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SBHCI
2016
In partnership with tct & G2

Mitos e verdades sobre o uso de antiplaquetários na intervenção percutânea.

Panorama dos antiplaquetários na prática médica atual

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2016

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Declaração de conflito de interesse

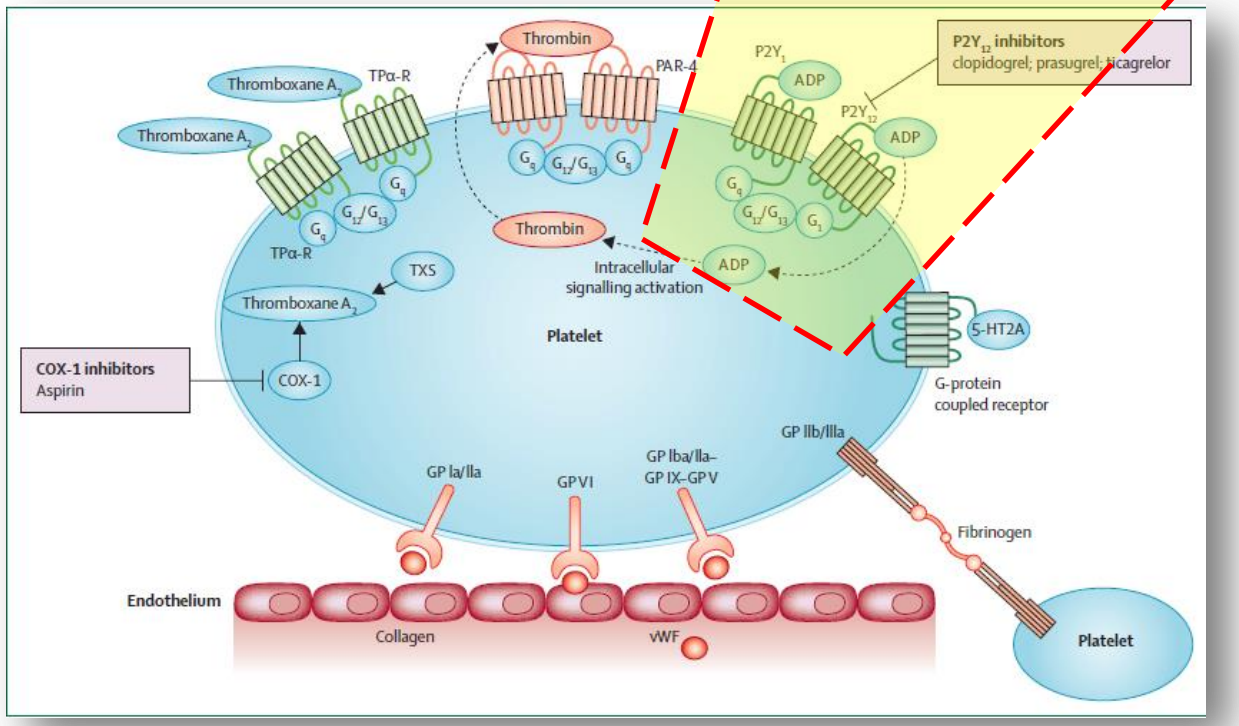
Dr. Roberto Esporcatte
CRM 359874 RJ

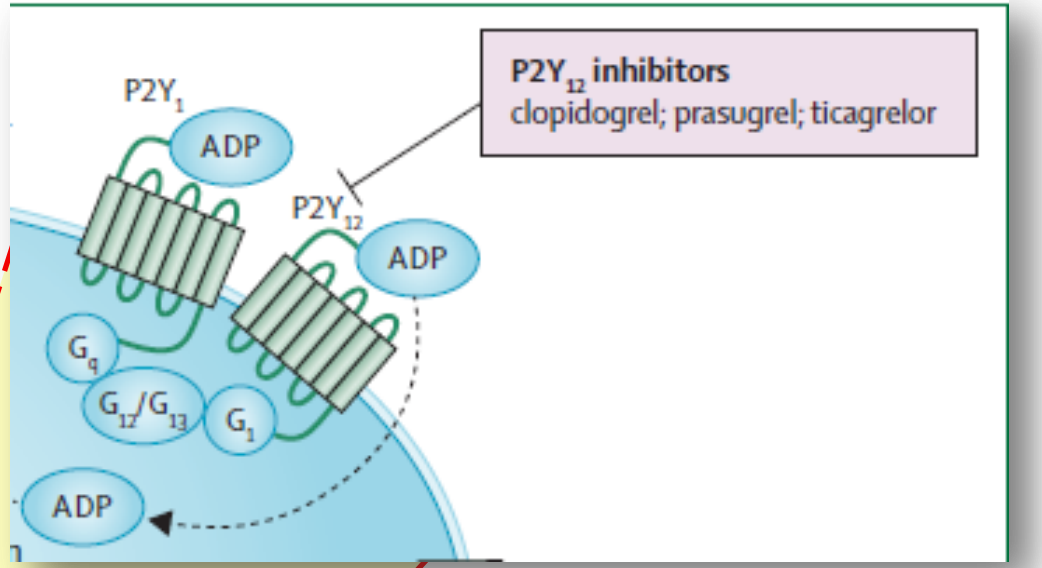
De acordo com a Norma 1595/2000 do Conselho Federal de Medicina e a Resolução RDC 96/2008 da Agência de Vigilância Sanitária declaro que:

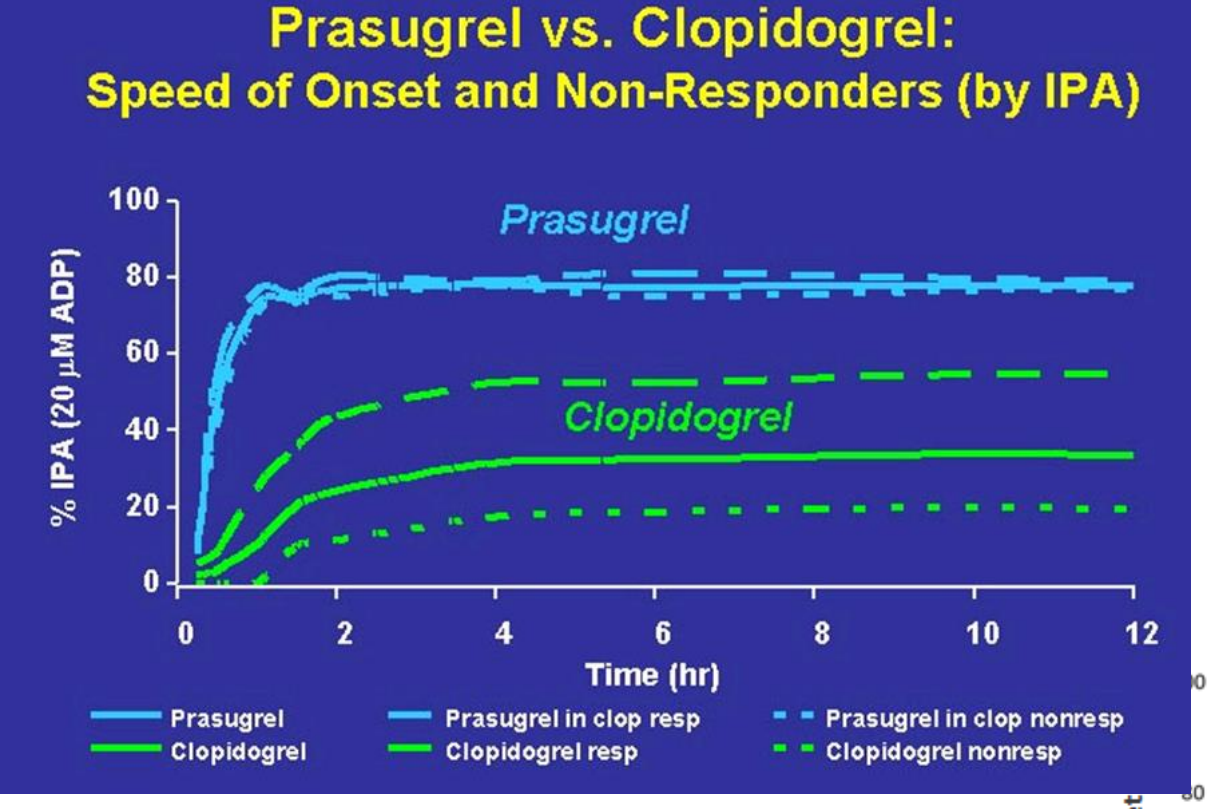
Palestrante/ Moderador:
AstraZeneca, Bayer, Daiichi-Sankyo, Pfizer

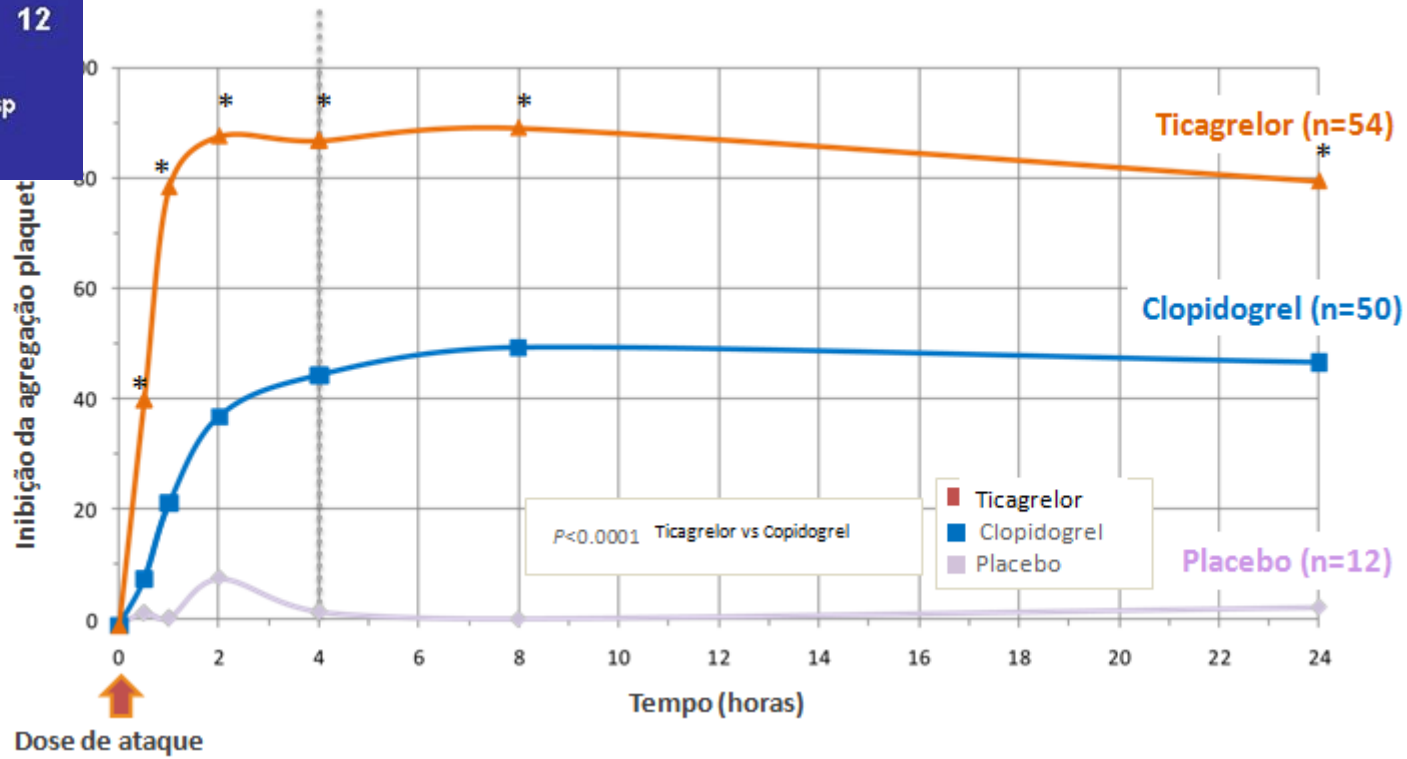
Panorama dos antiplaquetários na prática médica atual

1. Bases Farmacocinéticas: há diferença significativa entre as drogas?
2. Os Grandes Ensaios Clínicos
3. Risco Isquêmico ou Risco Hemorrágico?
4. Análise de Subgrupos:
   - Estratégias de Estratificação
   - Dose de Ataque Precoce vs Angiografia Precoce
5. Recomendações e Otimização Terapêutica


Thrombin
PAR-4
Thromboxane A2
TPα-R
Thromboxane A2
Gq
G12/G13
Gq
TPα-R
Thrombin
TXS
Intracellular
signalling activation
Thromboxane A2
Platelet
COX-1 inhibitors
Aspirin
COX-1
GP Ia/IIa
GPVI
GP Iba/IIa–
GP IX–GPV
Endothelium
Collagen
vWF
P2Y1
ADP
P2Y12
ADP
ADP
P2Y12 inhibitors
clopidogrel; prasugrel; ticagrelor
5-HT2A
G-protein
coupled receptor
GP IIb/IIIa
Fibrinogen
Platelet

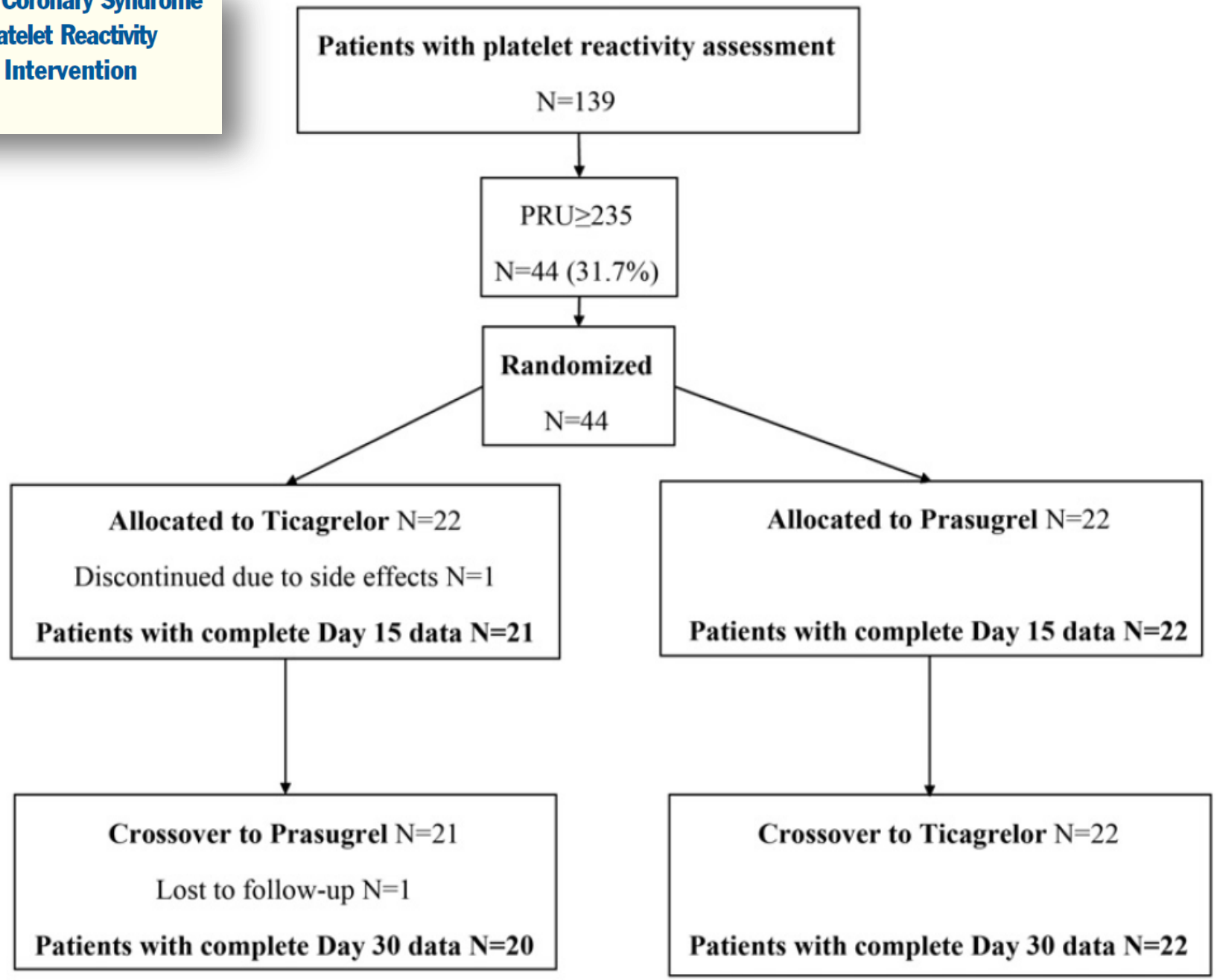

P2Y12 inhibitors
clopidogrel; prasugrel; ticagrelor
P2Y1
ADP
P2Y12
ADP
Gq
G12/G13
G1
ADP


Prasugrel vs. Clopidogrel:
Speed of Onset and Non-Responders (by IPA)
Prasugrel
Clopidogrel
% IPA (20 μM ADP)
100
80
60
40
20
0
0
2
4
6
8
10
12
Time (hr)
Prasugrel
Clopidogrel
Prasugrel in clop resp
Clopidogrel resp
Prasugrel in clop nonresp
Clopidogrel nonresp

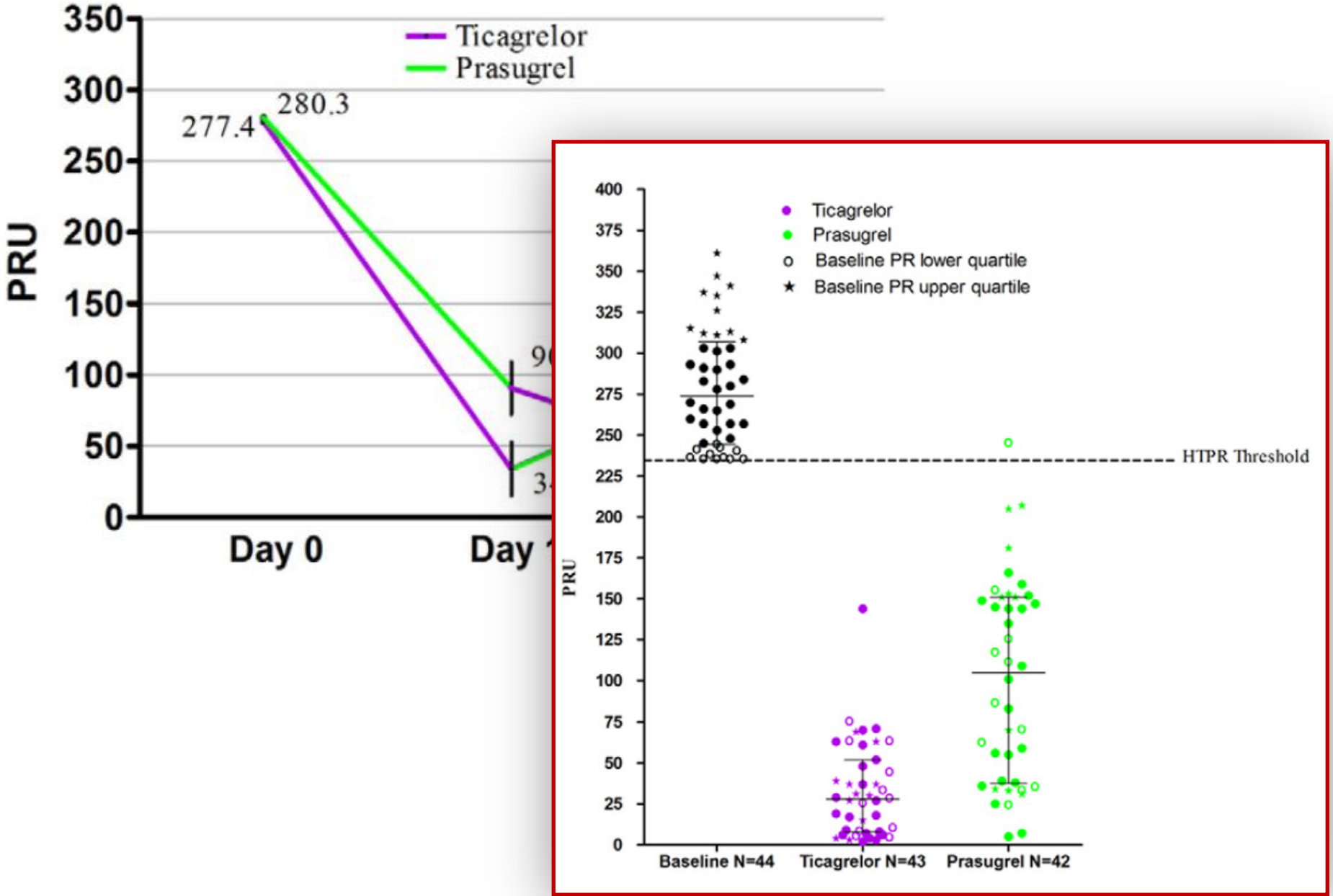

Inibição da agregação plaquet
Ticagrelor (n=54)
Clopidogrel (n=50)
Placebo (n=12)
P<0.0001 Ticagrelor vs Copidogrel
Ticagrelor
Clopidogrel
Placebo
0
20
40
60
0
2
4
6
8
10
12
14
16
18
20
22
24
Tempo (horas)
Dose de ataque

Ticagrelor Versus Prasugrel in Acute Coronary Syndrome Patients With High On-Clopidogrel Platelet Reactivity Following Percutaneous Coronary Intervention

A Pharmacodynamic Study



JACC 2012;60:193



JACC 2012;60:193

PLATO

SCA - SST(risco moderado a alto), IMCST (se IPC primária)
Tratados ou nunca tratados com clopidogrel;
randomizados dentro de 24 horas do evento índice
(N=18.624)

Clopidogrel
Se pré-tratados, sem dose de ataque adicional;
se nunca tratados, dose de ataque padrão 300 mg,
seguida por manutenção de 75 mg uma vez ao dia;
(300 mg adicionais permitidos pré- ICP)

Ticagrelor
dose de ataque de 180 mg, seguida por
manutenção de 90 mg duas vezes ao dia;
(90 mg adicionais pré- ICP)

6–12 meses de tratamento

Desfecho primário: Morte CV + IM + AVC
Desfecho primário de segurança: Sangramento Maior Total

SCA-SST = Síndrome Coronária Aguda sem elevação do segmento ST , IMCST = Infarto do Miocardio com elevação ST
ICP = intervenção coronária percutânea; AAS = ácido acetilsalicílico;
CV = cardiovascular; AIT= ataque isquêmico transitório

NEJM 2009;361(11):1045

TRITON TIMI-38

Desenho do Estudo

SCA (CSST ou AI/SSST) & ICP PLANEJADA
AAS n = 13.600

Duplo-cego

CLOPIDOGREL
300 mg DA/ 75 mg Man.

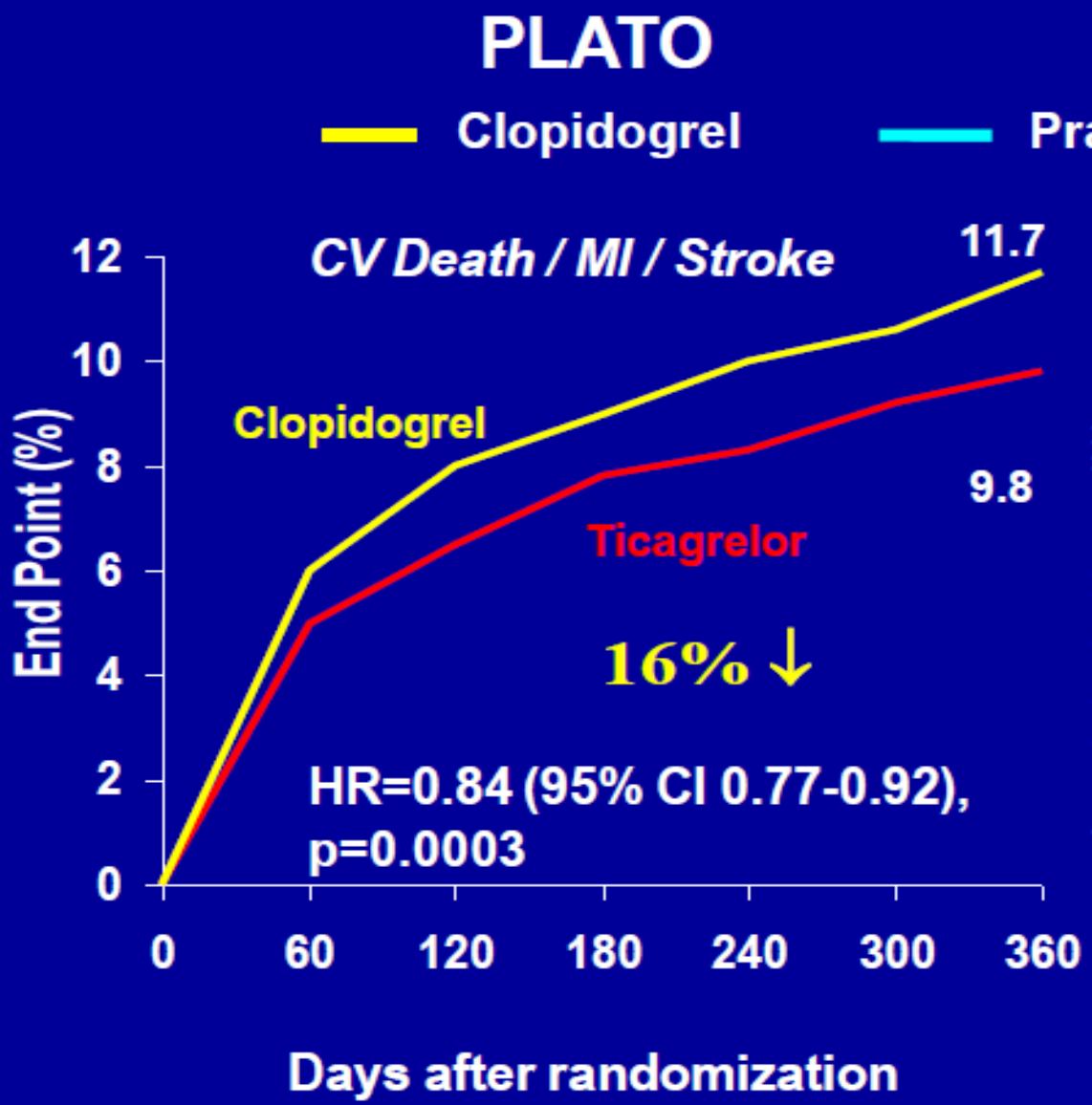
PRASUGREL
60 mg DA/ 10 mg Man

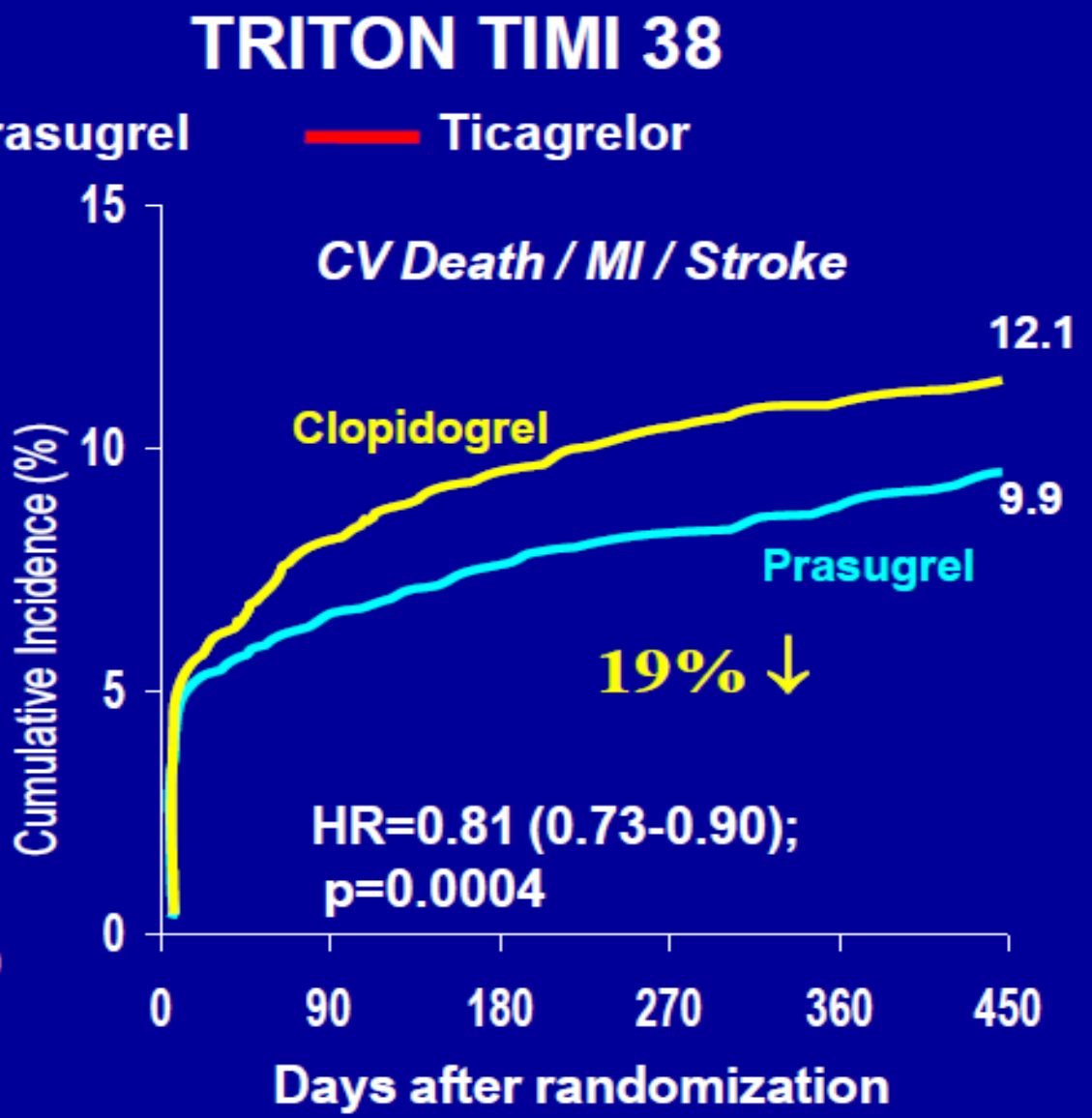
Duração Média Tratamento - 12 meses

1º desfechos: Morte CV , IAM, AVC
2º desfechos: Morte CV , IAM, RVTU
Trombose Stent (ARC definitiva/provável)
Desfechos Segurança:Sang. maioresTIMI, Sang. c/risco de vida
Sub-estudos: Farmacocinéticos, Genomicos

Wiviott SD, Antman EM et al AHJ 2006

Desfecho 1º:Morte CV , IAM, AVC

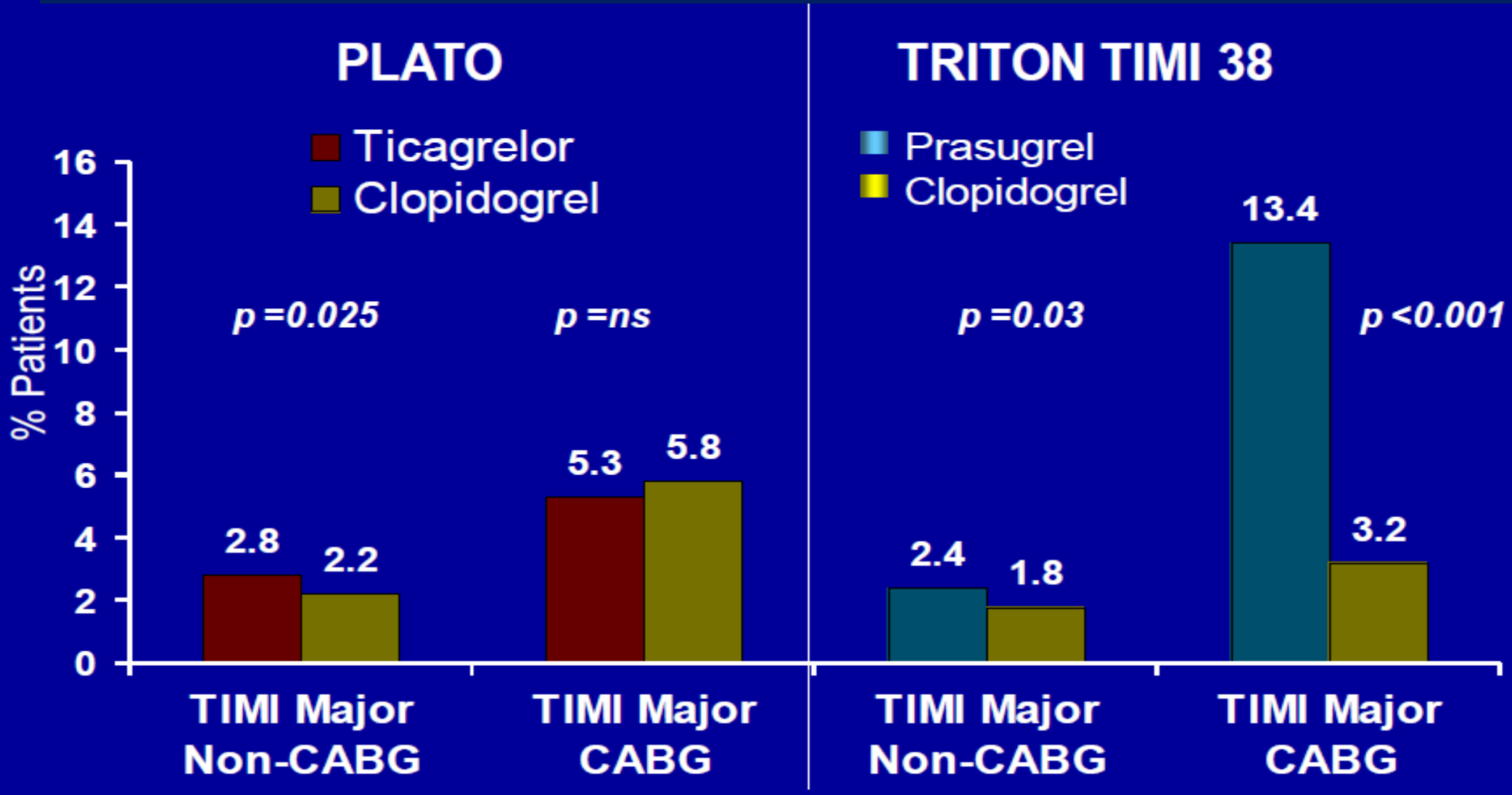




Wallentin et al. N Engl J Med 2009;361:1045-57

Wiviott et al. N Engl J Med 2007;357:2001-2015

Hemorragia Maior TIMI: PLATO & TRITON TIMI 38



Wallentin et al. N Engl J Med 2009;361:1045-57

Wiviott et al. N Engl J Med 2007;357:2001-2015

Clinical evidence for oral antiplatelet therapy in acute coronary syndromes

Stephen D Wiviott, Philippe Gabriel Steg

SCACSST

ALTO RISCO HEMORRÁGICO FIBRINÓLISE OU OUTROS CUIDADOS?

SIM → **CLOPIDOGREL**

NÃO

ATC 1ª Programada

Dose de Ataque Prasugrel ou Ticgrelor, *se rapidamente disponível*

Coronariografia Diagnóstica

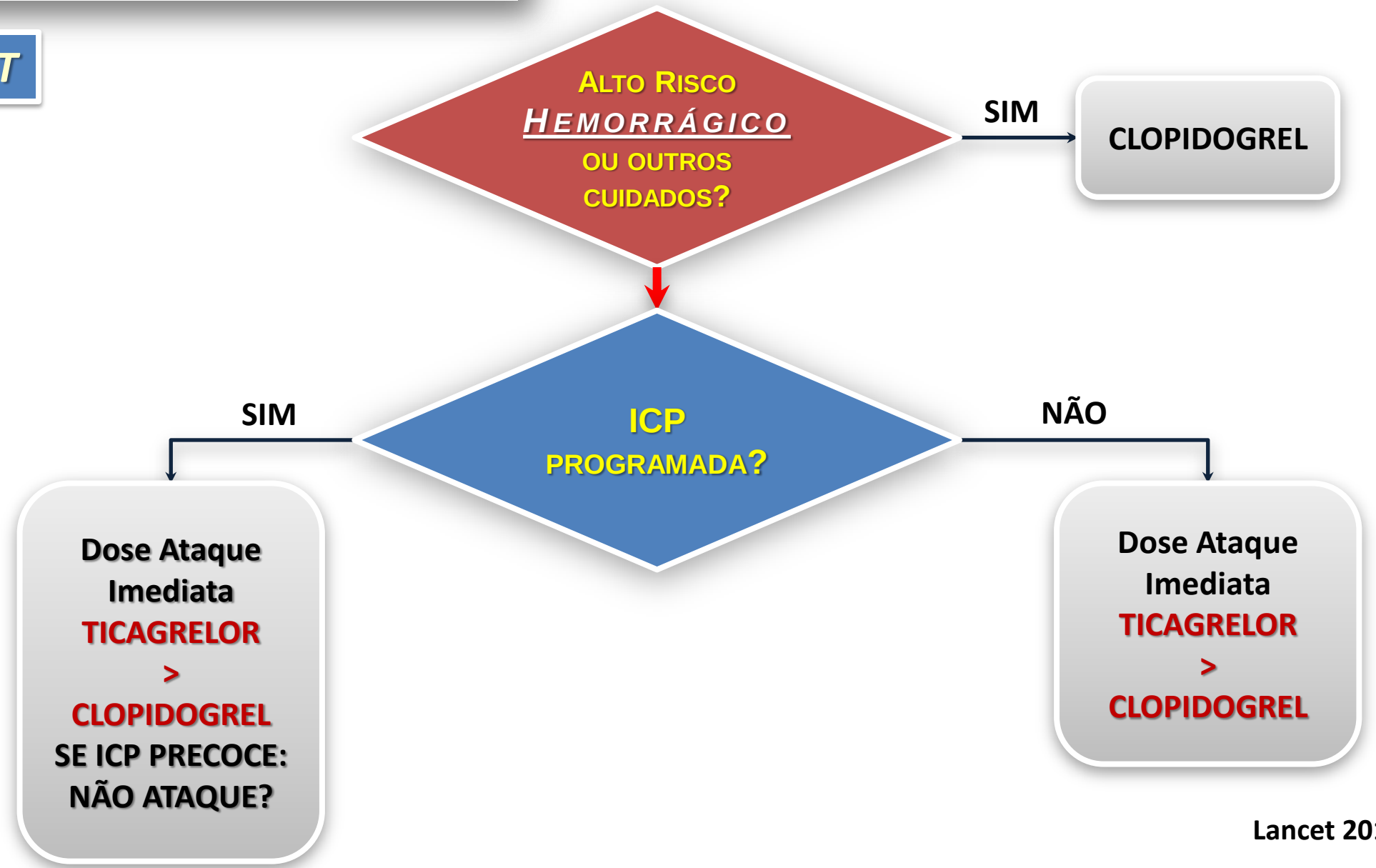
RM Cirúrgica	ATC 1ª	Tratamento Clínico
Interromper $P2Y_{12}$ Avaliar Ticagrelor Pós-Op	Prasugrel ou Ticagrelor	Ticagrelor > Clopidogrel

Lancet 2015; 386: 292-302

Clinical evidence for oral antiplatelet therapy in acute coronary syndromes

Stephen D Wiviott, Philippe Gabriel Steg

SCASSST



Lancet 2015; 386: 292-302

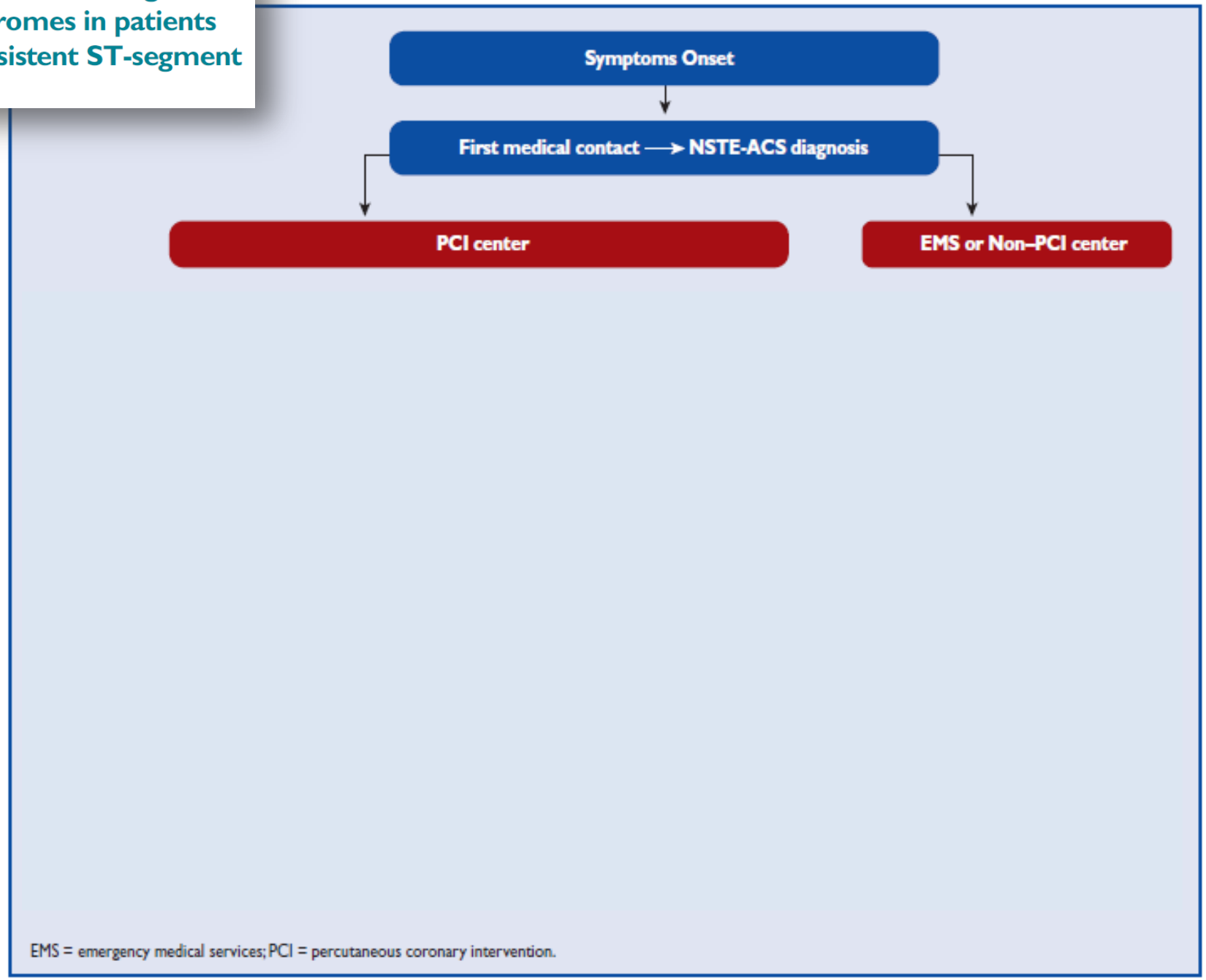
SCAssST: Análise de Subgrupos

Estratificação

Invasiva vs Não-Invasiva

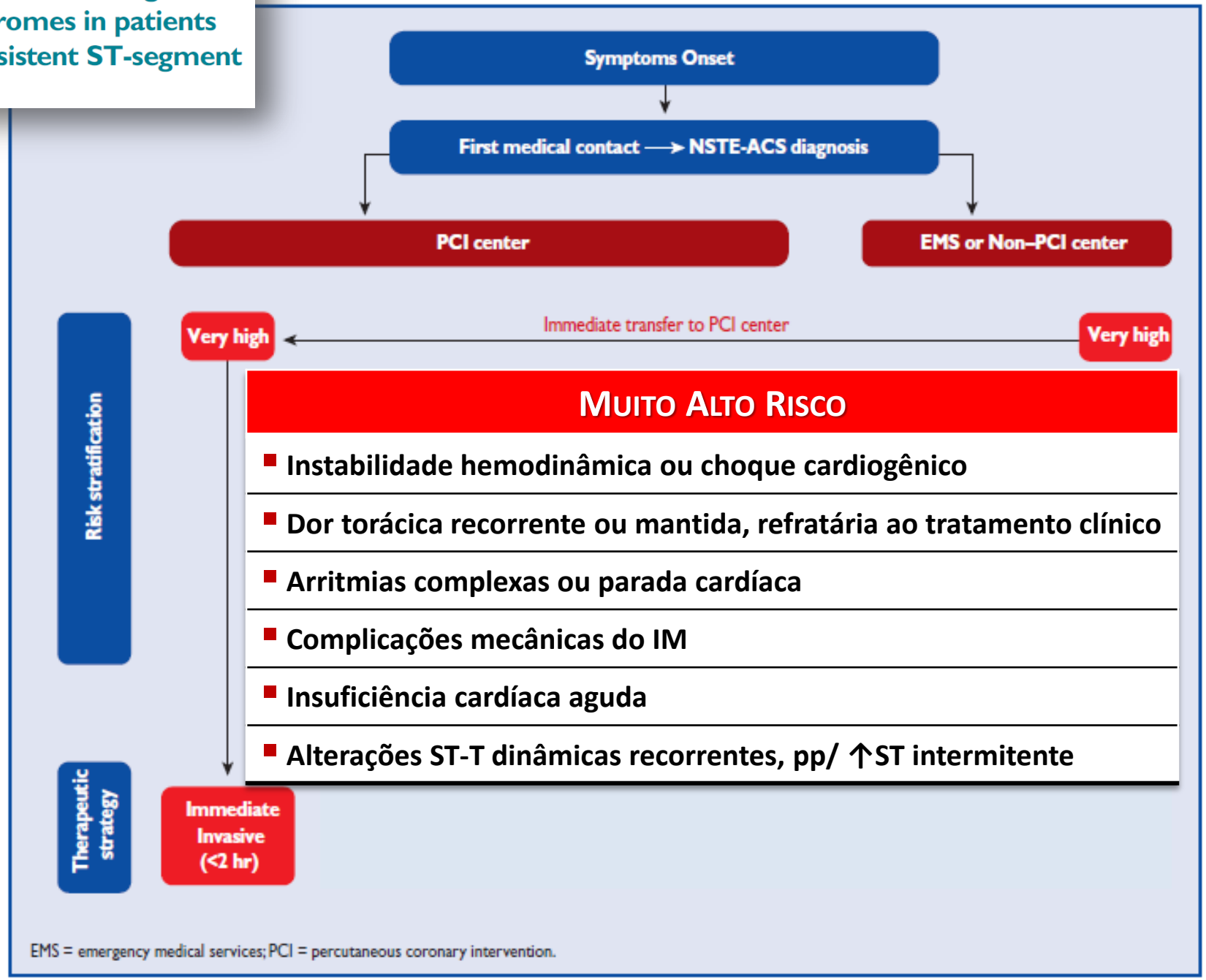
Imediata vs 24 h vs 72 h

2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

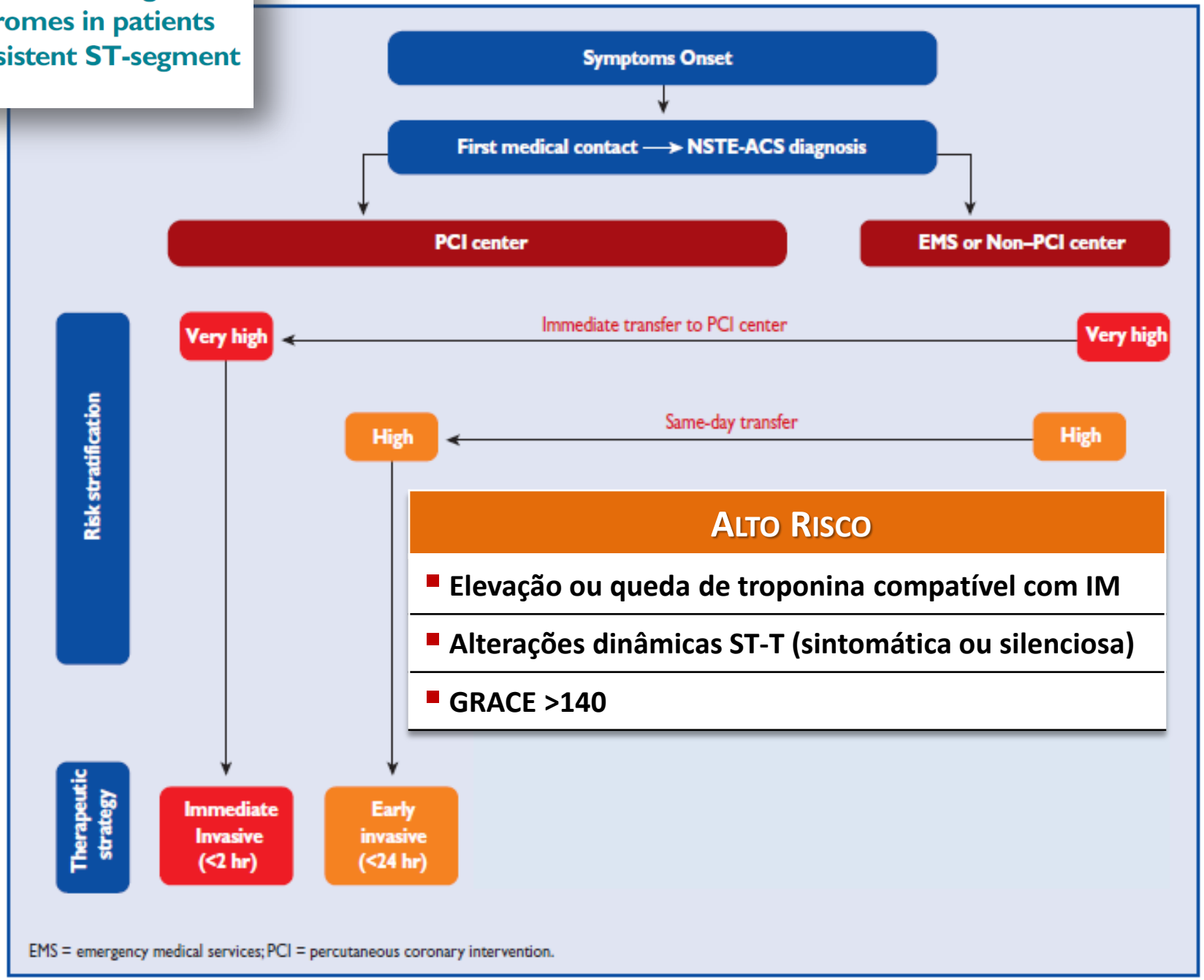


EMS = emergency medical services; PCI = percutaneous coronary intervention.

2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation



2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation



ALTO RISCO

- Elevação ou queda de troponina compatível com IM
- Alterações dinâmicas ST-T (sintomática ou silenciosa)
- GRACE >140

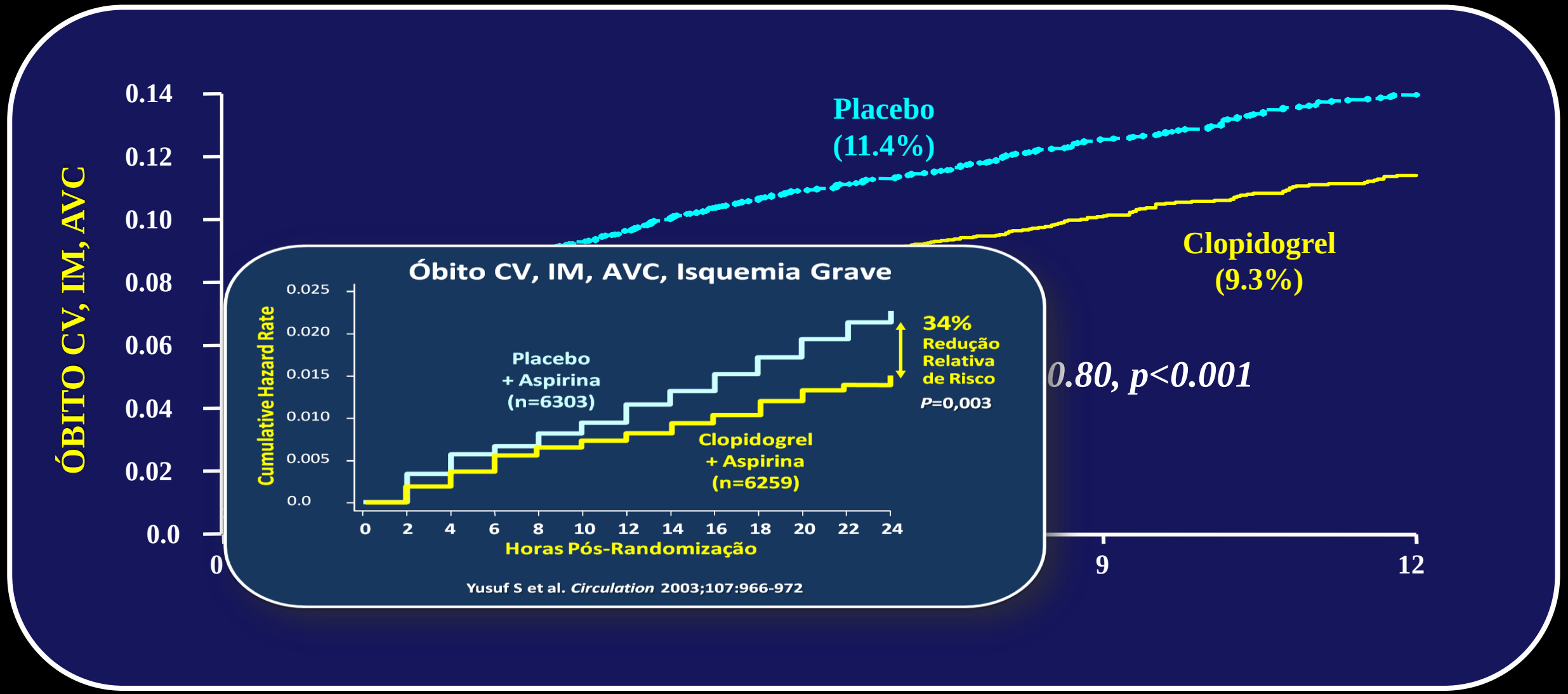
Panorama dos antiplaquetários na prática médica atual

Ataque Precoce

vs

Angiografia Precoce

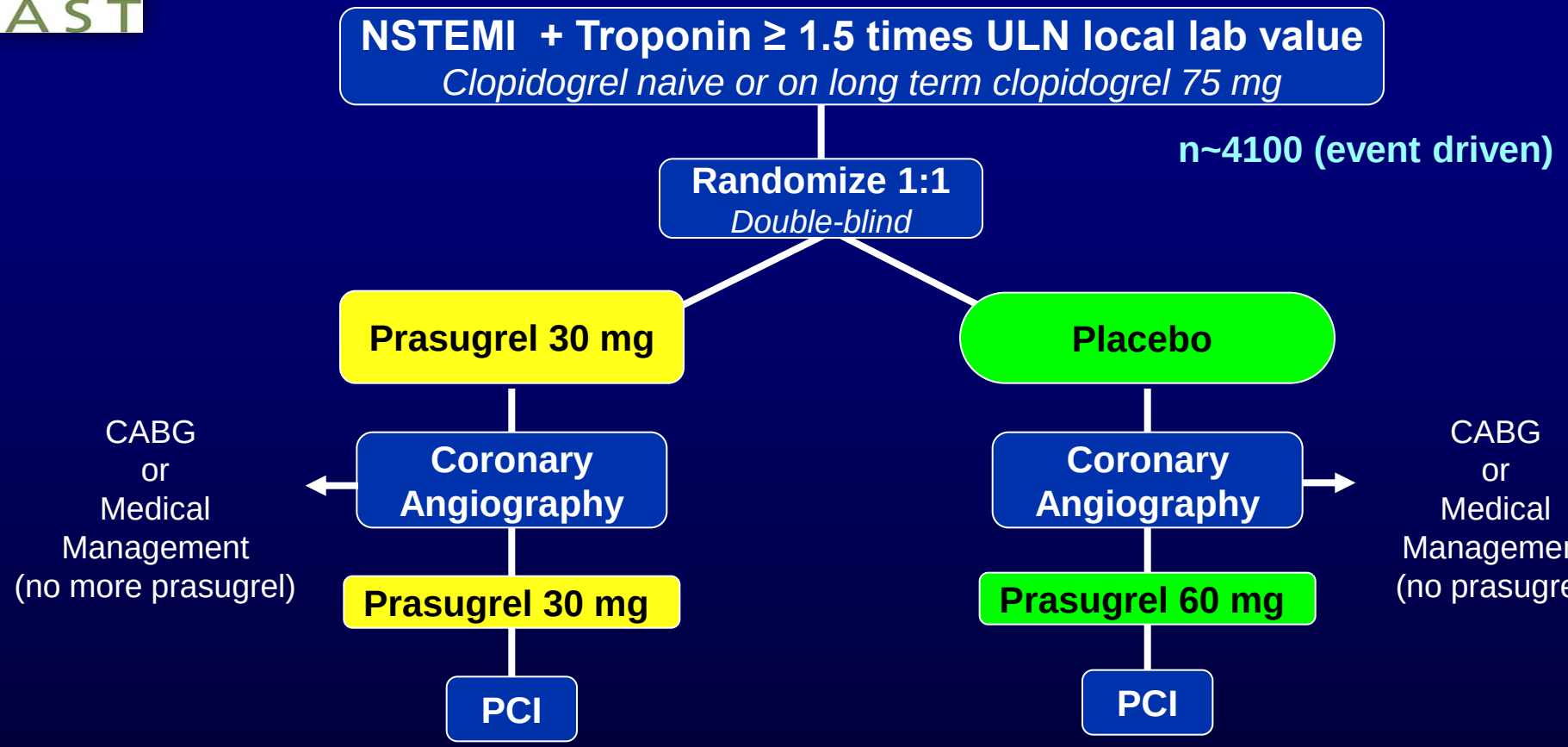
CURE: DESFECHO PRIMÁRIO (ÓBITO CV, IM, AVC)



Angiografia: 43,7% **CRM: 16,5%** **ATC: 21,2%**

CURE. *NEJM* 2001;345:494-502

ACCOAST



Prasugrel 10 mg or 5 mg (based on weight and age) for 30 days

1° Endpoint: CV Death, MI, Stroke, Urg Revasc, GP IIb/IIIa bailout, at 7 days

Montalescot G et al. *Am Heart J* 2011;161:650-656

Main Inclusion/Exclusion Criteria

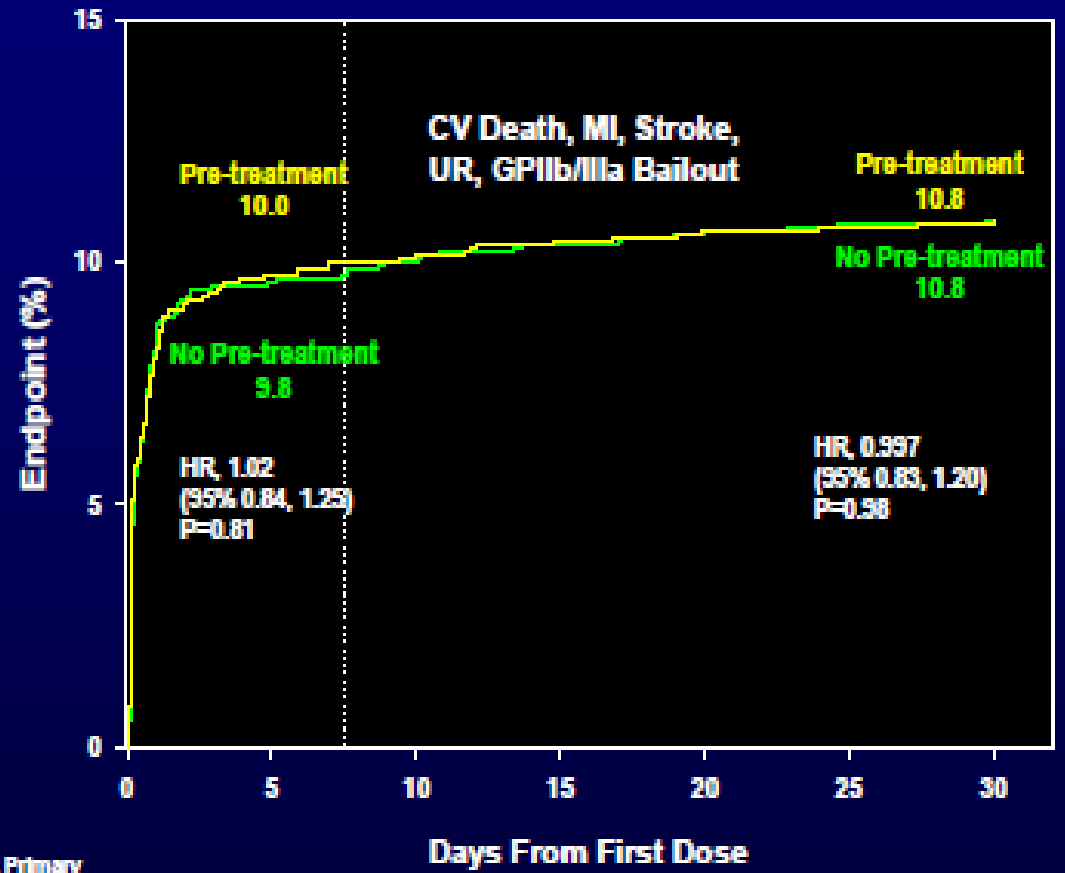
Inclusion

- NSTEMI symptoms within 48 hours prior to study entry
- Elevated troponin (≥1.5 times ULN) per local lab(s)
- Patient to be scheduled for coronary angiography and PCI within 2 hours to 24 hours of randomization and no later than 48 hours after randomization

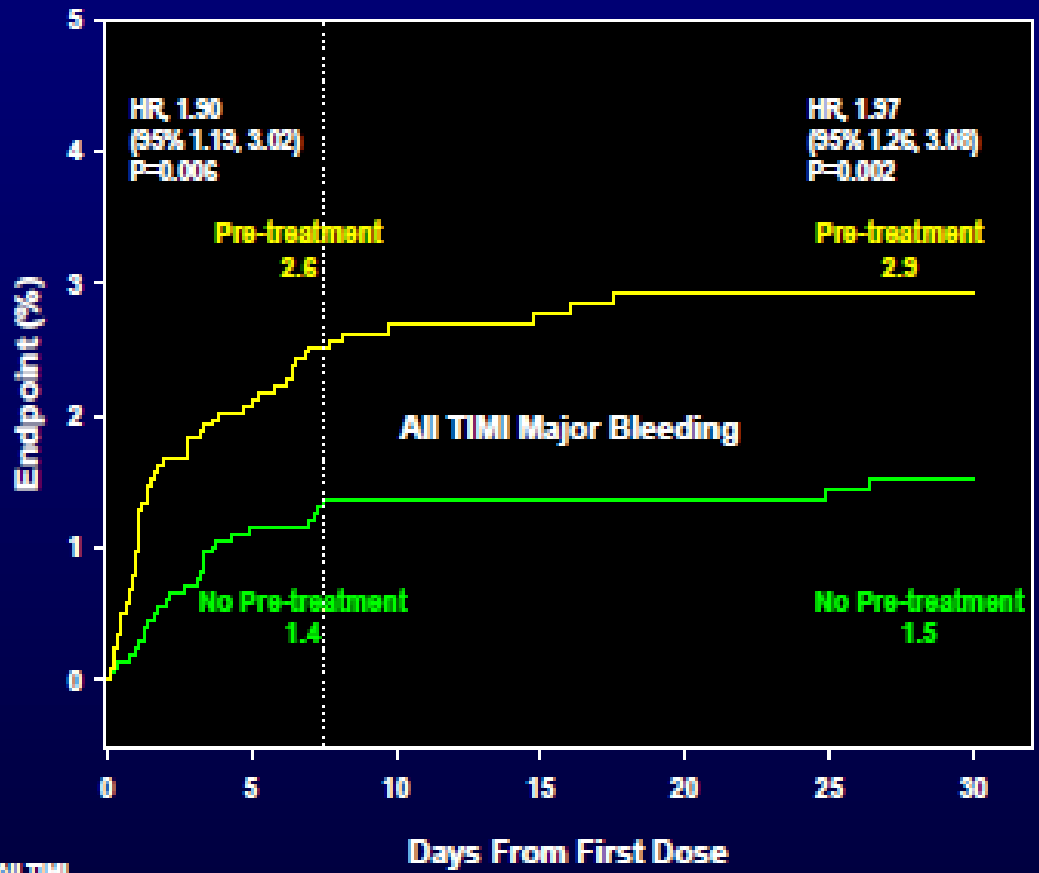
Exclusion

- STEMI patients
- Medical history contraindicating therapy with prasugrel
- History of stroke or transient ischemic attack (TIA)
- LD of any $P2Y_{12}$ antagonist ≤7 days of study entry

Desfecho Primário
(óbito CV, IM, AVC, RM urg, GP IIb/IIIa - 7d)
e Segurança (Hemorragia TIMI Mj)



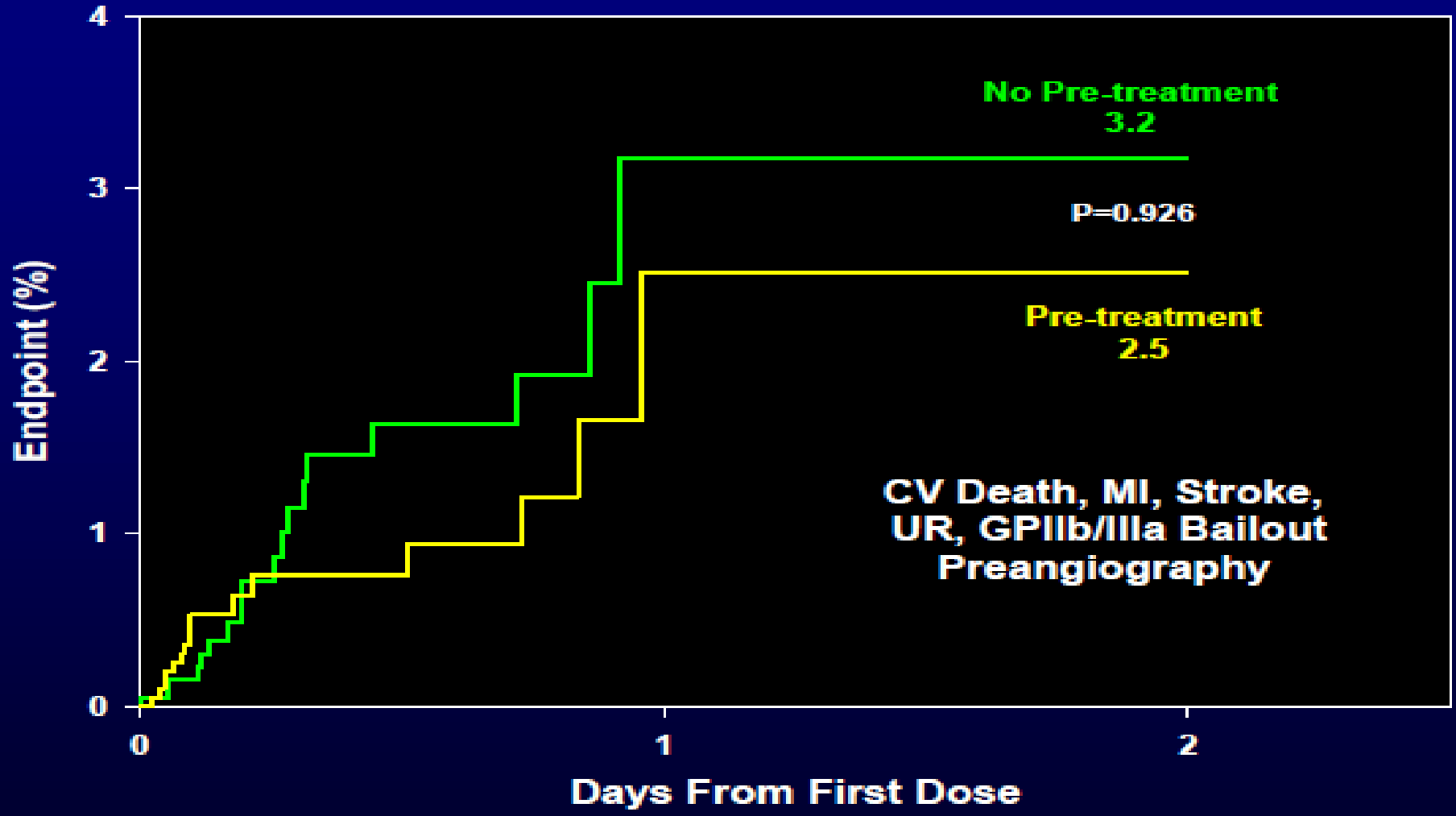
No. at Risk, Primary Efficacy End Point:							
No pre-treatment	1888	1788	1775	1788	1782	1752	1621
Pre-treatment	2037	1821	1809	1802	1797	1791	1618



No. at Risk, All TIMI Major Bleeding:							
No pre-treatment	1898	1847	1328	1297	1288	1284	1283
Pre-treatment	2037	1872	1338	1310	1298	1297	1289

Is there a risk of waiting to treat?

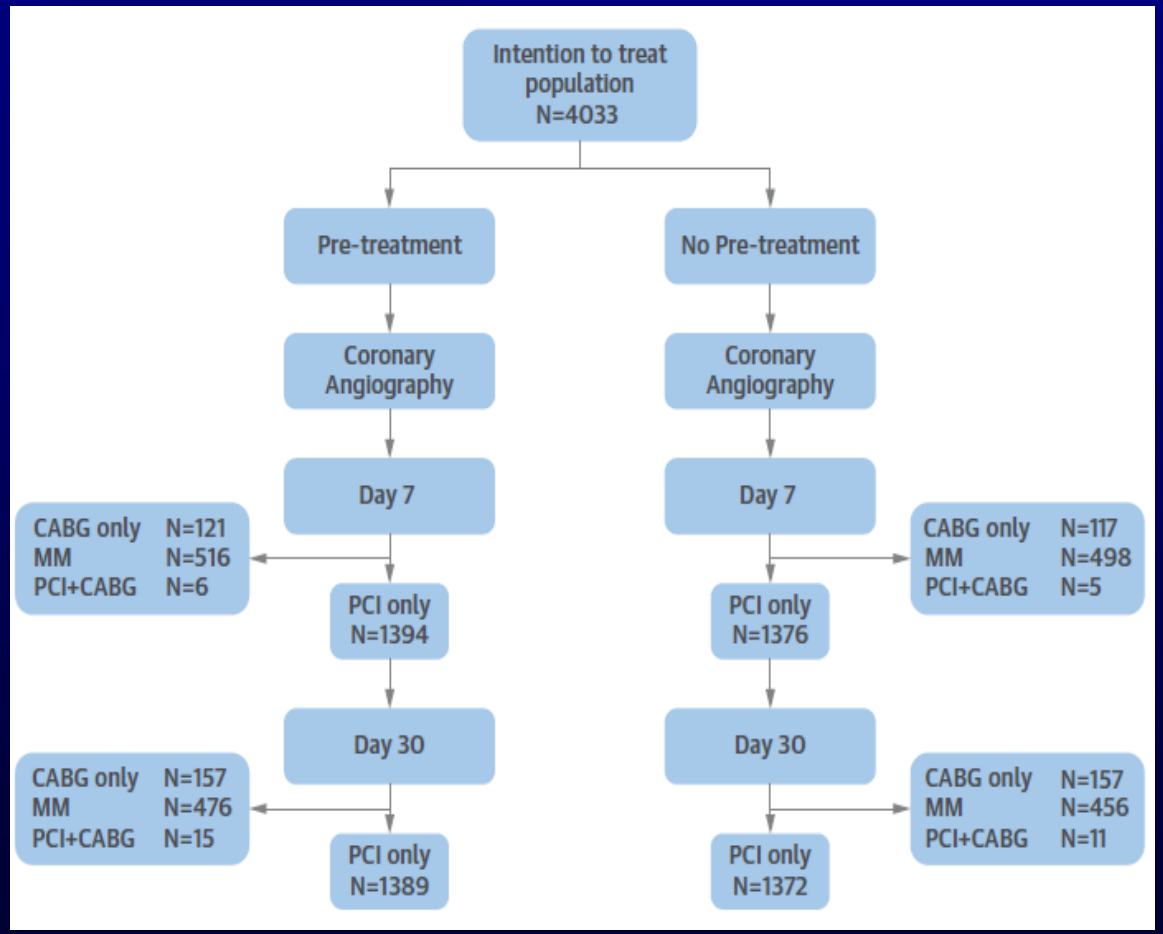
Primary Efficacy Endpoint Prior to Angiography

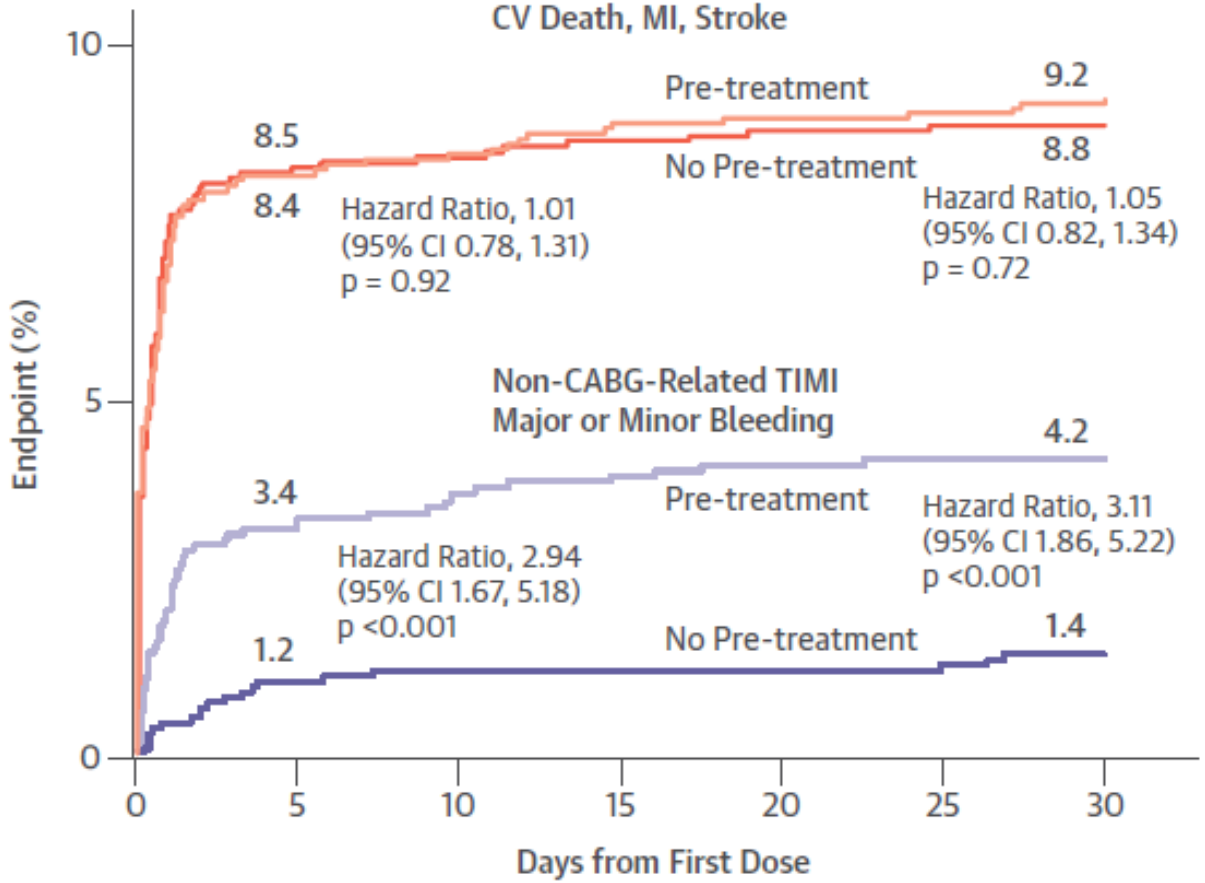


No. at Risk:			
No pre-treatment	1981	134	134
Pre-treatment	2014	113	113

ACCOAST – PCI

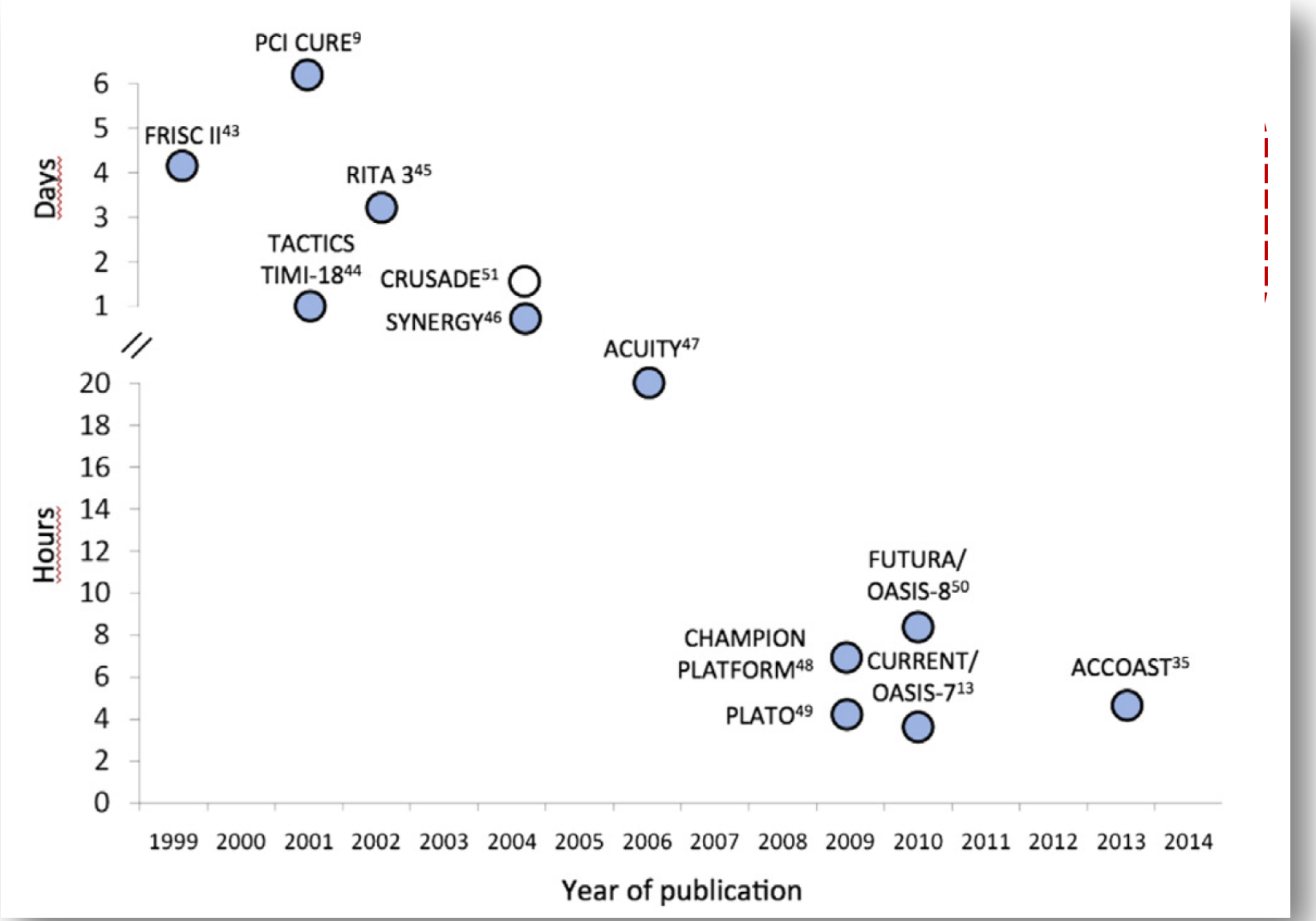
(n = 2761; 68,7%)





J Am Coll Cardiol 2014;64:2563

ΔT CAT (médio)
(randomização / admissão)



De Luca et al. Am J Cardiol 2015

5.2.3 Timing of $P2Y_{12}$ inhibitor administration

cussed extensively and the topic remains controversial.[165,166] As the optimal timing of ticagrelor or clopidogrel administration in NSTE-ACS patients scheduled for an invasive strategy has not been adequately investigated, no recommendation for or against pretreatment with these agents can be formulated. Based on the ACCOAST results, pretreatment with prasugrel is not recommended. In NSTE-ACS patients planned for conservative management, $P2Y_{12}$ inhibition (preferably with ticagrelor) is recommended, in the absence of contraindications, as soon as the diagnosis is confirmed.

A $P2Y_{12}$ inhibitor is recommended, in addition to aspirin, for 12 months unless there are contraindications such as excessive risk of bleeds.	I	A
prasugrel or who require oral anticoagulation.		

ATLANTIC

Administration of **T**icagrelor in the cath **L**ab or in the **A**mbulance for **N**ew S**T** elevation myocardial **I**nfarction to open the **C**oronary artery

G. Montalescot, A.W. van't Hof, F. Lapostolle, J Silvain, J.F. Lassen, L. Bolognese, W.J. Cantor, A. Cequier, M. Chettibi, S.G. Goodman, C.J. Hammett, K. Huber, M. Janzon, B. Merkely, R.F. Storey, U. Zeymer, O. Stibbe, P. Ecollan, W.M.J.M. Heutz, E. Swahn, J.P. Collet, F.F. Willems, C. Baradat, M. Licour, A. Tsatsaris, E. Vicaut, C.W. Hamm, for the ATLANTIC investigators

G. Montalescot, COI are available at www.action-coeur.org

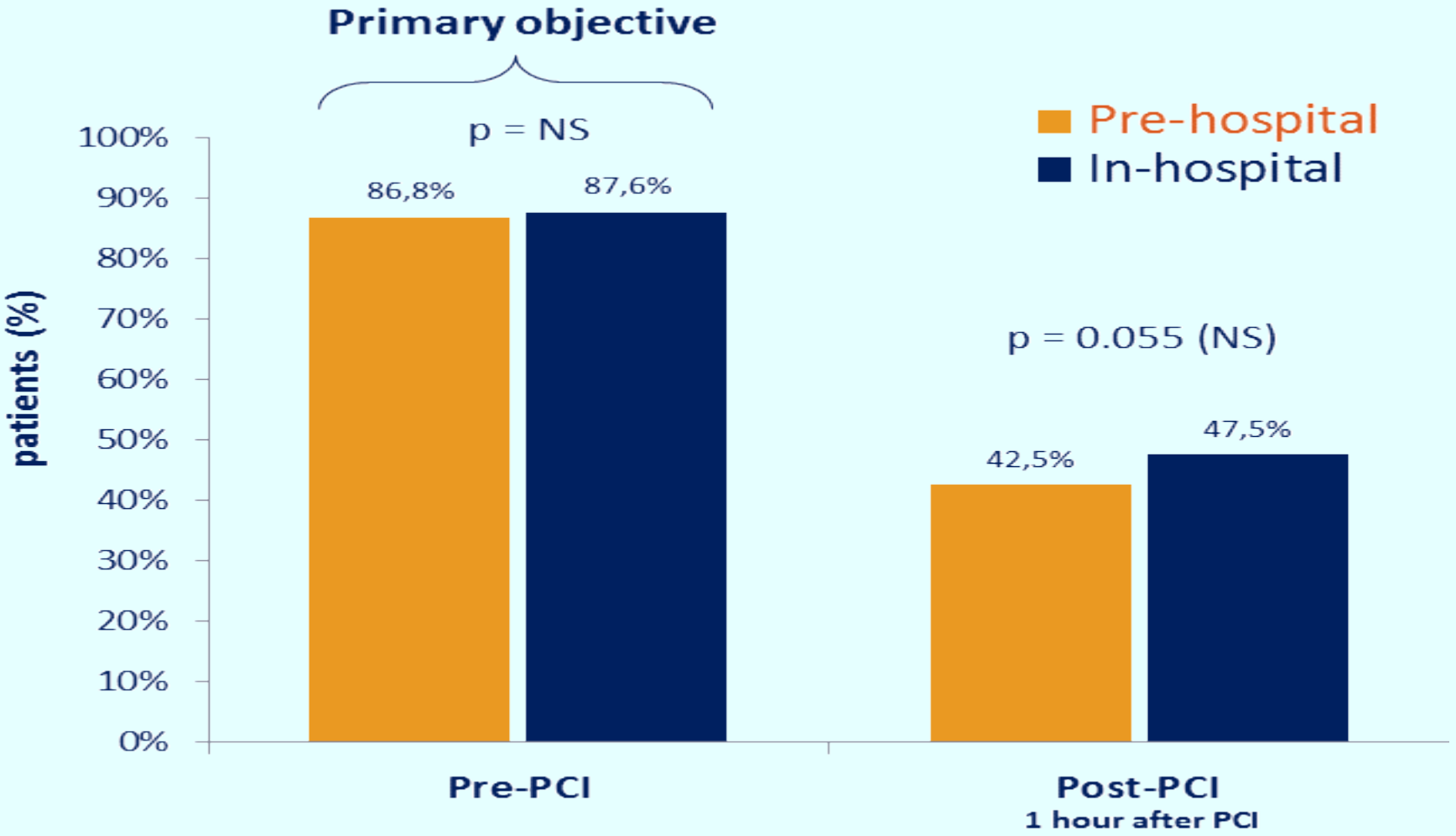
Table 1. Demographic Characteristics and Treatment of the Patients at Baseline.*

Characteristic	Prehospital Ticagrelor (N=909)	In-Hospital Ticagrelor (N=953)
Age		
Mean age — yr	60.6±12.4	61.0±12.5
≥75 yr — no. (%)	144 (15.8)	160 (16.8)
Female sex — no. (%)	173 (19.0)	196 (20.6)
Body weight — kg	80.4±15.9	79.7±15.6
BMI ≥30 — no. (%)†	177 (19.5)	178 (18.7)
Diabetes mellitus — no. (%)	115 (12.7)	138 (14.5)
TIMI risk score — no. (%)‡		
0–2	552 (60.7)	573 (60.1)
3–6	337 (37.1)	365 (38.3)
>6	20 (2.2)	15 (1.6)
Killip class I — no. (%)	819 (90.1)	862 (90.5)
First medical contact — no. (%)§		
In ambulance	689 (75.8)	723 (75.9)
In emergency department before ambulance transfer	220 (24.2)	229 (24.0)
Procedures for index event		
Coronary angiography — no. (%)	890 (97.9)	937 (98.3)
Femoral access — no./total no. (%)	280/890 (31.5)	309/937 (33.0)
Radial access — no./total no. (%)	604/890 (67.9)	625/937 (66.7)
Missing data — no./total no. (%)	6/890 (0.7)	3/937 (0.3)
Thromboaspiration — no. (%)	471 (51.8)	470 (49.3)
PCI — no. (%)	800 (88.0)	830 (87.1)
With stent¶	760 (83.6)	776 (81.4)
Drug-eluting stent	467 (51.4)	479 (50.3)
Bare-metal stent	305 (33.6)	312 (32.7)
Without stent	40 (4.4)	54 (5.7)
CABG — no. (%)	10 (1.1)	15 (1.6)
No PCI or CABG — no. (%)	99 (10.9)	108 (11.3)

ΔT
Sintoma – Diagnóstico = 73 min
Random – Cat = 48 min
Dose pré vs hosp = 31 min

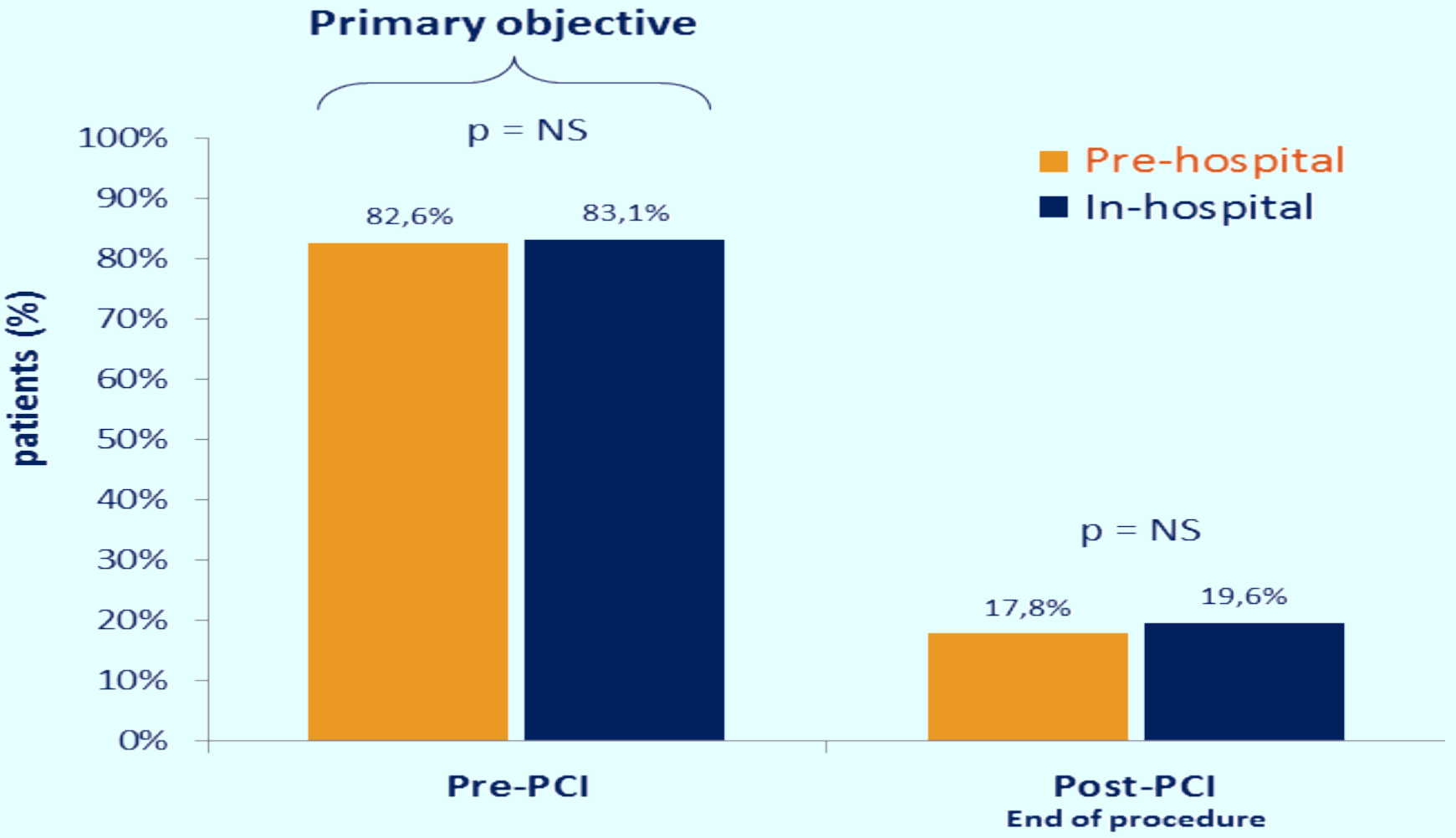
N Engl J Med 2014; 371:1016-1027

Defecho Co-primário Principal
Ausência Resolução ST (≥70%)



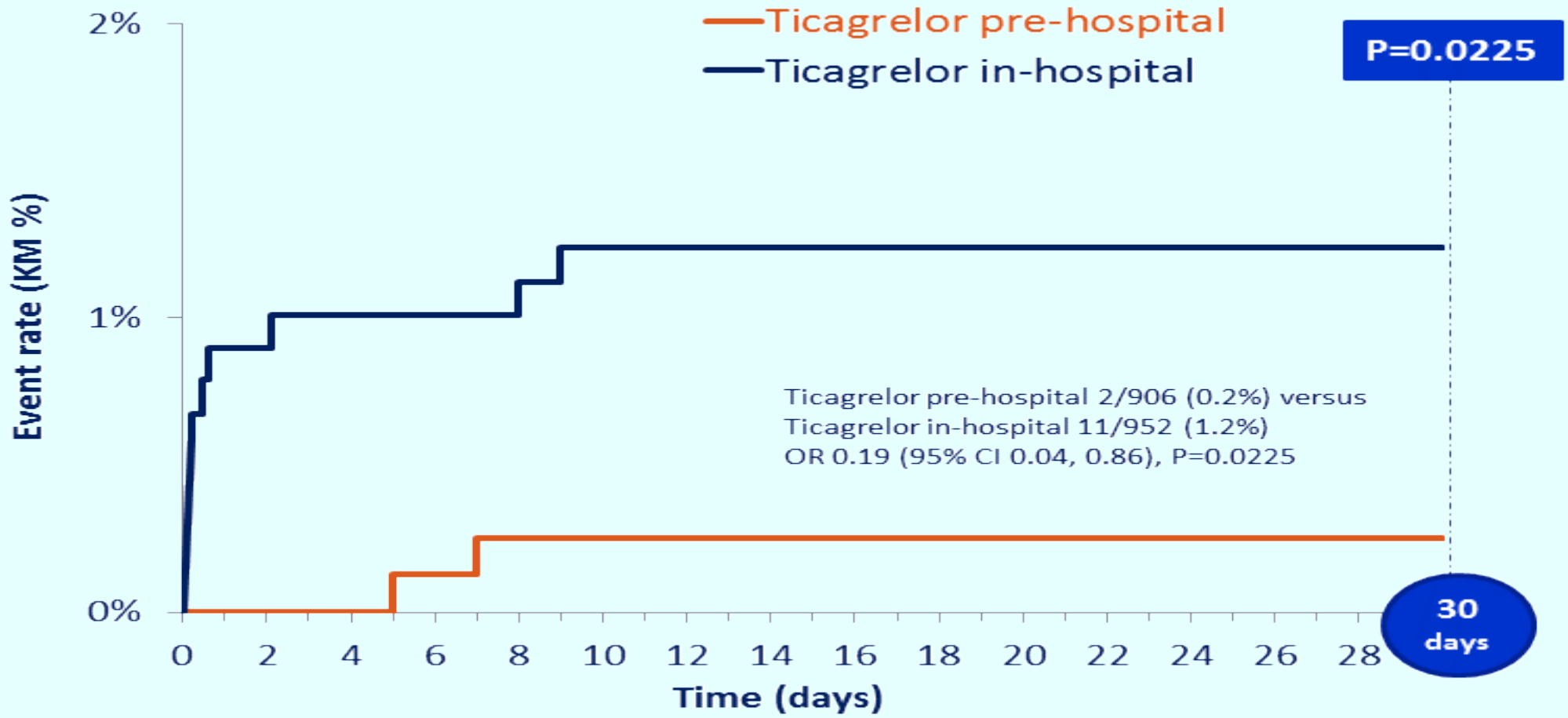
N Engl J Med 2014; 371:1016-1027

Desfecho Co-primário Secundário
Ausência Fluxo TIMI 3 na ARI



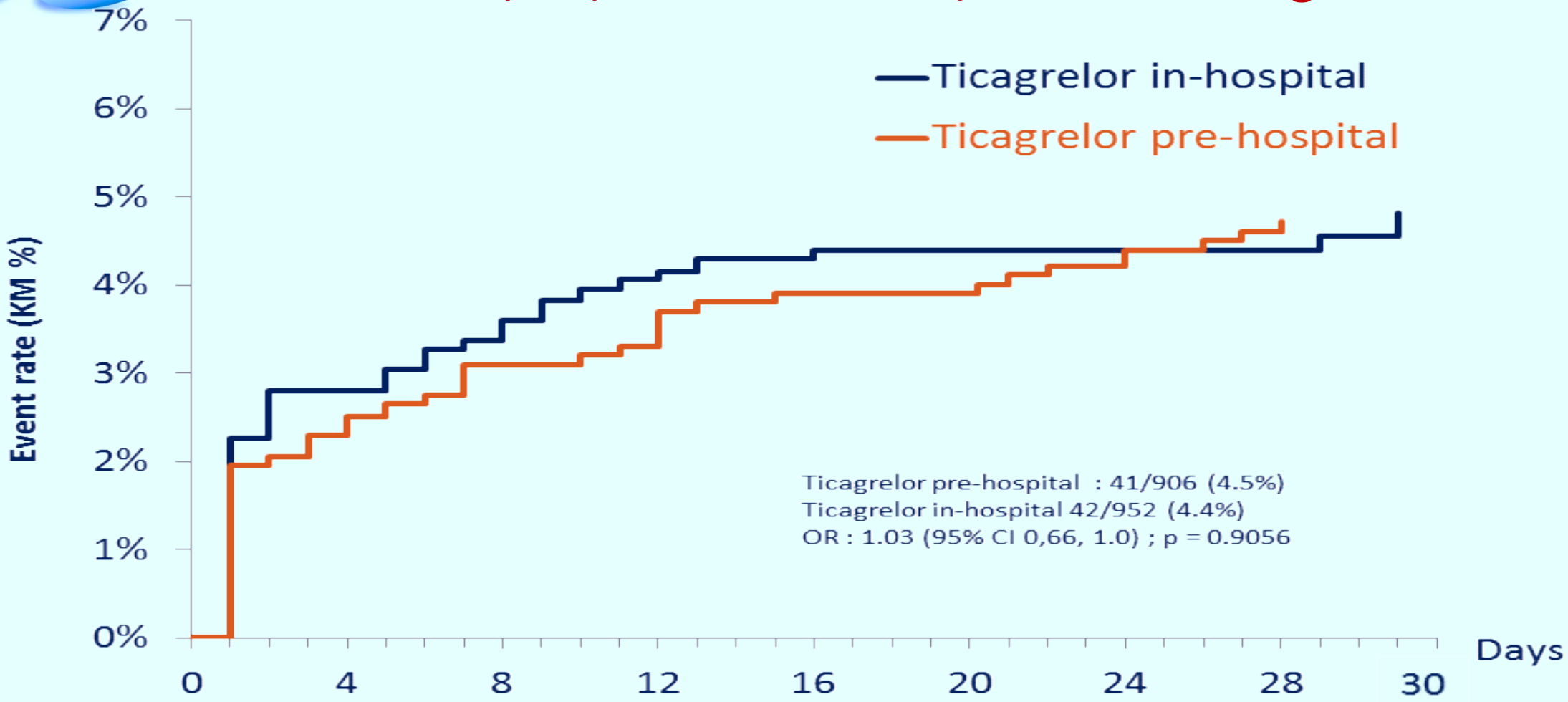
N Engl J Med 2014; 371:1016-1027

Trombose Stent Definitiva (30 d)



N Engl J Med 2014; 371:1016-1027

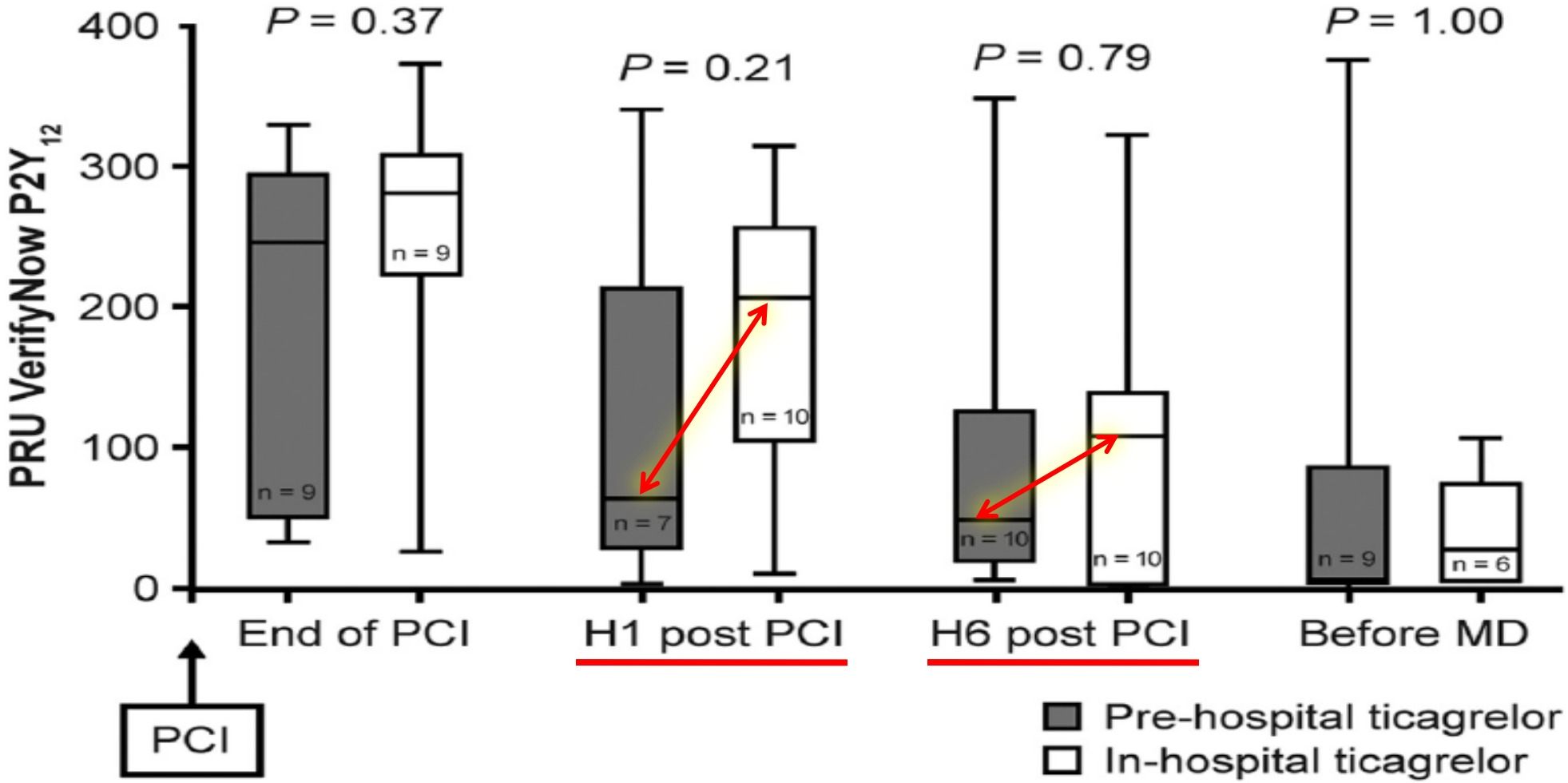
MACE (30d):
óbito, IM, trombose stent, AVC ou RM urgente



N Engl J Med 2014; 371:1016-1027

Effect of Pre-Hospital Ticagrelor During the First 24 h After Primary Percutaneous Coronary Intervention in Patients With ST-Segment Elevation Myocardial Infarction

The ATLANTIC-H^{24} Analysis

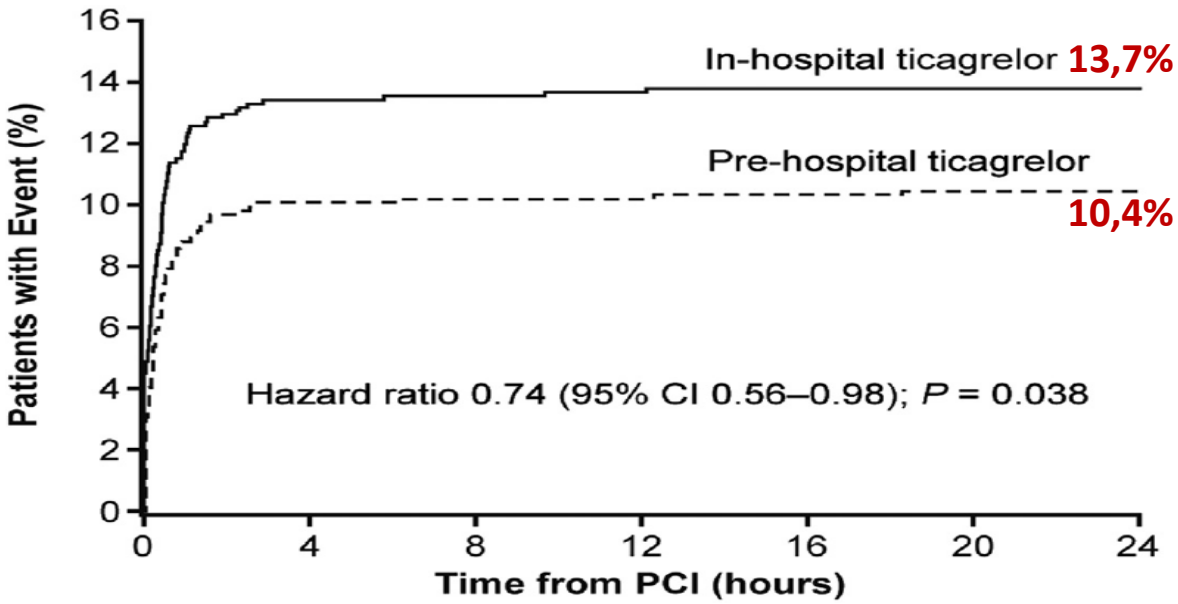


J Am Coll Cardiol Intv 2016;9:646–56

Effect of Pre-Hospital Ticagrelor During the First 24 h After Primary Percutaneous Coronary Intervention in Patients With ST-Segment Elevation Myocardial Infarction

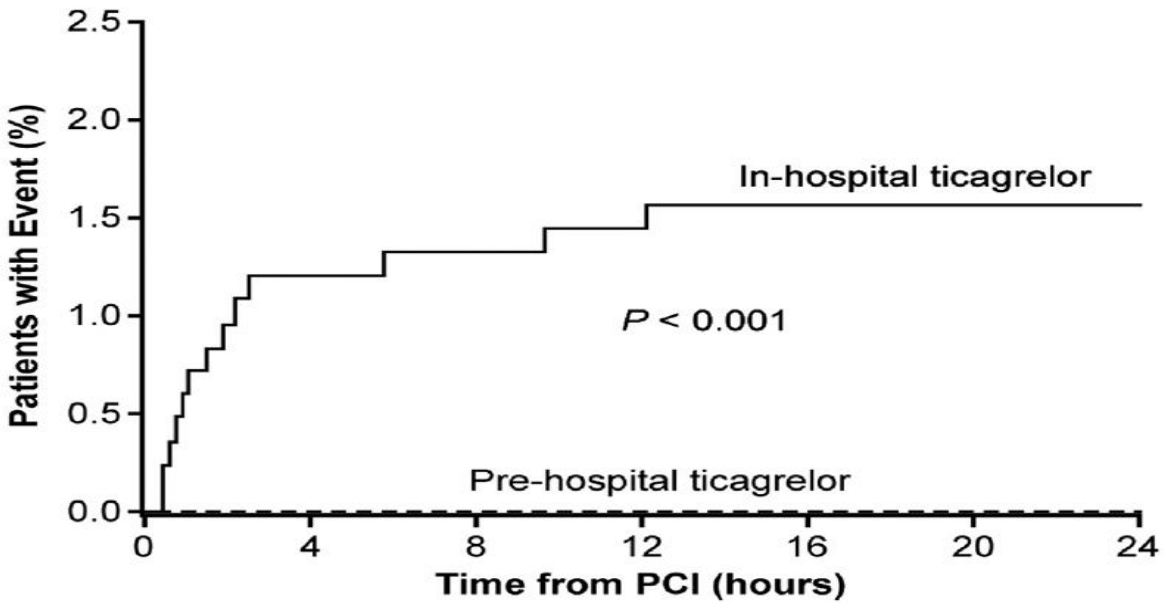
The ATLANTIC-H^{24} Analysis

Óbito/IM/ RM Urg/ Trombose Stent Def / GPIIIbIIIa



	Patients with event, no. (%)	Total no. of patients
Pre-hospital ticagrelor	83 (10.4)	799
In-hospital ticagrelor	114 (13.7)	830

IM / Trombose Stent Definitiva



	Patients with event, no. (%)	Total no. of patients
Pre-hospital ticagrelor	0 (0)	799
In-hospital ticagrelor	13 (1.6)	830

J Am Coll Cardiol Intv 2016;9:646–56

Effect of Pre-Hospital Ticagrelor During the First 24 h After Primary Percutaneous Coronary Intervention in Patients With ST-Segment Elevation Myocardial Infarction

The ATLANTIC-H^{24} Analysis

TABLE 4 Clinical Endpoints Within 24 h of the Index PCI

Endpoint	Pre-Hospital Ticagrelor (n = 799)	In-Hospital Ticagrelor (n = 830)	Odds Ratio (95% CI)	p Value
Composite of death/new MI/urgent revascularization/ definite stent thrombosis/ bail-out glycoprotein IIb/IIIa inhibitor use	83 (10.4)	114 (13.7)	0.728 (0.539–0.984)	0.039
Composite of death/new MI/urgent revascularization/ definite stent thrombosis	10 (1.3)	17 (2.0)	0.606 (0.276–1.332)	0.213
New MI or definite acute stent thrombosis	0 (0.0)	13 (1.6)	0.027 (0.017–0.184)*	<0.001*
All-cause mortality	9 (1.1)	2 (0.2)	4.716 (1.016–21.896)	0.048

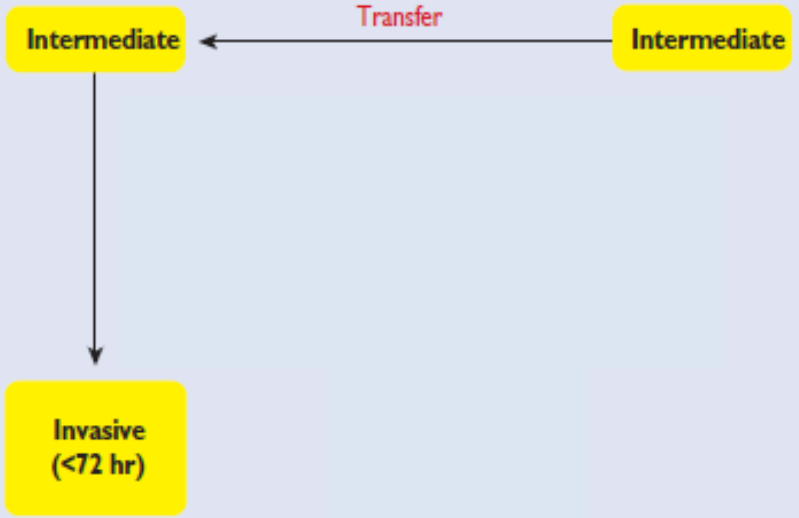
CONCLUSIONS The effects of pre-hospital ticagrelor became apparent after PCI, with numerical differences in platelet reactivity and immediate post-PCI reperfusion, associated with reductions in ischemic endpoints, over the first 24 h, whereas there was a small excess of mortality. (Administration of Ticagrelor in the cath Lab or in the Ambulance for New ST elevation myocardial infarction to open the Coronary artery [ATLANTIC, NCT01347580]) (J Am Coll Cardiol Intv 2016;9:646–56)

2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

RISCO INTERMEDIÁRIO

- Diabetes mellitus
- Insuficiência renal ($ClCr_{est}$ <60 mL/min/1,73 m^2)
- FEVE <40% ou insuficiência cardíaca congestiva
- Angina pós-infarto precoce
- ATC prévia
- RM cirúrgica prévia
- GRACE >109 - <140

Cardiopatia
Coronariopatia
GRAVES



PLATO

Ticagrelor Versus Clopidogrel : *SUBGRUPOS*

SCASSST

≥2 critérios

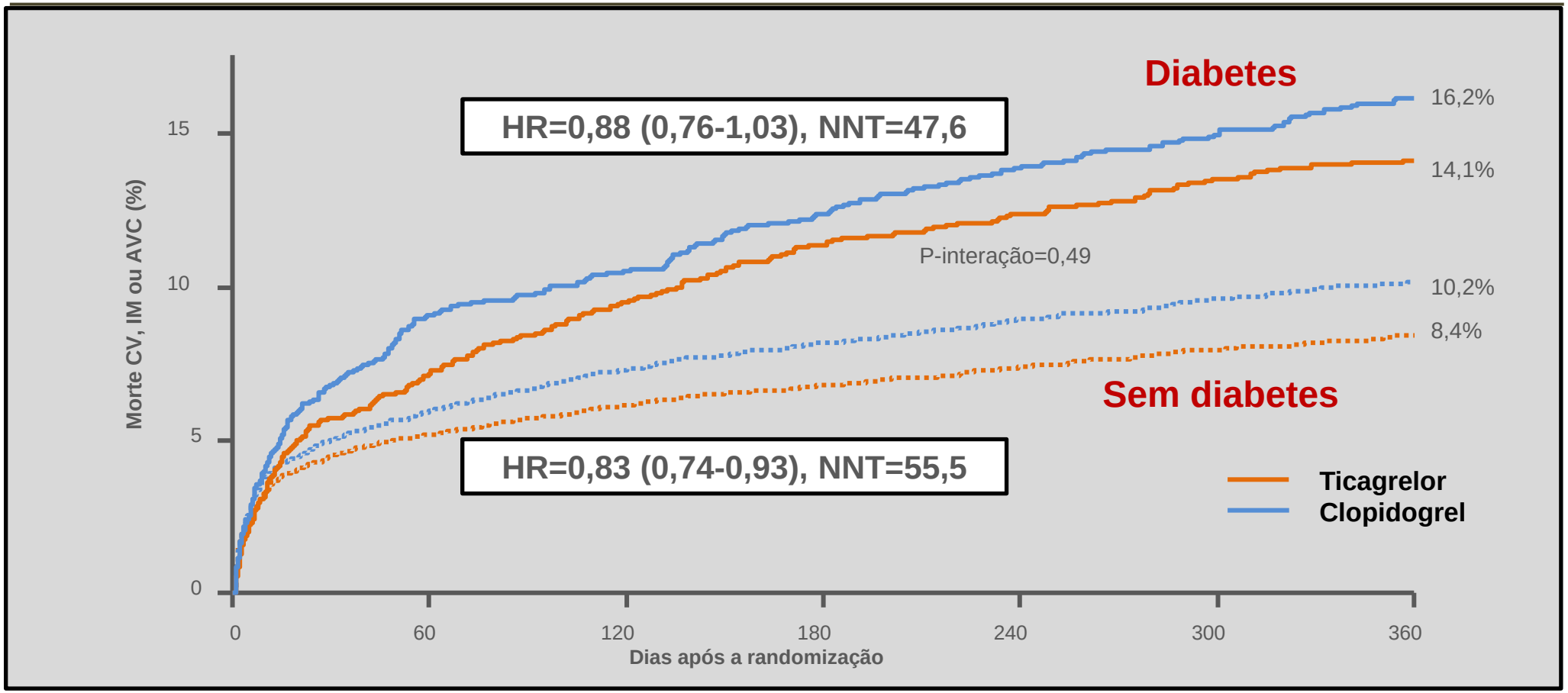
1. ST isquemia, depressão; elevação transitória
2. MNM (+)
3. Um dos abaixo:

- ≥60 a
- IM ou RMC prévia
- DAC ≥50% em ≥2 vasos
- AVC, AIT, Carótida ≥50%
- Diabetes Mellitus
- DAP
- I. renal crônica (ClCr <60 mL/min)

Ticagrelor vs. clopidogrel in patients with acute coronary syndromes and diabetes: a substudy from the PLATelet inhibition and patient Outcomes (PLATO) trial

Diabetes mellitus n = 4662 (DMID = 1036) vs Não DM = 13.951

Desfecho composto primário: Morte CV, IAM ou AVC

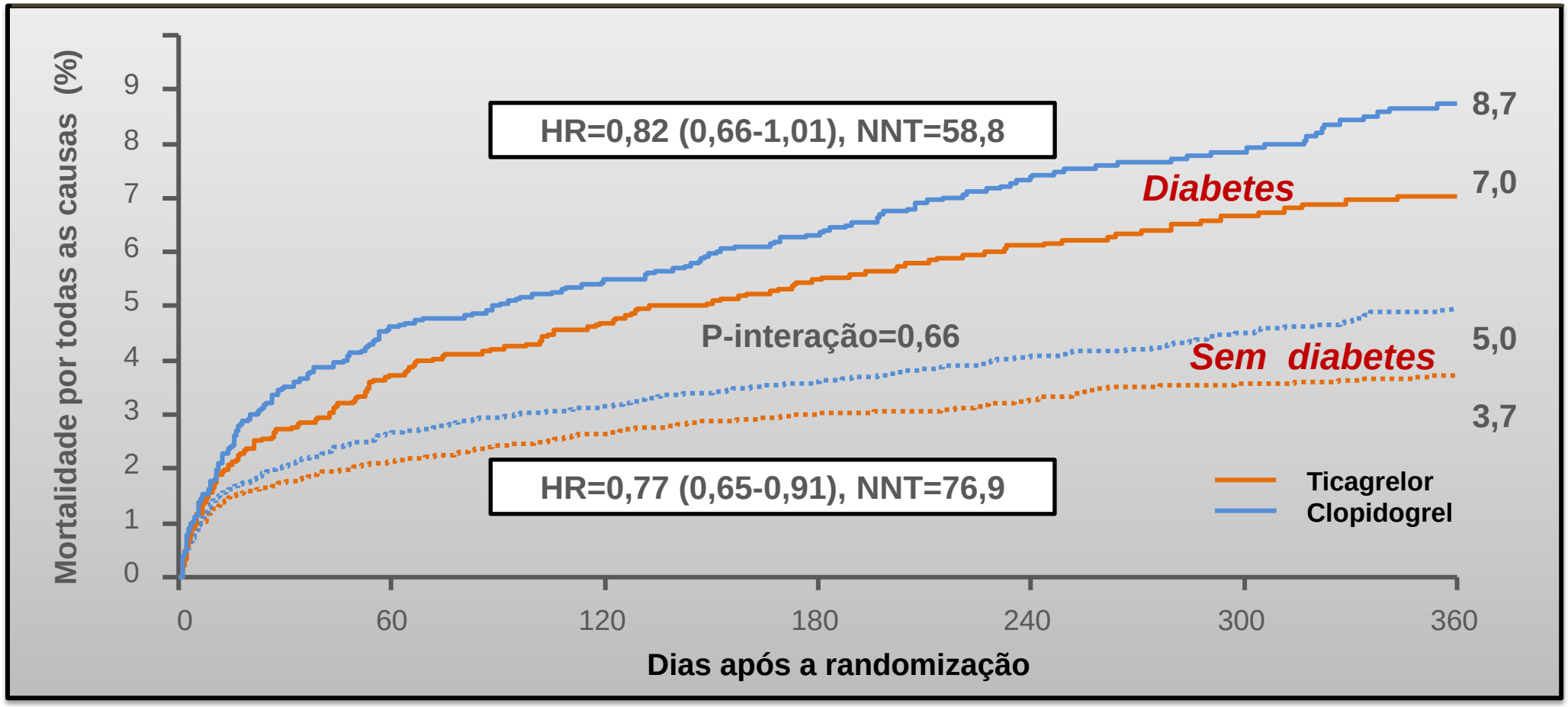


James S. et al. Eur Heart J 2010; 31: 3006-16.

Ticagrelor vs. clopidogrel in patients with acute coronary syndromes and diabetes: a substudy from the PLATelet inhibition and patient Outcomes (PLATO) trial

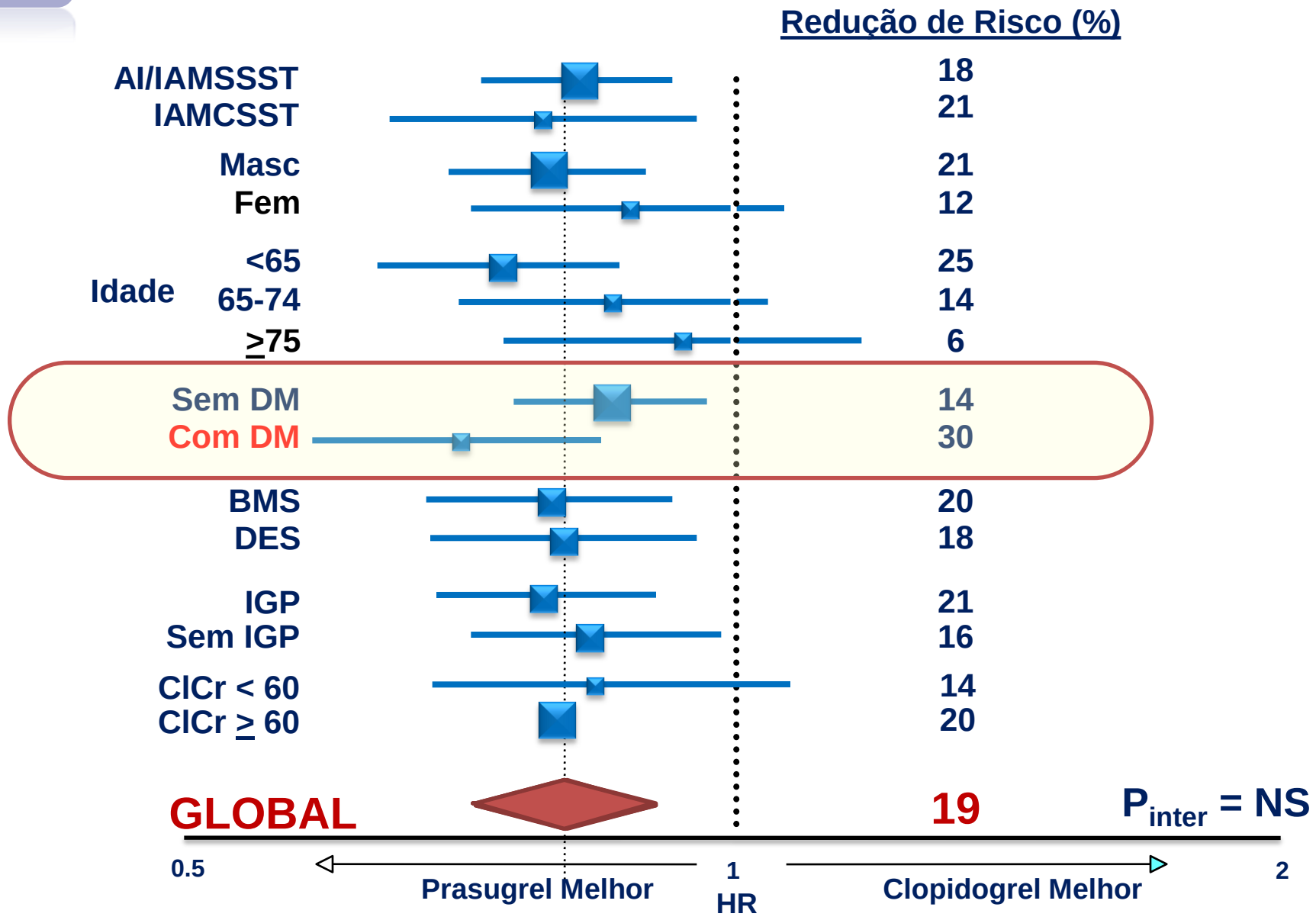
Diabetes mellitus n = 4662 (DMID = 1036) vs Não DM = 13.951

Mortalidade total



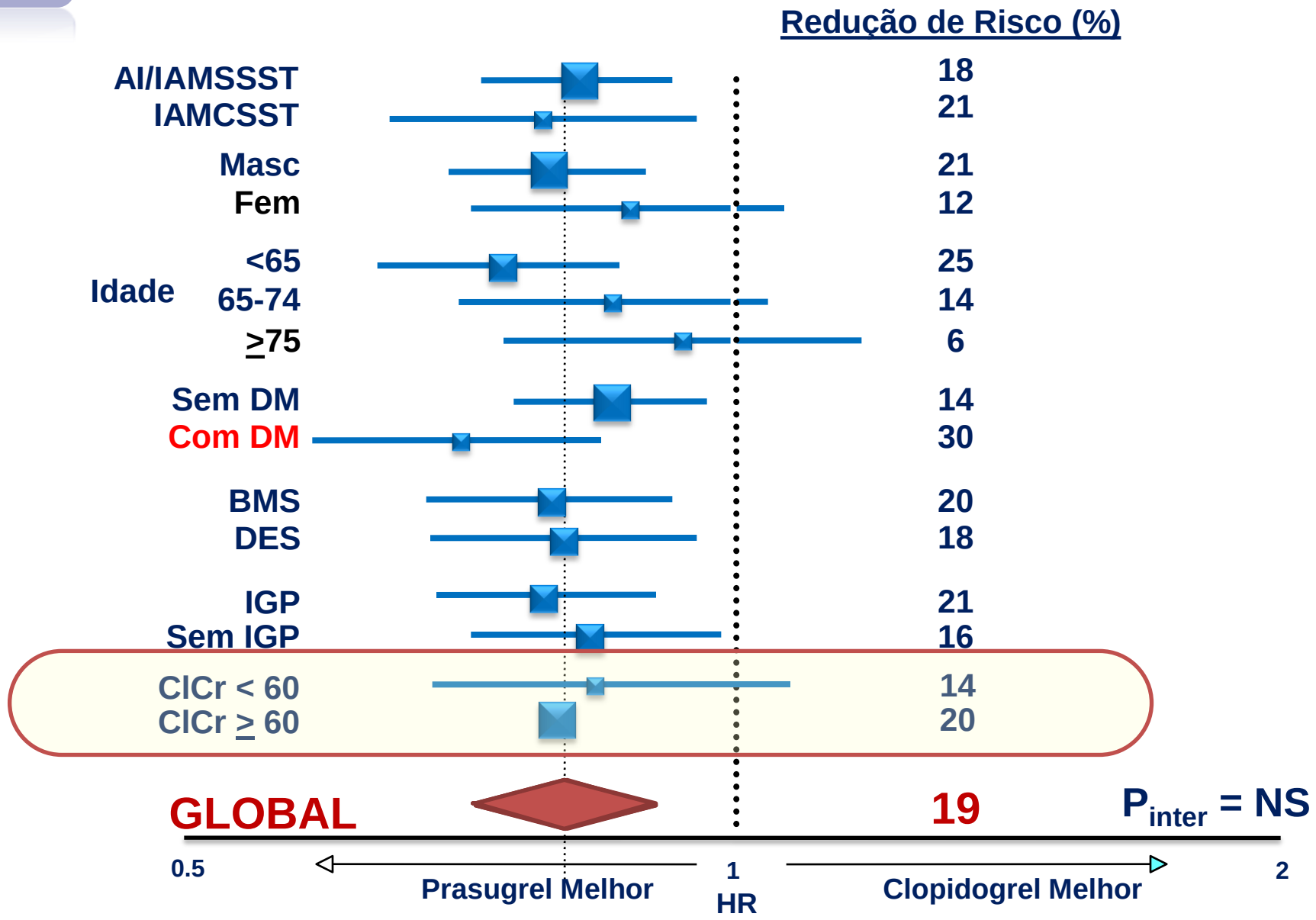
James S. et al. Eur Heart J 2010; 31: 3006-16.

Morte CV, IAM, AVC: Análise de Subgrupos



Wiviott SD, Braunwald E, McCabe CH et al NEJM2007

Morte CV, IAM, AVC: Análise de Subgrupos



Wiviott SD, Braunwald E, McCabe CH et al NEJM2007

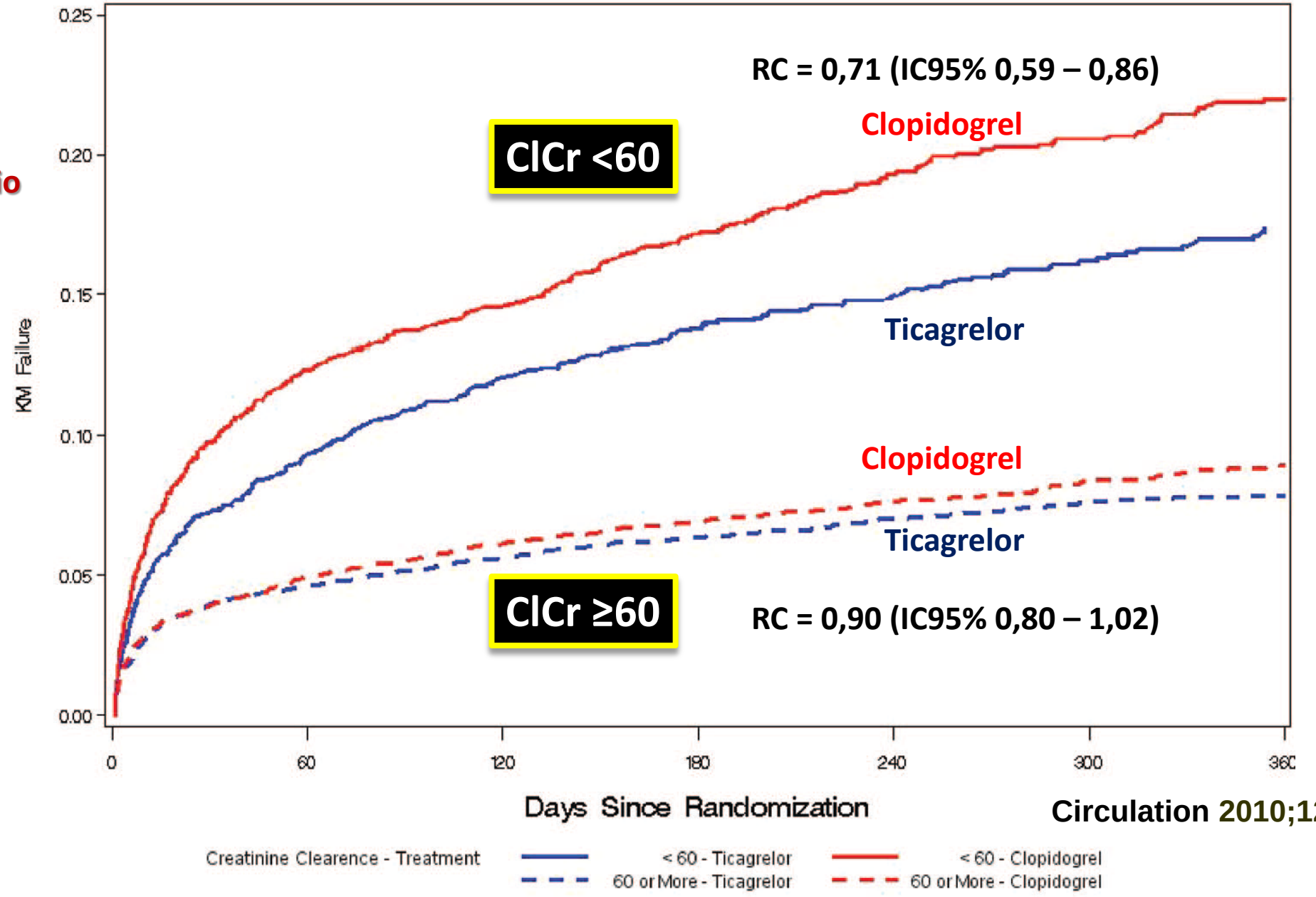
Ticagrelor Versus Clopidogrel in Acute Coronary Syndromes in Relation to Renal Function

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

$ClCr_{est}$ em 15 202 (81.9%)
$ClCr_{est}$ < 60 mL/min: n=3237),

PLATO

Desfecho Primário
Óbito CV
I Miocárdio
AVC



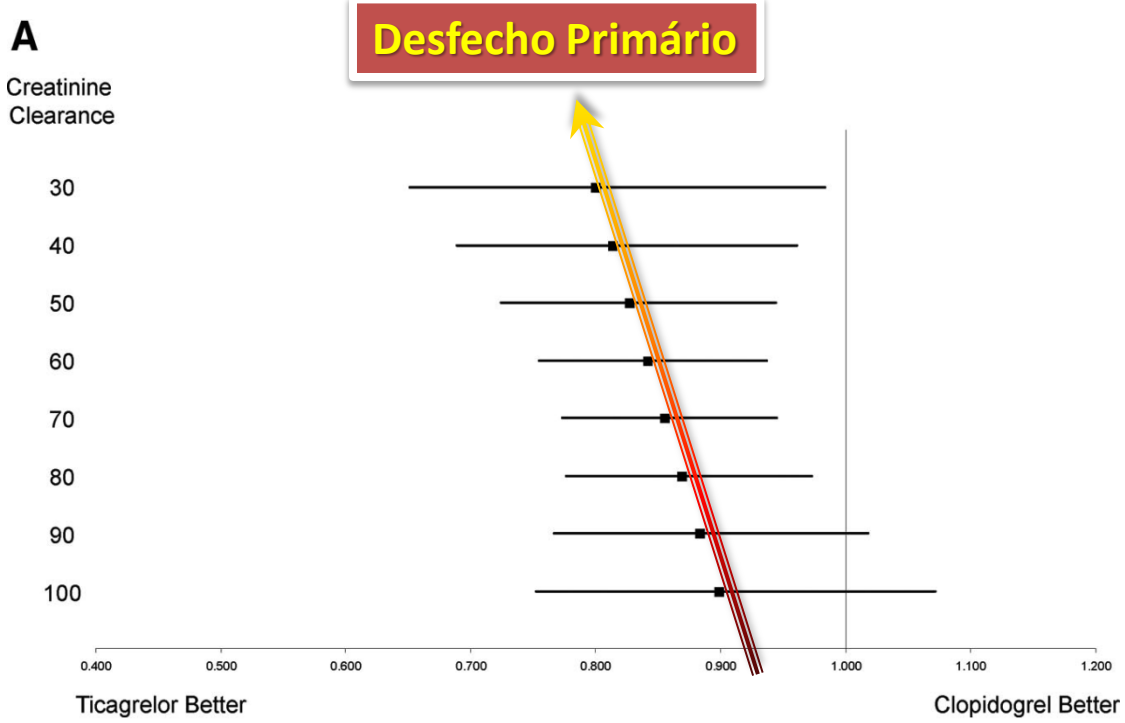
Circulation 2010;122:1056-1067

Ticagrelor Versus Clopidogrel in Acute Coronary Syndromes in Relation to Renal Function

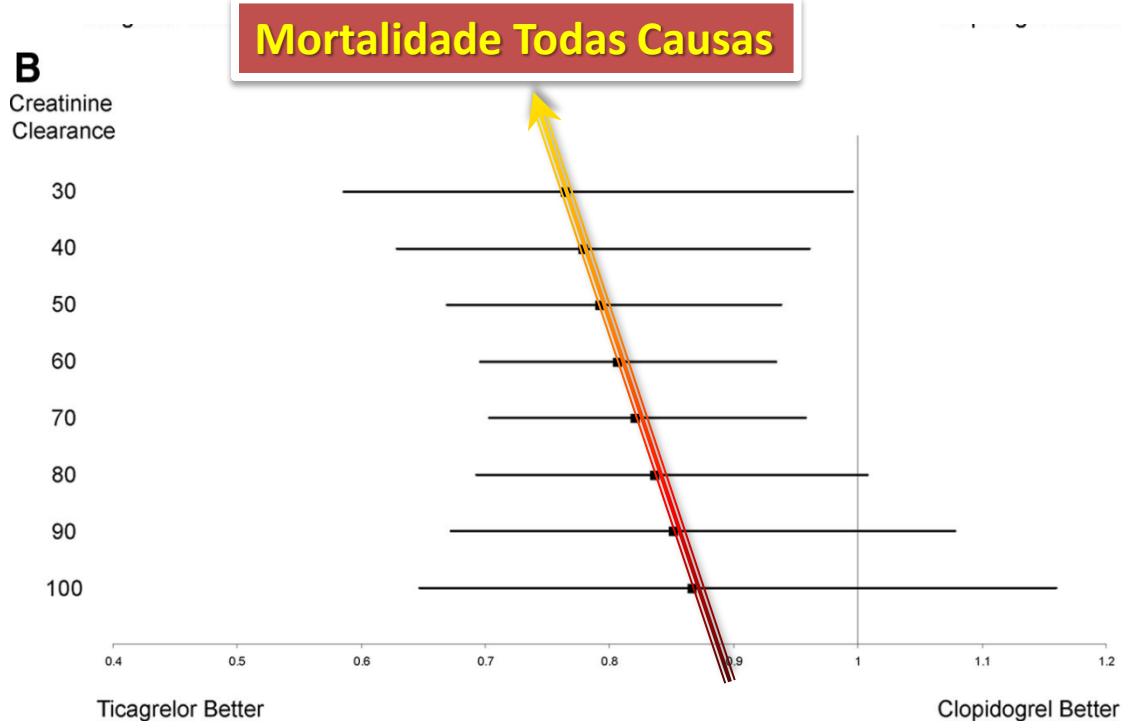
Results From the Platelet Inhibition and Patient Outcomes (PLATO) Trial

PLATO

Desfecho Primário



Mortalidade Todas Causas



Circulation 2010;122:1056-1067

Ticagrelor Versus Clopidogrel in Acute Coronary Syndromes in Relation to Renal Function

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

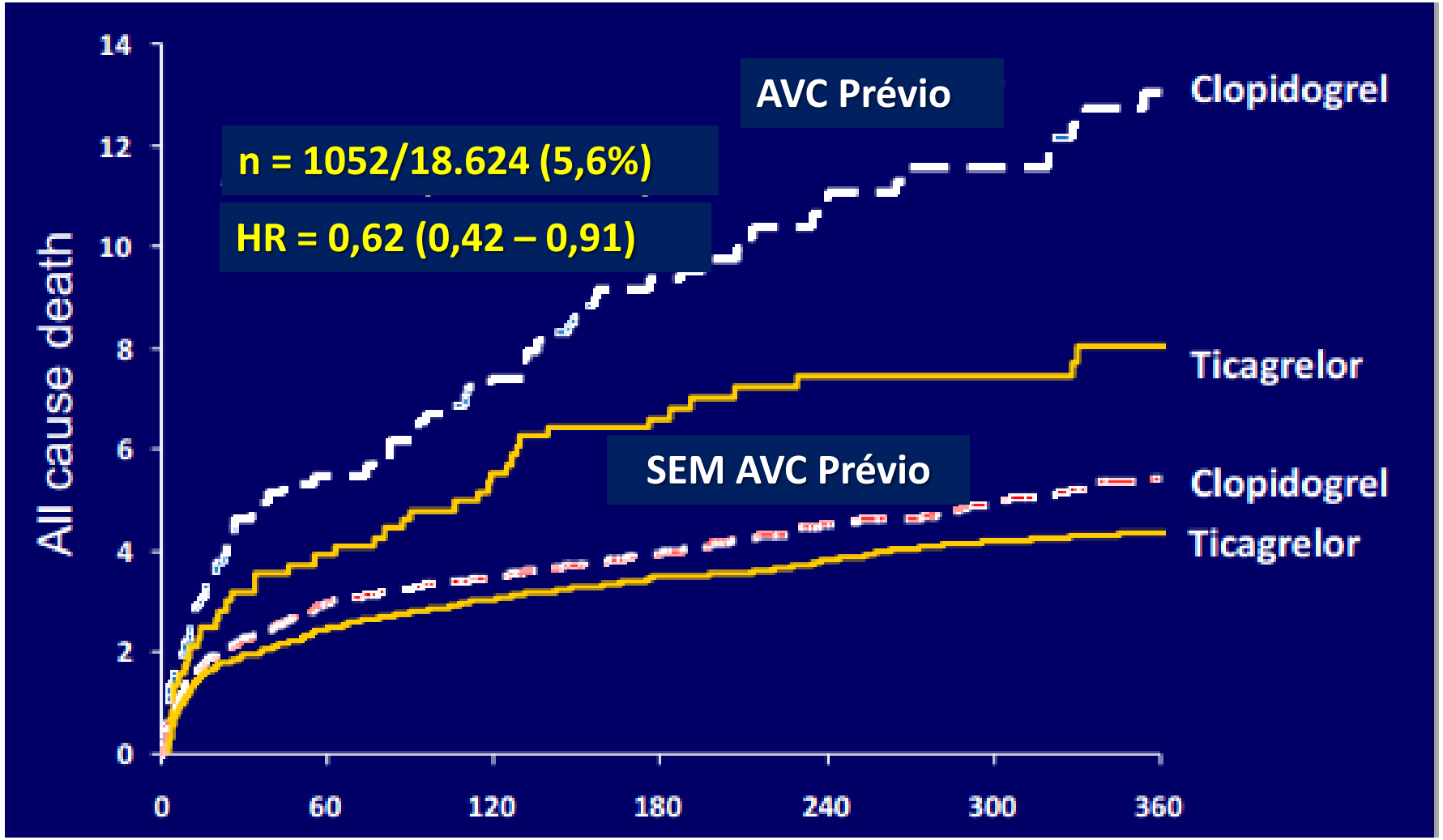
PLATO

CrCl, mL/min	Random	Overall n	Overall %/y	Ticagrelor n	Ticagrelor %/y	Clopidogrel n	Clopidogrel %/y	HR (95% CI)	*P* for Interaction
Primary outcome: cardiovascular death/ myocardial infarction/stroke									
Overall	15 202	1538	10.8	703	9.8	835	11.7	0.84 (0.76–0.93)	
<60	2562	457	19.4	189	16.4	268	22.4	0.71 (0.59–0.86)	0.03
≥60	12 640	1081	9.1	514	8.5	567	9.6	0.90 (0.80–1.02)	
Mortalidade Todas Causas									
Overall	15 202	728	5.2	321	4.5	407	5.8	0,79 (0,68 – 0,92)	
<60	2,562	282	12.3	109	9.6	173	14.9	0,64 (0,50 – 0,81)	0.02
≥60	12 640	446	3.8	212	3.5	234	4.0	0,91 (0,75 – 1,09)	
Hemorragia maior, PLATO									
Overall	15 202	1518	11.1	781	11.5	737	10.7	1,07 (0,97 – 1,19)	
<60	2562	319	14.3	161	14.5	158	14.2	1,08 (0,87 – 1,34)	0.98
≥60	12 640	1199	10.5	620	10.9	579	10.1	1,08 (0,96 – 1,20)	

Circulation. 2010;122:1056

PLATO

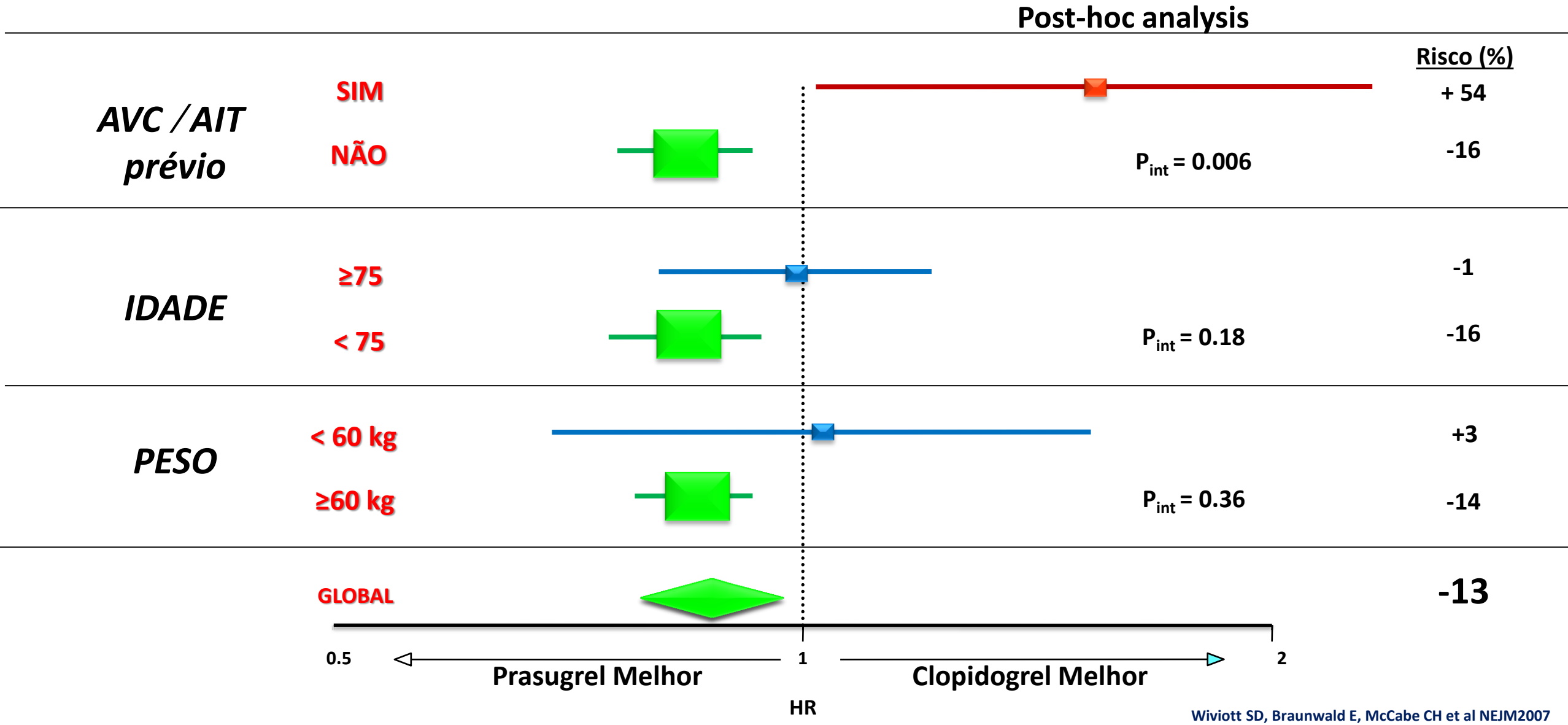
Ticagrelor Versus Clopidogrel e *AVC PRÉVIO*



Circulation 2012;125:2914

Benefício Clínico Líquido

Análise de Sub-grupos de Riscos de Sangramentos Maiores



Wiviott SD, Braunwald E, McCabe CH et al NEJM2007

2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

Developed in Collaboration with American Association for Thoracic Surgery, American Society of Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists,
and Society of Thoracic Surgeons

Endorsed by Preventive Cardiovascular Nurses Association and
Society for Vascular Surgery

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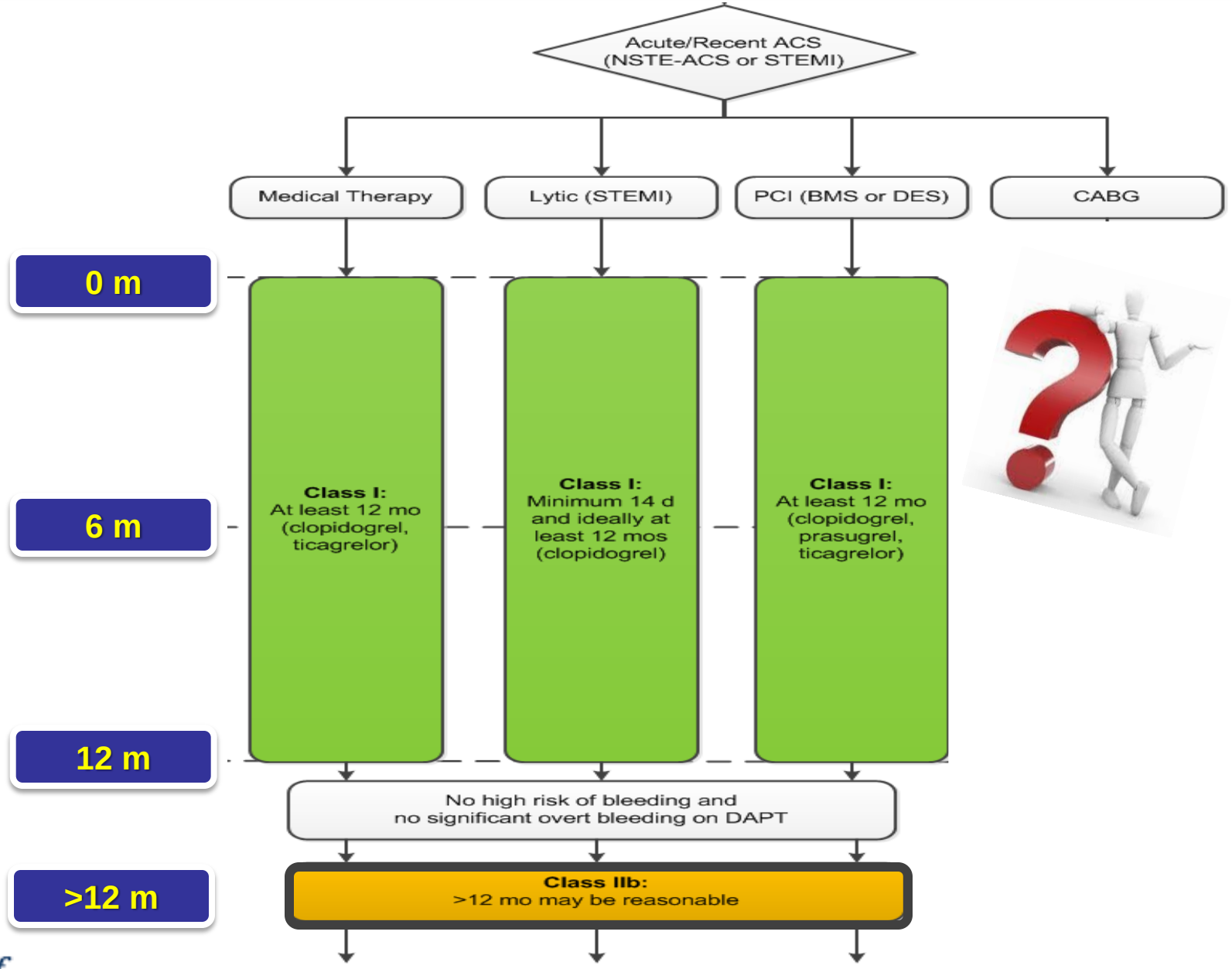
CR	NE	Recomendações
Inibidores Específicos $P2Y_{12}$		
IIa	B-R	▪ SCA (SCAssST ou SCAcsST) + Stent, ou ▪ SCAssST + Tratamento clínico (sem RM): ➔ Ticagrelor em preferência ao clopidogrel é RAZOÁVEL
IIa	B-R	▪ SCA (SCAssST ou SCAcsST) + Stent; ▪ Não alto risco hemorrágico ▪ Sem história de AVC ou AIT ➔ Prasugrel em preferência ao clopidogrel é RAZOÁVEL
III: Harm	B-R	▪ Prasugrel NÃO deve ser administrado a pacientes com AVC ou AIT prévios
Dose de Aspirina para Pacientes em DTAP		
I	B-NR	▪ Em pacientes em DTAP, dose de aspirina: ***81*** mg/dia (75 mg -100 mg)

SCA: Duração da DTAP (AAS + inibidor $P2Y_{12}$)



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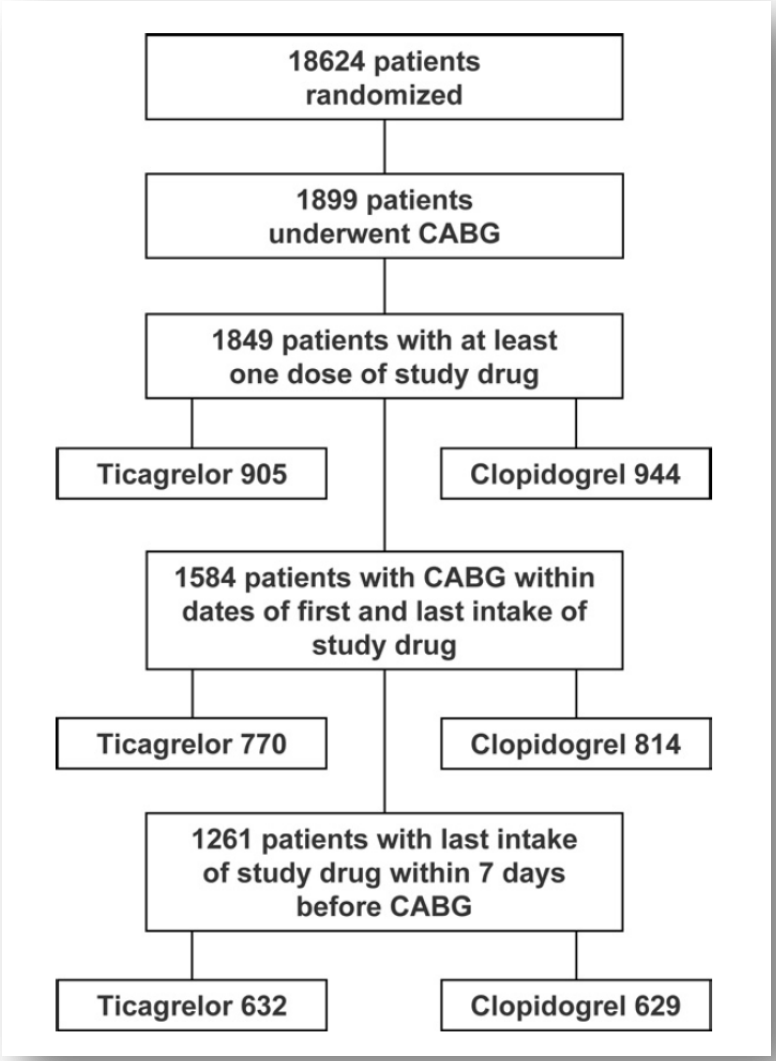
Ticagrelor Versus Clopidogrel in Patients With Acute Coronary Syndromes Undergoing Coronary Artery Bypass Surgery

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



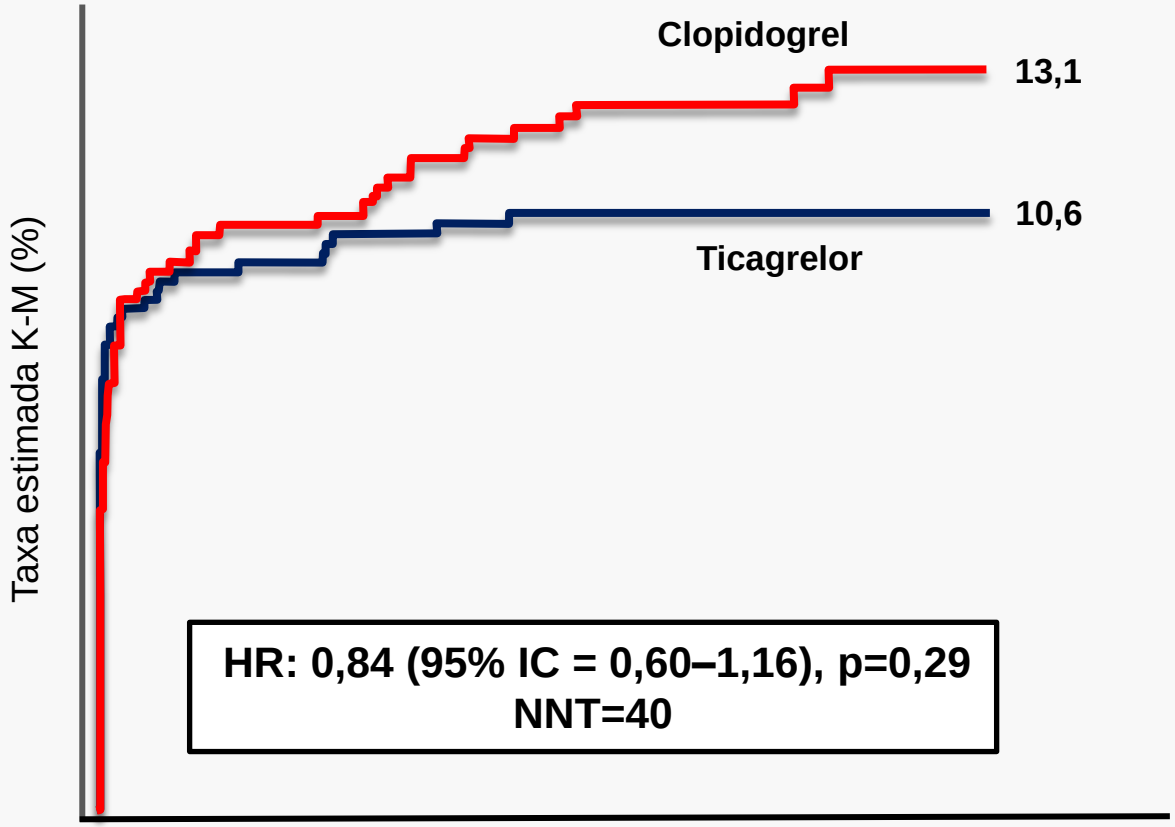
Characteristic	Ticagrelor (n = 632)	Clopidogrel (n = 629)
Treatment duration, days	226 (24–364)	223 (28–363)
Delay from start of pain, h	14.4 (6.9–20.4)	13.5 (6.7–20.8)
Delay from hospital admission, h	9.0 (2.3–17.0)	6.8 (2.2–15.7)
Study drug stopped before CABG		
1 day before CABG	84 (13.3)	88 (14.0)
2 days before CABG	106 (16.8)	86 (13.7)
3 days before CABG	114 (18.0)	73 (11.6)
4 days before CABG	84 (13.3)	69 (11.0)
5 days before CABG	79 (12.5)	96 (15.3)
6 days before CABG	91 (14.4)	110 (17.5)
7 days before CABG	74 (11.7)	107 (17.0)
Restarted drug after CABG		
Did not restart	234 (37.0)	238 (37.8)
<7 days	227 (35.9)	225 (35.8)
7–14 days	111 (17.6)	100 (15.9)
>14 days	60 (9.5)	66 (10.5)

Held C et al. JACC 2011;57:672-84

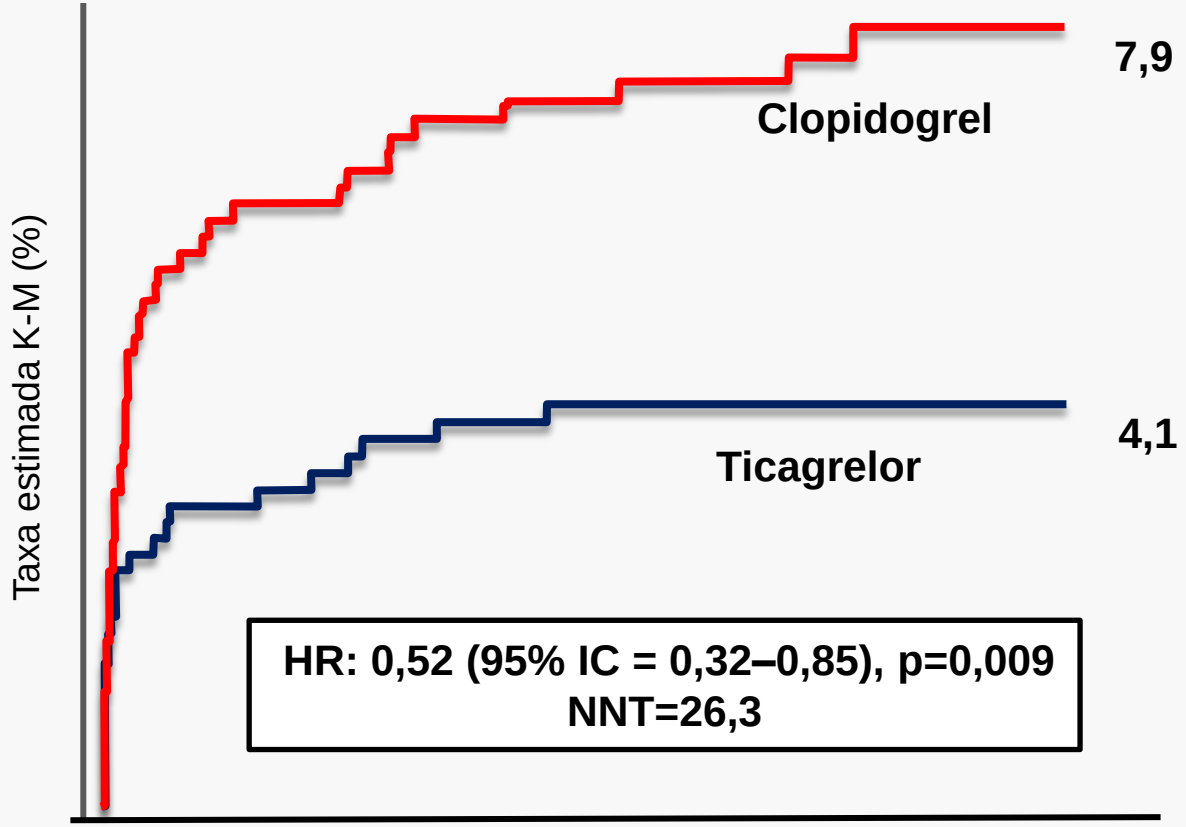
Ticagrelor Versus Clopidogrel in Patients With Acute Coronary Syndromes Undergoing Coronary Artery Bypass Surgery

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

Desfecho primário de morte CV, IM ou AVC



Morte cardiovascular



Held C et al. JACC 2011;57:672-84

SCAssST: Antiplaquetários

Classe de recomendação	Indicações	Nível de evidência
I	AAS (162 – 300mg em dose de ataque, com dose de manutenção de 81 – 100mg/dia), a todos os pacientes, salvo contraindicação, independentemente da estratégia de tratamento e por tempo indeterminado.	A
	Clopidogrel (300mg em dose de ataque, com dose de manutenção de 75mg/dia) em adição ao AAS, em pacientes portadores de angina instável de risco intermediário ou alto, além de IAMSEST, por 12 meses.	A
	Uso de terapia antiplaquetária dupla por 12 meses após o evento agudo, salvo contraindicações.	A
	Ticagrelor (180mg de ataque seguido por 90mg 2x/dia) em pacientes portadores de angina instável de risco moderado ou alto, além do IAMSEST, independentemente da estratégia de tratamento posterior (clínico, cirúrgico ou percutâneo), por 12 meses.	B
	Prasugrel 60mg de ataque seguido por 10mg ao dia em pacientes portadores de angina instável de risco moderado ou alto, além do IAMSEST, com anatomia coronária conhecida, submetidos à angioplastia e sem fatores de risco para sangramento (maior ou igual a 75 anos de idade; menos de 60kg; AVC ou AIT prévios).	B
	Adição de um inibidor da GP IIb/IIIa em pacientes com baixo risco hemorrágico, sob dupla antiagregação plaquetária, submetidos à ICP de alto risco (presença de trombos, complicações trombóticas da ICP).	A
IIa	Clopidogrel (600mg em dose de ataque, seguida por 150mg ao dia por 7 dias e dose posterior de 75mg ao dia), em adição ao AAS, em pacientes submetidos a ICP com alto risco de eventos isquêmicos e baixo risco de sangramento.	B
	Reiniciar ticagrelor ou clopidogrel após cirurgia de revascularização miocárdica, assim que seguro	**B**

Arq Bras Cardiol 2013; 101 (3Supl.3): 1-93

2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

MANEJO PEROPERATÓRIO DE TERAPIA ANTIPLAQUETÁRIA EM PACIENTES COM SCASSST E INDICAÇÃO CIRÚRGICA (CARDÍACA E NÃO CARDÍACA)

	Classe	NE
AAS em 6-24hs após cirurgia de revascularização miocárdica na ausência de hemorragias	I	A
AAS em baixa dose até a cirurgia de revascularização miocárdica	I	B
Suspender **ticagrelor e clopidogrel** no **mínimo 5 dias antes** de cirurgia *cardíaca* Cirurgia não cardíaca	IIa IIa	B C
Suspender **prasugrel no mínimo 7 dias antes** de cirurgia *cardíaca* Cirurgia não cardíaca	IIa IIa	B C
Após CRM, retorno de inibidor $P2Y_{12}$ tão logo considerado seguro	IIa	C
Em caso de **cirurgia inadiável** suspender dupla antiagregação plaquetária **após mínimo de um mês de uso** para **stent convencional**	IIb	C
Em caso de **cirurgia inadiável** suspender dupla antiagregação plaquetária **após mínimo de 3 meses de uso** para **stent farmacológico**	IIb	C

2016

Revascularização Miocárdica Cirúrgica e DTAP

CR	NE	Recomendações
I	C-EO	**Pacientes em DTAP pós stent, submetidos a RMC:** **Reiniciar inibidor $P2Y_{12}$ no pós-op e continuar até completar duração recomendada**
I	C-LD	**Pacientes em DTAP pós SCA, submetidos a RMC:** **Reiniciar inibidor $P2Y_{12}$ no pós-op e completar 12 meses de DTAP pós SCA**
I	B-NR	**Em pacientes em DTAP, dose de aspirina é de 81 mg/dia (75 mg -100 mg)**
IIb	B-NR	**Pacientes com DAC estável:** **DTAP com clopidogrel no pós-op precoce e mantido por 12 meses para manutenção de patência de enxerto venoso pode ser razoável**

EO: *expert opinion* **LD:** *limited data* **NR:** *nonrandomized*

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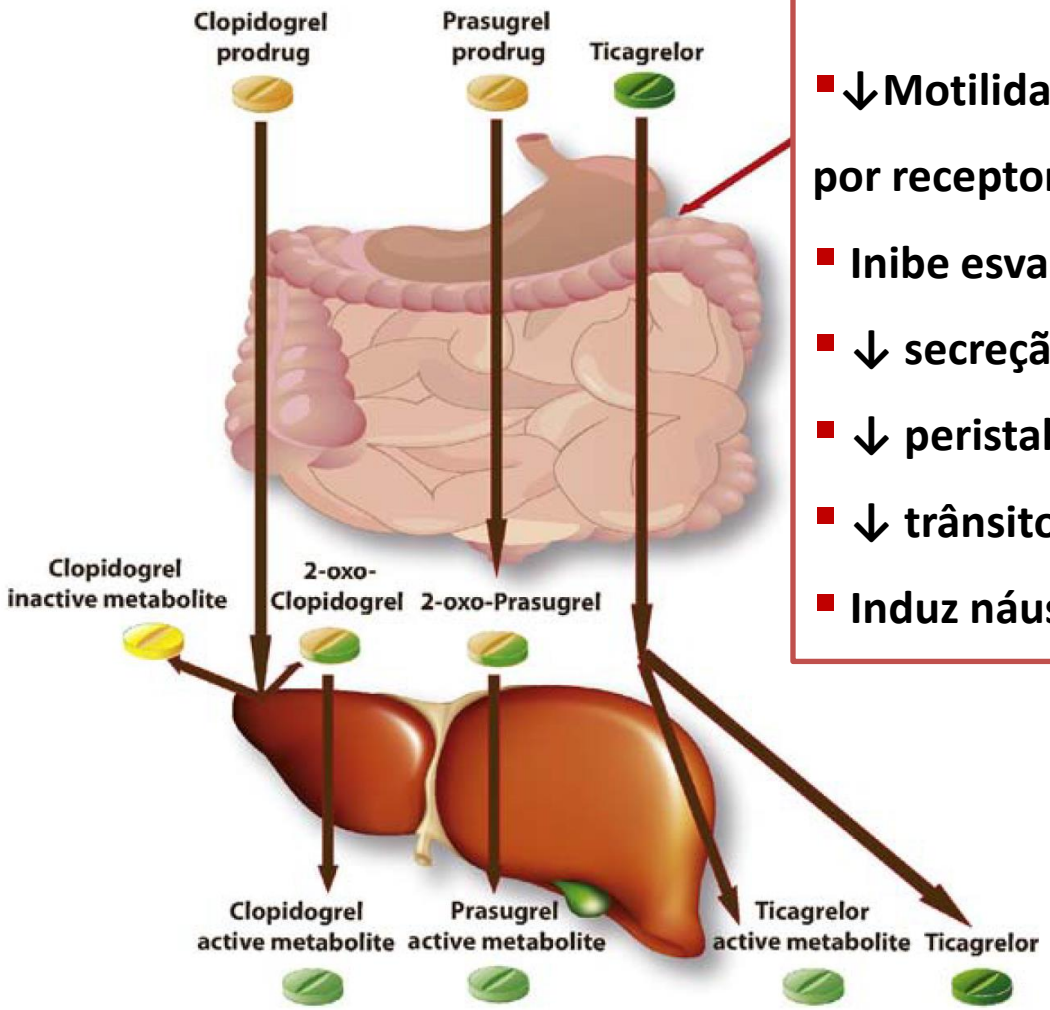


MORFINA

- ↓Motilidade intestinal via plexo mesentérico, mediado por receptores opóides μ
- Inibe esvaziamento gástrico
- ↓ secreção intestinal
- ↓ peristalse intestinal
- ↓ trânsito intestinal
- Induz náuseas e vômitos

European Heart Journal Advance Access published October 21, 2015

European Heart Journal
doi:10.1093/eurheartj/ehv547

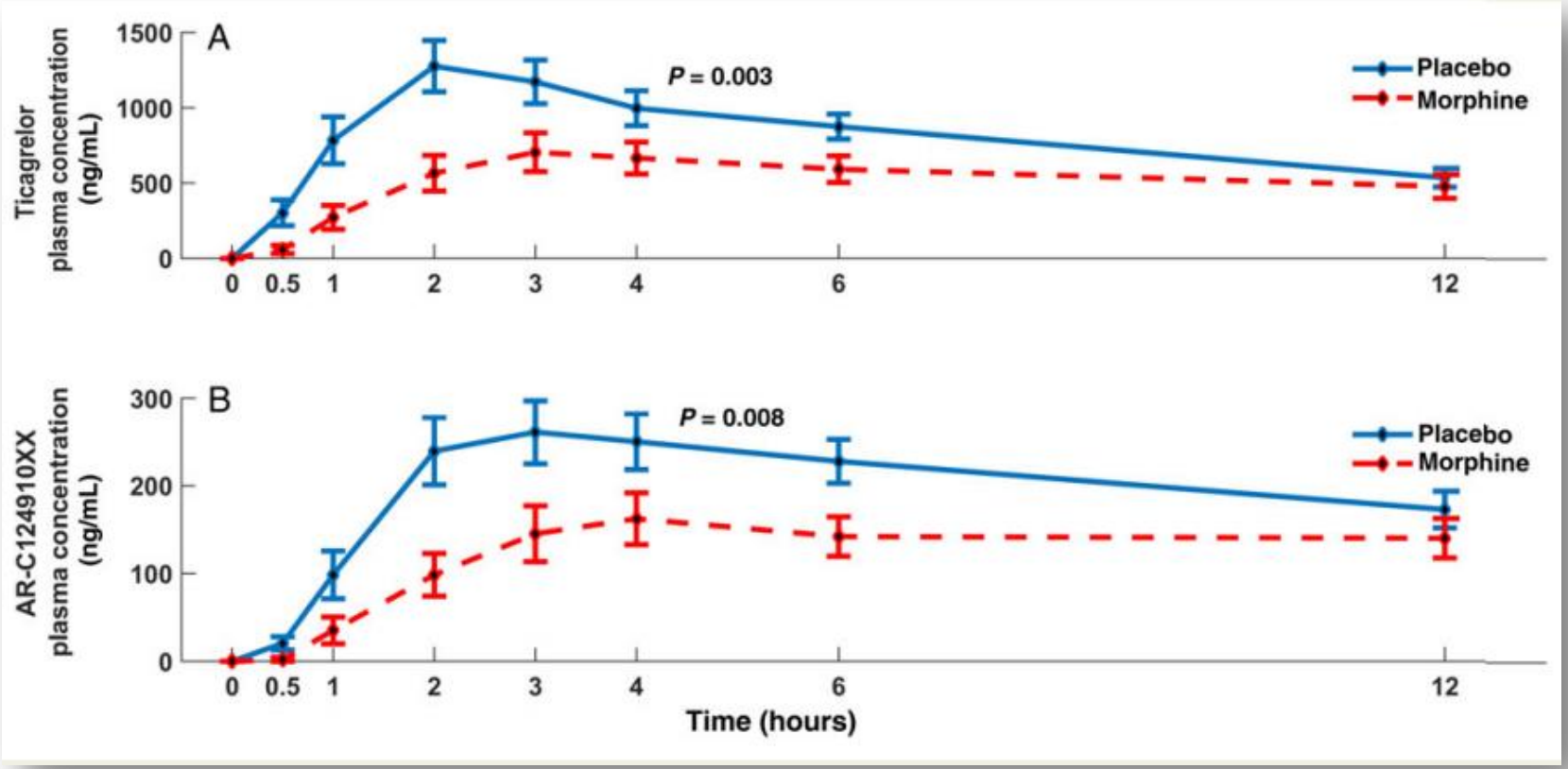
FASTTRACK CLINICAL RESEARCH
Acute coronary syndromes

Morphine delays and attenuates ticagrelor exposure and action in patients with myocardial infarction: the randomized, double-blind, placebo-controlled IMPRESSION trial

N = 70
IAMcsST = 64%

Ticagrelor

Metabólito Ativo Ticagrelor



Thromb Haemost. 2015 May 19;116(2). [Epub ahead of print]

P2Y12 receptor inhibition and effect of morphine in patients undergoing primary PCI for ST-segment elevation myocardial infarction. The PRIVATE-ATLANTIC study.

Silvain J, Storey RF, Cayla G, Esteve JB, Dillinger JG, Rousseau H, Tsatsaris A, Baradat C, Salhi N, Hamm CW, Lapostolle F, Lassen JF, Collet JP, Ten Berg JM, Van't Hof AW, Montalescot G[1].

Author information

Abstract

PRIVATE-**ATLANTIC** (P2Y12 Receptor Inhibition with VASP Testing using Elisa kit during the **ATLANTIC** study) is a pre-specified substudy of the randomised, double-blind **ATLANTIC trial** in patients with ST-segment elevation myocardial infarction, designed to help interpret the main **trial** results. The primary objective of **ATLANTIC** was to assess coronary reperfusion prior to percutaneous coronary intervention (PCI) with pre- vs in-hospital ticagrelor 180 mg loading dose (LD). PRIVATE-**ATLANTIC** assessed platelet inhibition in 37 patients by measurement of vasodilator-associated stimulated phosphoprotein (VASP) platelet reactivity index (PRI) and VerifyNow platelet reactivity units (PRU) before angiogram (T1), immediately after PCI (T2), 1 (T3), and 6 (T4) hours (h) after PCI, and before next study drug administration (T5). The median time difference between the two ticagrelor LD was 41 minutes. Platelet reactivity was unaffected at T1 when measured by VASP-PRI (89.8 vs 93.9 % for pre- and in-hospital ticagrelor, respectively; p = 0.18) or PRU (239 vs 241; p = 0.82). Numerical differences were apparent at T2 and maximal at T3. Morphine administration significantly delayed onset of platelet inhibition at T3 (VASP-PRI 78.2 vs 23.4 % without morphine; p = 0.0116) and T4 (33.1 vs 11.0 %; p = 0.0057). In conclusion, platelet inhibition in **ATLANTIC** was unaffected by pre-hospital ticagrelor administration at the time of initial angiogram due to the short transfer delay. The maximum difference in platelet inhibition was detected 1 h after PCI (T3). Morphine administration was associated with delayed onset of action of ticagrelor and appeared more important than timing of ticagrelor administration.

Thromb Haemost. 2016 Apr 21;116(1). [Epub ahead of print]

Morphine delays the onset of action of prasugrel in patients with prior history of ST-elevation myocardial infarction.

Thomas MR, Morton AC, Hossain R, Chen B, Luo L, Shahari NN, Hua P, Beniston RG, Judge HM, Storey RF[1].

Author information

Abstract

Delays in the onset of action of prasugrel during primary percutaneous coronary intervention (PPCI) have been reported and could be related to the effects of morphine on gastric emptying and subsequent intestinal absorption. The study objective was to determine whether morphine delays the onset of action of prasugrel in patients with a prior history of ST-elevation myocardial infarction (STEMI) treated with PPCI. This was a crossover study of 11 aspirin-treated patients with prior history of STEMI treated with PPCI, for which prasugrel and morphine had been previously administered. Patients were randomised to receive either morphine (5 mg) or saline intravenously followed by 60 mg prasugrel. Blood samples were collected before randomised treatment and over 24 hours after prasugrel administration. The inhibitory effects of prasugrel on platelets were determined using the VerifyNow P2Y12 assay and light transmission aggregometry. Plasma levels of prasugrel and prasugrel active metabolite were measured. Platelet reactivity determined by VerifyNow PRU, VerifyNow % Inhibition and LTA was significantly higher at 30-120 minutes (min) when morphine had been co-administered compared to when saline had been co-administered. Morphine, compared to saline, significantly delayed adequate platelet inhibition after prasugrel administration (158 vs 68 min; p = 0.006). Patients with delayed onset of platelet inhibition also had evidence of delayed absorption of prasugrel. In conclusion, prior administration of intravenous morphine significantly delays the onset of action of prasugrel. Intravenous drugs may be necessary to reduce the risk of acute stent thrombosis in morphine-treated STEMI patients undergoing PPCI.

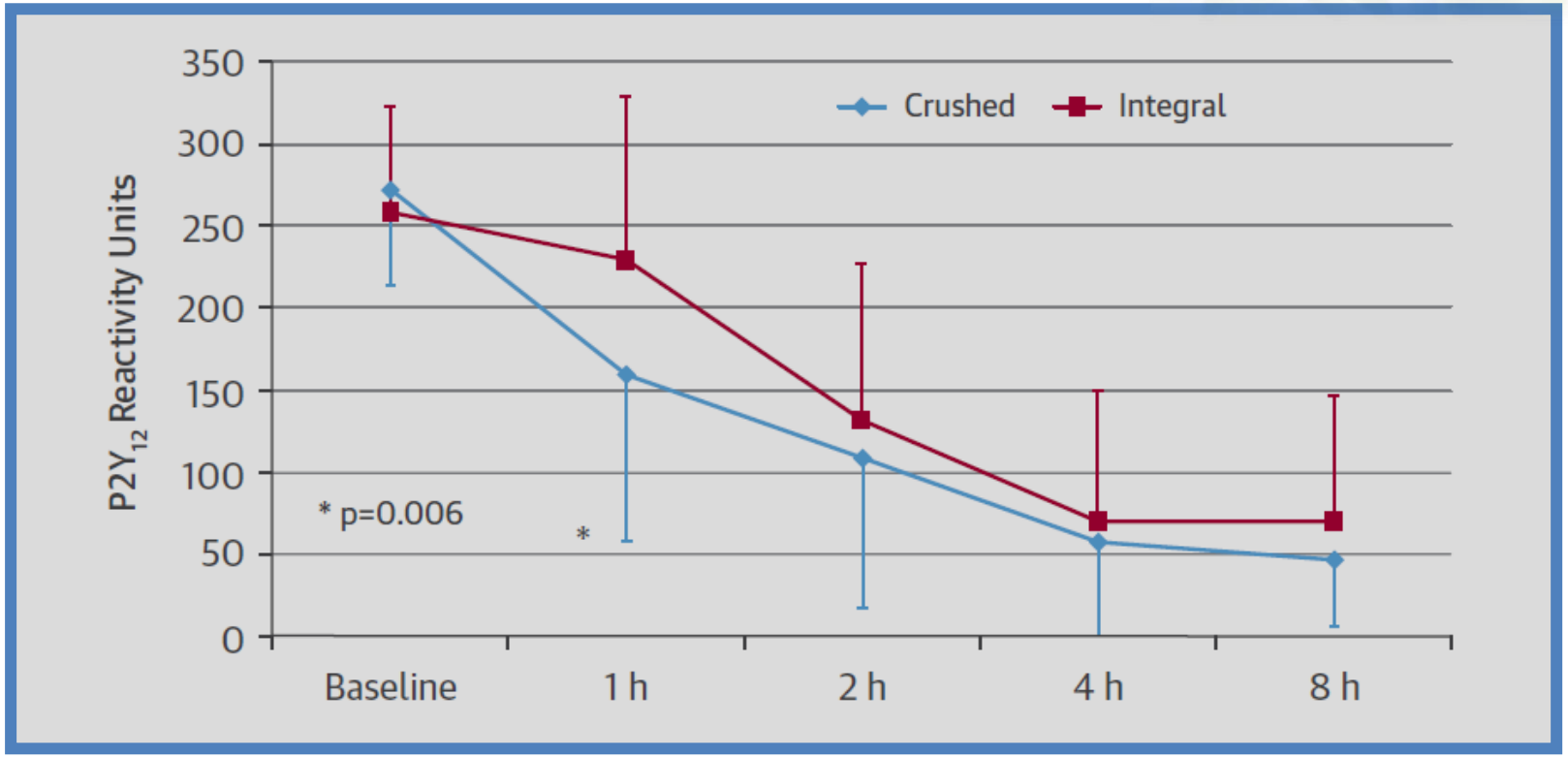
MOJITO (Mashed Or Just Integral pill of TicagrelOr)

n = 82 IAMcsST + ATC 1ª

Interação Morfina/$P2Y_{12}$

Estratégias (?)

- $P2Y_{12}$ IV (cangrelor)
- iGPIIb/IIIa
- Procinéticos
- Maceração
- Analgesia curta duração (alfentanil)



PREDITORES INDEPENDENTES (1ª HORA):

- DROGA MACERADA
- USO DE MORFINA (↑PRU)

JACC 2015,65:511

J. Kubica et al.
International Journal of Cardiology
2016;215:201–208

Antiplaquetários: Custo/Efetividade

Economic Analysis of Ticagrelor Therapy From a U.S. Perspective

Results From the PLATO Study

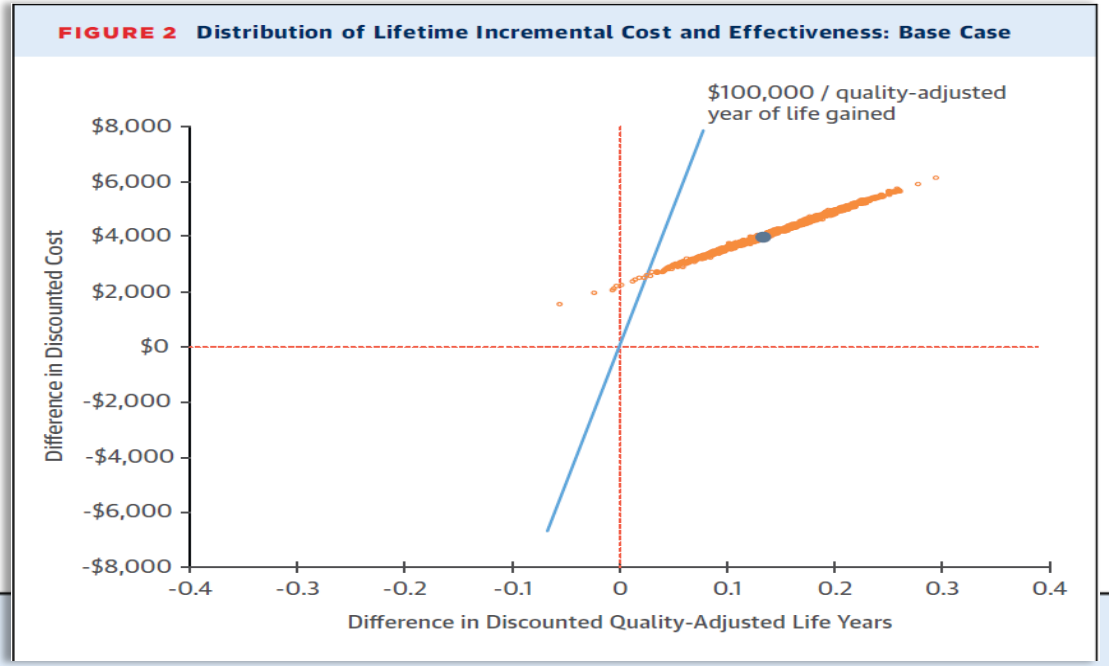


FIGURE 2 Distribution of Lifetime Incremental Cost and Effectiveness: Base Case

TABLE 3 Cumulative 1-Year Within-Trial Costs for U.S. Low-Dose Cohort*

Cost	Ticagrelor Group (n = 284)	Clopidogrel Group (n = 263)	Difference (95% CI)†	p Value
Medical costs (observed)	29,223 (26,655–31,790)	30,716 (27,155–34,277)	−1,493 (−5,884 to 2,897)	0.50
Medical costs (Winsorized)	29,191 (26,648–31,735)	29,907 (26,999–32,815)	−716 (−4,579 to 3,147)	0.72
Study drug	2,204 (2,072–2,336)	32 (30–34)	2,172 (2,040 to 2,304)	<0.001
Total (Winsorized)	31,395 (28,848–33,942)	29,939 (27,031–32,847)	1456 (−2410 to 5,322)	0.46

CONCLUSIONS For PLATO-eligible ACS patients, a U.S. perspective comparison of the current standard of dual antiplatelet therapy of aspirin with clopidogrel versus aspirin plus ticagrelor showed that the ticagrelor regimen increased life expectancy at an incremental cost well within accepted benchmarks of good value for money. (A Comparison of

JACC 2015;65:465

Antiplaquetários: Custo/Efetividade

Intervention and compared intervention strategy	Patient group	ICER (Euro) per QALY or LY gained	References
Early invasive strategy vs. medical treatment in patients with unstable coronary artery disease	FRISC II	2 330 QALY	Janzon et al. (2003)*
Ticagrelor vs. clopidogrel in patients with ACS	PLATO	2 370 Life Year, 2 750 QALY	Janzon et al. (2011)***
Prasugrel vs. clopidogrel in patients with ACS and planned PCI	TRITON-TIMI 38	6 710 Life Year	Mahoney et al. (2010)**
Clopidogrel vs. placebo in patients with acute coronary syndromes	CURE	7 280 Life Year	Weintraub et al. (2005)*
Early invasive vs. conservative strategy for the treatment of unstable angina and NSTE myocardial infarction	TACTICS-TIMI	12 040 Life Year	Mahoney et al. (2002)*
Early interventional vs. conservative strategy for patients with NSTE-ACS	RITA 3 medium risk	24 840 QALY	Henriksson et al. (2008)*

Threshold, National Board of Health and Welfare: €40 000-€50 000/QALY

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Mitos e verdades sobre o uso de antiplaquetários na intervenção percutânea.

Panorama dos antiplaquetários na prática médica atual

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