudio
Vida media (h)	8	4	6-12	3-5min	12
Metabolismo	Esterasas plasmáticas/ Hepático	Hepático	Directo/Ninguno	Directo/Ninguno	Directo/Ninguno
Ruta de eliminación	Renal/biliar	Renal	Biliar	Plasmática	En estudio
Tiempo para inhibición máxima (min)	240	60	120	<5	15
Suspender antes de cirugía (d)	5	7	5	-	-
Reacciones adversas	Reacciones anafilactoides, dolor abdominal, agranulocitosis, sangrado, dispepsia, aumento enzimas hepáticas, rash, mialgias, síndrome Steven –Johnson, PTT	Reacciones anafilactoides, anemia, FA, sangrado, bradicardia, dolor torácico, tos, disnea, fatiga, sangrado, neutropenia, trombocitopenia, vómito	FA, bloqueo AV, bradicardia, dolor torácico, sangrado, tos, diarrea, fatiga, HTA, náuseas, sangrado intracraneal, síncope	Sangrado, aumento ALT	En estudio
Contraindicaciones y precauciones	Sangrado, sangrado GI, sangrado intracraneano, ACV, cirugía, descontinuación abrupta, lactancia, embarazo	Sangrado, sangrado GI, sangrado intracraneano, ACV, anticoagulación, cirugía revascularización coronaria, descontinuación abrupta, embarazo, lactancia, peso < 60kg, edad > 75 años	Sangrado, sangrado intracraneal, sangrado GI, cirugía revascularización coronaria, descontinuación abrupta, lactancia, embarazo	En estudio	En estudio

ALT: alanino aminotransferasa, AV: atrioventricular, BID: dos veces al día, FA: fibrilación auricular, GI: gastrointestinal, HTA: hipertensión arterial, IV: intravenoso, QD: una vez al día, PTT: púrpura trombocitopénica trombótica.

PRASUGREL

Inhibicion Agregacion Plaquetaria en voluntarios sanos



- **Data are expressed as mean ± SEM. Arrows (↓) indicate day of dose administration**

IPA=Inhibition of platelet aggregation; ADP=Adenosine diphosphate

Payne CD et al. *J Cardiovasc Pharmacol* 2007;50(5):555-562

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 15, 2007 VOL. 357 NO. 20

Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes

TRITON–TIMI 38

UA/NSTEMI (TIMI Risk Score ≥ 3)* or STEMI (Primary PCI or Post-STEMI)
&
Planned PCI

ASA ⇩ N = 13,000

Double-blind (Stratified)

Prasugrel	Clopidogrel
60 mg LD/ 10 mg MD	300 mg LD/ 75 mg MD

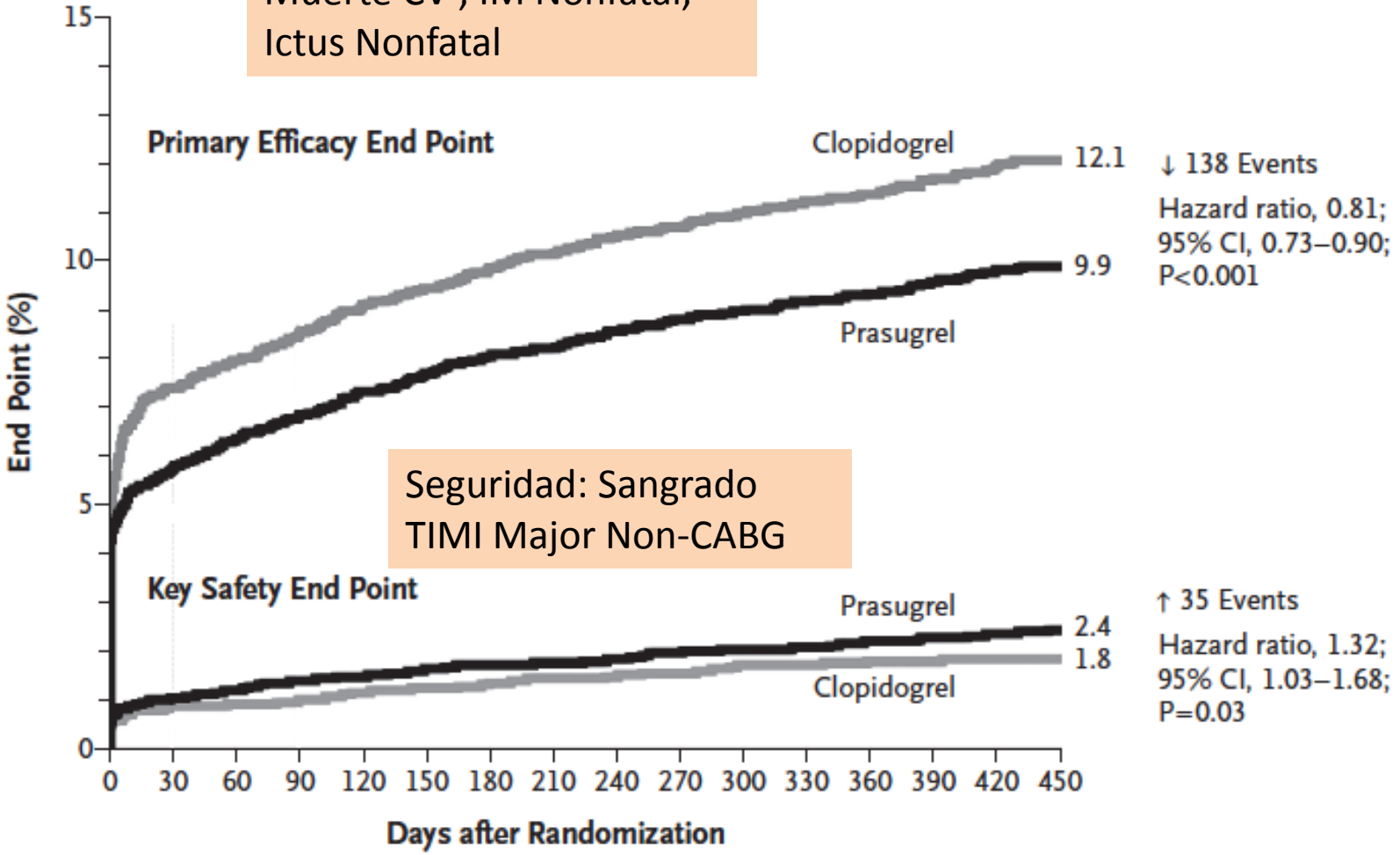
Median duration of therapy – 12 months
Maximum duration of therapy – 15 months

UA = unstable angina
NSTEMI = non-ST-segment elevation MI
STEMI = ST-segment elevation MI

Incidencia acumulada de todas las cohortes de SCA para el endpoint primario y el sangrado mayor TIMI

A

Eficacia Primaria:
Muerte CV , IM Nonfatal,
Ictus Nonfatal



No. at Risk

Clopidogrel	6795 6169	6036	5835	5043	4369	3017
Prasugrel	6813 6305	6177	5951	5119	4445	3085

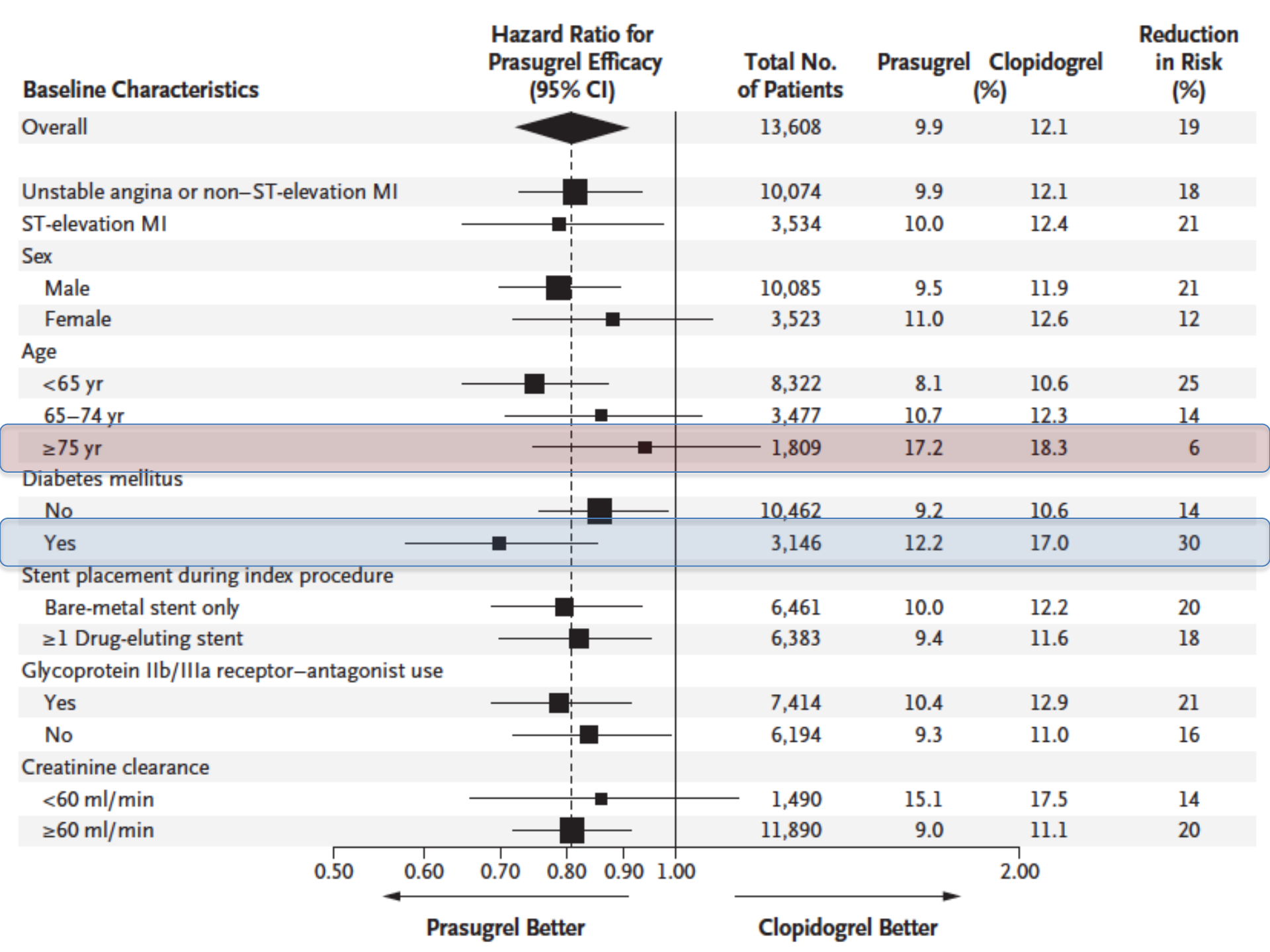
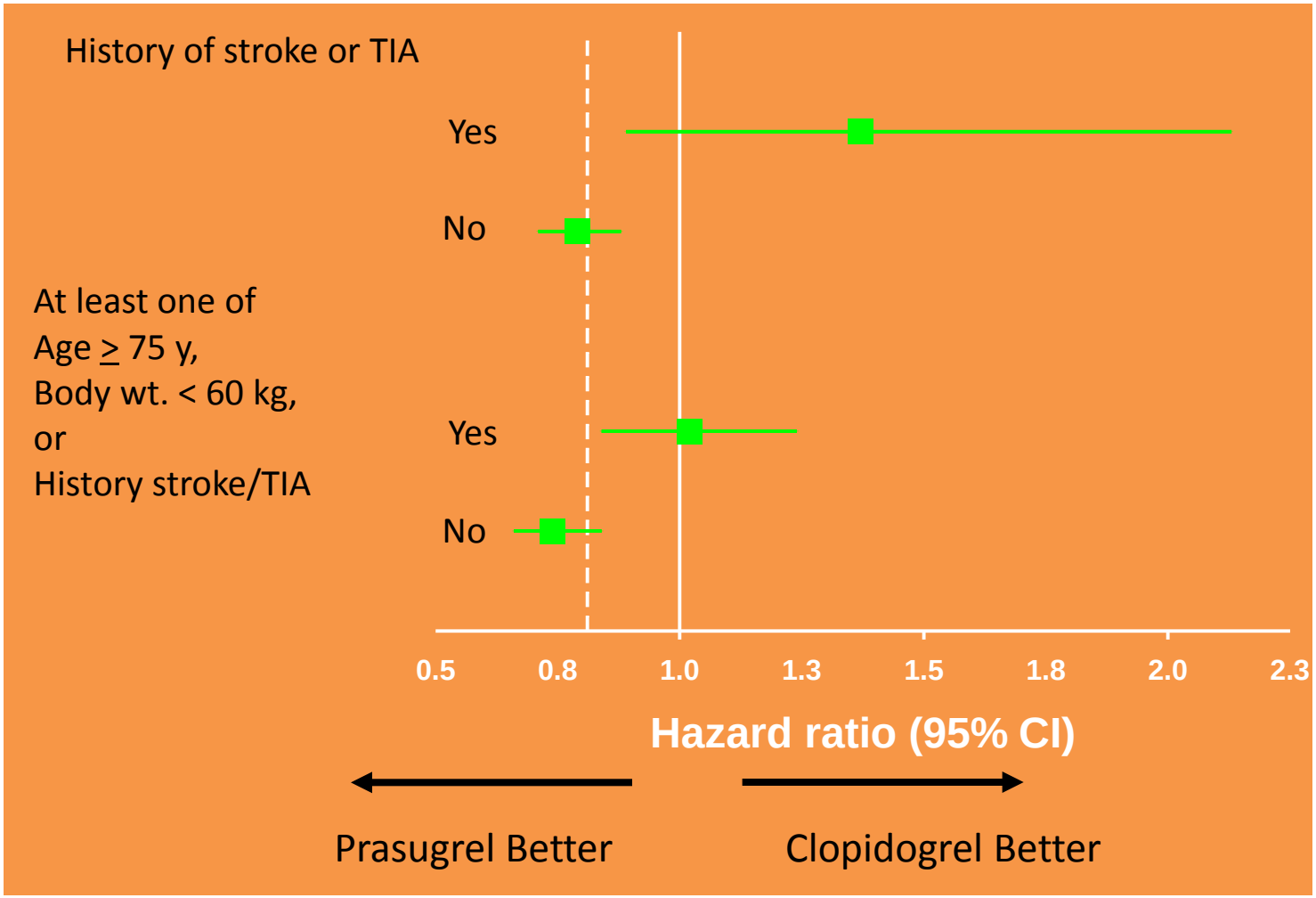

Baseline Characteristics
Hazard Ratio for Prasugrel Efficacy (95% CI)
Total No. of Patients
Prasugrel (%)
Clopidogrel (%)
Reduction in Risk (%)
Overall 13,608 9.9 12.1 19
Unstable angina or non–ST-elevation MI 10,074 9.9 12.1 18
ST-elevation MI 3,534 10.0 12.4 21
Sex
Male 10,085 9.5 11.9 21
Female 3,523 11.0 12.6 12
Age
<65 yr 8,322 8.1 10.6 25
65–74 yr 3,477 10.7 12.3 14
≥75 yr 1,809 17.2 18.3 6
Diabetes mellitus
No 10,462 9.2 10.6 14
Yes 3,146 12.2 17.0 30
Stent placement during index procedure
Bare-metal stent only 6,461 10.0 12.2 20
≥1 Drug-eluting stent 6,383 9.4 11.6 18
Glycoprotein IIb/IIIa receptor–antagonist use
Yes 7,414 10.4 12.9 21
No 6,194 9.3 11.0 16
Creatinine clearance
<60 ml/min 1,490 15.1 17.5 14
≥60 ml/min 11,890 9.0 11.1 20
0.50 0.60 0.70 0.80 0.90 1.00 2.00
Prasugrel Better
Clopidogrel Better

Table 3. Thrombolysis in Myocardial Infarction (TIMI) Bleeding End Points in the Overall Cohort at 15 Months.*

End Point	Prasugrel (N=6741)	Clopidogrel (N=6716)	Hazard Ratio for Prasugrel (95% CI)	P Value
	no. of patients (%)			
Non–CABG-related TIMI major bleeding (key safety end point)	146 (2.4)	111 (1.8)	1.32 (1.03–1.68)	0.03
Related to instrumentation	45 (0.7)	38 (0.6)	1.18 (0.77–1.82)	0.45
Spontaneous	92 (1.6)	61 (1.1)	1.51 (1.09–2.08)	0.01
Related to trauma	9 (0.2)	12 (0.2)	0.75 (0.32–1.78)	0.51
Life-threatening†	85 (1.4)	56 (0.9)	1.52 (1.08–2.13)	0.01
Related to instrumentation	28 (0.5)	18 (0.3)	1.55 (0.86–2.81)	0.14
Spontaneous	50 (0.9)	28 (0.5)	1.78 (1.12–2.83)	0.01
Related to trauma	7 (0.1)	10 (0.2)	0.70 (0.27–1.84)	0.47
Fatal‡	21 (0.4)	5 (0.1)	4.19 (1.58–11.11)	0.002
Nonfatal	64 (1.1)	51 (0.9)	1.25 (0.87–1.81)	0.23
Intracranial	19 (0.3)	17 (0.3)	1.12 (0.58–2.15)	0.74
Major or minor TIMI bleeding	303 (5.0)	231 (3.8)	1.31 (1.11–1.56)	0.002
Bleeding requiring transfusion§	244 (4.0)	182 (3.0)	1.34 (1.11–1.63)	<0.001
CABG-related TIMI major bleeding¶	24 (13.4)	6 (3.2)	4.73 (1.90–11.82)	<0.001

CV Death/ Nonfatal MI/ Nonfatal Stroke: Post-hoc Analysis by Selected Subgroups*



	P** value	P*** interaction
History of stroke or TIA: Yes	0.15	-
History of stroke or TIA: No	<0.001	0.02
At least one of Age ≥ 75 y, Body wt. < 60 kg, or History stroke/TIA: Yes	0.83	-
At least one of Age ≥ 75 y, Body wt. < 60 kg, or History stroke/TIA: No	<0.001	0.008

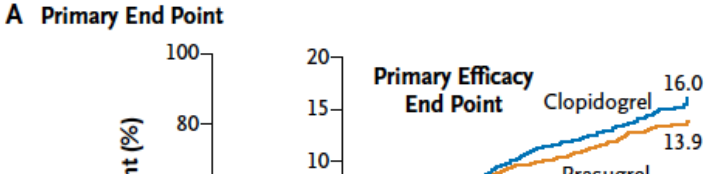
*Kaplan-Meier estimates intention-to-treat cohort
**Tests hazard ratio =1.0 within subgroups
***Tests equality hazard ratio between subgroups

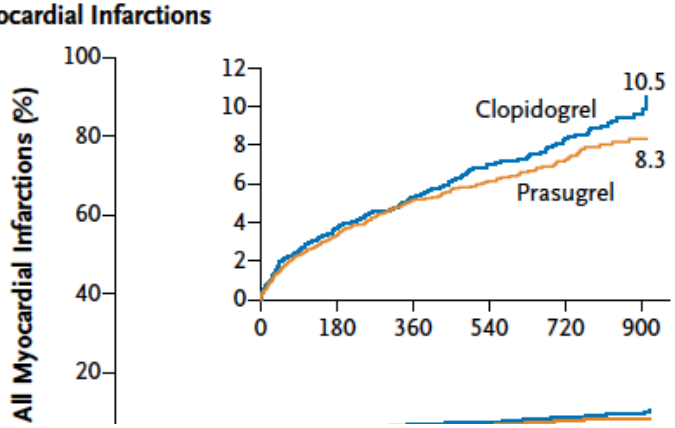
CONCLUSIONS

In patients with acute coronary syndromes with scheduled percutaneous coronary intervention, prasugrel therapy was associated with significantly reduced rates of ischemic events, including stent thrombosis, but with an increased risk of major bleeding, including fatal bleeding. Overall mortality did not differ significantly between treatment groups. (ClinicalTrials.gov number, NCT00097591.)

Prasugrel versus Clopidogrel for Acute Coronary Syndromes without Revascularization

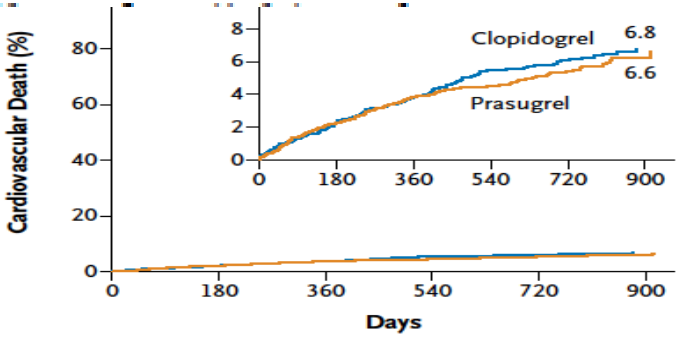
TRILOGY ACS

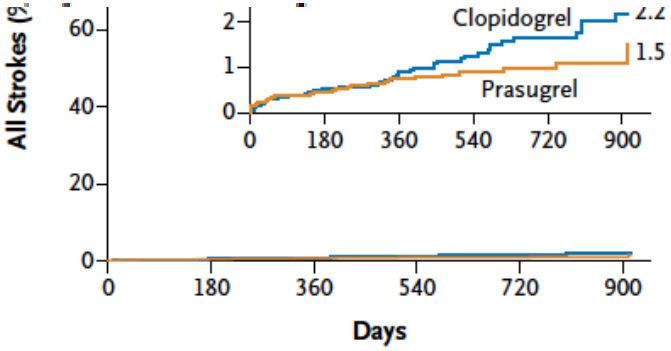




CONCLUSIONS

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





The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 12, 2013 VOL. 369 NO. 11

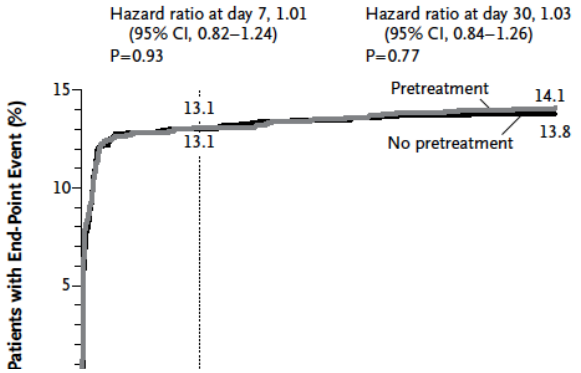
Pretreatment with Prasugrel in Non–ST-Segment Elevation Acute Coronary Syndromes

ACCOAST

POBLACION TOTAL

POBLACION PCI

A Primary Efficacy End Point, PCI Group



A Primary Efficacy End Point

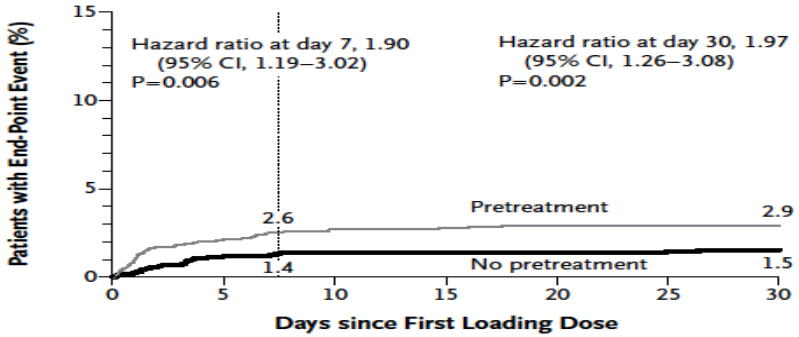
CONCLUSIONS

Among patients with NSTE acute coronary syndromes who were scheduled to undergo catheterization, pretreatment with prasugrel did not reduce the rate of major ischemic events up to 30 days but increased the rate of major bleeding complications. (Funded by Daiichi Sankyo and Eli Lilly; ACCOAST ClinicalTrials.gov number,

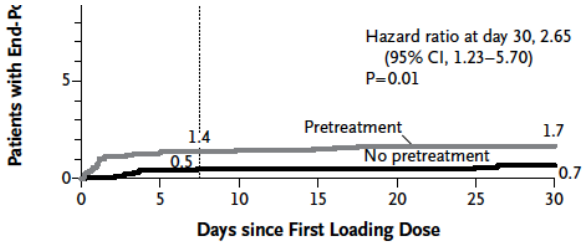
Days since First Loading Dose

No. at Risk							
No pretreatment	1996	1788	1775	1769	1762	1752	1621
Pretreatment	2037	1821	1809	1802	1797	1791	1616

B All TIMI Major Bleeding



No. at Risk							
No pretreatment	1996	1947	1328	1297	1288	1284	1263
Pretreatment	2037	1972	1339	1310	1299	1297	1280

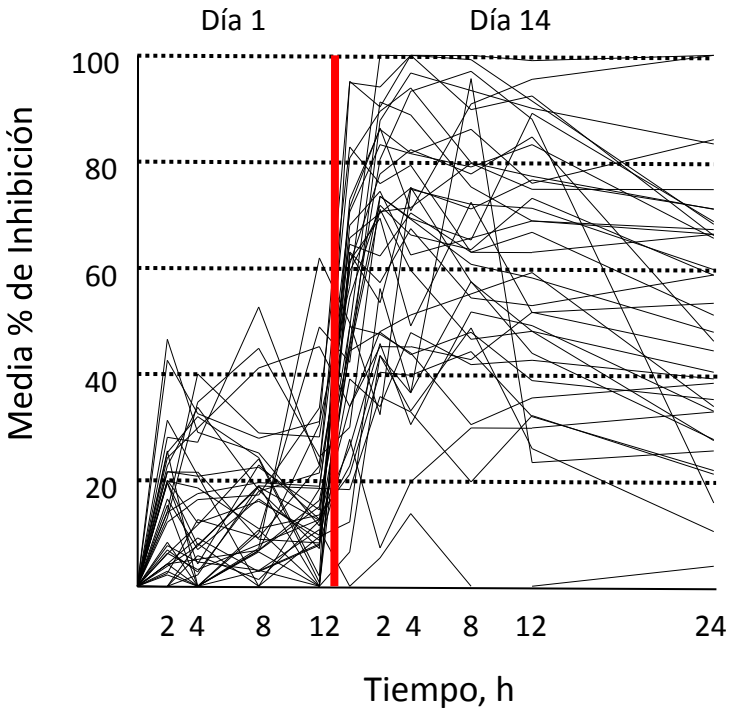


No. at Risk							
No pretreatment	1372	1356	1302	1280	1272	1268	1249
Pretreatment	1389	1364	1314	1293	1282	1280	1269

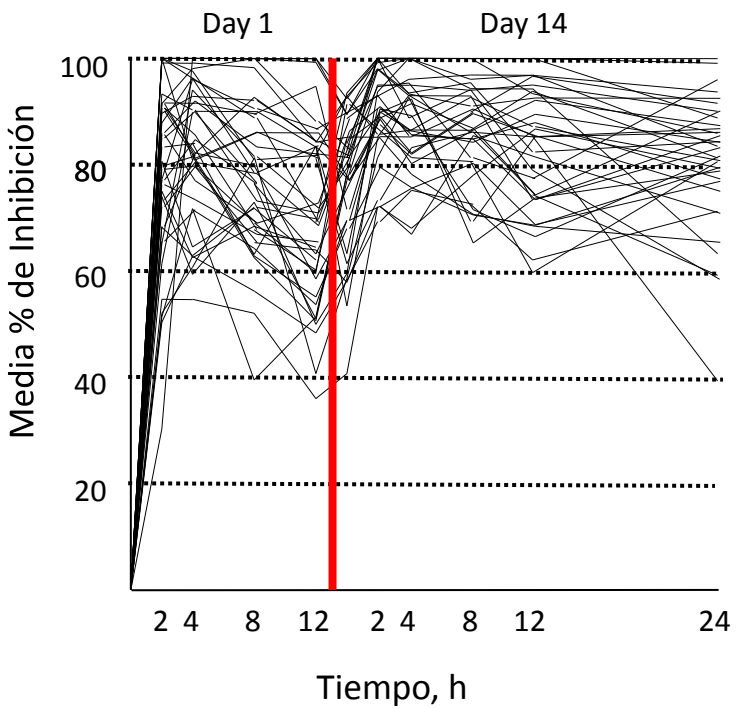
TICAGRELOR

IPA – Estudio DISPERSE I

Mayor y más consistente IPA que clopidogrel



75 mg de Clopidogrel qd



100 mg de Ticagrelor bd

Husted SE, et al. Eur Heart J. 2006;27:1038-47.

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

PLATO

SCASEST (riesgo moderado/alto) y SCACEST (si PCI primaria).
Todos recibiendo AAS
Tratados previamente con Clopidogrel o no;
aleatorizados en <24 horas desde evento índice
(N=18,624)
Manejo Médico o Invasivo

Clopidogrel
Pretratados: no dosis de carga adicional,
No pretratados: 300-mg dosis carga
(o 600-mg a discreción del investigador);
+ 75-mg od mantenimiento

Ticagrelor
180-mg dosis de carga
+ 90-mg bd mantenimiento
(90mg adicional si PCI >24 horas)

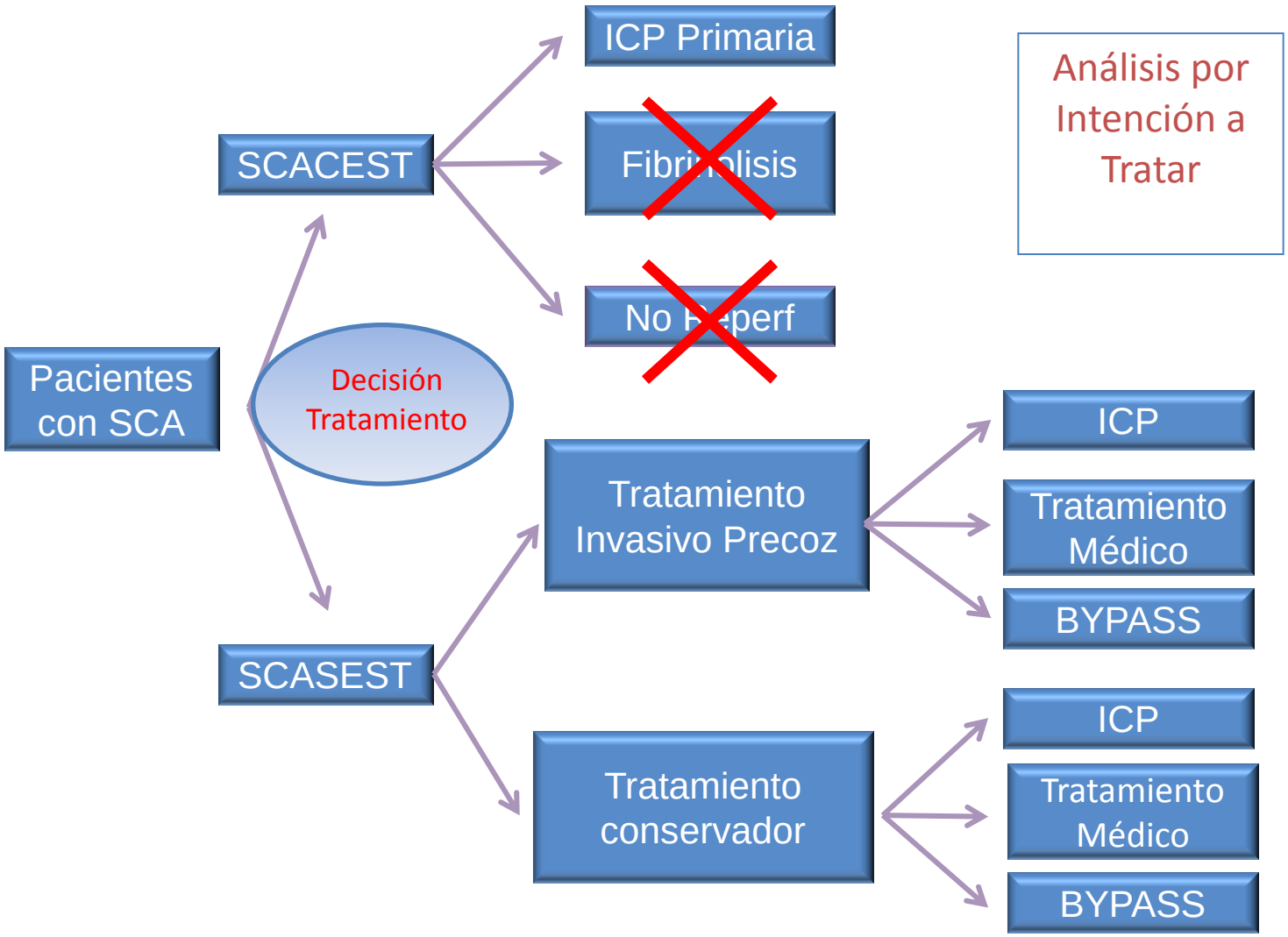
6-12 meses de tratamiento

Objetivo Primario de eficacia: Muerte CV + IM + Ictus
Objetivo Primario de Seguridad: Sangrado Mayor Total

James S, et al. *Am Heart J.* 2009;157:599-605;
Wallentin L et al. N Engl J Med 2009;361:1045-57.

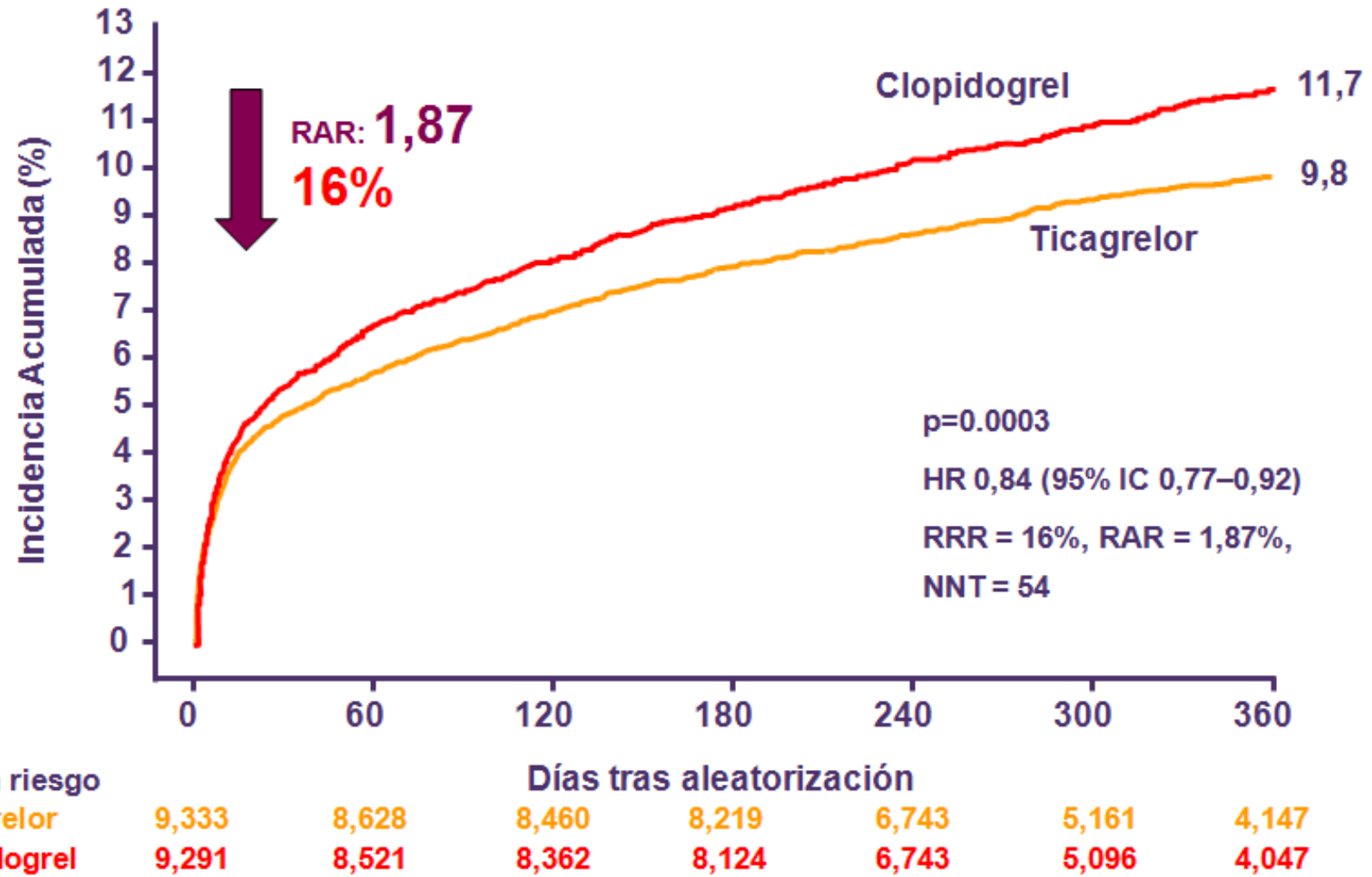
PLATO: Inclusión de pacientes

Población SCA con Tratamiento Invasivo o No

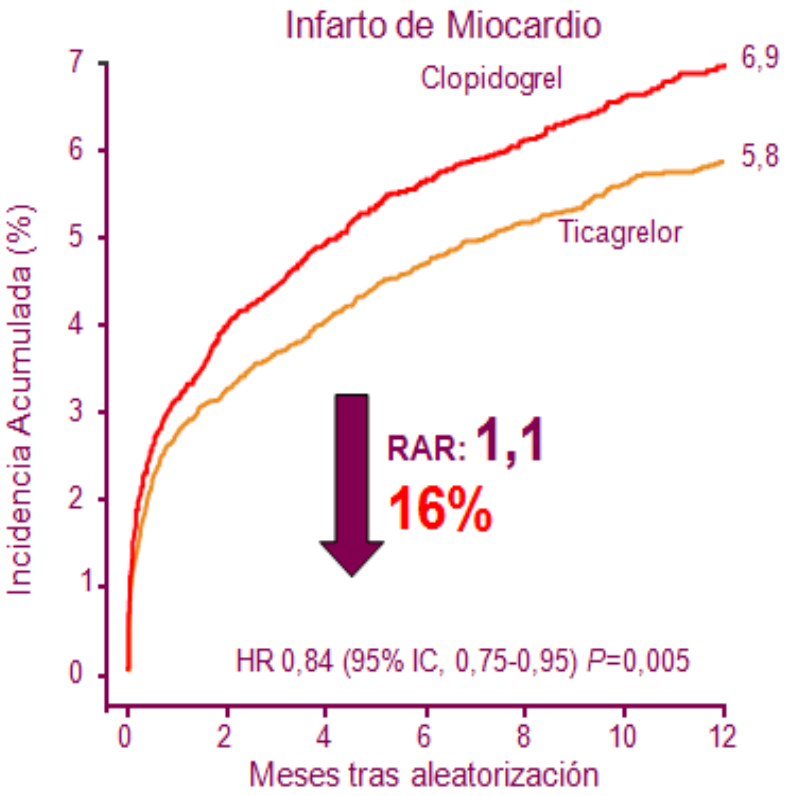


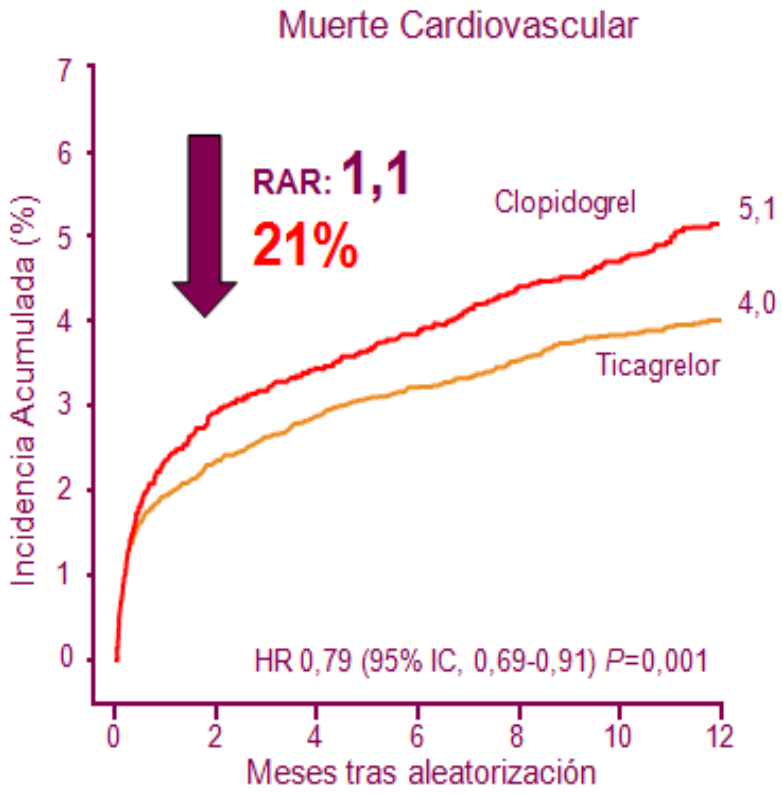
Wallentin L, et al. N Engl J Med. 2009;361:1045–1057

Estimación de K-M del tiempo hasta evento del objetivo de eficacia primario (Objetivo compuesto de Muerte CV, IM e Ictus)



Wallentin L, et al. N Engl J Med. 2009;361:1045–1057





No. en riesgo

Ticagrelor	9333	8678	8520	8279	6796	5210	4191
Clopidogrel	9291	8560	8405	8177	6703	5136	4109

9333	8294	8822	8626	7119	5482	4419
9291	8865	8780	8589	7079	5441	4364

PLATO: Objetivos 2rios de Eficacia

Table 3. Major Efficacy End Points at 12 Months.*

End Point	Ticagrelor Group	Clopidogrel Group	Hazard Ratio for Ticagrelor Group (95% CI)	P Value†
Primary end point: death from vascular causes, MI, or stroke — no./total no. (%)	864/9333 (9.8)	1014/9291 (11.7)	0.84 (0.77–0.92)	<0.001‡
Secondary end points — no./total no. (%)				
Death from any cause, MI, or stroke	901/9333 (10.2)	1065/9291 (12.3)	0.84 (0.77–0.92)	<0.001‡
Death from vascular causes, MI, stroke, severe recurrent ischemia, recurrent ischemia, TIA, or other arterial thrombotic event	1290/9333 (14.6)	1456/9291 (16.7)	0.88 (0.81–0.95)	<0.001‡
MI	504/9333 (5.8)	593/9291 (6.9)	0.84 (0.75–0.95)	0.005‡
Death from vascular causes	353/9333 (4.0)	442/9291 (5.1)	0.79 (0.69–0.91)	0.001‡
Stroke	125/9333 (1.5)	106/9291 (1.3)	1.17 (0.91–1.52)	0.22
Ischemic	96/9333 (1.1)	91/9291 (1.1)		0.74
Hemorrhagic	23/9333 (0.2)	13/9291 (0.1)		0.10
Unknown	10/9333 (0.1)	2/9291 (0.02)		0.04
Other events — no./total no. (%)				
Death from any cause	399/9333 (4.5)	506/9291 (5.9)	0.78 (0.69–0.89)	<0.001
Death from causes other than vascular causes	46/9333 (0.5)	64/9291 (0.8)	0.71 (0.49–1.04)	0.08
Severe recurrent ischemia	302/9333 (3.5)	345/9291 (4.0)	0.87 (0.74–1.01)	0.08

Wallentin L, et al. N Engl J Med. 2009;361:1045–1057

Table 4. Safety of the Study Drugs.*

End Point	Ticagrelor Group	Clopidogrel Group	Hazard or Odds Ratio for Ticagrelor Group (95% CI)†	P Value
Primary safety end points — no./total no. (%)				
Major bleeding, study criteria	961/9235 (11.6)	929/9186 (11.2)	1.04 (0.95–1.13)	0.43
Major bleeding, TIMI criteria‡	657/9235 (7.9)	638/9186 (7.7)	1.03 (0.93–1.15)	0.57
Bleeding requiring red-cell transfusion	818/9235 (8.9)	809/9186 (8.9)	1.00 (0.91–1.11)	0.96
Life-threatening or fatal bleeding, study criteria	491/9235 (5.8)	480/9186 (5.8)	1.03 (0.90–1.16)	0.70
Fatal bleeding	20/9235 (0.3)	23/9186 (0.3)	0.87 (0.48–1.59)	0.66
Nonintracranial fatal bleeding	9/9235 (0.1)	21/9186 (0.3)		0.03
Intracranial bleeding	26/9235 (0.3)	14/9186 (0.2)	1.87 (0.98–3.58)	0.06
Fatal	11/9235 (0.1)	1/9186 (0.01)		0.02
Nonfatal	15/9235 (0.2)	13/9186 (0.2)		0.69
Secondary safety end points — no./total no. (%)				
Non–CABG-related major bleeding, study criteria	362/9235 (4.5)	306/9186 (3.8)	1.19 (1.02–1.38)	0.03
Non–CABG-related major bleeding, TIMI criteria	221/9235 (2.8)	177/9186 (2.2)	1.25 (1.03, 1.53)	0.03
CABG-related major bleeding, study criteria	619/9235 (7.4)	654/9186 (7.9)	0.95 (0.85–1.06)	0.32
CABG-related major bleeding, TIMI criteria	446/9235 (5.3)	476/9186 (5.8)	0.94 (0.82–1.07)	0.32
Major or minor bleeding, study criteria	1339/9235 (16.1)	1215/9186 (14.6)	1.11 (1.03–1.20)	0.008
Major or minor bleeding, TIMI criteria‡	946/9235 (11.4)	906/9186 (10.9)	1.05 (0.96–1.15)	0.33

Principales Eventos Adversos

Pausas Ventriculares

- **No diferencias significativas en la tasa de manifestaciones clínicas de bradiarritmia.**
- **Monitorización por Holter de Pausas Ventriculares de ≥ 3 seg:**
  - **1ª Semana →** 84/1451 (5,8%) en grupo ticagrelor vs 51/1415 (3,6%) (p=0,01).
  - **A los 30 días →** 21/985 (2,1%) en grupo ticagrelor vs 17/1006 (1,7%) (p=0,52).
- **Raramente asociadas a síntomas.**

Holter monitoring — no./total no. (%)	Ticagrelor Group	Clopidogrel Group	P Value
First week			
Ventricular pauses ≥3 sec	84/1451 (5.8)	51/1415 (3.6)	0.01
Ventricular pauses ≥5 sec	29/1451 (2.0)	17/1415 (1.2)	0.10
At 30 days			
Ventricular pauses ≥3 sec	21/985 (2.1)	17/1006 (1.7)	0.52
Ventricular pauses ≥5 sec	8/985 (0.8)	6/1006 (0.6)	0.60

Wallentin L, et al. N Engl J Med. 2009;361:1045–1057

Principales Eventos Adversos

Disnea

- **Mas frecuente en el brazo de ticagrelor:**

  13,8% versus 7,8% (IC95%: 1,68-2,02; p<0,001)

- **Baja interrupción del tratamiento por disnea:**

  0,9% versus 0,1% (IC95%: 3,41-11,01 ; p< 0,001)

- **Aproximadamente sólo 1/100 discontinuaron el tratamiento por disnea.**

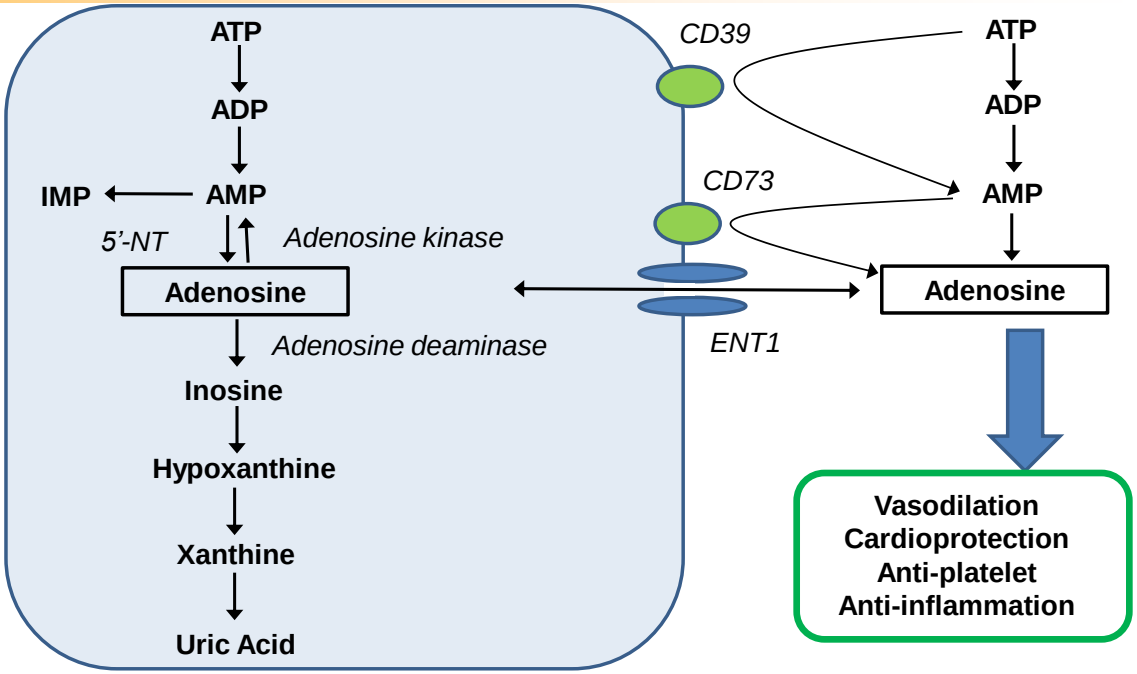
- **Episodios de leves a moderados y con duración menor a una semana.**

Wallentin L, et al. N Engl J Med. 2009;361:1045–1057

Ticagrelor: doble mecanismo de acción

Equilibrative Nucleoside Transporter Type 1 (ENT1): Ticagrelor Additional Mode of Action

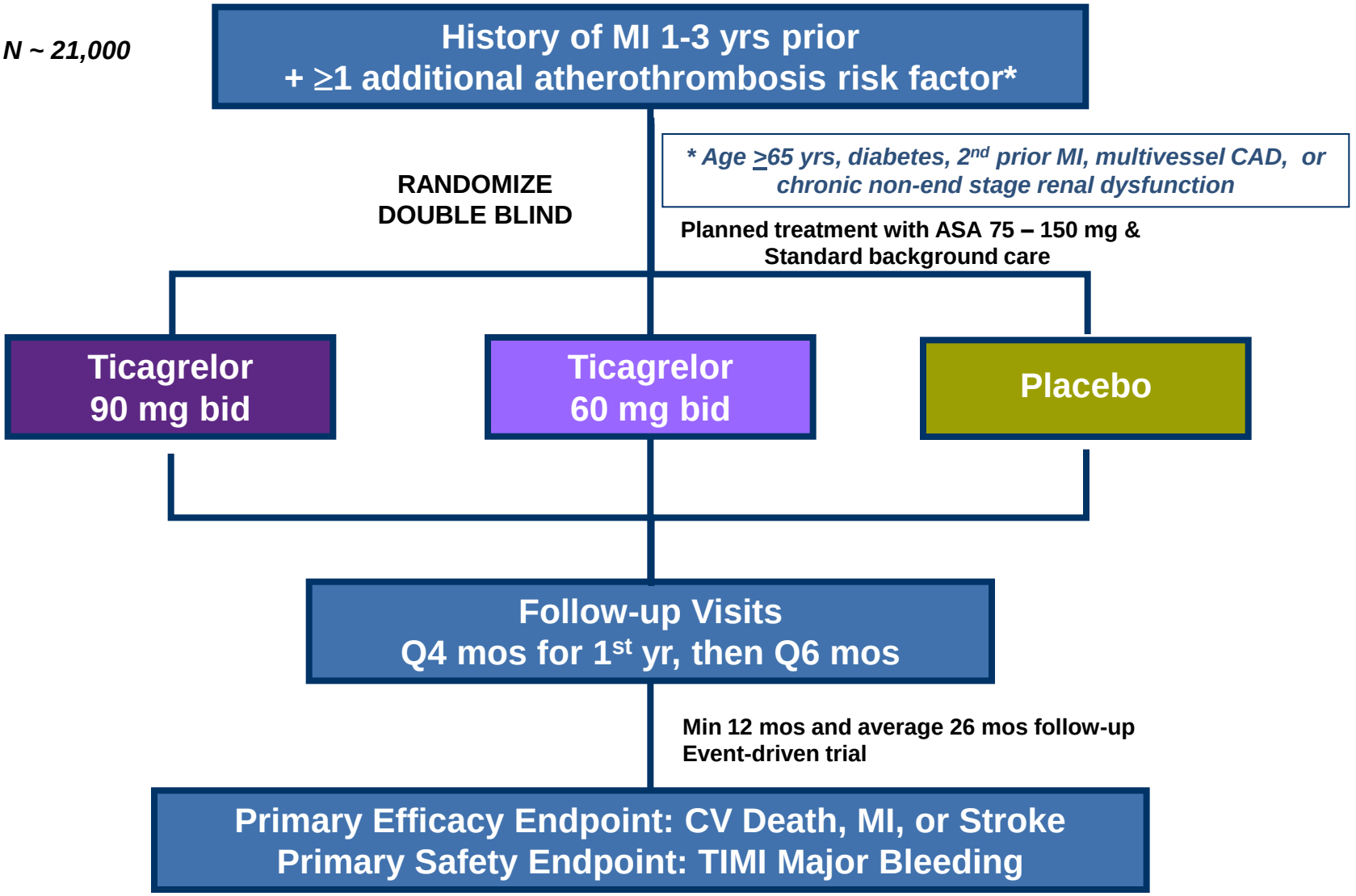
- Hypoxia prohibits regeneration of ATP from Adenosine leading to a large increase in intracellular adenosine concentration
- Adenosine transporter maintains equal intra- and extra-cellular concentrations, i.e. starts pumping adenosine out of the cell
- So, hypoxia or tissue damage result in locally increased circulating adenosine levels



CONCLUSIONS

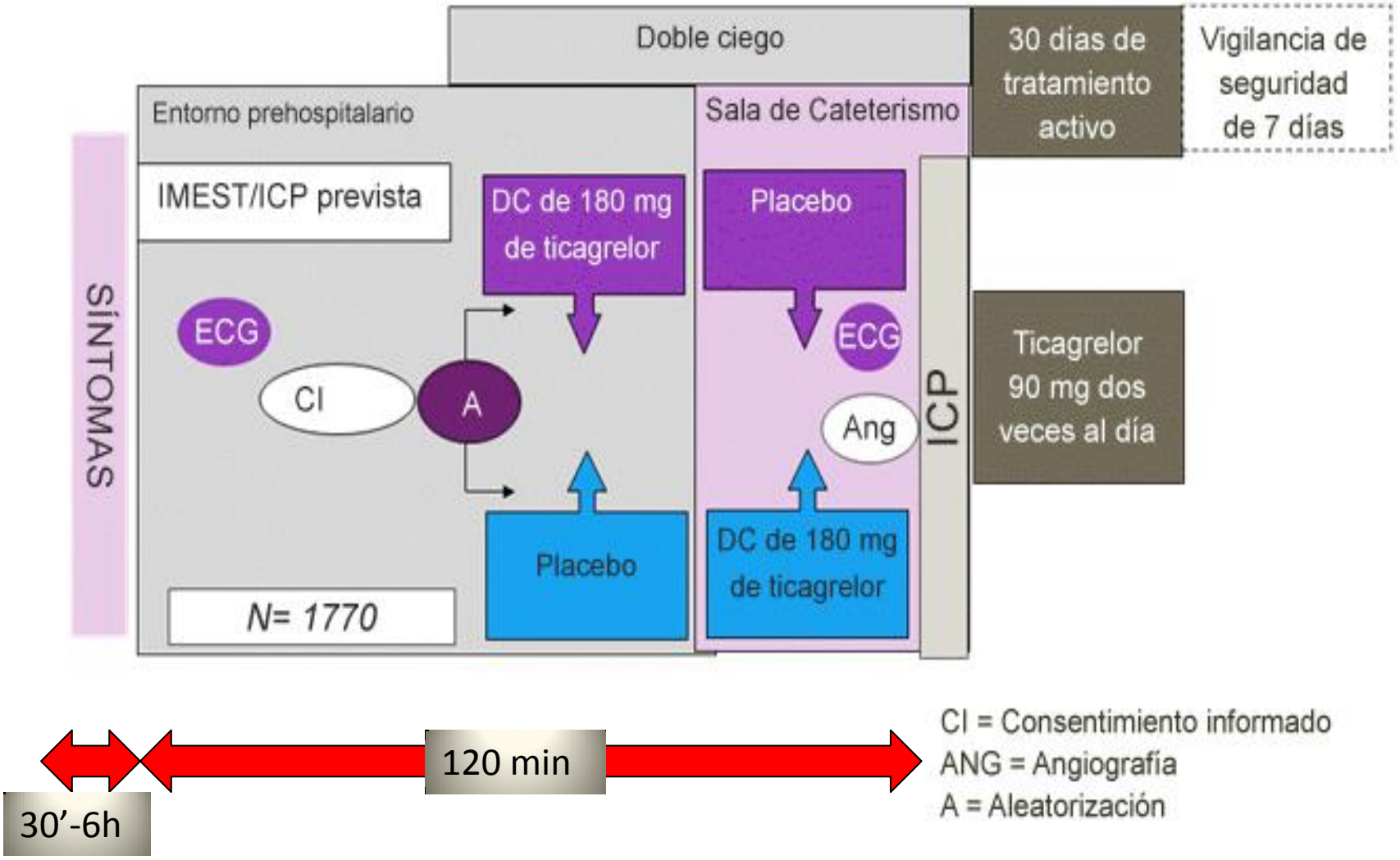
In patients who have an acute coronary syndrome with or without ST-segment elevation, treatment with ticagrelor as compared with clopidogrel significantly reduced the rate of death from vascular causes, myocardial infarction, or stroke without an increase in the rate of overall major bleeding but with an increase in the rate of non–procedure-related bleeding. (ClinicalTrials.gov number, NCT00391872.)

Estudio Pegasus



http://www.clinicaltrials.gov/ct2/show/NCT01225562?term=pegasus&rank=3

Estudio ATLANTIC



http://clinicaltrials.gov/ct2/show/NCT01347580?term=atlantic&rank=1

Guías: 'Pretratamiento'

ESC STEMI 2012

3.5.3.2 Periprocedural pharmacotherapy (Table 12)
Patients undergoing primary PCI should receive a combination of DAPT with aspirin and an adenosine diphosphate (ADP) receptor blocker, as early as possible before angiography, and a parenteral anticoagulant. No trials to date have evaluated the commencement

AHA/ACC STEMI 2013

3. A loading dose of a $P2Y_{12}$ receptor inhibitor should be given as early as possible or at time of primary PCI to patients with STEMI.

Steg G, et al. Eur Heart.J (2012) 33 (20): 2569 – 2619.
O'Gara et al. *Circulation. 2013;127:00-00*

Guidelines: 'Pretratamiento'

ESC STEMI 2012

3.5.3.2 Periprocedural pharmacotherapy (Table 12)

Patients undergoing primary PCI should receive a combination of DAPT with aspirin and an adenosine diphosphate (ADP) receptor blocker, as early as possible before angiography, and a parenteral anticoagulant. No trials to date have evaluated the commencement of DAPT prior to hospital admission, rather than in hospital, nor its use before, rather than during, angiography in the setting of STEMI, but this is common practice in Europe and is consistent with the pharmacokinetic data for oral antithrombotic agents, suggesting that the earliest administration would be preferable to achieve early efficacy.

Steg G, et al. Eur Heart.J (2012) 33 (20): 2569 – 2619.

2014 ESC M.I. Revascularisation: ICPp

Recommendations	Class[a]	Level[b]	Ref[c]
Antiplatelet therapy			
ASA is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (or 80–150 mg i.v.) and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A	776,794
A $P2Y_{12}$ inhibitor is recommended in addition to ASA and maintained over 12 months unless there are contraindications such as excessive risk of bleeding. Options are:	I	A	–
• Prasugrel (60 mg loading dose, 10 mg daily dose) if no contraindication	I	B	828
• Ticagrelor (180 mg loading dose, 90 mg twice daily) if no contraindication	I	B	823
• Clopidogrel (600 mg loading dose, 75 mg daily dose), only when prasugrel or ticagrelor are not available or are contraindicated.	I	B	812
It is recommended to give $P2Y_{12}$ inhibitors at the time of first medical contact.	I	B	777,846–848
GP IIb/IIIa inhibitors should be considered for bail-out or evidence of no-reflow or a thrombotic complication.	IIa	C	–
Upstream use of a GP IIb/IIIa inhibitor (vs. in-lab use) may be considered in high-risk patients undergoing transfer for primary PCI.	IIb	B	271,834, 835,849

Kolh P et al. Eur Heart J August 29 2014;
DOI:10.1093/eurheart/ehu278 [Epub ahead of print]

Background:

- Los trabajos en los que se apoya esta recomendación IB de las guías de revascularización 2014 están realizados con Clopidogrel.

- En ellos se sugiere que podría haber un beneficio en el pretratamiento con Clopidogrel (STEMI e ICPp), en terminos de eventos isquémicos, y que además no llevaría aparejado un exceso de sangrados.

- Ticagrelor demostró una mayor eficacia que Clopidogrel durante el estudio PLATO en un amplio espectro de pacientes con SCA, y en concreto en el subgrupo de pacientes STEMI que van a ICPp.

- En el estudio ATLANTIC se evalua la eficacia y seguridad de la administración prehospitalaria de Ticagrelor vs a la administración hospitalaria.

The NEW ENGLAND JOURNAL of MEDICINE

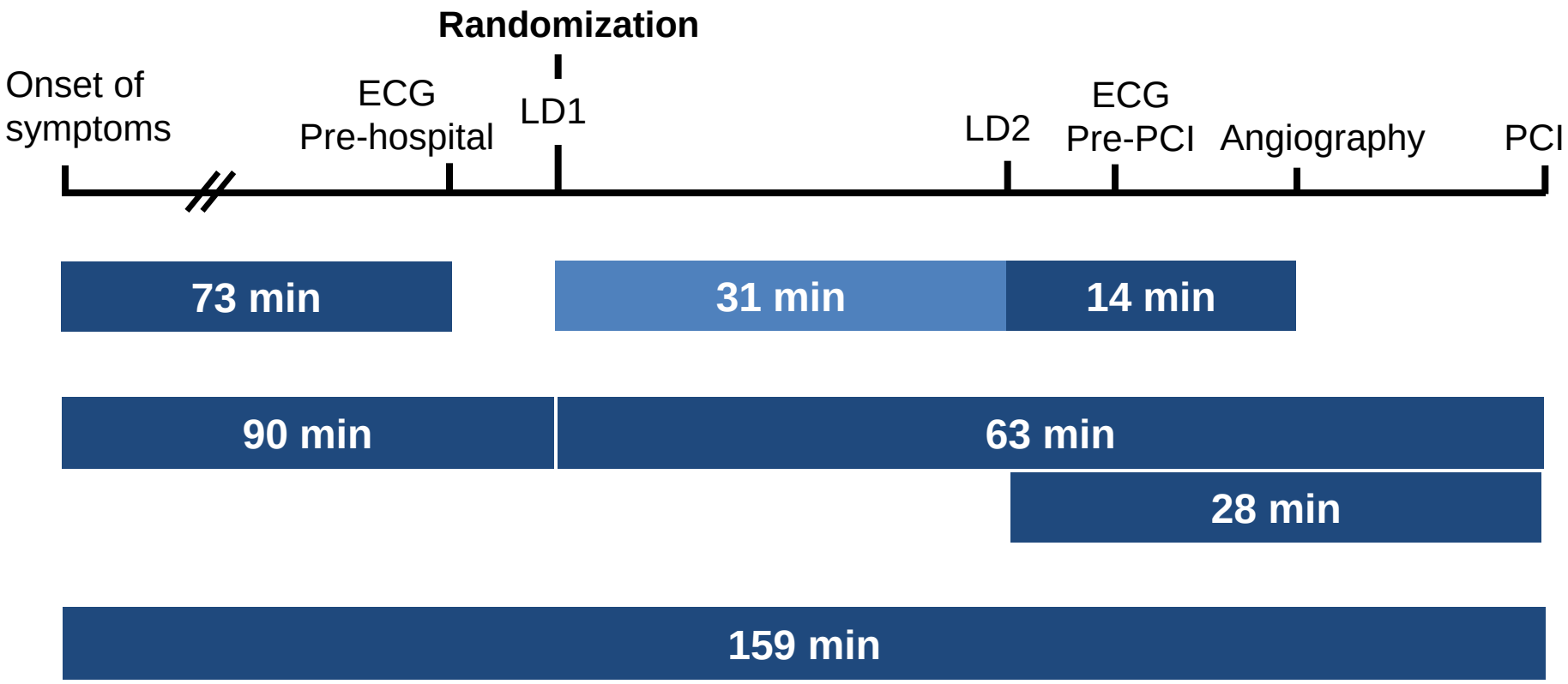
ORIGINAL ARTICLE

Prehospital Ticagrelor in ST-Segment Elevation Myocardial Infarction

Gilles Montalescot, M.D., Ph.D., Arnoud W. van 't Hof, M.D., Ph.D., Frédéric Lapostolle, M.D., Ph.D., Johanne Silvain, M.D., Ph.D., Jens Flensted Lassen, M.D., Ph.D., Leonardo Bolognese, M.D., Warren J. Cantor, M.D., Ángel Cequier, M.D., Ph.D., Mohamed Chettibi, M.D., Ph.D., Shaun G. Goodman, M.D., Christopher J. Hammett, M.B., Ch.B., M.D., Kurt Huber, M.D., Magnus Janzon, M.D., Ph.D., Béla Merkely, M.D., Ph.D., Robert F. Storey, M.D., D.M., Uwe Zeymer, M.D., Olivier Stibbe, M.D., Patrick Ecollan, M.D., Wim M.J.M. Heutz, M.D., Eva Swahn, M.D., Ph.D., Jean-Philippe Collet, M.D., Ph.D., Frank F. Willems, M.D., Ph.D., Caroline Baradat, M.Sc., Muriel Licour, M.Sc., Anne Tsatsaris, M.D., Eric Vicaut, M.D., Ph.D., and Christian W. Hamm, M.D., Ph.D., for the ATLANTIC Investigators*

Montalescot G et al. N Engl J Med September 1, 2014 [Epub ahead of print; DOI: 10.1056/NEJMoa1407024]

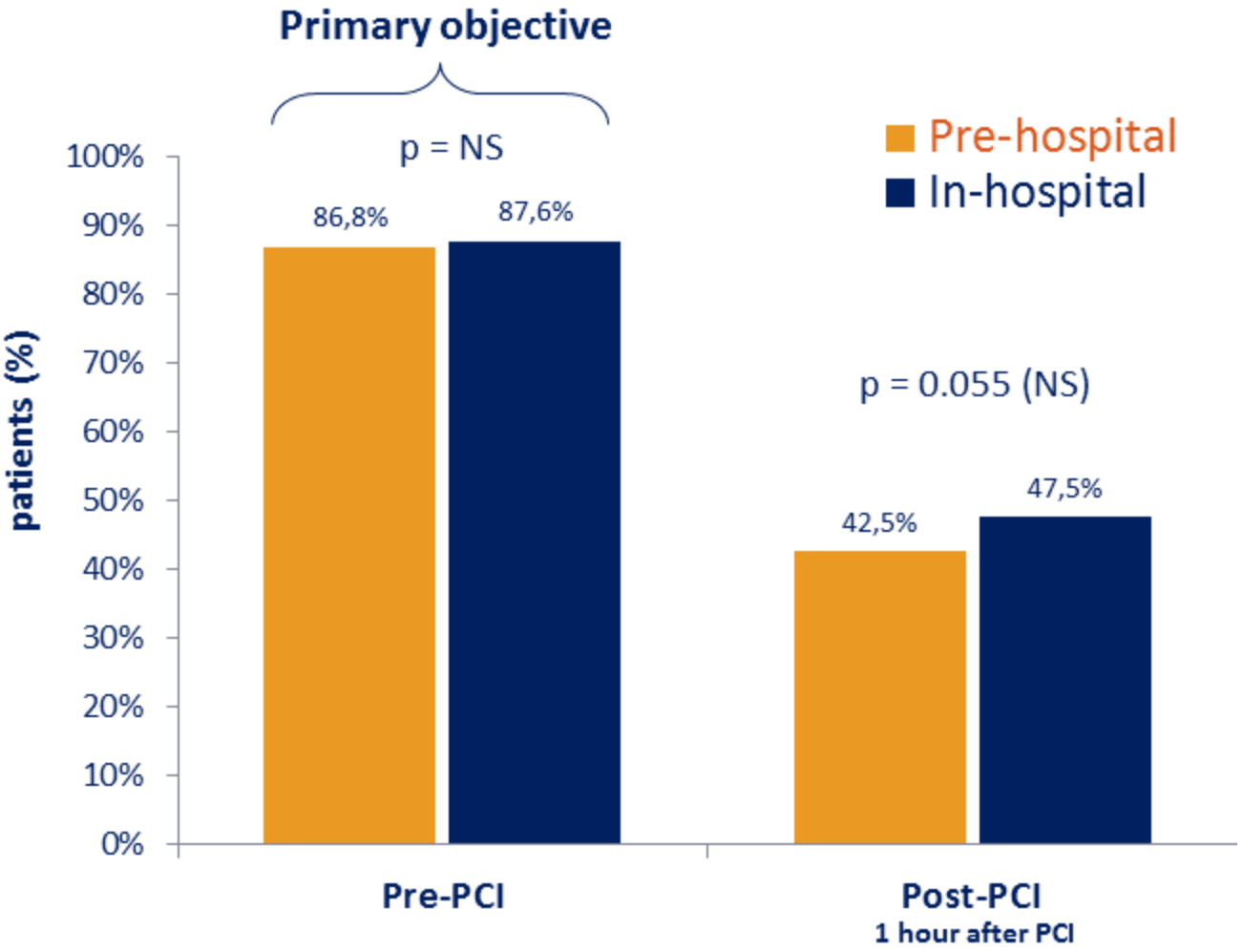
Median times to pre- and in-hospital steps



Montalescot G et al. N Engl J Med September 1, 2014 [Epub ahead of print; DOI: 10.1056/NEJMoa1407024]

1st Co-primary endpoint

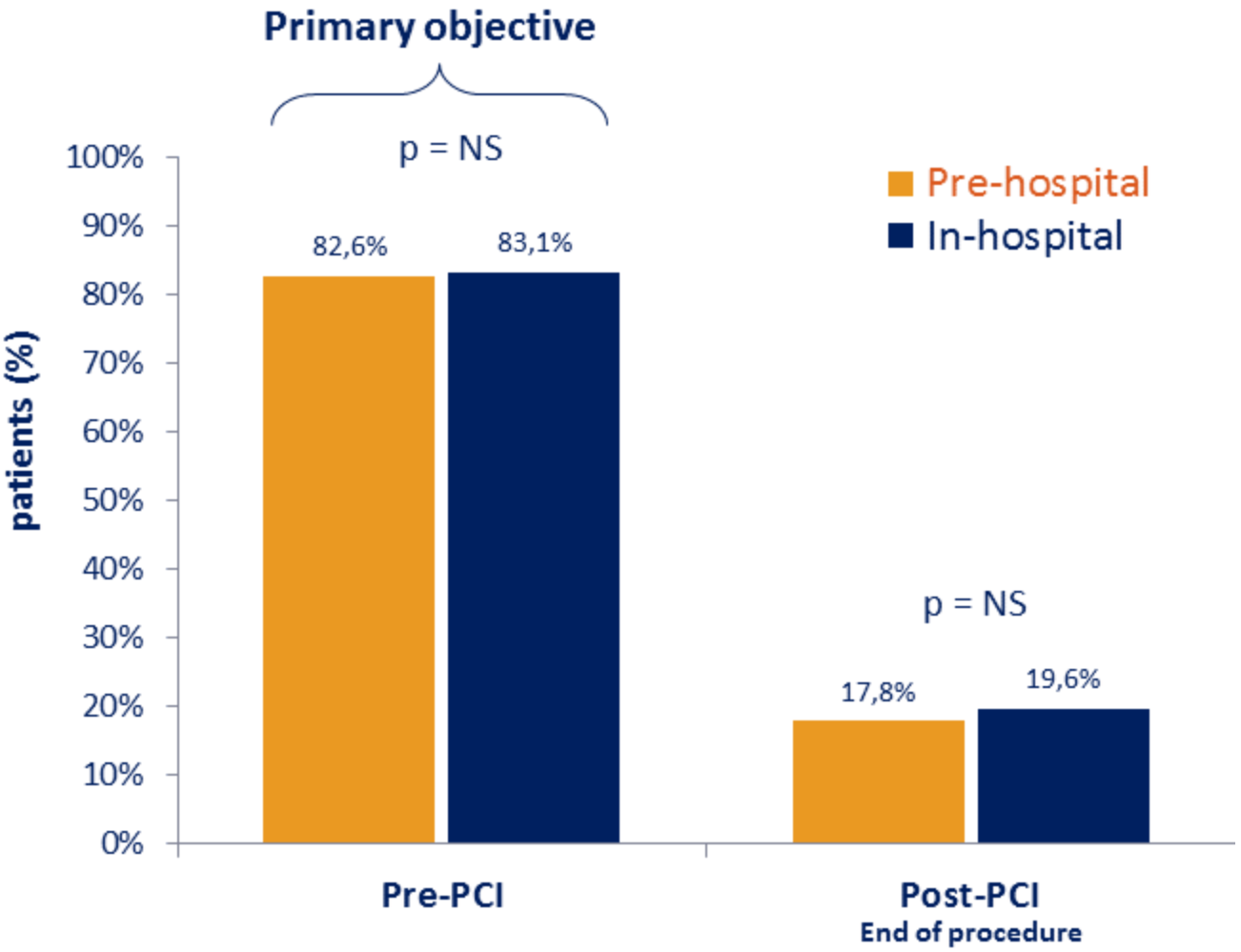
No ST-segment resolution (≥70%)



Montalescot G et al. N Engl J Med September 1, 2014 [Epub ahead of print; DOI: 10.1056/NEJMoa1407024]

2nd Co-primary endpoint

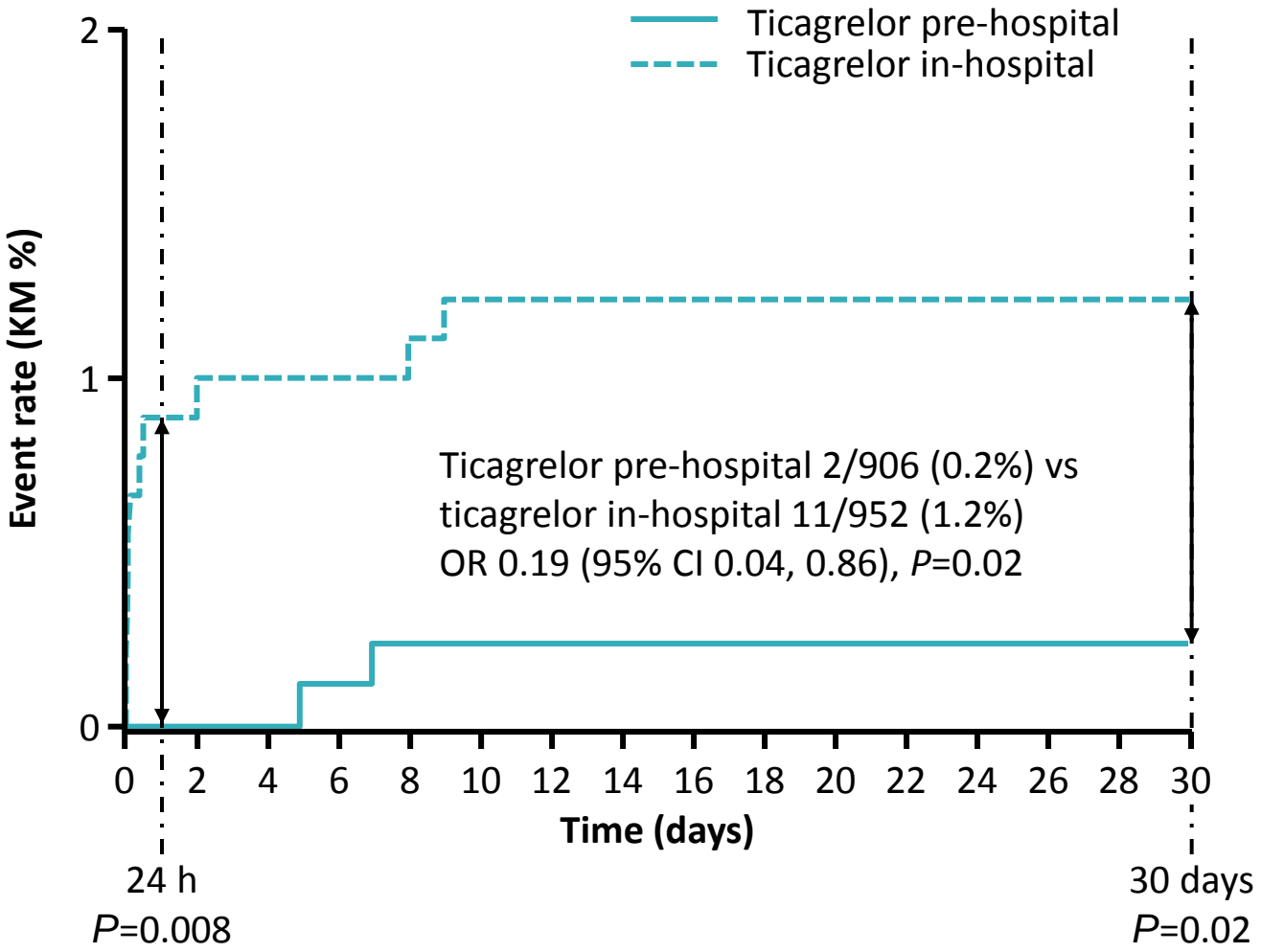
No TIMI 3 flow in infarct-related artery



Montalescot G et al. N Engl J Med September 1, 2014 [Epub ahead of print; DOI: 10.1056/NEJMoa1407024]

Definite stent thrombosis up to 30 days

Kaplan–Meier curves



Montalescot G et al. N Engl J Med September 1, 2014 [Epub ahead of print; DOI: 10.1056/NEJMoa1407024]

Clinical endpoints at 30 days

n (%)	Ticagrelor pre-hosp (n=906)	Ticagrelor in-hosp (n=952)	Odds ratio (95% CI)	*P* value	Difference (95% CI)
Death (all-cause)*	30 (3.3)	19 (2.0)	1.68 (0.94, 3.01)	0.08†	0.013 (–0.001, 0.028)
MI	7 (0.8)	10 (1.1)	0.73 (0.28, 1.94)	0.53†	–0.003 (–0.011, 0.006)
Stroke	4 (0.4)	2 (0.2)	2.11 (0.39, 11.53)	0.39†	0.002 (–0.004, 0.009)‡
TIA	0	1 (0.1)		Not estimable	–0.001 (–0.006, 0.003)‡
Urgent coronary revascularization	5 (0.6)	8 (0.8)	0.66 (0.21, 2.01)	0.46†	–0.003 (–0.010, 0.005)
Bail-out with GP IIb/IIIa inhibitors	78 (8.6)	100 (10.5)	0.80 (0.59, 1.10)	0.17	–0.019 (–0.046, 0.008)

*Almost all causes of death were related to cardiogenic shock, cardiac arrest, or cardiac rupture rather than bleeding or ischaemic events. Patient records have been specifically examined and no treatment related effect can be discerned

†Fisher's exact test

‡Probable stent thrombosis was defined as any death occurring in a stented patient within 30 days

Events occurring up to the date of last study visit (to a maximum of 32 days) are included in the table. Patients could be on study treatment or not when the event occurred

mITT analysis: Each event is counted once in each row. A single event may be counted in more than one row. Odds ratios for pre-hospital group versus in hospital group, two-sided 95% CIs and *P* values were calculated from a logistic regression model, with treatment as the only explanatory variable Difference in binomial proportions calculated for pre-hospital – in-hospital ticagrelor

Montalescot G et al. N Engl J Med September 1, 2014 [Epub ahead of print; DOI: 10.1056/NEJMoa1407024]

ATLANTIC: Conclusion

Pre-hospital ticagrelor administration a short time before PCI in patients with ongoing STEMI is **safe** but **does not improve pre-PCI coronary reperfusion**. It may, however, **reduce the risk of post-PCI stent thrombosis**.

Main study characteristics of novel P2Y12 antagonists vs clopidogrel in medically treated ACS

	PLATO substudy	TRILOGY-ACS
Design	Pre-specified substudy of PLATO	Ad hoc double blind randomised trial
N° of patients randomised	5,216	9,326
Type of ACS	STEMI/NSTE-ACS	NSTE-ACS
N° of patients with NSTE-ACS	4,751	9,326
Risk Factors		
Age (Median, IQ range)	65, 57-73	66, 58-74
Women (%)	36.5	39.2
% Hypertension	72.1	82.0
% Current smoking	25.5	20.0
% Diabetes	29.8	38.0
Prior MI	39.6	43.1
Tested		
Loading	Ticagrelor 180mg	Prasugrel 30mg (if<72h and not on clopidogrel)
Maintenance	Ticagrelor 90mg BID	Prasugrel 10mg daily (5mg if weight <60kg or age >75 years).
Comparator		
Loading	Clopidogrel 300 mg	Clopidogrel 300 mg
Maintenance	Clopidogrel 75mg daily	Clopidogrel 75mg daily
Aspirin background	75-100mg daily	<100 mg daily in 33.3%
Follow-up, months, median	9.2	14.8
Crossover to PCI (%)	40.0	7.9

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. BMJ 2011;342:d3527.

Prasugrel versus clopidogrel for acute coronary syndromes without revascularization. N Engl J Med 2012;367:1297-309

Main study outcomes of novel P2Y12 antagonists vs clopidogrel in medically treated ACS

	PLATO substudy	TRILOGY-ACS
Primary endpoint	CV death, MI and stroke (all patients randomised)	CV death, MI and stroke in patients <75 years
HR (95% CI)	0.85 (0.73 to 1.00)	0.91 (0.78-1.05)
p	0.045	0.21
CV death, MI and stroke (all patients randomised)		
HR (95% CI)	0.85 (0.73 to 1.00)	0.96 (0.86-1.07)
p	0.045	0.45
All cause death		
HR (95% CI)	0.75 (0.61 to 0.93)	0.94 (0.82-1.08)
p	0.010	0.40

TRITON (Prasugrel):

- Pacientes entraban en el estudio después de conocer la anatomía coronaria.
- Todos los pacientes fueron mayoritariamente a ICP. No se consideraron otras estrategias de tratamiento: manejo médico 1,1% o CABG 3,2%.
- No se permitió el pre-tratamiento con Clopidogrel.
- DC de Clopidogrel: 300mg

PLATO (Ticagrelor):

- Pacientes entraban en el estudio en las fases iniciales. No había necesidad de conocer la anatomía coronaria.
- No sólo ICP, sino también otras estrategias de tratamiento: manejo médico 34% y CABG 10,2%.
- Podían ser pre-tratados con clopidogrel en abierto (46%). En el brazo de Ticagrelor fue cambiado a Ticagrelor en el momento de la randomización.
- DC de Clopidogrel: 300 ó 600 mg (según criterio clínico)

Wallentin L, et al. N Engl J Med 2009;361:1045–1057; Wiviott, S et al. N Engl J Med 2007;357:2001-15

COMPARACIÓN DE ESTUDIOS CLÍNICOS DE LOS NUEVOS ANTIAGREGANTES PLAQUETARIOS.

Parámetro			
Características del estudio	**CURRENT OASIS 7 (12)**	**TRITON TIMI 38 (13)**	**PLATO (14)**
Criterios de inclusión	Síntomas compatibles con SCA (con o sin elevación del ST) y evidencia electrocardiográfica de isquemia o aumento de los biomarcadores, programados para PCI en < 72 horas.	SCA con o sin elevación del ST programados para PCI	SCA con o sin elevación del ST, con inicio de los síntomas < 24 horas.
Grupos de tratamiento	Clopidogrel 600 mg en día 1, seguido de 150 mg /día en días 2-7, luego 75 mg/día; ASA 300 mg en día 1, seguido 300-325 mg/día	Prasugrel (dosis de carga 60 mg, luego 10 mg/día)	Ticagrelor (dosis de carga 180 mg, luego 90 mg/BID)
Grupo control	Clopidogrel 300 mg día 1, luego 75 mg día ASA 300 mg en día 1, seguido 75-100 mg/día	Clopidogrel (dosis de carga 300 mg, luego 75 mg/día)	Clopidogrel (dosis de carga 300-600 mg, luego 75 mg/día)
Diseño del estudio	Estudio 2x2 factorial, aleatorizado, doble ciego	Aleatorizado, doble ciego	Multicéntrico, aleatorizado, doble ciego
Tamaño muestra	25.086	13.608	18.624
Características de base de los pacientes			
Diagnóstico	SCA con o sin elevación del ST	SCA con o sin elevación del ST	SCA con o sin elevación del ST
SCA sin elevación ST	63%	74%	59%
SCA con elevación ST	37%	26%	38%
Edad media (años)	61,2	61	62
Desenlaces			
Muerte cardiovascular, infarto del miocardio o ACV	Clopidogrel dosis altas 3,9% vs. clopidogrel dosis bajas 4,5% (p = 0,039)	Prasugrel 9,9% vs. clopidogrel 12,1% (p = < 0,001)	Ticagrelor 9.8% vs. clopidogrel 11,7% (p = 0,001)
Muerte cardiovascular	Clopidogrel dosis altas 1,9% vs. clopidogrel dosis bajas 1,9% (p = 0,71)	Prasugrel 2,1% vs. clopidogrel 2,4% (p = < 0,31)	Ticagrelor 4,0% vs. clopidogrel 6,9% (p = 0,001)
Infarto del miocardio	Clopidogrel dosis altas 2,0% vs. clopidogrel dosis bajas 2,6% (p = 0,018)	Prasugrel 7,3% vs. clopidogrel 9,5% (p = < 0,001)	Ticagrelor 5,8% vs. clopidogrel 6,9% (p = 0,005)
ACV	Clopidogrel dosis altas 0,4% vs. clopidogrel dosis bajas 0,4% (p = 0,56)	Prasugrel 1,0% vs. clopidogrel 1,0% (p = < 0,93)	Ticagrelor 1,5% vs. clopidogrel 1,3% (p = 0,22)
Trombosis del stent	Clopidogrel dosis altas 0,7% vs. clopidogrel dosis bajas 1,3% (p = 0,0001)	Prasugrel 1.1% vs. clopidogrel 2,4% (p = < 0,001)	Ticagrelor 1,3% vs. clopidogrel 1,9% (p = 0,009)
Sangrado mayor	Clopidogrel dosis altas 1,6% vs. clopidogrel dosis bajas 1,1% (p = 0,009)	Prasugrel 2,4% vs. clopidogrel 1,8% (p = < 0,003)	Ticagrelor 7,9% vs. clopidogrel 7,7% (p = 0,57)

ACV: accidente cerebrovascular; BID: dos veces al día; PCI: intervención coronaria percutánea, SCA: síndrome coronario agudo.

Guías de Práctica Clínica
Contenidos

- **Guías Americanas AHA:**
  - 2011 ACCF/AHA/SCAI Guidelines for PCI
  - 2011 ACCF/AHA Guidelines for CABG
  - 2012 ACCP Antithrombotic Therapy Guidelines
  - 2012 ACCF/AHA Guidelines for UA/NSTEMI
  - 2013 ACCF/AHA Guidelines for STEMI
  - 2014 ACC/AHA Guidelines NSTE-ASC

- **Guías Europeas ESC:**
  - 2010 ESC Myocardial Revascularization Guidelines
  - 2011 ESC NSTE-ACS Guidelines
  - 2012 ESC STEMI Guidelines
  - 2014 ESC Myocardial Revascularisation

2014 AHA/ACC NSTE-ASC GUIDELINE

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Ezra A. Amsterdam, Nanette K. Wenger, Ralph G. Brindis, Donald E. Casey, Jr., Theodore G. Ganiats, David R. Holmes, Jr., Allan S. Jaffe, Hani Jneid, Rosemary F. Kelly, Michael C. Kontos, Glenn N. Levine, Philip R. Liebson, Debabrata Mukherjee, Eric D. Peterson, Marc S. Sabatine, Richard W. Smalling and Susan J. Zieman

Circulation. published online September 23, 2014;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

2014 AHA/ACC NSTE-ASC GUIDELINE

4.3. Initial Antiplatelet/Anticoagulant Therapy in Patients With Definite or Likely NSTE-ACS

4.3.1. Initial Oral and Intravenous Antiplatelet Therapy in Patients With Definite or Likely NSTE-ACS Treated With an Initial Invasive or Ischemia-Guided Strategy: Recommendations

See Table 7 for a summary of recommendations from this section and Online Data Supplement 15 for additional information on initial oral and intravenous antiplatelet therapy in patients with definite or likely NSTE-ACS treated with an early invasive or an ischemia-guided strategy.

Class I[‡]

1. **Non–enteric-coated, chewable aspirin (162 mg to 325 mg) should be given to *all* patients with NSTE-ACS without contraindications as soon as possible after presentation, and a maintenance dose of aspirin (81 mg/d to 162 mg/d) should be continued indefinitely (288-290). *(Level of Evidence: A)***
2. **In patients with NSTE-ACS who are unable to take aspirin because of hypersensitivity or major gastrointestinal intolerance, a loading dose of clopidogrel followed by a daily maintenance dose should be administered (291). *(Level of Evidence: B)***
3. **A $P2Y_{12}$ inhibitor (either clopidogrel or ticagrelor) in addition to aspirin should be administered for up to 12 months to all patients with NSTE-ACS without contraindications who are treated with either an early invasive[§] or ischemia-guided strategy. Options include:**
   - **Clopidogrel: 300-mg or 600-mg loading dose, then 75 mg daily (289, 292) *(Level of Evidence: B)***
   - **Ticagrelor[‖]: 180-mg loading dose, then 90 mg twice daily (293, 294) *(Level of Evidence: B)***

Amsterdam EA et al., *Circulation. 2014;000:000–000*

2014 AHA/ACC NSTE-ASC GUIDELINE

4.3. Initial Antiplatelet/Anticoagulant Therapy in Patients With Definite or Likely NSTE-ACS

4.3.1. Initial Oral and Intravenous Antiplatelet Therapy in Patients With Definite or Likely NSTE-ACS Treated With an Initial Invasive or Ischemia-Guided Strategy: Recommendations

See Table 7 for a summary of recommendations from this section and Online Data Supplement 15 for additional information on initial oral and intravenous antiplatelet therapy in patients with definite or likely NSTE-ACS treated with an early invasive or an ischemia-guided strategy (http://jaccjacc.cardiosource.com/acc_documents/2014_NSTE-ACS_Data_Supplement_Tables.pdf).

Class IIa

1. **It is reasonable to use ticagrelor in preference to clopidogrel for $P2Y_{12}$ treatment in patients with NSTE-ACS who undergo an early invasive or ischemia-guided strategy (293, 294). *(Level of Evidence: B)***

Class IIb

1. **In patients with NSTE-ACS treated with an early invasive strategy and dual antiplatelet therapy (DAPT) with intermediate/high-risk features (e.g., positive troponin), a GP IIb/IIIa inhibitor may be considered as part of initial antiplatelet therapy. Preferred options are eptifibatide or tirofiban (43, 94, 295). (*Level of Evidence: B*)**

2014 AHA/ACC NSTE-ASC GUIDELINE

5.1.2. PCI—Antiplatelet and Anticoagulant Therapy

5.1.2.1. Oral and Intravenous Antiplatelet Agents: Recommendations

Class I

1. **Patients already taking daily aspirin before PCI should take 81 mg to 325 mg non–enteric-coated aspirin before PCI (26, 368-370). *(Level of Evidence: B)***
2. **Patients not on aspirin therapy should be given non–enteric-coated aspirin 325 mg as soon as possible before PCI (26, 368-370). *(Level of Evidence: B)***
3. **After PCI, aspirin should be continued indefinitely at a dose of 81 mg to 325 mg daily (27, 288, 371). *(Level of Evidence: B)***
4. **A loading dose of a $P2Y_{12}$ receptor inhibitor should be given before the procedure in patients undergoing PCI with stenting (26, 293, 302, 331, 372-375). *(Level of Evidence: A)* Options include:**
    a. **Clopidogrel: 600 mg (331, 372-374, 376-378) *(Level of Evidence: B)* or**
    b. **Prasugrel[#]: 60 mg (302) *(Level of Evidence: B)* or**
    c. **Ticagrelor[‖]: 180 mg (293) *(Level of Evidence: B)***
5. **In patients with NSTE-ACS and high-risk features (e.g., elevated troponin) not adequately pretreated with clopidogrel or ticagrelor, it is useful to administer a GP IIb/IIIa inhibitor (abciximab, double-bolus eptifibatide, or high-dose bolus tirofiban) at the time of PCI (379-382). *(Level of Evidence: A)***
6. **In patients receiving a stent (bare-metal stent or drug-eluting stent [DES]) during PCI for NSTE-ACS, $P2Y_{12}$ inhibitor therapy should be given for at least 12 months (330). Options include:**
    a. **Clopidogrel: 75 mg daily (296, 331) *(Level of Evidence: B)* or**
    b. **Prasugrel[#]: 10 mg daily (302) *(Level of Evidence: B)* or**
    c. **Ticagrelor[‖]: 90 mg twice daily (293) *(Level of Evidence: B)***

Amsterdam EA et al., *Circulation. 2014;000:000–000*

2014 AHA/ACC NSTE-ASC GUIDELINE

5.1.2. PCI—Antiplatelet and Anticoagulant Therapy

5.1.2.1. Oral and Intravenous Antiplatelet Agents: Recommendations

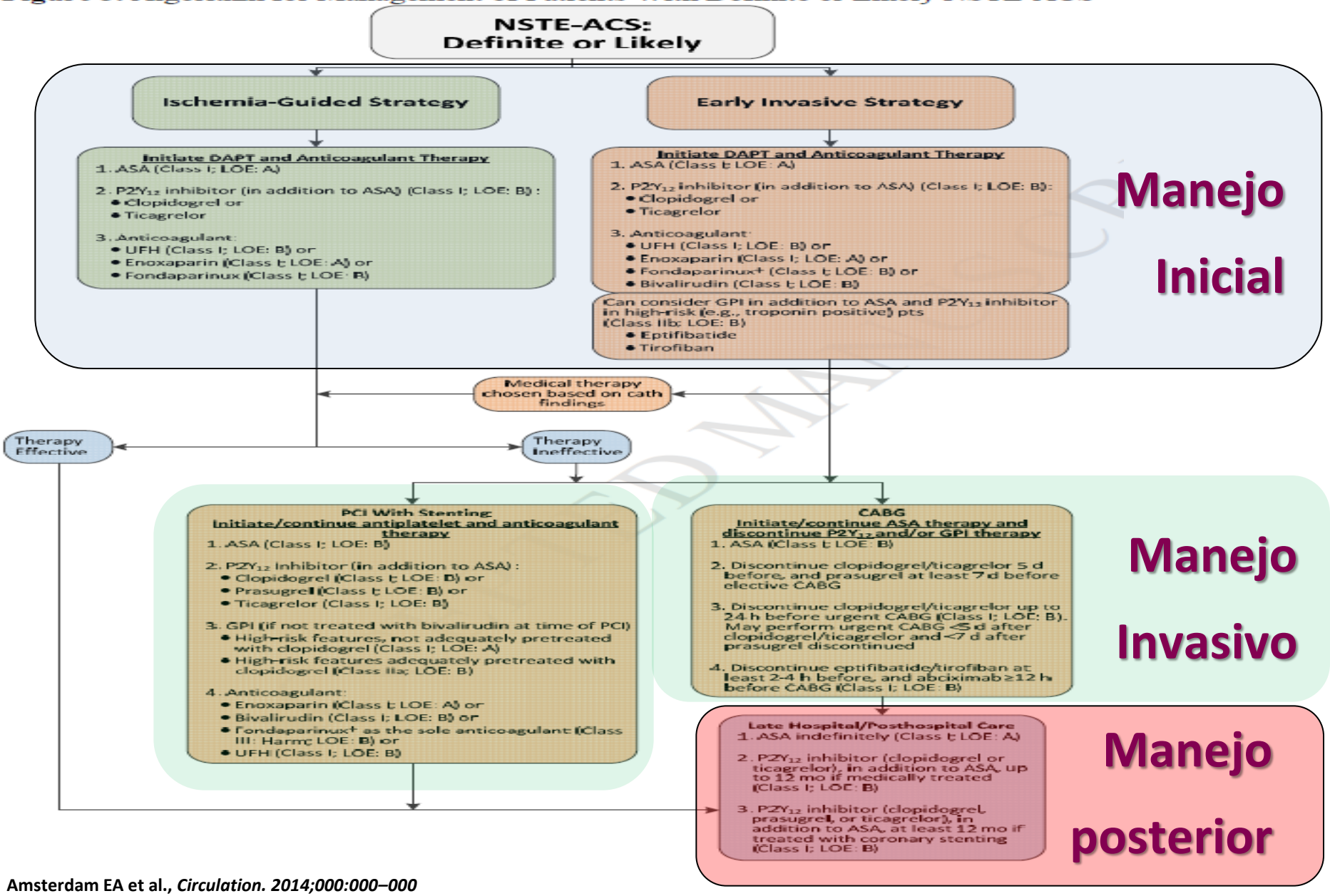
Class IIa

1. **It is reasonable to choose ticagrelor over clopidogrel for $P2Y_{12}$ inhibition treatment in patients with NSTE-ACS treated with an early invasive strategy and/or coronary stenting (293, 294). *(Level of Evidence: B)***
2. **It is reasonable to choose prasugrel over clopidogrel for $P2Y_{12}$ treatment in patients with NSTE-ACS who undergo PCI who are not at high risk of bleeding complications (302, 303). *(Level of Evidence: B)***
3. **In patients with NSTE-ACS and high-risk features (e.g., elevated troponin) treated with UFH and adequately pretreated with clopidogrel, it is reasonable to administer a GP IIb/IIIa inhibitor (abciximab, double-bolus eptifibatide, or high-bolus dose tirofiban) at the time of PCI (195, 383, 384). (*Level of Evidence: B*)**
4. **After PCI, it is reasonable to use 81 mg per day of aspirin in preference to higher maintenance doses (331, 368, 385-388). *(Level of Evidence: B)***

[#]Patients should receive a loading dose of prasugrel, provided that they were not pretreated with another $P2Y_{12}$ receptor inhibitor.
[‖]The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily (290).

2014 AHA/ACC NSTE-ASC GUIDELINE

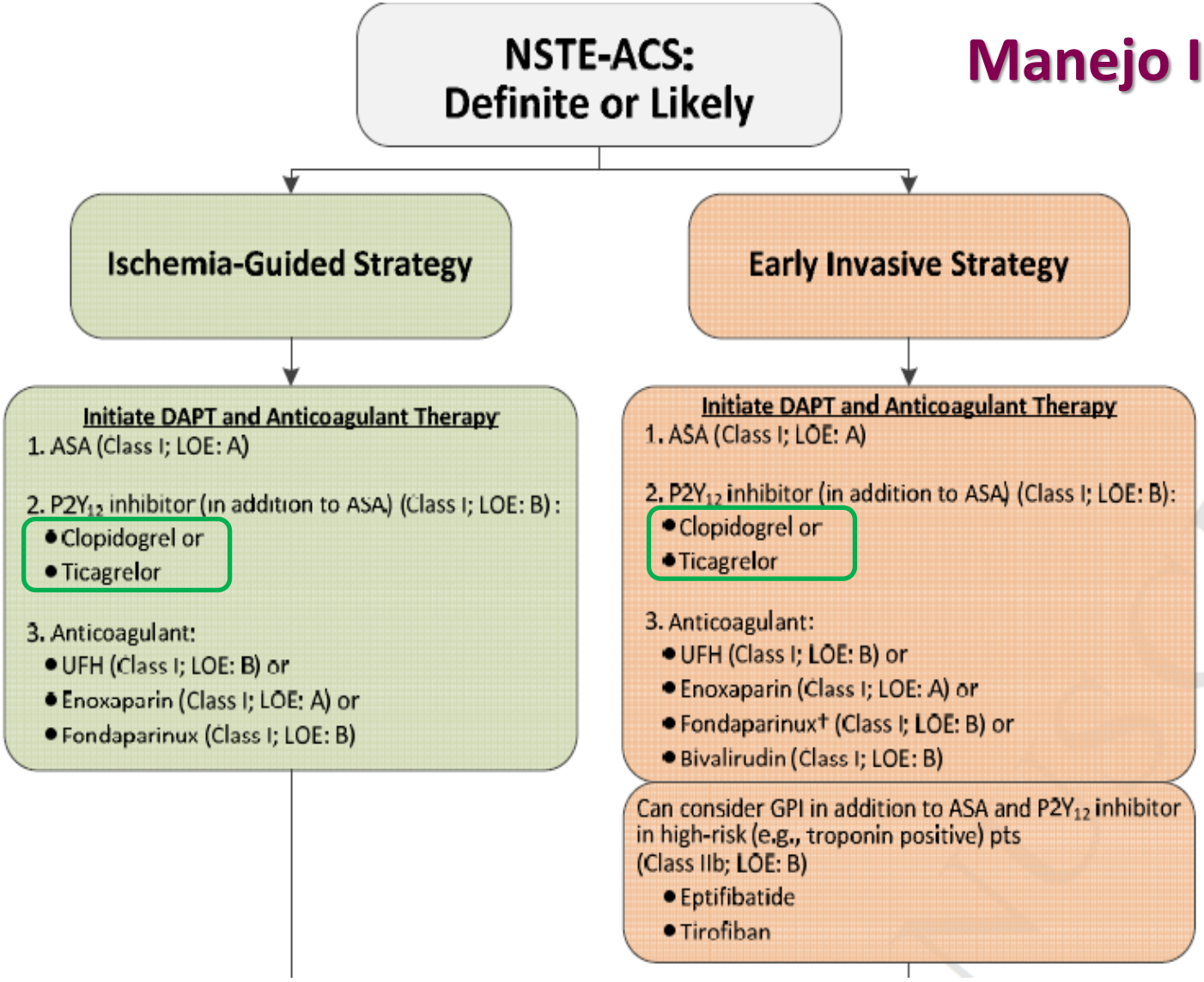
Figure 3. Algorithm for Management of Patients With Definite or Likely NSTE-ACS*



Amsterdam EA et al., *Circulation. 2014;000:000–000*

2014 AHA/ACC NSTE-ASC GUIDELINE

Manejo Inicial



Amsterdam EA et al., *Circulation. 2014;000:000–000*

2014 AHA/ACC NSTE-ASC GUIDELINE

PCI With Stenting

Initiate/continue antiplatelet and anticoagulant therapy

1. ASA (Class I; LOE: B)

2. $P2Y_{12}$ Inhibitor (in addition to ASA):
   - Clopidogrel (Class I; LOE: B) or
   - Prasugrel (Class I; LOE: B) or
   - Ticagrelor (Class I; LOE: B)

3. GPI (if not treated with bivalirudin at time of PCI)
   - High-risk features, not adequately pretreated with clopidogrel (Class I; LOE: A)
   - High-risk features adequately pretreated with clopidogrel (Class IIa; LOE: B)

4. Anticoagulant:
   - Enoxaparin (Class I; LOE: A) or
   - Bivalirudin (Class I; LOE: B) or
   - Fondaparinux† as the sole anticoagulant (Class III: Harm; LOE: B) or
   - UFH (Class I; LOE: B)

CABG

Initiate/continue ASA therapy and discontinue $P2Y_{12}$ and/or GPI therapy

1. ASA (Class I; LOE: B)

2. Discontinue clopidogrel/ticagrelor 5 d before, and prasugrel at least 7 d before elective CABG

3. Discontinue clopidogrel/ticagrelor up to 24 h before urgent CABG (Class I; LOE: B). May perform urgent CABG <5 d after clopidogrel/ticagrelor and <7 d after prasugrel discontinued

4. Discontinue eptifibatide/tirofiban at least 2-4 h before, and abciximab ≥12 h before CABG (Class I; LOE: B)

Manejo Invasivo

Amsterdam EA et al., *Circulation. 2014;000:000–000*

2011 ESC NSTE-ACS Guidelines

European Heart Journal (2011) **32**, 2999–3054
doi:10.1093/eurheartj/ehr236

ESC GUIDELINES

ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

Hamm CW, et al. Eur Heart.J (2011) 32: 2999-3054

ESC SCASEST 2011: Estratificación del riesgo

Recomendaciones para el diagnóstico y la estratificación del riesgo

Recomendaciones	Clase[a]	Nivel[b]	Ref[c]
En pacientes con sospecha de SCASEST, el diagnóstico y la estratificación del riesgo isquémico/hemorrágico a corto plazo se debe basar en la combinación de la historia clínica, síntomas, hallazgos físicos, ECG (monitorización del segmento ST continua o repetida) y biomarcadores	I	A	16, 18, 27, 30, 56-58
Se recomienda el uso de clasificaciones de riesgo establecidas para el pronóstico y el sangrado (p. ej., GRACE, CRUSADE)	I	B	50, 83
y antes del alta hospitalaria			
Se recomiendan otras derivaciones para el ECG (V_{3R}, V_{4R}, V_7-V_9) cuando las derivaciones habituales no son concluyentes	I	C	18
Se debe tomar una muestra de sangre rápidamente para la determinación de troponinas (troponina cardiaca T o I). Los resultados deben estar disponibles en un plazo de 60 min. La prueba debe repetirse a las 6-9 h de la evaluación inicial si la primera determinación no es concluyente. Es aconsejable repetir la determinación después de 12-24 h si el estado clínico sigue indicando SCA	I	A	27, 30
Se recomienda un protocolo rápido de exclusión (0 y 3 h) cuando se disponga de pruebas de alta sensibilidad para determinación de troponinas	I	B	20, 21, 23
Se recomienda un ecocardiograma a todos los pacientes para evaluar la función ventricular izquierda general y regional y para descartar o confirmar un diagnóstico diferencial	I	C	–
La angiografía coronaria está indicada en pacientes en los que se tenga que determinar la extensión de la enfermedad coronaria o de la lesión causal (véase la sección 5.4)	I	C	–
La angiografía coronaria por TC se debe considerar como una alternativa a la angiografía invasiva para excluir un SCA cuando hay una probabilidad baja a intermedia de enfermedad coronaria y cuando las troponinas y el ECG no sean concluyentes	IIa	B	37-41
En pacientes sin dolor recurrente, con ECG normal, troponinas negativas y clasificación de riesgo baja, se recomienda una prueba de estrés no invasiva para inducción de isquemia antes de decidir sobre la estrategia invasiva	I	A	35, 54, 55

CRUSADE: Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines; ECG: electrocardiograma; GRACE: Global Registry of Acute Coronary Events; SCA: síndrome coronario agudo; SCASEST: síndrome coronario agudo sin elevación del segmento ST; TC: tomografía computarizada.

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

ESC SCASEST 2011: Momento de la Revascularización

Recomendaciones para la evaluación invasiva y la revascularización

Recomendaciones	Clase[a]	Nivel[b]	Ref.[c]
Está indicada una estrategia invasiva (en las primeras 72 h tras la presentación) para pacientes con: • Al menos un criterio de alto riesgo (tabla 9) • Síntomas recurrentes	I	A	148
Está indicada la angiografía coronaria urgente (< 2 h) para pacientes con riesgo isquémico muy alto (angina refractaria, insuficiencia cardiaca	I	C	148, 209
Está recomendada una estrategia invasiva precoz (< 24 h) para pacientes con una clasificación de riesgo GRACE > 140 o al menos un criterio principal de alto riesgo	**I**	**A**	**212, 215**
de la enfermedad, es decir, distribución y características angiográficas de la lesión (p. ej., clasificación SYNTAX), de acuerdo con el protocolo local del «Equipo del Corazón»			
Como no hay problemas de seguridad relacionados con el uso de *stents* farmacoactivos en los SCA, la indicación de estos se debe basar en las características basales individuales, la anatomía coronaria y el riesgo de hemorragia	I	A	225, 226
No está recomendada la ICP de lesiones no significativas	III	C	–
No está recomendada la evaluación invasiva por sistema de los pacientes de bajo riesgo	III	A	148, 208

CABG: cirugía de revascularización aortocoronaria; GRACE: Global Registry of Acute Coronary Events; ICP: intervención coronaria percutánea; SCA: síndrome coronario agudo; SYNTAX: SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery.
[a]Clase de recomendación.
[b]Nivel de evidencia.
[c]Referencias.

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

2011 ESC NSTE-ACS Guidelines

Antiplatelets Therapy Recommendations

Recommendations	Class [a]	Level [b]
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 $P2Y_{12}$ 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
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 $P2Y_{12}$-inhibitor-naïve patients (especially diabetics) in whom coronary anatomy is known and who are proceeding to PCI unless there is a high risk of life-threatening bleeding or other contraindications.[d]	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
A higher maintenance dose of clopidogrel 150 mg daily should be considered for the first 7 days in patients managed with PCI and without increased risk of bleeding.	IIa	B

Hamm CW, et al. Eur Heart.J (2011) 32: 2999-3054

2011 ESC NSTE-ACS Guidelines

Management strategy (treatments).

Table 13 Checklist of treatments when an ACS diagnosis appears likely

Aspirin	Initial dose of 150–300 mg non-enteric formulation followed by 75–100 mg/day (i.v. administration is acceptable)
$P2Y_{12}$ inhibitor	Loading dose of ticagrelor or clopidogrel[a]
Anticoagulation	Choice between different options depends on strategy: • Fondaparinux 2.5 mg/daily subcutaneously • Enoxaparin 1 mg/kg twice daily subcutaneously • UFH i.v. bolus 60–70 IU/kg (maximum 5000 IU) followed by infusion of 12–15 IU/kg/h (maximum 1000 IU/h) titrated to aPTT 1.5–2.5 × control • Bivalirudin is indicated only in patients with a planned invasive strategy
Oral ß-Blocker	If tachycardic or hypertensive without signs of heart failure

aPTT = activated partial thromboplastin time; IU = international units; i.v. = intravenous; UFH = unfractionated heparin.

[a]Prasugrel is not mentioned as it is not approved as medical therapy before invasive strategy, but only after angiography when anatomy is known.

Table 14 Checklist of antithrombotic treatments prior to PCI

Aspirin	Confirm loading dose prior to PCI.
$P2Y_{12}$ inhibitor	Confirm loading dose of ticagrelor or clopidogrel prior to PCI. If $P2Y_{12}$ naïve, consider prasugrel (if <75 years age, >60 kg, no prior stroke or TIA)
Anticoagulation	• Fondaparinux pre-treated: add UFH for PCI • Enoxaparin pre-treated: add if indicated • UFH pre-treated: titrate to ACT >250 s, or switch to bivalirudin (0.1 mg/kg bolus followed by 0.25 mg/kg/h)
GP IIb/IIIa receptor inhibitor	• Consider tirofiban or eptifibatide in patients with high-risk anatomy or troponin elevation • Abciximab only prior to PCI in high-risk patients.

ACT = activated clotting time; GP, glycoprotein; PCI = percutaneous coronary intervention; TIA = transient ischaemic attack; UFH = unfractionated heparin.

Hamm CW, et al. Eur Heart.J (2011) 32: 2999-3054

2011 ESC NSTE-ACS Guidelines

Antiplatelets Therapy for CABG

A higher maintenance dose of clopidogrel 150 mg daily should be considered for the first 7 days in patients managed with PCI and without increased risk of bleeding.	IIa	B
Increasing the maintenance dose of clopidogrel based on platelet function testing is not advised as routine, but may be considered in selected cases.	IIb	B
Genotyping and/or platelet function testing may be considered in selected cases when clopidogrel is used.	IIb	B
In patients pre-treated with $P2Y_{12}$ inhibitors who need to undergo non-emergent major surgery (including CABG), postponing surgery at least for 5 days after cessation of ticagrelor or clopidogrel, and 7 days for prasugrel, if clinically feasible and unless the patient is at high risk of ischaemic events should be considered.	IIa	C
Ticagrelor or clopidogrel should be considered to be (re-) started after CABG surgery as soon as considered safe.	IIa	B
The combination of aspirin with an NSAID (selective COX-2 inhibitors and non-selective NSAID) is not recommended.	III	C

[a]Class of recommendation.
[b]Level of evidence.
[c]References.
[d]Prasugrel is in the 'Guidelines on Revascularization'[148] given a IIa recommendation as the overall indication including clopidogrel-pre-treated patients and/or unknown coronary anatomy. The class I recommendation here refers to the specifically defined subgroup.
CABG = coronary artery bypass graft; COX = cyclo-oxygenase; DAPT = dual (oral) antiplatelet therapy; NSAID = non-steroidal anti-inflammatory drug; PCI = percutaneous coronary intervention.

Según FT Ticagrelor debe suspenderse 7 días antes de una intervención quirúrgica programada.

Hamm CW, et al. Eur Heart.J (2011) 32: 2999-3054

European Heart Journal
doi:10.1093/eurheartj/ehs149

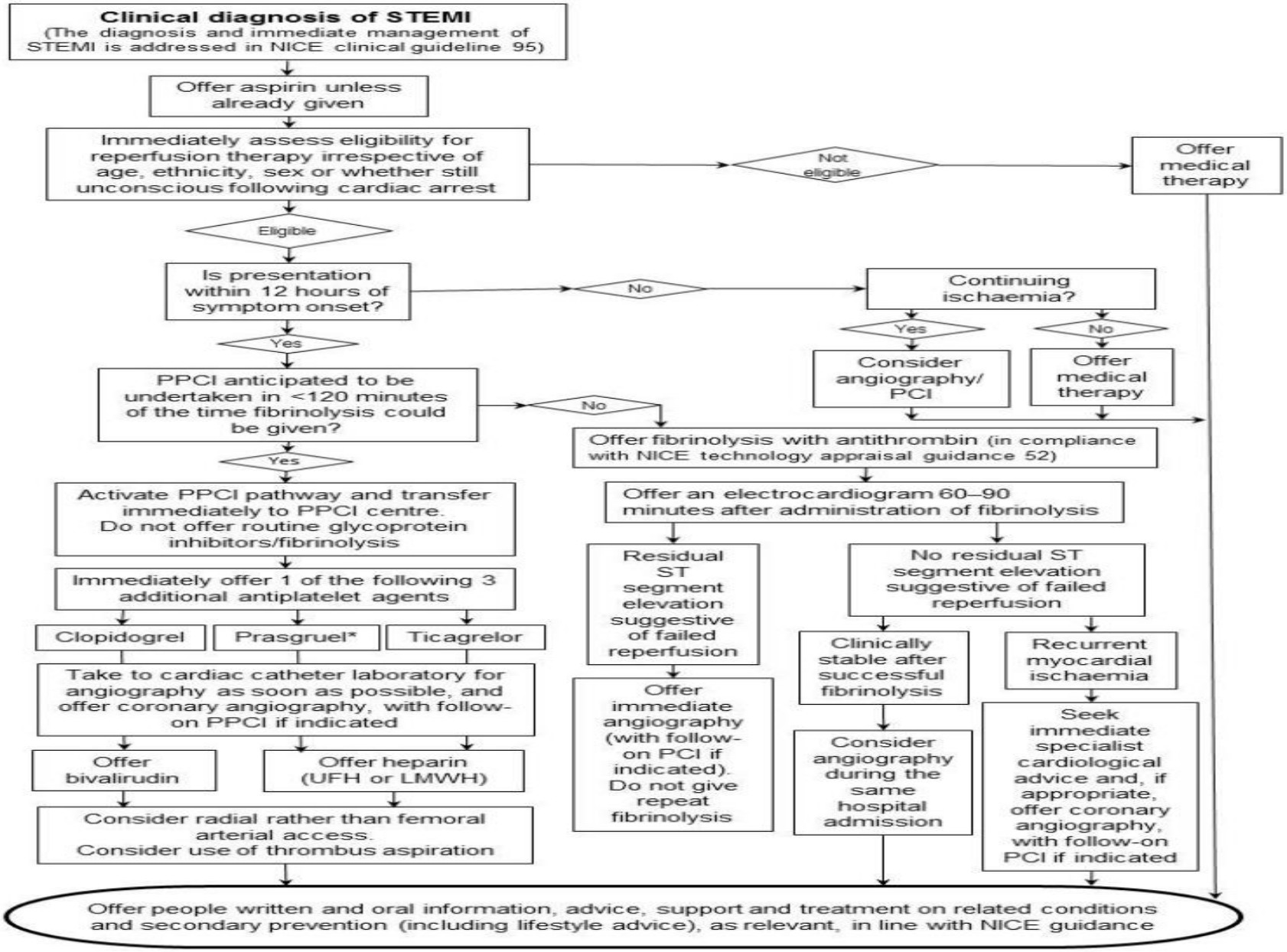
Cost-effectiveness of treating acute coronary syndrome patients with ticagrelor for 12 months: results from the PLATO study

Conclusion Based on clinical and health-economic evidence from the PLATO study, treating ACS patients with ticagrelor for 12 months is associated with a cost per QALY below generally accepted thresholds for cost-effectiveness.
ClinicalTrials.gov Identifier: NCT00391872.

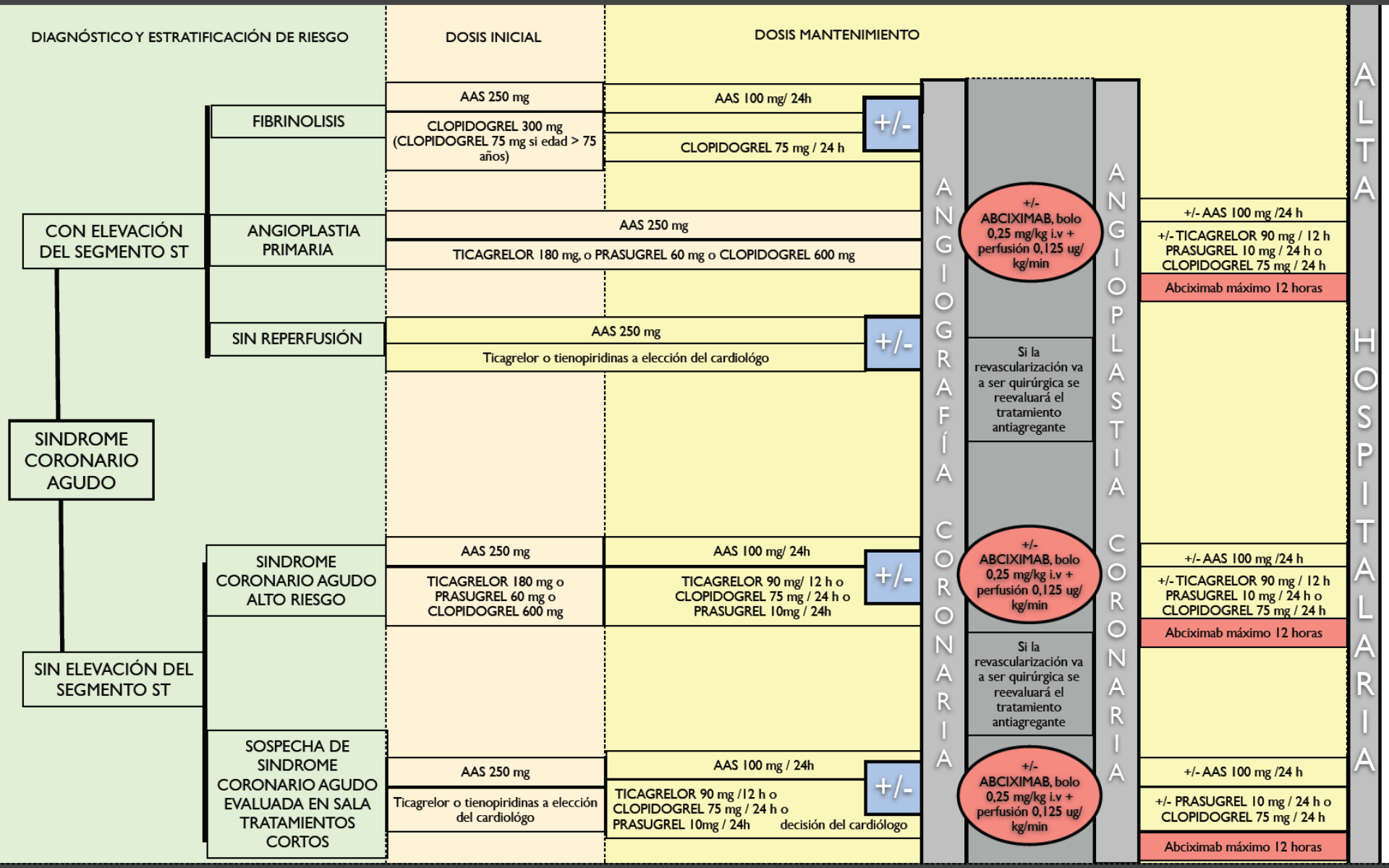
NICE National Institute for Health and Care Excellence

The Committee noted that the incremental cost-effectiveness ratios (ICERs) produced with this analysis were within the range normally considered to be a cost-effective use of NHS resources.	4.12

NICE National Institute for Health and Care Excellence



PROTOCOLO ANTIAGREGACIÓN EN SINDROME CORONARIO AGUDO



TICAGRELOR	Implica tomar dos dosis diarias... valorar cumplimiento terapéutico No usar si disfunción sinusal o bloqueo av	
PRASUGREL	Razones a favor de su uso: - Diabetes - Anatomía coronaria conocida, se cree no quirúrgico a priori - Evento agudo pese a clopidogrel	Razones en contra de su uso: - antecedentes de AIT o ICTUS. - peso < 60 kg y edad > 75 años - > riesgo de sangrado.

- TICAGRELOR/PRASUGREL no han sido evaluados en combinación con anti IIb/IIIa o fibrinolíticos

- SCA en tratamiento previo con clopidogrel: se puede hacer el switch, simplemente suspendiendo clopidogrel e iniciando carga y dosis de mantenimiento habitual de ticagrelor o prasugrel.
- Si ya se ha dado carga de alguno de ellos lo razonable es continuar con el mismo (no mezclar cargas de distintos fármacos)