Uso de los NACOs en pacientes que precisen antiagregación plaquetaria

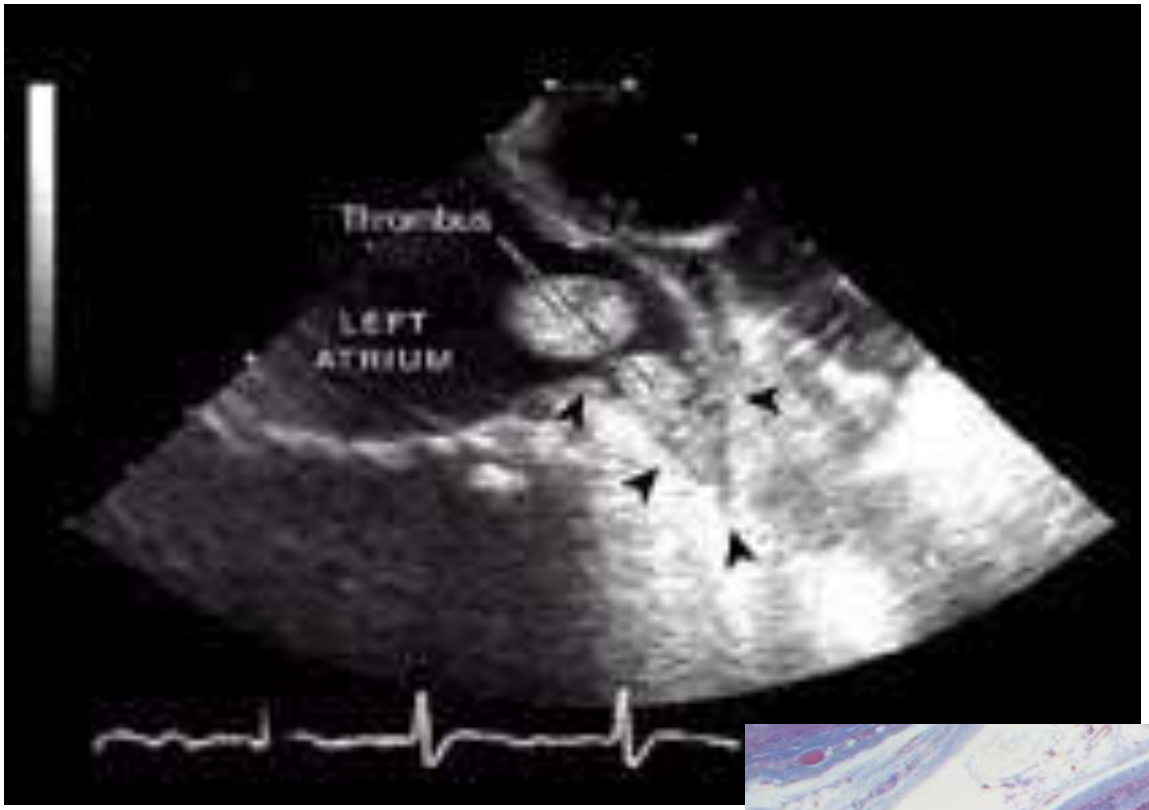
Francisco Marín
Servicio de Cardiología
Hospital Universitario Virgen de la Arrixaca
Murcia

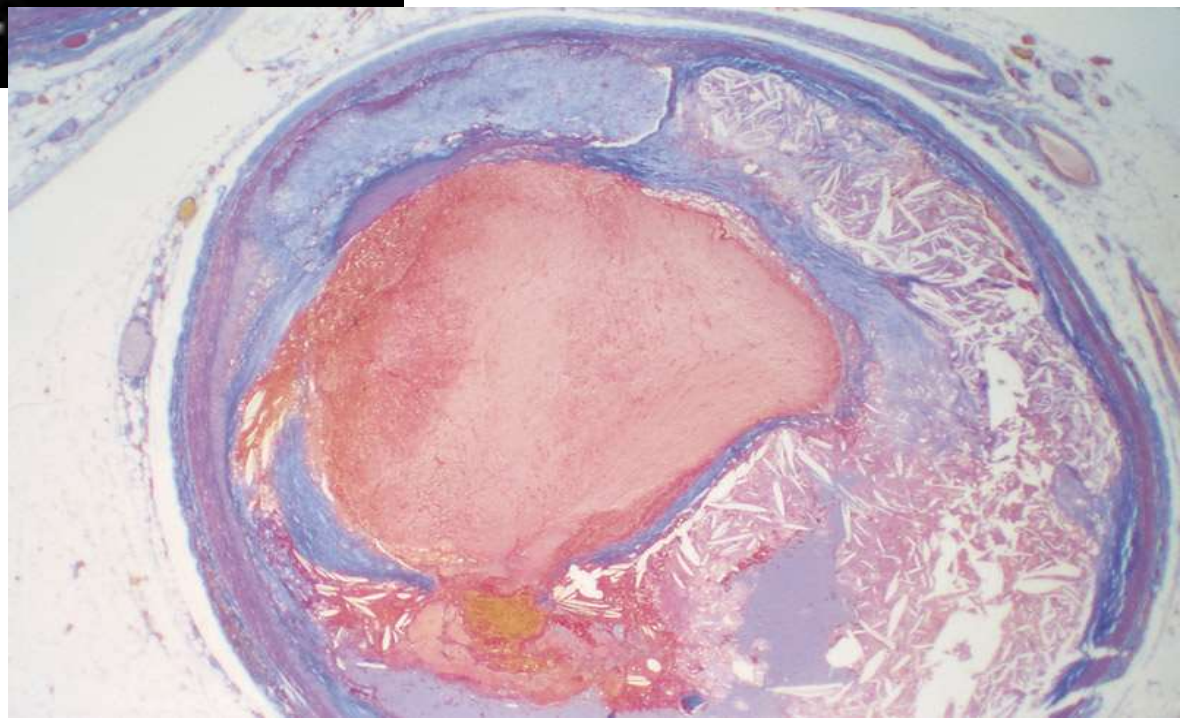
IMIB
Instituto Murciano de Investigación Biosanitaria Virgen de la Arrixaca

Declaración de potenciales conflictos de intereses

Relativas a esta presentación existen las siguientes relaciones que podrían ser percibidas como potenciales conflictos de intereses:

- Consultoría: Bayer, BMS-Pfizer, Boehringer-Ingelheim, Daiichi-Sankyo y AFNET-EHRA
- Becas de Investigación: Abbott, Boston Scientific, Astra-Zeneca, Pfizer, Bayer, Boehringer-Ingelheim, Menarini y Daiichi-Sankyo
- Remuneración por desarrollo de presentaciones educativas: Daiichi-Sankyo, Bayer, BMS-Pfizer, Astra-Zeneca, Boehringer-Ingelheim, Servier y Menarini


Thrombus
LEFT
ATRIUM

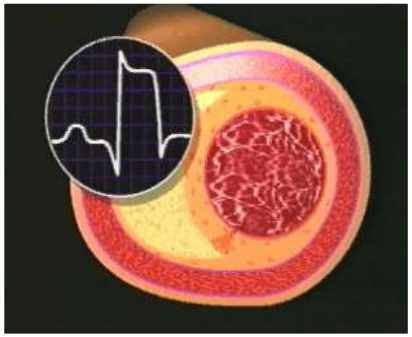


Tratamiento antitrombótico

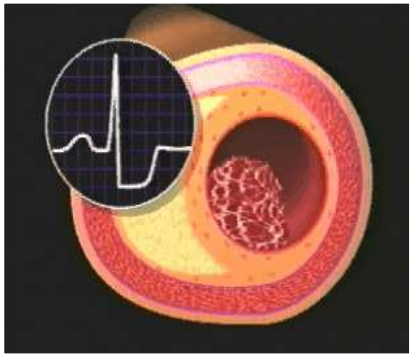
Reducción de eventos trombóticos

Incremento del riesgo hemorrágico

No son pacientes especiales: son pacientes habituales



SCACEST  **11%**



SCASEST  **9%**

- **Frecuente coexistencia.**
  - 8-15% SCA presentan Fibrilación auricular.
  - 20-25% Fibrilación auricular presentan cardiopatía isquémica.
- **Implicación pronóstica bidireccional.**
- **Población compleja con múltiples co-morbilidades.**

Registros Diocles y GYSCA

Table 1 Clinical Characteristics of the Studied Population (N = 1,370)

Heart failure	433 (32)
History of stroke or TIA	364 (19)
Coronary artery disease	254 (18)
Current alcoholic consumption	49 (4)
Previous bleeding episode	111 (9)
Renal impairment	141 (10)
Liver impairment	18 (1)
HAS-BLED score	2 (2–3)
HAS-BLED ≥3	479 (35)
$CHADS_2$ score	2 (2–3)
$CHADS_2$ ≥2	1,027 (75)
CHA_2DS_2-VASc score	4 (3–5)
CHA_2DS_2-VASc ≥2	1,289 (94)
Concomitant treatment	
Antiplatelet therapy	246 (18)
ACE inhibitors/angiotensin receptor blockers	712 (52)
Calcium antagonist	342 (25)
Beta-blockers	466 (34)
Statins	329 (24)
Digoxin	274 (20)
Diuretics	616 (45)

Values are n (%) or median (interquartile range).

ACE = angiotensin-converting enzyme; $CHADS_2$ = congestive heart failure, hypertension, 75 years of age or older, diabetes mellitus, and previous stroke or transient ischemic attack; CHA_2DS_2-VASc = congestive heart failure, hypertension, 75 years of age and older, diabetes mellitus, previous stroke or transient ischemic attack, vascular disease, 65 to 74 years of age, female; HAS-BLED: hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly; TIA = transient ischemic attack.

Roldán et al. J Am Coll Cardiol 2013

Características y pronóstico

Table 1 Baseline Characteristics of the Study Population

	Whole Cohort n = 426	Chronic n = 256 (60.1%)	Paroxysmal n = 170 (39.9%)	p Value
Men, n (%)	70.9	69.0	73.7	0.31
Age (yrs)	71.5 ± 8.5	72.3 ± 8.5	70.0 ± 8.5	<0.01
Medical history				
Diabetes (%)	40.2	41.5	38.2	0.49
Hypertension (%)	74.5	75.4	73	0.58
Previous heart failure (%)	26.7	32.4	17.4	<0.01
Previous stroke or thromboembolism (%)	15.9	18	12.4	0.14
Renal failure	14.9	12.8	21.4	0.39
Number of embolic factors	2.5 ± 1.1	2.7 ± 1	1.9 ± 1.1	<0.01
Any embolic factor	95.8	96.9	92.3	0.21
$CHADS_2$ risk score	2 (1–3)	2 (2–3)	2 (1–2)	<0.01
Previous ischemic events (%)	43.7	45.1	40.3	0.29
Treatment on admission (%)				
Previous aspirin	36.2	31.5	43.6	0.01
Previous clopidogrel	13.8	13.4	14.5	0.77
Previous oral anticoagulation	50.1	69.2	16.0	<0.01

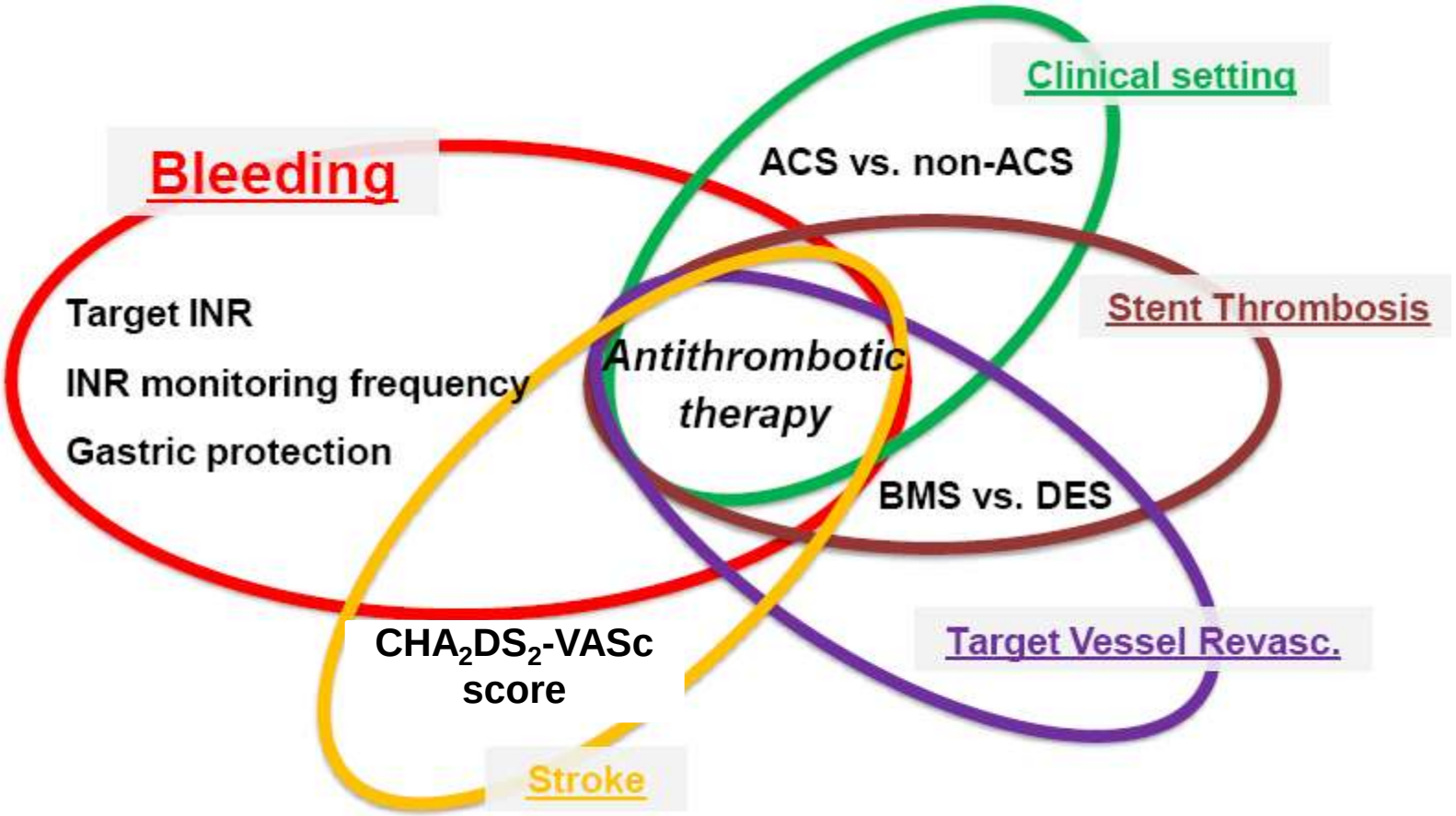
Ruiz-Nodar et al. JACC 2008:51:818-25

Características y pronóstico

Table 5 Events During Follow-Up — **Median 594 days. Range 0 to2190**

	Whole Cohort n = 373	Anticoagulated n = 195	Not Anticoagulated n = 178	p Value
Major bleeding (%)	12.3	14.9	9.0	0.19
Minor bleeding (%)	11.0	12.6	9.0	0.32
Embolism (%)	4.2	1.7	6.9	0.02
Death (%)	22.6	17.8	27.8	0.02
Acute myocardial infarction (%)	8.4	6.5	10.4	0.14
Target vessel revascularization (%)	7.7	7.1	8.4	0.3
Target vessel failure (%)	9.2	9.2	16.7	<0.01
Revascularization of other lesions (%)	7.1	5.9	8.5	0.25
Subacute or late thrombosis (%)	1.2	1.2	1.3	0.65
MACE (%)	32.3	26.5	38.7	0.01
MAE (%)	36.6	31.8	41.9	0.03

Ruiz-Nodar et al. JACC 2008:51:818-25


Clinical setting
ACS vs. non-ACS
Bleeding
Target INR
INR monitoring frequency
Gastric protection
Stent Thrombosis
Antithrombotic therapy
BMS vs. DES
Target Vessel Revasc.
CHA2DS2-VASc score
Stroke

Rubboli A.

European Heart Journal (2014) **35**, 3155–3179
doi:10.1093/eurheartj/ehu298

CURRENT OPINION

Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions: a joint consensus document of the European Society of Cardiology Working Group on Thrombosis, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS)

Task Force Members: Gregory Y.H. Lip* (UK, Chairman), Stephan Windecker (Switzerland)†, Kurt Huber (Austria)†, Paulus Kirchhof (UK)†, Francisco Marin (Spain), Jurriën M. Ten Berg (Netherlands), Karl Georg Haeusler (Germany), Giuseppe Boriani (Italy), Davide Capodanno (Italy), Martine Gilard (France), Uwe Zeymer (Germany), Deirdre Lane (UK, Patient Representative).
Document Reviewers: Robert F. Storey (Review Co-ordinator), Hector Bueno, Jean-Philippe Collet, Laurent Fauchier, Sigrun Halvorsen, Maddalena Lettino, Joao Morais, Christian Mueller, Tatjana S. Potpara, Lars Hvilsted Rasmussen, Andrea Rubboli, Juan Tamargo, Marco Valgimigli, and Jose L. Zamorano

Lip et al. Eur Heart J 2014

DEFINICIONES

- **TERAPIA PUENTE**: administración de un anticoagulante de acción rápida parenteral (HNF/HBPM) durante el periodo de cese del tratamiento anticoagulante oral
  - Dosis terapéuticas
  - Dosis profilácticas
  - Dosis intermedias

- **Pacientes con alto riesgo trombótico**
  - Las recomendaciones van orientadas en primer lugar a reducir el riesgo trombótico y segundo el hemorrágico
- **Pacientes de bajo riesgo trombótico**
  - Las recomendaciones van dirigidas en primer lugar a minimizar el riesgo hemorrágico y 2º reducir el riesgo trombótico

RIESGO TROMBÓTICO

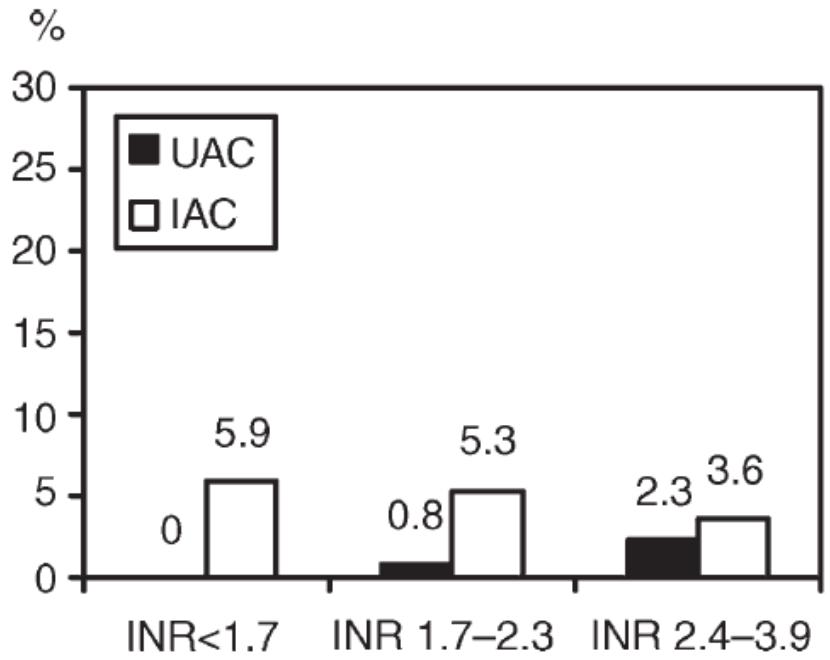
ACCP, 9ª Conferencia. 2012

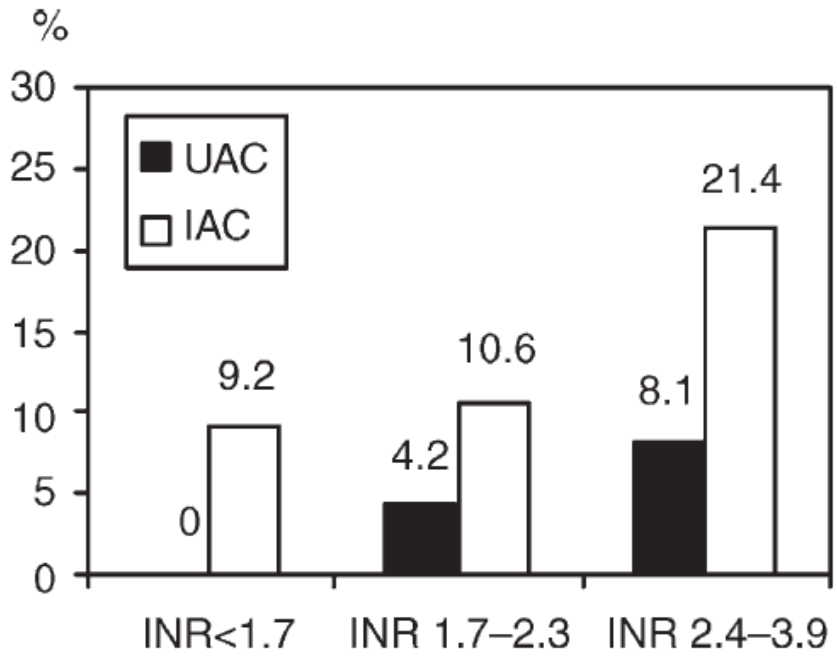
	MOTIVO ANTICOAGULACION		
RIESGO	**Válvulas cardiacas mecánicas**	**Fibrilación auricular**	**Tromboembolismo venoso (TEV)**
ALTO **>10%/año evento arterial y >10%/m ETV**	Posición mitral Posición aórtica (antiguas) ACV/TIA < 6 m	$CHADS_2$: 5-6 ACV/TIA <3 m V reumática mitral	VTE reciente (<3 m) Trombofilia severa
MODERADO **4-10%/año evento arterial y 4-10%/m ETV**	Posición aortica con FA, ACV/TIA previo, DM, IC, edad>75	$CHADS_2$: 3-4	VTE 3-12 m Trombofilia no severa TEV recurrente TEV + cáncer
BAJO **<4%/año evento arterial y <4%/m ETV**	Posición aórtica sin factores riesgo	$CHADS_2$: 0-2 sin ACV/TIA previo	VTE > 12 m

RIESGO HEMORRÁGICO SEGÚN PROCEDIMIENTO

Riesgo bajo	Riesgo intermedio	Riesgo alto
·Extracciones dentarias únicas ·Cataratas con anestesia tópica ·Herida traumática periférica ·Inyección intramuscular ·Endoscopias sin biopsia ·Resto de biopsias y punciones ·Dilataciones del tracto gastrointestinal y genitourinario ·Cirugía menor ·Reducciones no quirúrgicas de fracturas ·Implante de catéter central ·Cateterismo arterial por vía radial ·Colocación de DIU	·Varias extracciones e implantes dentarios ·Cataratas con anestesia retrobulbar ·Desprendimiento de retina ·Endoscopia con biopsia ·Punción lumbar ·Biopsia de próstata ·Legrado uterino ·Cateterismo arterial por vía femoral ·Absceso perianal ·Implante de marcapasos ·Polipectomía	·Prostatectomía y cirugía mayor urológica ·Cirugía abdominal ·Traumatismos craneoencefálicos ·Biopsia hepática/renal ·Cirugía cardiaca ·Neurocirugía

Interrumpir la ACO se asocia a mayor riesgo de hemorragia





21% de acceso radial

Karjalainen PP et al. Eur Heart J 2008;29:1001-10

Heparin Bridging vs. Uninterrupted Oral Anticoagulation in Patients With Atrial Fibrillation Undergoing Coronary Artery Stenting

– Results From the AFCAS Registry –

Table 4. Outcome Events

	Overall series			Propensity score-matched pairs		
	UAC (n=290)	BT (n=161)	P-value	UAC (n=114)	BT (n=114)	P-value
No. patients with MACCE	11 (3.8)	10 (6.2)	0.25	6 (5.3)	8 (7.0)	0.58
Death	6 (2.1)	4 (2.5)	0.73	5 (4.4)	4 (3.5)	1.00
Myocardial infarction	3 (1.0)	3 (1.9)	0.67	0	0	–
Re-revascularization	2 (0.7)	4 (2.5)	0.19	0	3 (2.6)	0.25
Stent thrombosis	6 (2.1)	2 (1.2)	0.72	1 (0.9)	0	1.00
Definite	2 (0.7)	0		0	0	
Probable	4 (1.4)	2 (1.2)		1 (0.9)	0	
Stroke	1 (0.3)	0	1.0	0	0	–
All bleeding events	35 (12.1)	30 (18.6)	0.07	18 (15.8)	17 (14.9)	1.00
Major bleeding	4 (1.4)	4 (2.5)	0.25	3 (2.6)	3 (2.6)	1.00
Blood transfusion	3 (1.0)	1 (0.6)	1.0	3 (2.6)	1 (0.9)	0.62
Access site bleeding	16 (5.5)	18 (11.2)	0.030	10 (8.8)	10 (8.8)	1.00

Data given as n (%).
UAC, uninterrupted oral anticoagulation; BT, bridging therapy; MACCE, major adverse cardiac and cerebrovascular events (death, myocardial infarction, target vessel revascularization and/or stent thrombosis and stroke).

n=963 19% de acceso radial tras el propensity

Lahtela. Circulation Journal 2012;76:1363-8

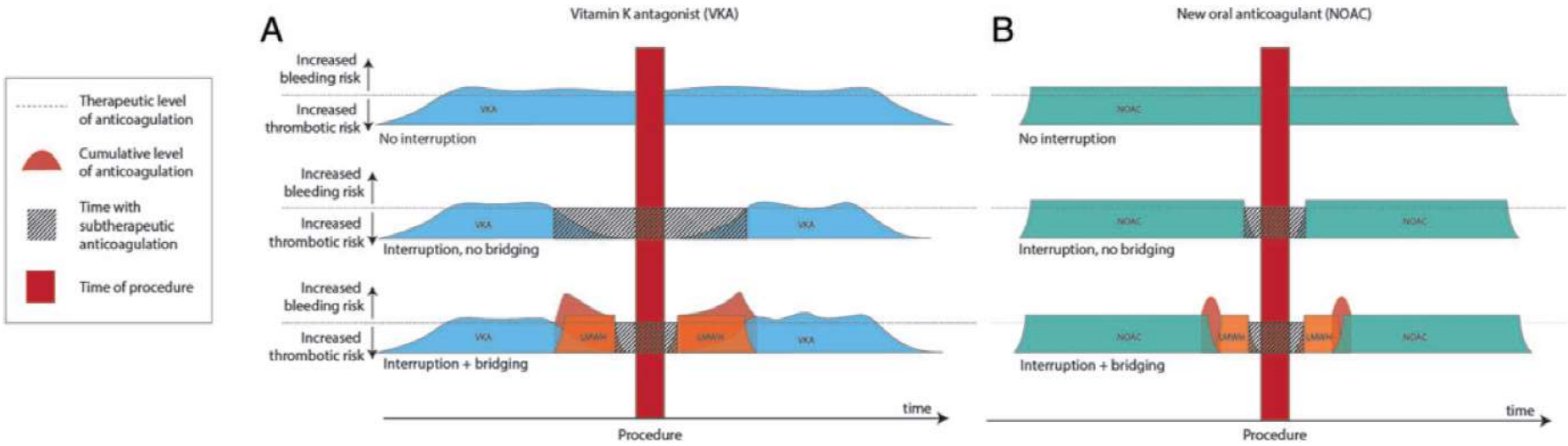
Terapia puente con NOAC

Dresden NOAC registry:

-Las complicaciones cardiovasculares y sangrados mayores son más altos en **procedimientos mayores**

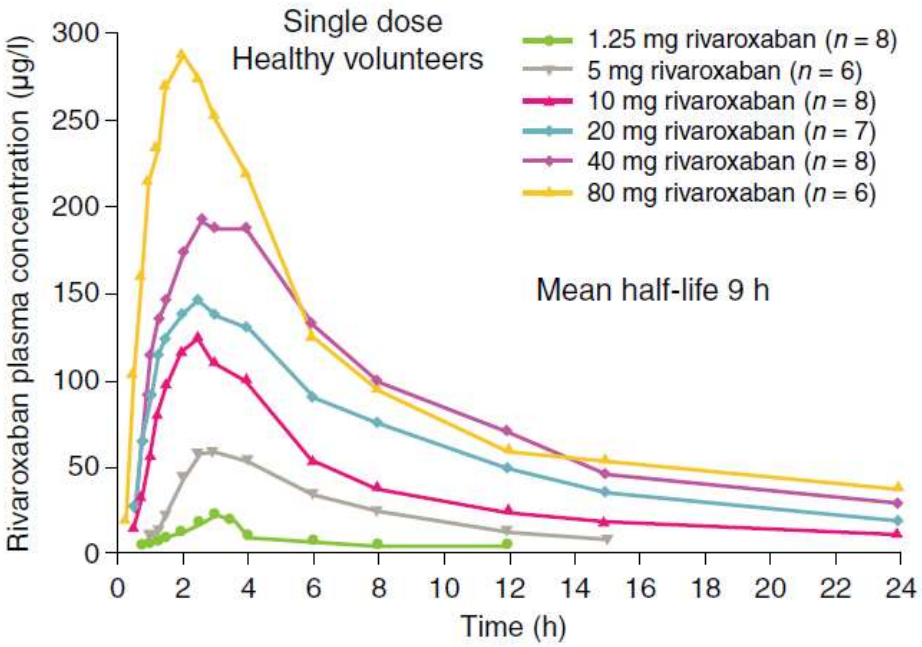
-Las **terapias puentes** no reducen los eventos cardiovasculares pero sí **aumentan los sangrados mayores**

-En procedimientos invasivos: la estrategia más segura es la **continuación o interrupción corta del NOAC**



Vannasche et al. Eur Heart J 2014: 35:1831–3

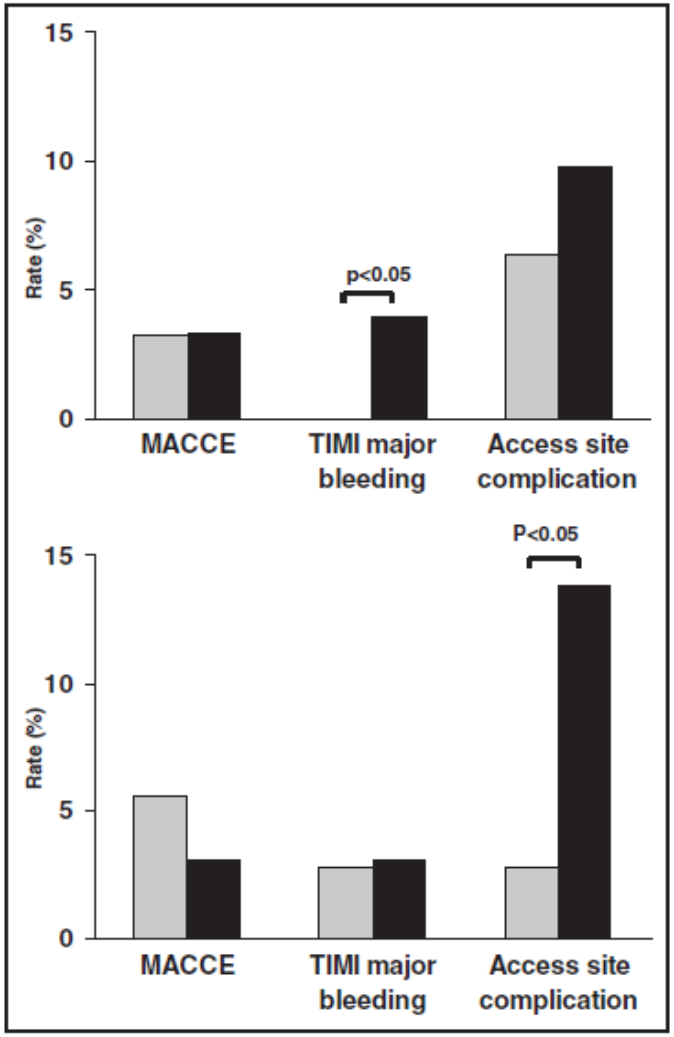
Problemática de los NACOs y la terapia puente



- Utilizar HBPM como terapia puente en el preoperatorio puede ocasionar incrementos indeseados del riesgo hemorrágico, por solapamiento de actividades anticoagulantes

Si el INR es correcto, no añadamos heparina

INR= 2-2,5



Sí Hep Na

No Hep Na

INR=2,6-3,5

Kiviniemi et al. Am J Cardiol 2012;110:30 –35

Comparison of Additional Versus No Additional *Heparin During* Therapeutic Oral Anticoagulation in Patients Undergoing Percutaneous Coronary Intervention

Variable	Overall Series			Propensity Score-Matched Pairs		
	Additional AC		p Value	Additional AC		p Value
	No (n = 196)	Yes (n = 218)		No (n = 122)	Yes (n = 122)	
Major adverse cardiac and cerebrovascular events	8 (4.1%)	7 (3.2%)	0.79	6 (4.9%)	1 (0.8%)	0.12
Death	2 (1.0%)	4 (1.8%)	0.69	2 (1.6%)	1 (0.8%)	0.56
Myocardial infarction	3 (1.5%)	3 (1.4%)	1.00	1 (0.8%)	0	1.00
Target vessel revascularization	3 (1.5%)	1 (0.5%)	0.35	1 (0.8%)	0	1.00
Stent thrombosis	3 (1.5%)	1 (0.5%)	0.35	3 (2.5%)	0	0.08
Stroke	1 (0.5%)	0	0.47	1 (0.8%)	0	1.00
Thrombolysis In Myocardial Infarction major bleeding	2 (1.0%)	8 (3.7%)	0.11	[illegible]	[illegible]	[illegible]
Access site complications	10 (5.1%)	24 (11%)	0.032	7 (5.7%)	16 (13%)	0.049
Pseudoaneurysm	3 (1.5%)	8 (3.7%)	0.23	0	6 (4.9%)	0.013
Bleeding delaying discharge	3 (1.5%)	13 (6.0%)	0.022	3 (2.5%)	9 (7.4%)	0.14
Need for corrective surgery	1 (0.5%)	1 (0.5%)	1.00	1 (0.8%)	1 (0.8%)	1.00
Hemoglobin decrease >4 g/dl	1 (0.5%)	4 (1.8%)	0.38	0	3 (2.5%)	0.25
Blood transfusion	0	6 (2.8%)	0.031	0	5 (4.1%)	0.06

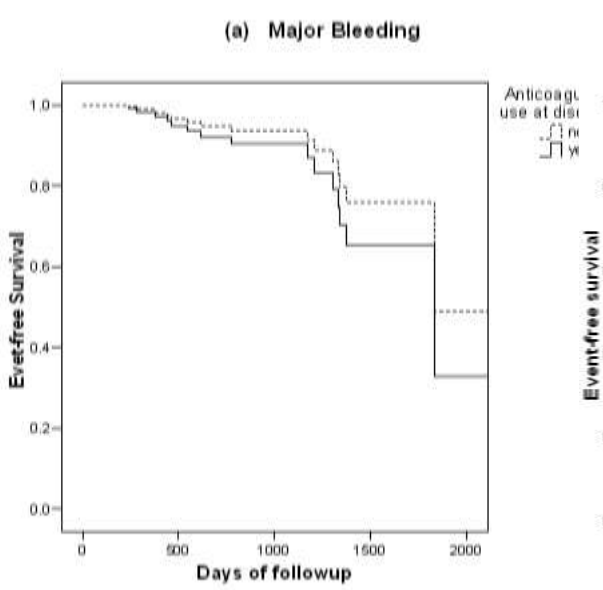
Kiviniemi et al. Am J Cardiol 2012;110:30 –35

Mensajes para casa

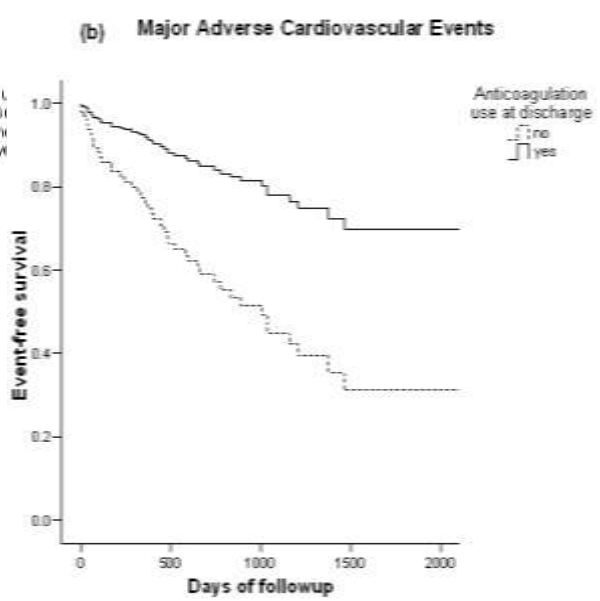
- Realizar angioplastia **sin interrupción** de los AVK o NACO
- Anticoagulación durante la angioplastia:
  - Si AVK e INR>2.5: No añadir heparina
  - Si AVK e INR<2.5 o NACO: dosis baja de heparina sódica (60 Us/Kgr)
- No pretratar con inhibidores P2Y12
- Evitar los inhibidores de la Gp IIb/IIIa

TRATAMIENTO ANTITROMBOTICO AL ALTA

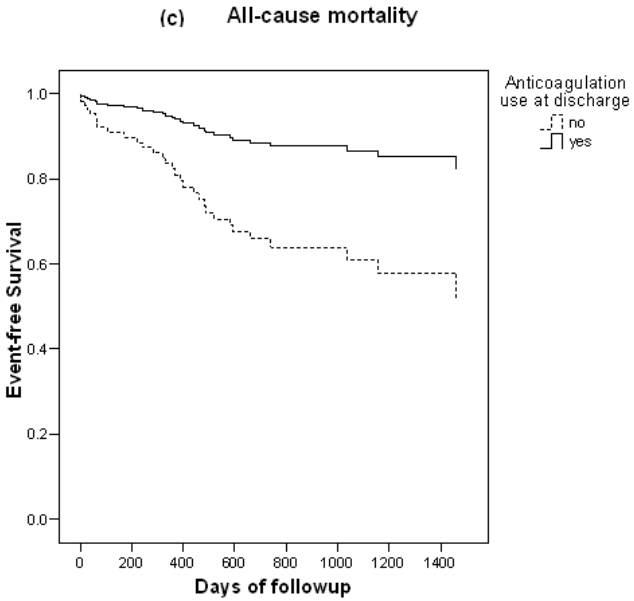
Triple terapia



Log-rank test, p=0.6
Number of patients follow-up:
Anticoagulation group n=195
No anticoagulation group n=178.



Log-rank test, P=0.02
Number of patients followup:
Anticoagulation group n=195
No anticoagulation group n=178.



Log rank test, P=0.03
Number of patients followed up:
Anticoagulation group n=195
No anticoagulation group n=178.

Ruiz-Nodar et al. JACC 2008:51:818-25

La triple terapia redujo el desarrollo de eventos mayores: muerte global y MACE

Cox Regression Analysis: PREDICTORS OF MACE and DEATH

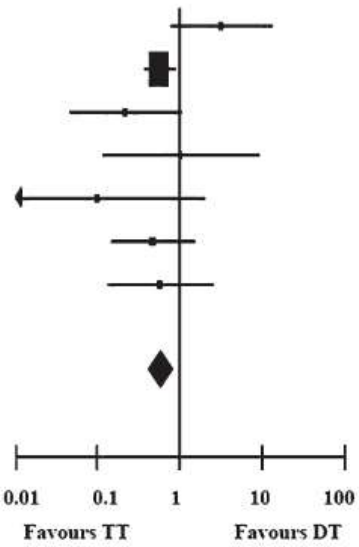
Variables	β	SE	p Value	HR	95% Confidence Interval
Age	0.06	0.02	0.02	1.07	1.01–1.12
Type of AF	0.41	0.53	0.44	1.51	0.53–4.31
Hypertension	−0.36	0.43	0.40	0.69	0.30–1.61
Diabetes	−0.23	0.35	0.51	0.80	0.40–1.58
Congestive heart failure or low LVEF	−0.15	0.35	0.67	0.86	0.43–1.71
Renal failure	−0.89	0.66	0.18	0.41	0.11–1.50
Previous stroke	0.22	0.49	0.65	1.24	0.48–3.25
Previous aspirin	0.23	0.41	0.58	1.25	0.57–2.78
Previous clopidogrel	−0.13	0.41	0.75	0.88	0.40–1.95
Previous oral anticoagulation	−0.76	0.50	0.12	0.47	0.18–1.23
Use of DES	−0.35	0.33	0.29	0.70	0.36–1.35
Non-anticoagulation at discharge	1.59	0.42	<0.01	4.9	2.17–11.09
Complete revascularization	−0.68	0.33	0.07	0.51	0.27–1.17

Ruiz-Nodar et al. JACC 2008:51:818-25

En este meta-ánalisis se confirma el beneficio clínico de la triple terapia

MACE

Study	Year	Triple Therapy Events	Triple Therapy Total	Dual Therapy Events	Dual Therapy Total	Weight (%)	Odds Ratio M-H Fixed, 95% CI
Mattichak[29]	2005	8	40	3	42	2.9%	3.25 (0.80. 13.27)
Ruiz-Nodar[16]	2008	52	195	69	178	66.4%	0.57 (0.37. 0.89)
Karjalainen[10]	2007	3	106	4	34	7.4%	0.22 (0.05. 1.03)
Maegdefessel[32]	2008	1	14	7	103	2.0%	1.05 (0.12. 9.28)
M-Fernández[14]	2008	0	51	3	39	4.9%	0.10 (0.01. 2.02)
Sarafoff[31]	2008	5	306	7	209	10.3%	0.48 (0.15. 1.53)
Rossini[15]	2008	3	102	5	102	6.1%	0.59 (0.14. 2.53)
Total (95% CI)			**814**		**707**	**100.0%**	**0.60 (0.42, 0.86)**
Total events		**72**		**98**			



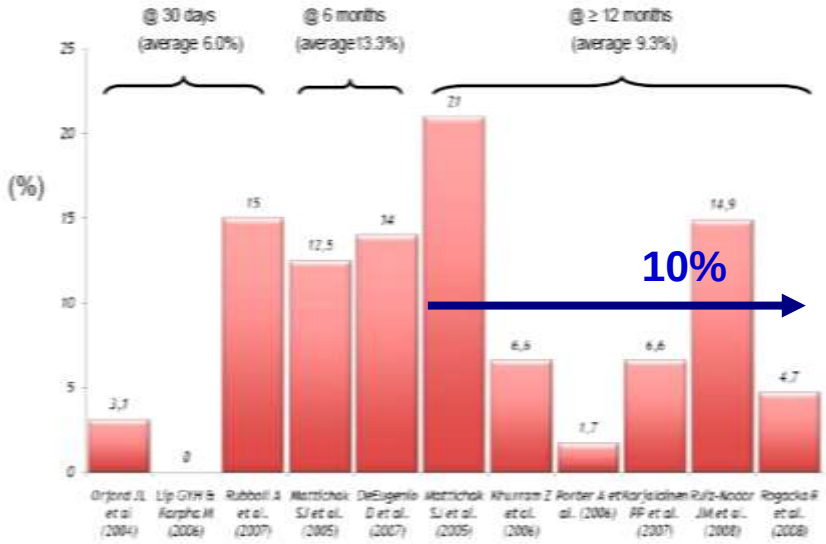
Heterogeneity: Chi^2 = 8.97, df = 6 (P = 0.18); I^2 = 33%

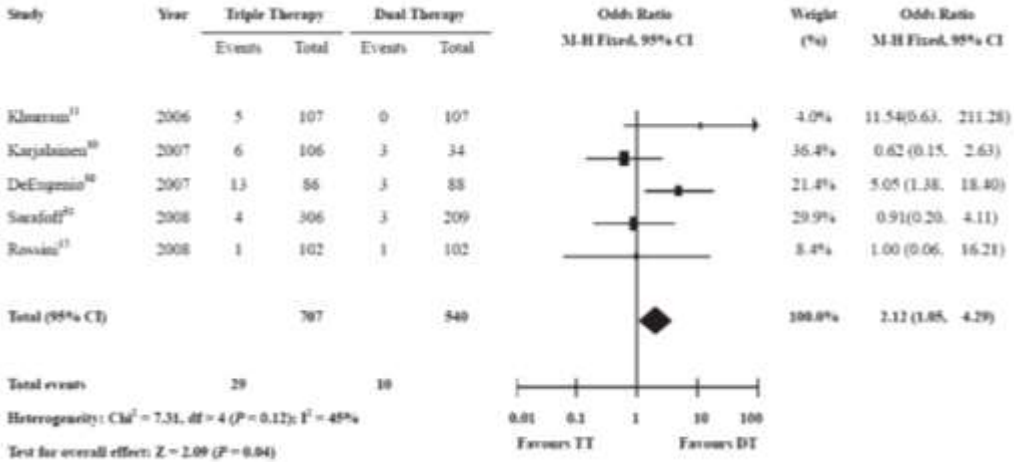
Test for overall effect: Z = 2.80 (P =0.005)

Zhao et al. CHEST 2011; 139:260–270

Pero con un incremento del sangrado mayor

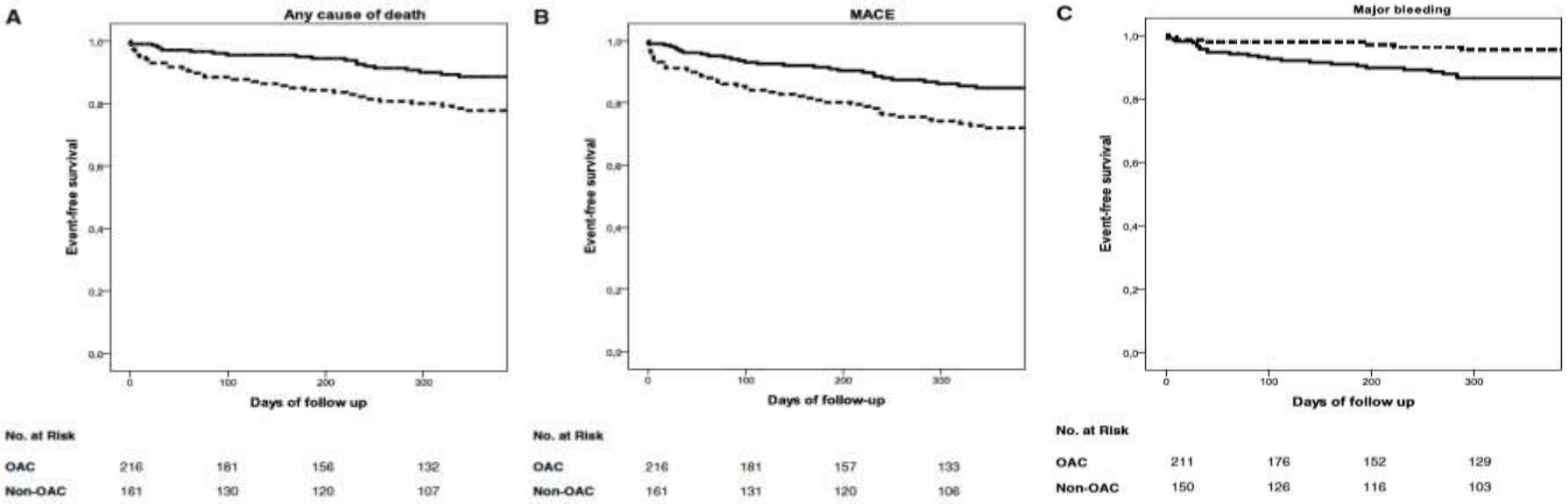
Mayor indicencia de sangrados mayores con TT





Rubboli et al. Ann Med 2008:40:428-36 Zhao et al. CHEST 2011; 139:260–270

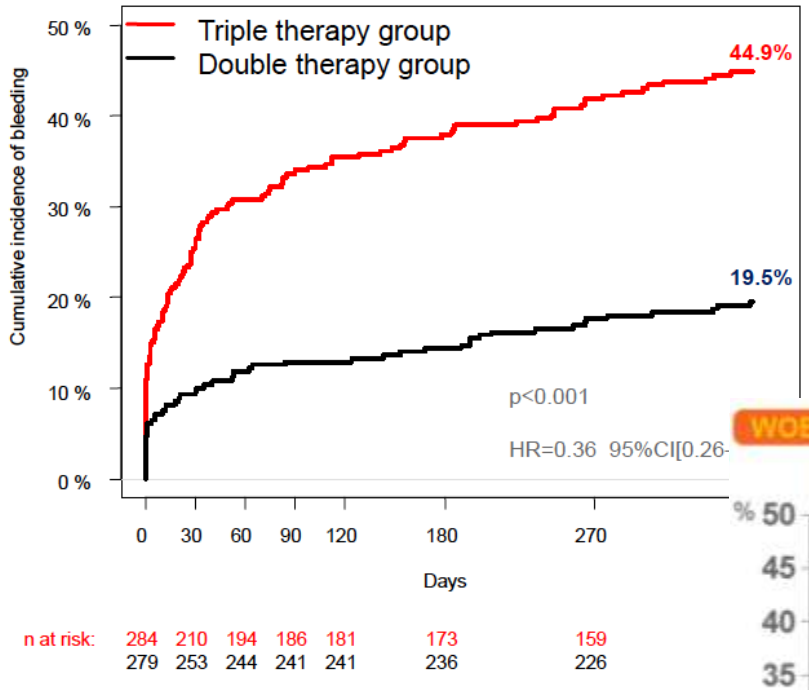
Beneficio ACO en FA + stent incluso con HAS-BLED>3



Ruiz-Nodar JM, et al. Circ Cardiovasc Interv 2012;5:459-66

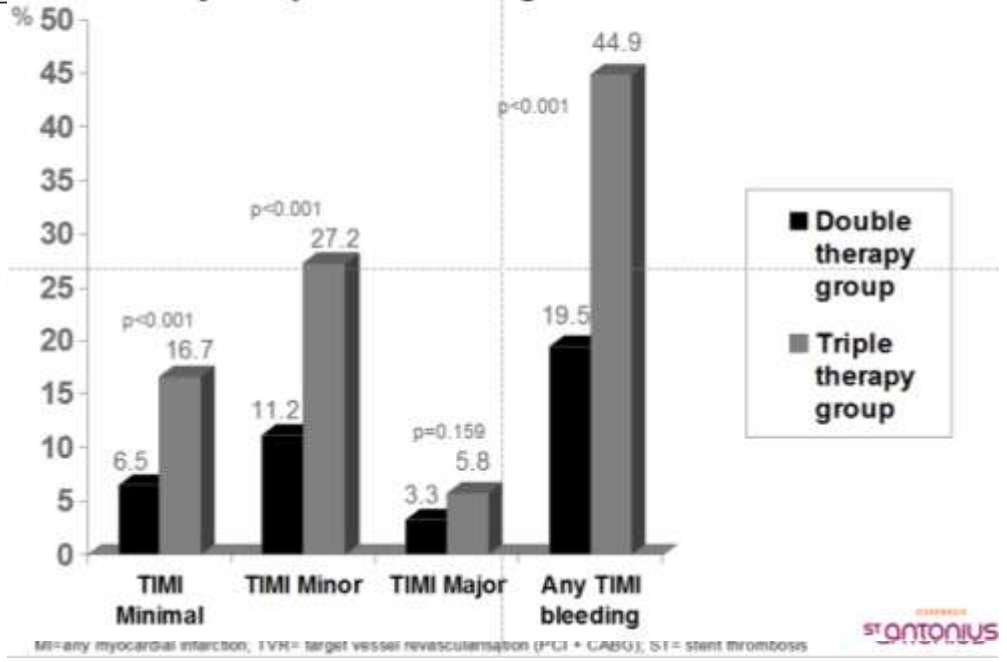
WOEST

Primary Endpoint: Total number of bleeding events (TIMI criteria)



WOEST

Primary Endpoint: Bleeding events TIMI classification



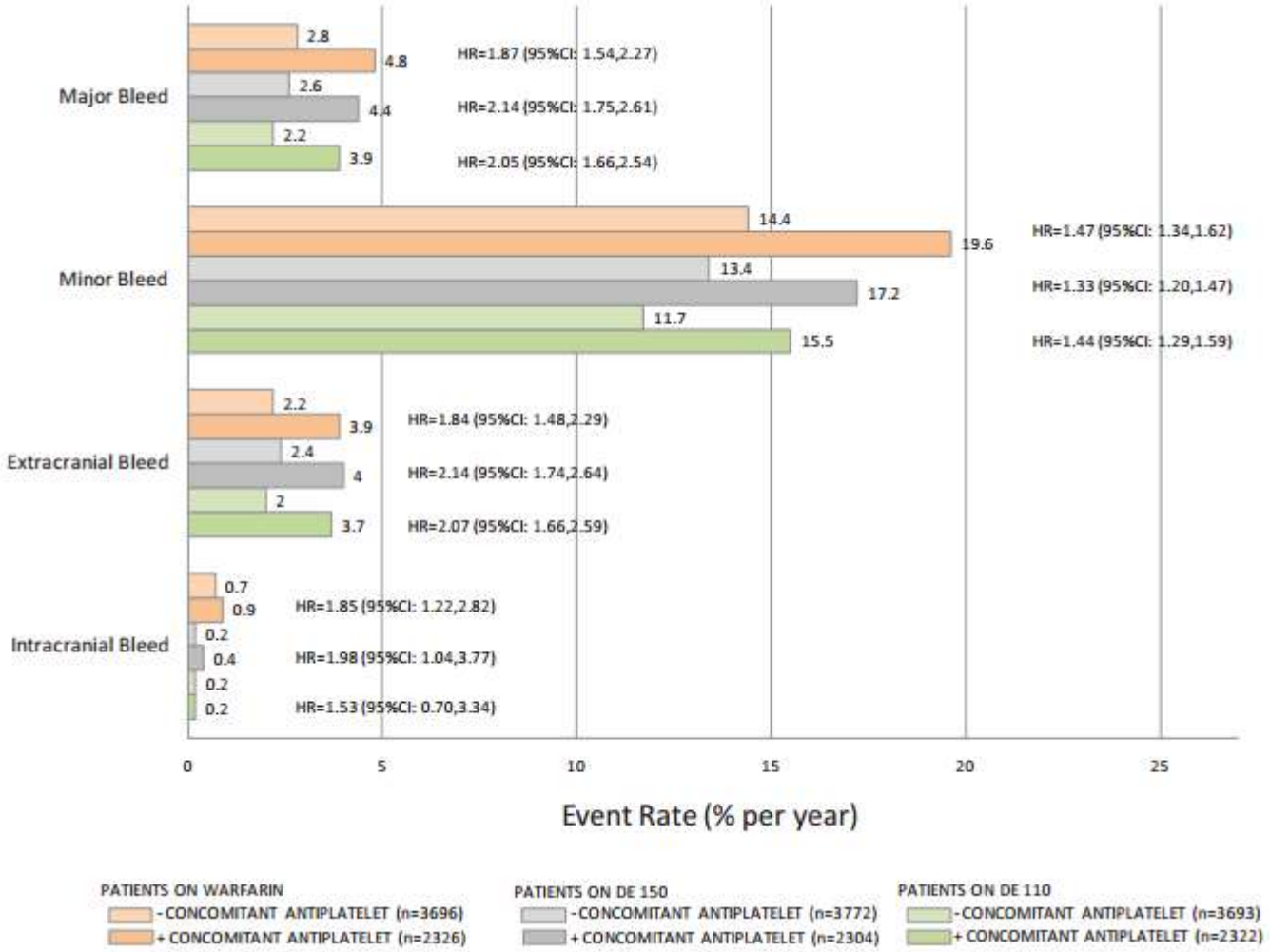
n=573

-SCA 27%
-Femoral 73%
-Triple terapia 1 año si Angina estable?
- Escaso uso de IBP

Dewilde et al. WOEST. The Lancet, 2013.dx.doi.org/10.1016/S0140-6736(12)62177-1

Concomitant Use of Antiplatelet Therapy with Dabigatran or Warfarin in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Trial

Antonio L. Dans, MD, MSc; Stuart J. Connolly, MD; Lars Wallentin, MD, PhD; Sean Yang, MSc; Juliet Nakamya, PhD; Martina Brueckmann, MD; Michael Ezekowitz, MBChB, DPhil; Jonas Oldgren, MD, PhD; John W. Eikelboom, MD; Paul A. Reilly, PhD; Salim Yusuf, DPhil, FRCPC, FRSC



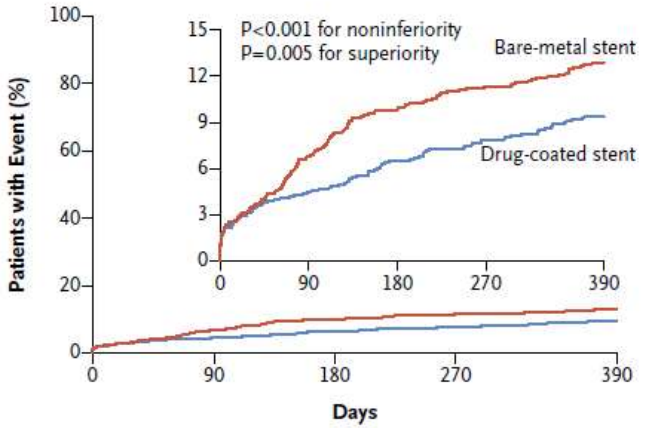
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Polymer-free Drug-Coated Coronary Stents in Patients at High Bleeding Risk

for the LEADERS FREE Investigators*

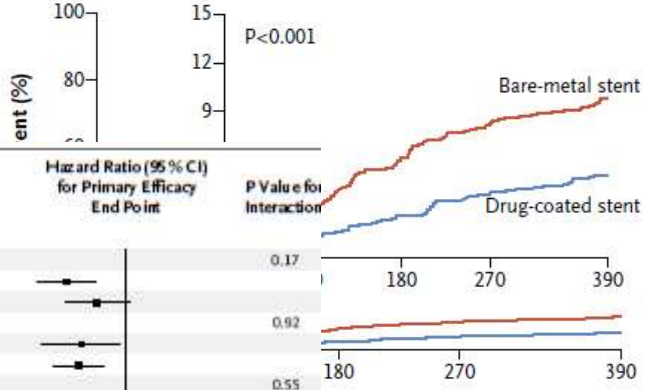
Primary Safety End Point



No. at Risk

Drug-coated stent	1221	1146	1105	1081	1045
Bare-metal stent	1211	1115	1066	1037	1000

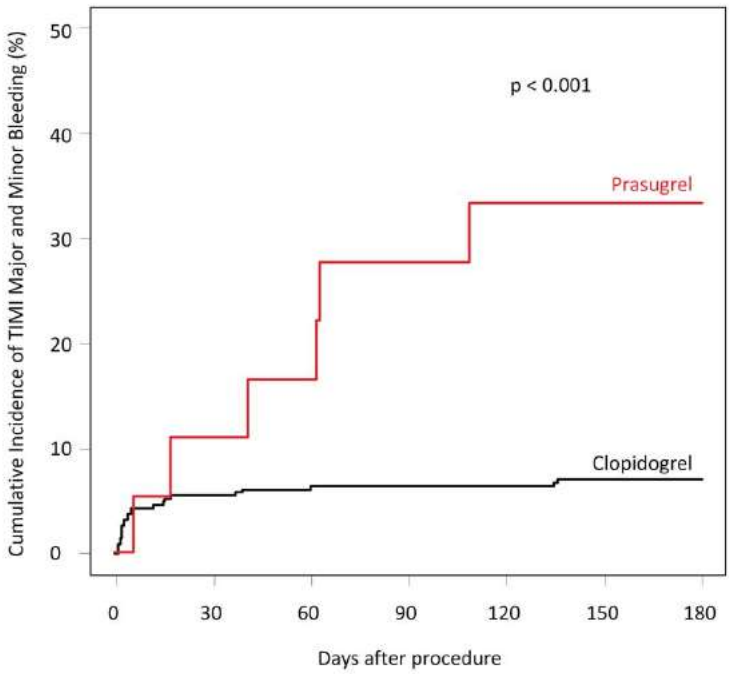
Primary Efficacy End Point

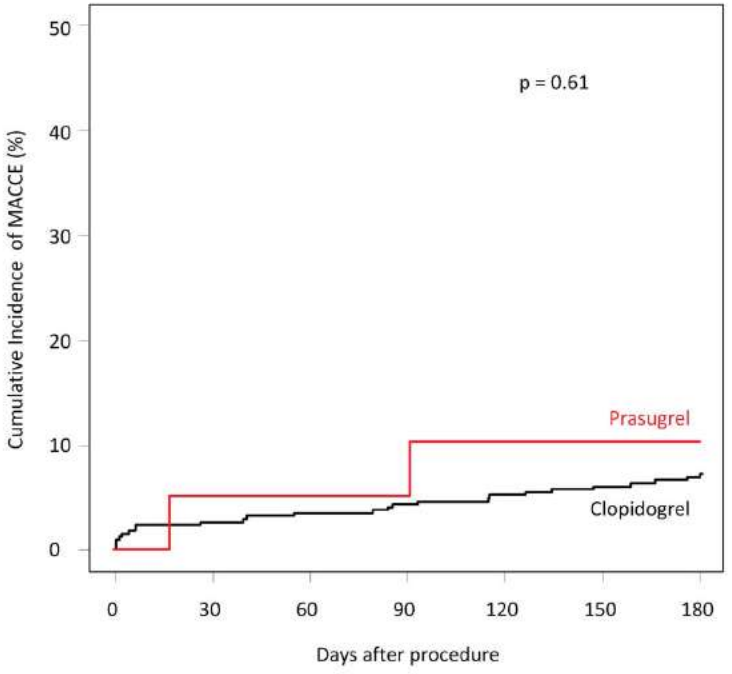


Subgroup	No. of Patients	Drug-Coated Stent	Bare-Metal Stent	Hazard Ratio (95% CI) for Primary Safety End Point	P Value for Interaction	Drug-Coated Stent	Bare-Metal Stent	Hazard Ratio (95% CI) for Primary Efficacy End Point	P Value for Interaction
		no. of events (% of patients)				no. of events (% of patients)			
Age					0.86				0.17
≤80 yr	1602	65 (8.3)	92 (11.6)			31 (4.0)	72 (9.4)		
>80 yr	830	47 (11.5)	62 (15.5)			28 (7.1)	41 (10.6)		
Sex					0.59				0.92
Female	738	34 (9.6)	53 (14.4)			17 (5.0)	33 (9.3)		
Male	1694	78 (9.3)	101 (12.3)			42 (5.1)	80 (10.0)		
ACS at admission					0.04				0.55
No	1773	82 (9.4)	95 (10.9)			47 (5.5)	86 (10.1)		
Yes	659	30 (9.3)	59 (18.5)			12 (3.9)	27 (9.0)		
Diabetes					0.90				0.57
No	1622	65 (8.3)	93 (11.5)			40 (5.3)	74 (9.4)		
Yes	805	47 (11.5)	61 (15.9)			19 (4.7)	39 (10.7)		
Renal failure at admission					0.46				0.02
No	1754	73 (8.3)	89 (10.4)			42 (4.9)	88 (10.6)		
Yes	466	31 (14.7)	53 (22.2)			16 (7.9)	15 (6.7)		
OAC planned to continue after PCI					0.44				0.61
No	1553	66 (8.7)	100 (13.0)			39 (5.3)	80 (10.7)		
Yes	879	46 (10.5)	54 (12.8)			20 (4.7)	33 (8.2)		

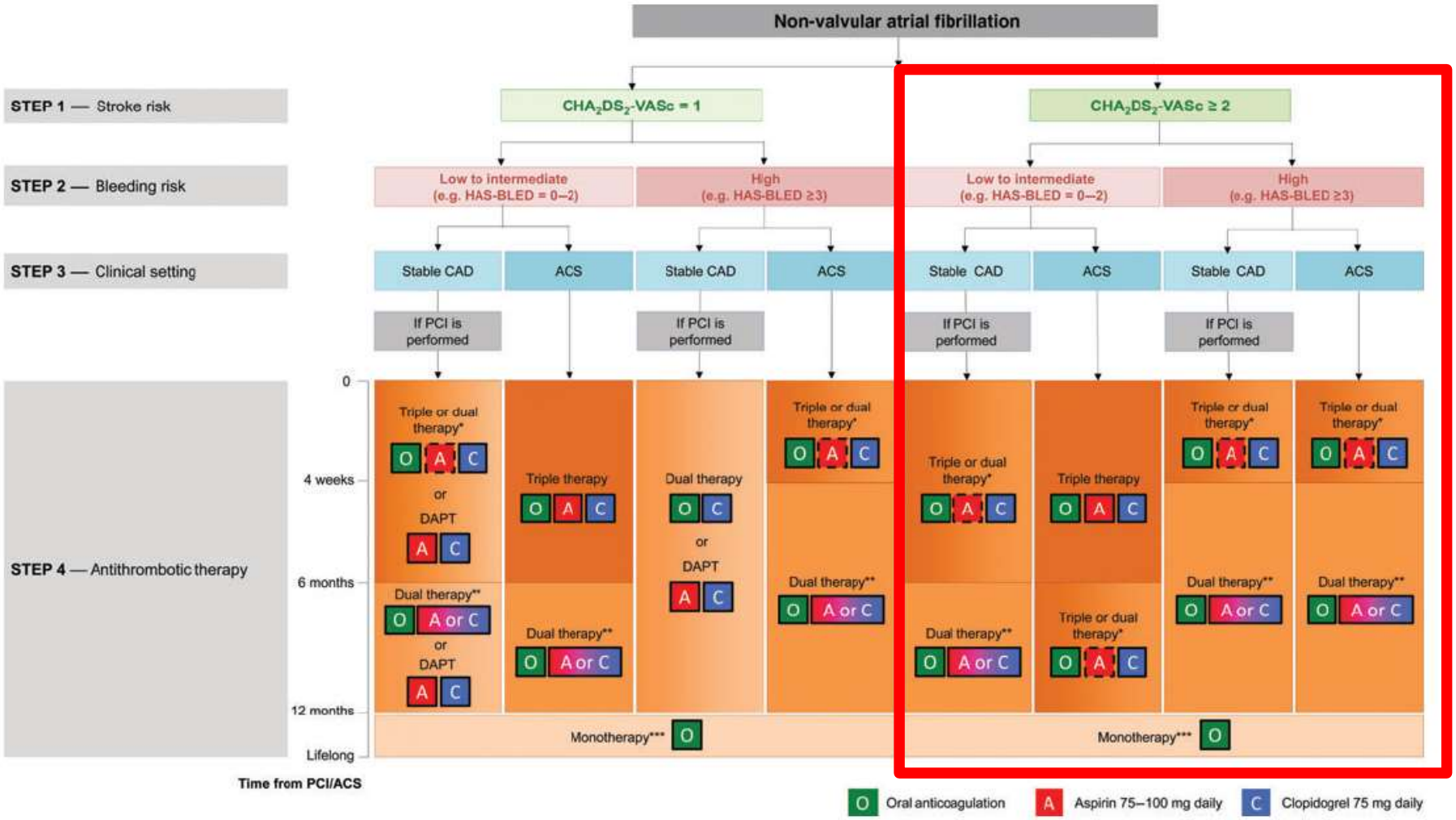
Urban et al. NEJM 2015:393:2038-47

Triple Terapia con nuevos antiagregantes





Sarafoff N, et al. JACC. 2013;61(10_S):. doi:10.1016/S0735-1097(13)61859-8



Lip et al. Documento de Consenso. Eur Heart J 2014;doi:10.1093/eurheartj/ehu298

Mensajes para casa

- En general, la **triple terapia al alta**, que debería ser lo más corta posible, seguido de ACO más un único antiagregante (clopidogrel 75 mgr/día o aspirina 100 mgr/día).

- La **duración de la triple terapia** dependerá de:
  - Riesgo hemorrágico (HAS-BLED)
  - Síndrome coronario agudo vs angioplastia electiva
  - Tipo de stent: DES de nueva generación o BMS

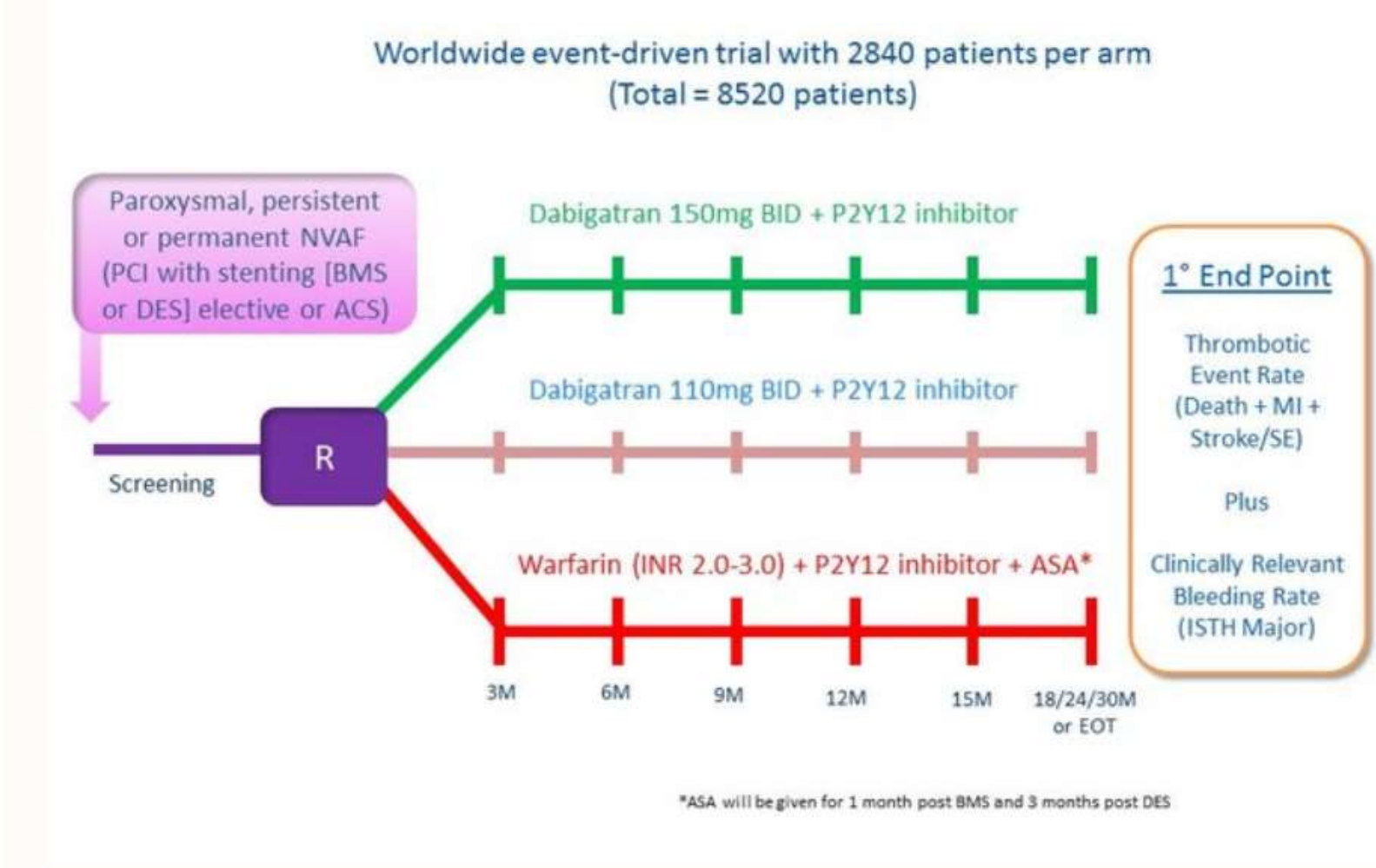
- En pacientes con mal control del INR o contraindicación a los antivitamina K: **NACOs**

- Deberemos evitar el uso de los **nuevos antiagregantes** en este contexto

- Los **stents recubiertos de nueva generación** ofrecen mayor seguridad

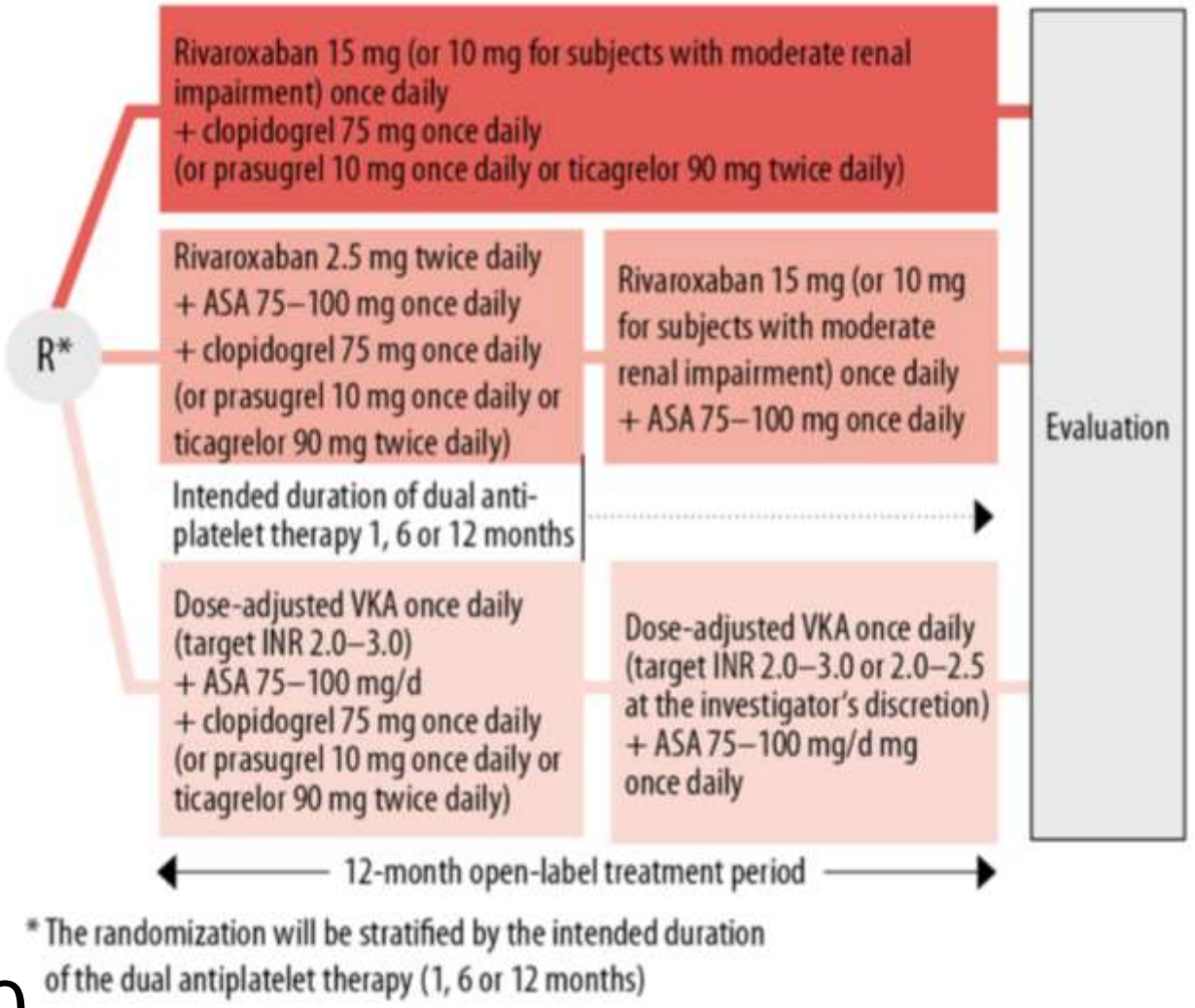
Evaluation of Dual Therapy With Dabigatran vs. Triple Therapy With Warfarin in Patients With AF That Undergo a PCI With Stenting (REDUAL-PCI)

RE-DUAL PCI™
Study in NVAF patients undergoing PCI



N= 8520

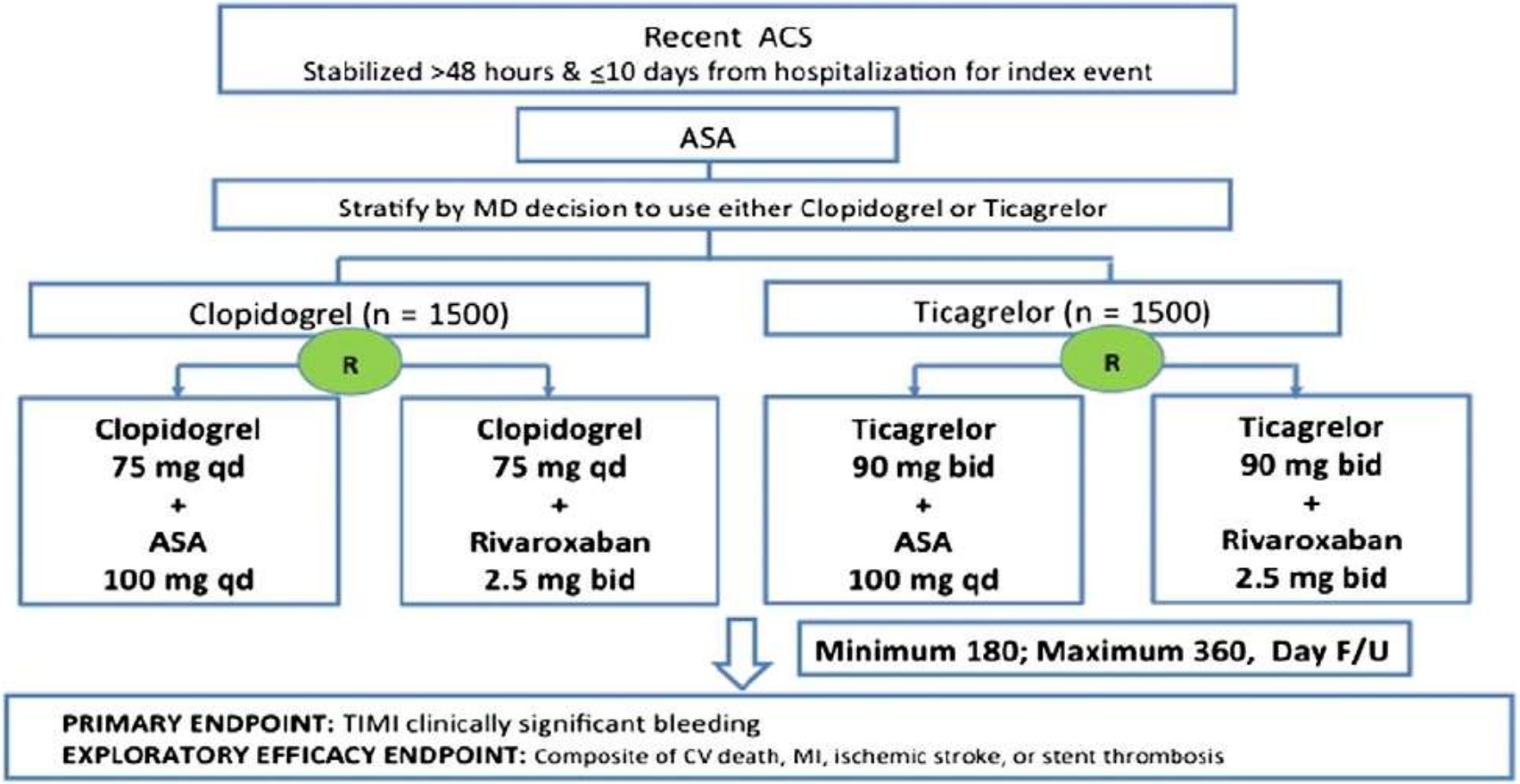
An open-label, randomized, controlled, multicenter study exploring two treatment strategies of rivaroxaban and a dose-adjusted oral vitamin K antagonist treatment strategy in subjects with atrial fibrillation who undergo percutaneous coronary intervention (PIONEER AF-PCI).



N= 2100

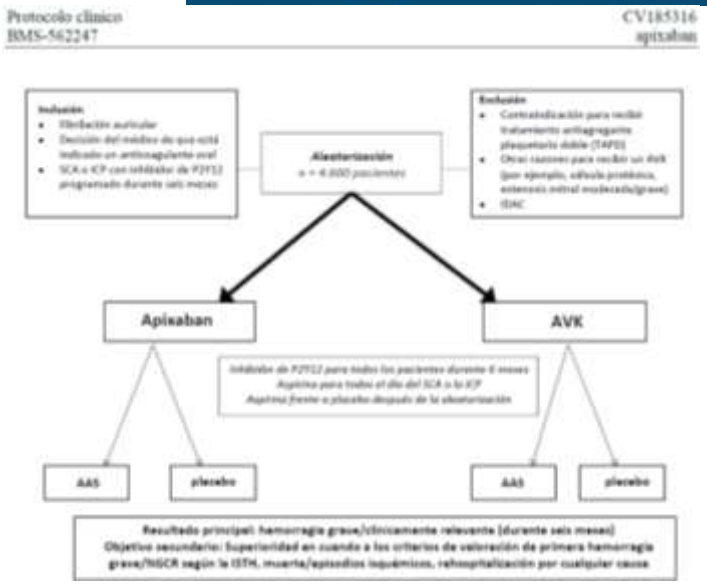
Gibson.Am Heart J 2015 Apr;169(4):472-8.e5. doi: 10.1016/j.ahj.2014.12.006. Epub 2014 Dec 20

GEMINI-ACS-1



GEMINI-ACS-1 trial design.

Study Apixaban to Vitamin K Antagonist for the Prevention of Stroke or Systemic Embolism and Bleeding in Patients With Non-valvular Atrial Fibrillation and Acute Coronary Syndrome/Percutaneous Coronary Intervention

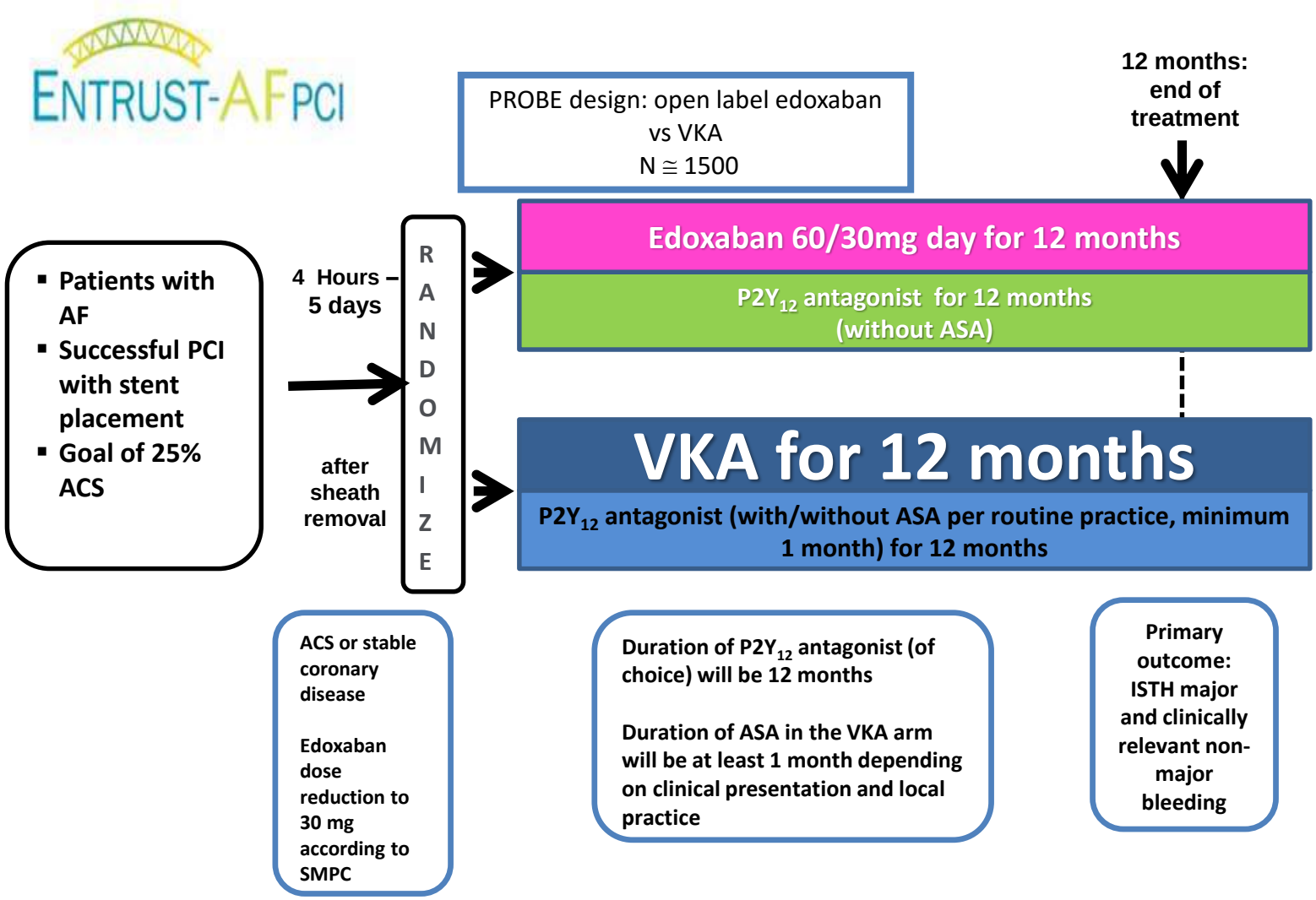


Apixaban (2.5 o 5mgr) → Aspirina o placebo → InhP2Y12

Anti Vit K → Aspirina o placebo → InhP2Y12

N= 4600

ENTRUST-AF PCI: CONFIDENTIAL



¿y a largo plazo qué tratamiento antitrombótico se debe recomendar?

Don't add aspirin for associated stable vascular disease in a patient with atrial fibrillation receiving anticoagulation

Gregory Y H Lip

BMJ | 15 MARCH 2008 | VOLUME 336

KEY POINTS

Adding aspirin to warfarin does not seem to prevent stroke and vascular events in patients with atrial fibrillation and stable vascular disease

Bleeding risks are much higher in patients prescribed both warfarin and aspirin

We should stop prescribing aspirin plus warfarin to prevent stroke and vascular events in stable patients with atrial fibrillation who are receiving anticoagulation treatment

Guidelines for the management of atrial fibrillation

The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC)

EUROPEAN SOCIETY OF CARDIOLOGY®

4.1.6.3 Stable vascular disease

Many anticoagulated AF patients have stable coronary or carotid artery disease and/or PAD, and common practice is to treat such patients with VKA plus one antiplatelet drug, usually aspirin. Adding aspirin to VKA does not reduce the risk of stroke or vascular events (including myocardial infarction), but substantially increases bleeding events.

Embolismo

Olesen et al. Thromb Haemost 2011

	Whole cohort (n=132,372)					HAS-BLED score ≤2 (n=93,826)	HAS-BLED score ≥3 (n=38,546)	No preMI (n=112,916)	With preMI (n=19,456)
	Years of exposure	TE events	Hazard ratio (CI)*	Hazard ratio (CI)†	Hazard ratio (CI)‡	Hazard ratio (CI)‡	Hazard ratio (CI)‡	Hazard ratio (CI)‡	Hazard ratio (CI)‡
High (2–9)									
VKA only	93,560	2,696	Reference	Reference	Reference	Reference	Reference	Reference	Reference
No treatment	132,737	8,380	1.93 (1.85–2.02)	1.72 (1.64–1.79)	1.86 (1.78–1.95)	1.94 (1.84–2.05)	1.77 (1.65–1.89)	1.92 (1.83–2.01)	1.59 (1.43–1.77)
ASA only	81,832	5,180	2.01 (1.92–2.11)	1.73 (1.65–1.81)	1.81 (1.73–1.90)	1.96 (1.84–2.08)	1.60 (1.49–1.72)	1.90 (1.80–2.00)	1.45 (1.30–1.61)
VKA + ASA	22,149	838	1.13 (1.04–1.22)	1.15 (1.06–1.24)	1.14 (1.06–1.23)	1.23 (1.09–1.38)	1.00 (0.90–1.11)	1.16 (1.06–1.27)	1.02 (0.87–1.19)

ASA: acetylsalicylic acid; $CHADS_2$, CHA_2DS_2-VASc, and HAS-BLED: see text; CI: confidence interval; preMI: previous myocardial infarction; TE: thromboembolism; VKA: vitamin K antagonist. * Unadjusted. † Adjusted for gender and age. ‡ Adjusted for all baseline characteristics.

Sangrado mayor

	Whole cohort (n=132,372)					HAS-BLED score ≤2 (n=93,826)	HAS-BLED score ≥3 (n=38,546)	No preMI (n=112,916)	With preMI (n=19,456)
	Years of exposure	Bleeding events	Hazard ratio (CI)*	Hazard ratio (CI)†	Hazard ratio (CI)‡	Hazard ratio (CI)‡	Hazard ratio (CI)‡	Hazard ratio (CI)‡	Hazard ratio (CI)‡
High (2–9)									
VKA only	93,634	4,061	Reference	Reference	Reference	Reference	Reference	Reference	Reference
No treatment	130,172	5,135	0.91 (0.87–0.95)	0.86 (0.83–0.90)	0.84 (0.81–0.88)	0.79 (0.75–0.84)	0.94 (0.88–1.01)	0.85 (0.81–0.89)	0.78 (0.71–0.87)
ASA only	82,638	3,682	1.04 (0.99–1.08)	0.94 (0.90–0.98)	0.93 (0.89–0.97)	0.91 (0.85–0.97)	0.92 (0.86–0.99)	0.95 (0.91–1.00)	0.82 (0.74–0.91)
VKA + ASA	22,137	1,669	1.66 (1.56–1.75)	1.63 (1.54–1.72)	1.64 (1.55–1.74)	1.76 (1.62–1.91)	1.47 (1.34–1.60)	1.69 (1.58–1.80)	1.46 (1.29–1.64)

ASA: acetylsalicylic acid; $CHADS_2$, CHA_2DS_2-VASc, and HAS-BLED: see text; CI: confidence interval; preMI: previous myocardial infarction; VKA: vitamin K antagonist. * Unadjusted. † Adjusted for gender and age. ‡ Adjusted for all baseline characteristics.

Pacientes con infarto n=3630

-aspirina

-warfarina

-aspirina+warfarina

The Waris Trial

Conclusions Warfarin, in combination with aspirin or given alone, was superior to aspirin alone in reducing the incidence of composite events after an acute myocardial infarction but was associated with a higher risk of bleeding. (N Engl J Med 2002;347:969-74.)

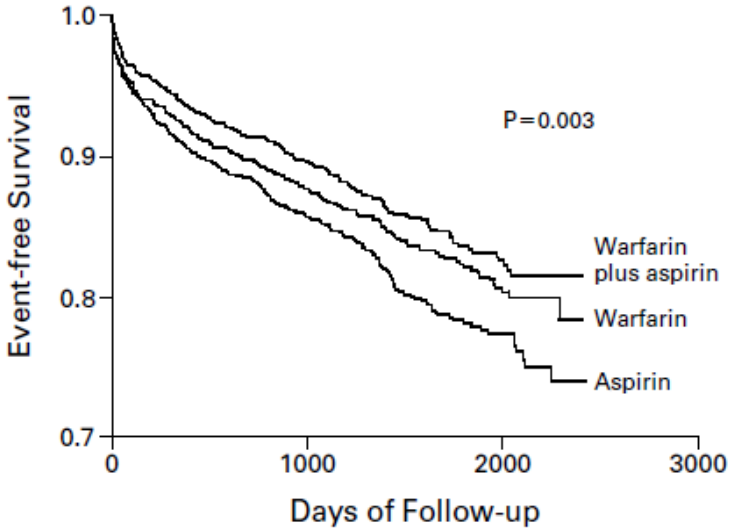


Figure 1. Event-free Survival Curves for the Composite End Point of Death, Nonfatal Reinfarction, and Thromboembolic Stroke. The P value refers to the overall difference among the curves (Tarone–Ware method).

TABLE 5. NONFATAL BLEEDING COMPLICATIONS ACCORDING TO TREATMENT GROUP.

COMPLICATION	ASPIRIN	WARFARIN	ASPIRIN PLUS WARFARIN
	no. of patients		
Major bleeding			
Cerebral	1	5	3
Gastrointestinal	6	18	21
Urinary	—	2	—
Muscle or skin	—	1	—
Other	1	7	4
Total	8	33	28
Minor bleeding			
Nose or airways	7	20	30
Gastrointestinal	18	30	45
Urinary	7	24	27
Muscle or skin	—	8	16
Other	7	21	15
Total	39	103	133

Hurlen. WARIS II. NEJM 2002;347:969-74

JACC Journals

From: Rivaroxaban in Patients Stabilized After a ST-Segment Elevation Myocardial Infarction: Results From the ATLAS ACS-2–TIMI-51 Trial (Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome–Thrombolysis In Myocardial Infarction-51)

J Am Coll Cardiol. 2013;61(18):1853-1859. doi:10.1016/j.jacc.2013.01.066

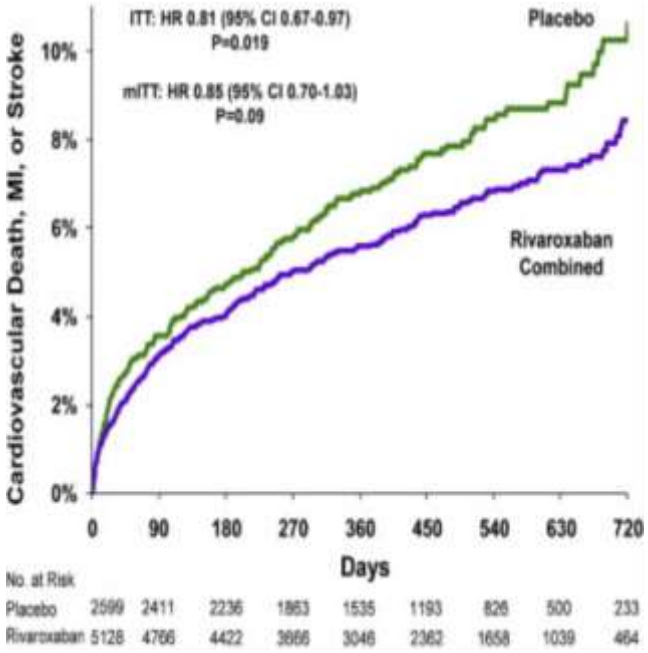


Figure Legend:

Incidence of the Primary Efficacy Endpoint

The primary efficacy endpoint consists of cardiovascular death, myocardial infarction (MI), or stroke. Data are presented for the rivaroxaban doses combined compared with placebo. CI = confidence interval; HR = hazard ratio; ITT = intention-to-treat; mITT = modified ITT.

JACC Journals

From: Rivaroxaban in Patients Stabilized After a ST-Segment Elevation Myocardial Infarction: Results From the ATLAS ACS-2–TIMI-51 Trial (Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome–Thrombolysis In Myocardial Infarction-51)

J Am Coll Cardiol. 2013;61(18):1853-1859. doi:10.1016/j.jacc.2013.01.066

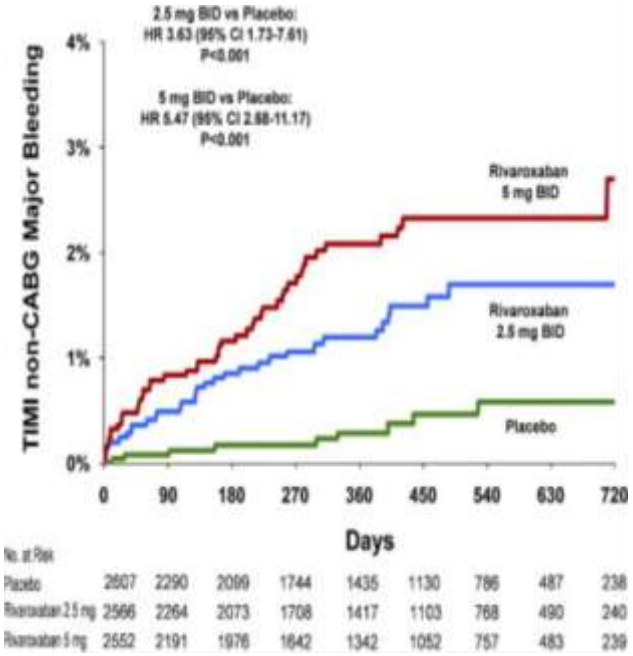


Figure Legend:

Incidence of TIMI non-CABG Major Bleeding

Data are presented for each of the rivaroxaban doses as compared with placebo. CABG = coronary artery bypass graft; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as Figures 1 and 4.

ORIGINAL RESEARCH

American Heart Association | American Stroke Association

Concomitant Use of Single Antiplatelet Therapy With Edoxaban or Warfarin in Patients With Atrial Fibrillation: Analysis From the ENGAGE AF-TIMI48 Trial

Haiyan Xu, MD; Christian T. Ruff, MD, MPH; Robert P. Giugliano, MD, SM; Sabina A. Murphy, MPH; Francesco Nordio, PhD; Indravadan Patel, MD; Minggao Shi, PhD; Michele Mercuri, MD, PhD; Elliott M. Antman, MD; Eugene Braunwald, MD

Background—We studied the concomitant use of single antiplatelet therapy (SAPT) on the efficacy and safety of the anti-Xa agent edoxaban in patients with atrial fibrillation (AF).

Methods and Results—ENGAGE AF-TIMI 48 was a randomized trial that compared 2 dose regimens of edoxaban with warfarin. We studied both the approved high-dose edoxaban regimen (HDER; 60 mg daily reduced by one half in patients with anticipated increased drug exposure), as well as a lower-dose edoxaban regimen (LDER; 30 mg daily, also reduced by one half in patients with anticipated increased drug regimen). SAPT (aspirin in 92.5%) was administered at the discretion of the treating physician. Cox proportional hazard regressions stratified by SAPT at 3 months with treatment as a covariate were performed. The 4912 patients who received SAPT were more frequently male, with histories of coronary artery disease and diabetes, and had higher $CHADS_2Vasc$ and HAS BLED scores than did the 14 977 patients not receiving SAPT. When compared to patients not receiving SAPT, those receiving SAPT had a higher incidence of major bleeding; (adjusted hazard ratio [HR_{adj}]=1.46; 95% CI, 1.27–1.67, $P<0.001$). SAPT did not alter the relative efficacy of edoxaban compared to warfarin in preventing stroke or systemic embolic events (SEEs): edoxaban versus warfarin without SAPT, hazard ratio (HR_{adj} for HDER)=0.94; (95% CI: 0.77–1.15) with SAPT, HR_{adj}=0.70 (95% CI: 0.50–0.98), *P* interaction (P_{int})=0.14. (HR_{adj} for LDER versus warfarin without SAPT=1.19 (95% CI 0.99–1.43) With SAPT, 1.03 (95% CI, 0.76–1.39) P_{int}=0.42. Major bleeding was lower with edoxaban than warfarin both without SAPT, HR_{adj} for HDER=0.80 (95% CI, 0.68–0.95), and with SAPT, HR_{adj}=0.82 (95% CI, 0.65–1.03; P_{int}=0.91). For LDER without SAPT (HR_{adj}=0.56 [95% CI 0.46–0.67]) and with SAPT (HR_{adj}=0.51 [95% CI 0.39–0.66]).

Conclusions—Patients with AF who were selected by their physicians to receive SAPT in addition to an anticoagulant had a similar risk of stroke/SEE and higher rates of bleeding than those not receiving SAPT. Edoxaban exhibited similar relative efficacy and reduced bleeding compared to warfarin, with or without concomitant SAPT.

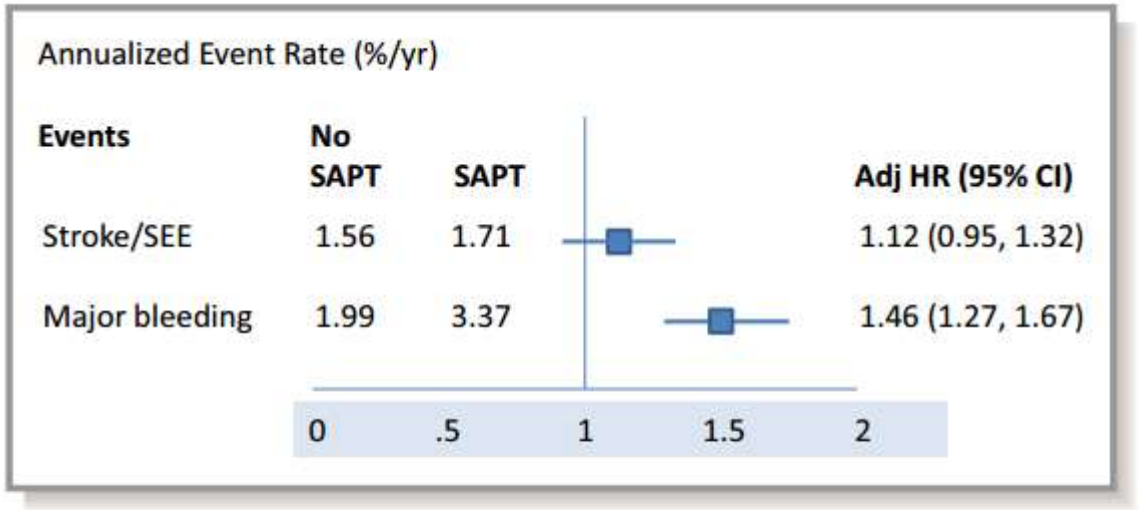
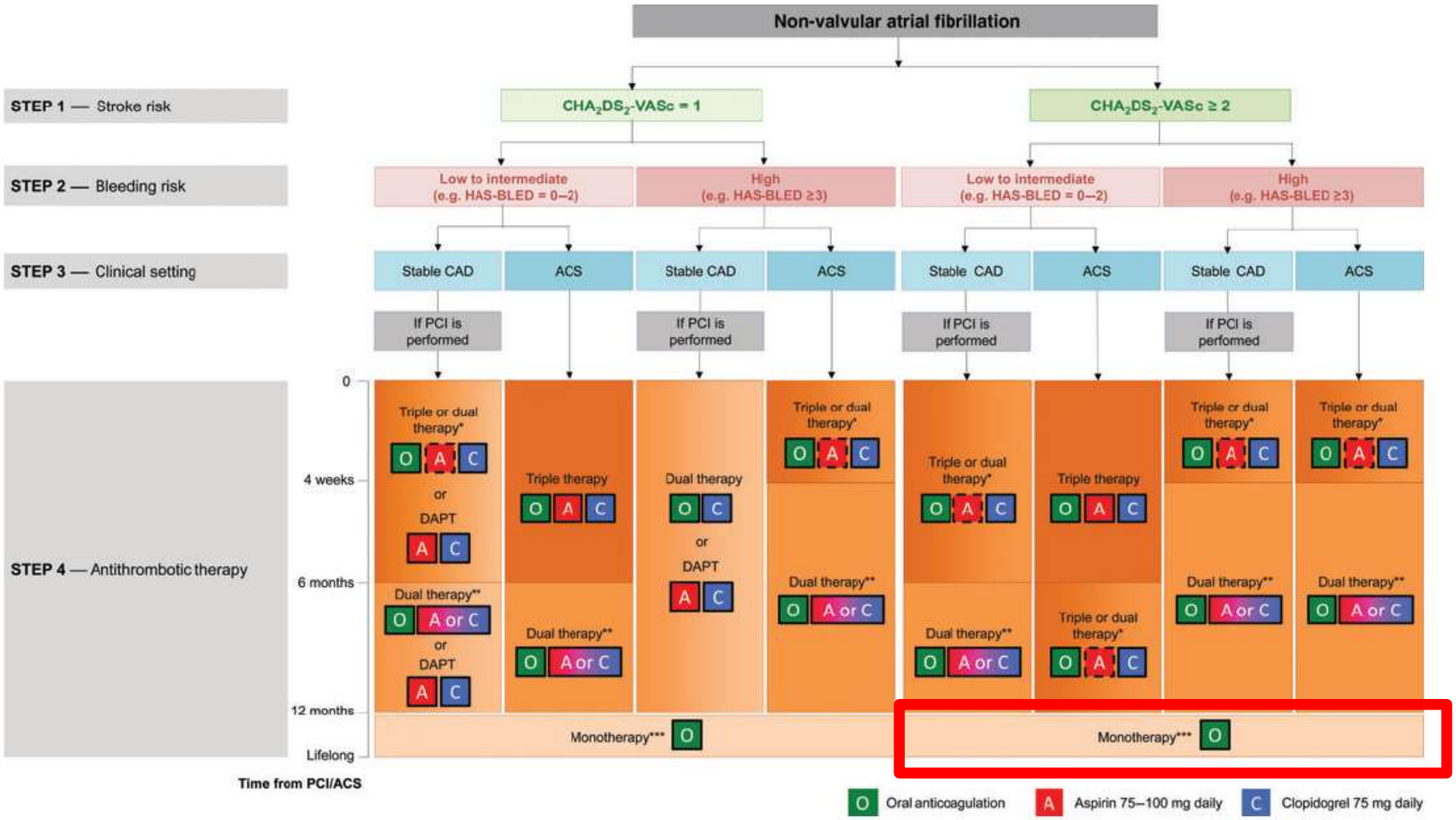


Figure 2. Outcomes in patients with and without antiplatelet therapy. Adj HR indicates adjusted hazard ratio; HR, hazard ratio; SAPT, single antiplatelet therapy; SEE, systemic embolic event.

We observed that the addition of SAPT to an anticoagulant (warfarin or edoxaban) was associated with a significantly greater risk of bleeding. However, the addition of SAPT did not modify the relative efficacy and safety of edoxaban as compared to warfarin. Notably, when compared to warfarin, both edoxaban regimens significantly reduced all forms of bleeding, including ICH and life-threatening bleeding, both in patients who were as well as those who were not, receiving a SAPT.



Lip et al. Documento de Consenso. Europ Heart J 2014;doi:10.1093/eurheartj/ehu298

Mensajes para casa

- A partir del año mantenter monoterapia con anticoagulantes en una gran mayoría de los casos
- Se deberá individualizar los casos especiales (trombosis del stent, alta carga trombótica, …)
- Los ensayos en marcha nos informarán del papel de los NACOs en este contexto, así como el papel de los nuevos antiagregantes

Gracias

Playa de Calblanque, Murcia