LA TRIPLICE TERAPIA ANTITROMBOTICA NELLA FANV CON CARDIOPATIA ISCHEMICA: UNA DIFFICILE SCELTA

Claudio Pascale

Il sottoscritto___Claudio PASCALE_____
in qualità di relatore all'evento

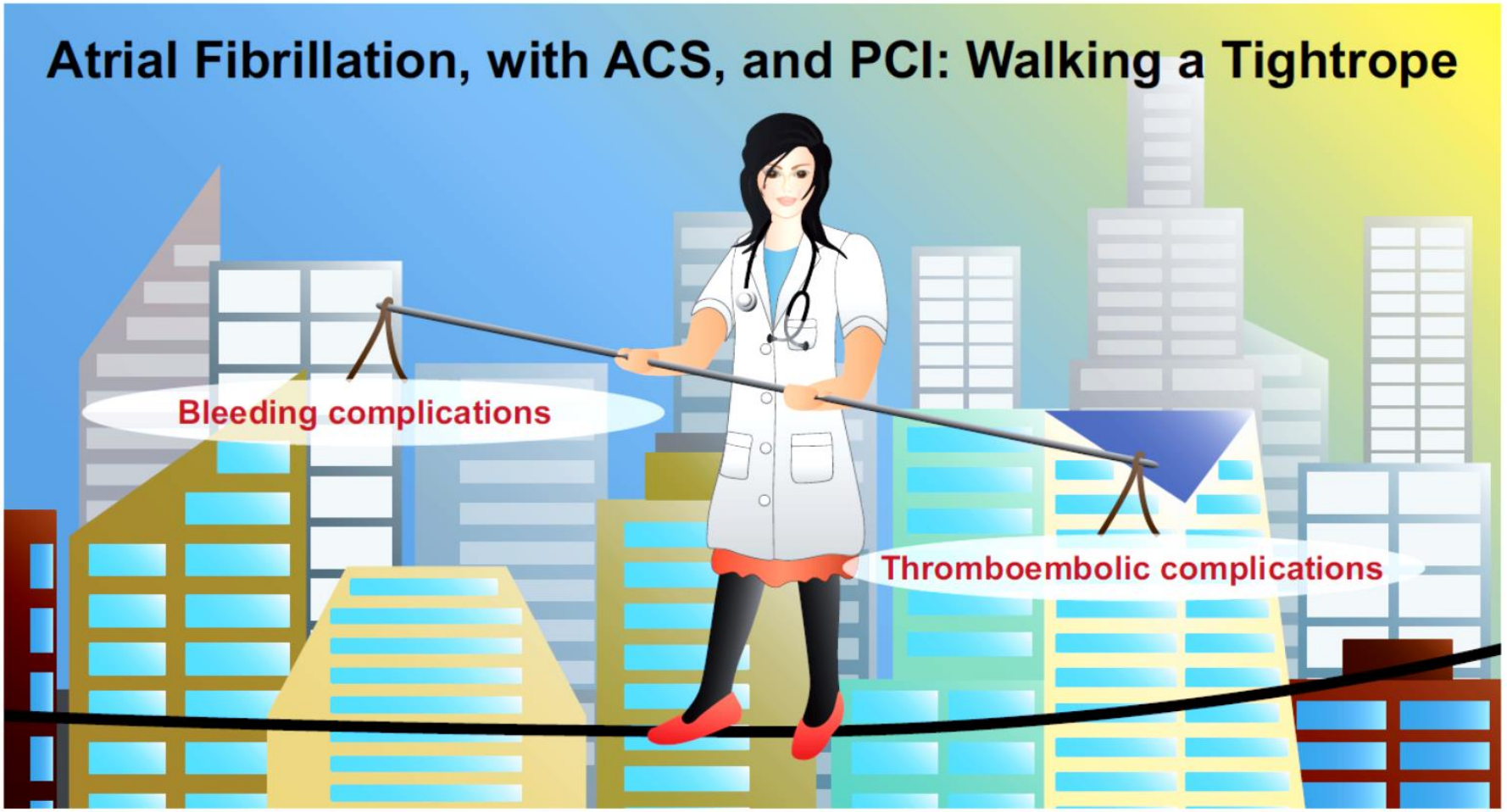
CONGRESSO INTERREGIONALE SIIA
PIEMONTE - LIGURIA - VALLE D'AOSTA
TORINO
10 OTTOBRE 2020

dichiara

che negli ultimi due anni non ha avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario

10 ottobre 2020

During and after PCI, management of patients with AF must balance the risk of bleeding with tha risk of thrombosis



Mehra R et al. European Heart Journal (2019) 40, 1563–1566

European Heart Journal Advance Access published August 27, 2016

European Heart Journal
doi:10.1093/eurheartj/ehw210

ESC GUIDELINES

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

The Task Force
European Soci

Developed with
Rhythm Associ

Endorsed by th

ESC European Society of Cardiology

European Heart Journal (2018) **00**, 1–64
doi:10.1093/eurheartj/ehy136

SPECIAL ARTICLE

The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antag with

Jan Steffe
Matthias
Holger R
Ronan C

ESC European Society of Cardiology

European Heart Journal (2018) **00**, 1–96
doi:10.1093/eurheartj/ehy394

ESC/EACTS GUIDELINES

2018 E revascu

The Task
Society o
Cardio-T

Develope
Associati

ESC European Society of Cardiology

Europace (2019) **21**, 192–193
doi:10.1093/europace/euy174

EHRA CONSENSUS DOCUMENT

2018 Joint European consensus document on the manag atrial fibril coronary s percutane joint conse Heart Rhy Society of Thrombos Percutane (EAPCI), a Cardiac Ca Rhythm So Rhythm Society (APHR Heart Rhythm Society (Arrhythmia Society of S (CASSA)

Circulation

WHITE PAPER

Antithrombotic Therapy in Patients With Atrial Fibrillati Undergo

A North Am

Circulation

ACC/AHA/HRS GUIDELINE

2019 AHA/ACC/HRS Foc ACC/HRS Guideline for With Atrial Fibrillation

A Report of the American College
Task Force on Clinical Practice Gu

ESC European Society of Cardiology

European Heart Journal (2020) **00**, 1–126
doi:10.1093/eurheartj/ehaa612

ESC GUIDELINES

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS)

The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC

AGENDA

1. Importanza e significato della duplice terapia antiaggregante nelle sindromi coronariche acute e/o PCI

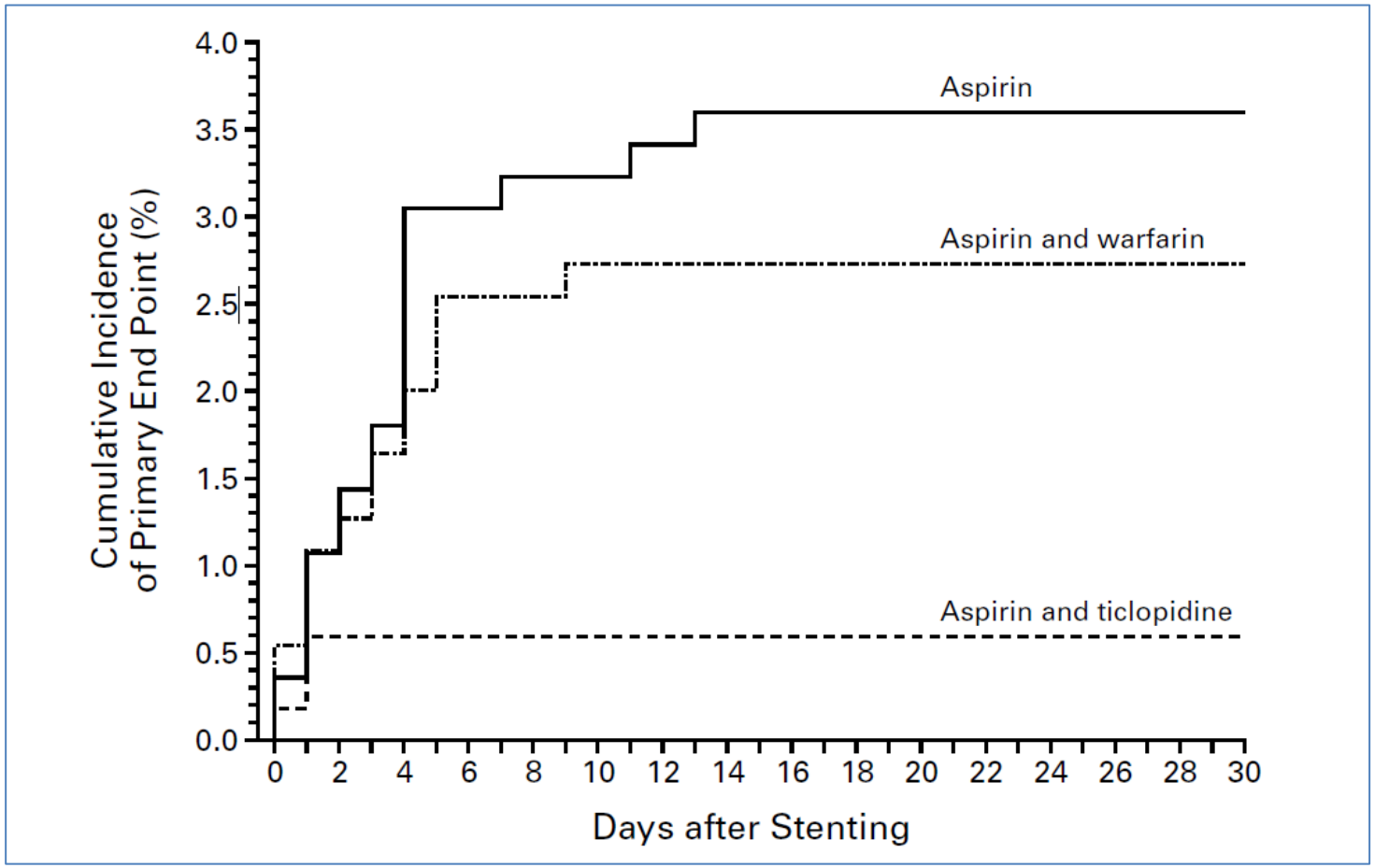
2. Duplice terapia antiaggregante nei pazienti in terapia anticoagulante orale: TRIPLICE TERAPIA ANTITROMBOTICA

3. NOACs, triplice e duplice terapia

4. Evoluzione delle raccomandazioni delle linee guida

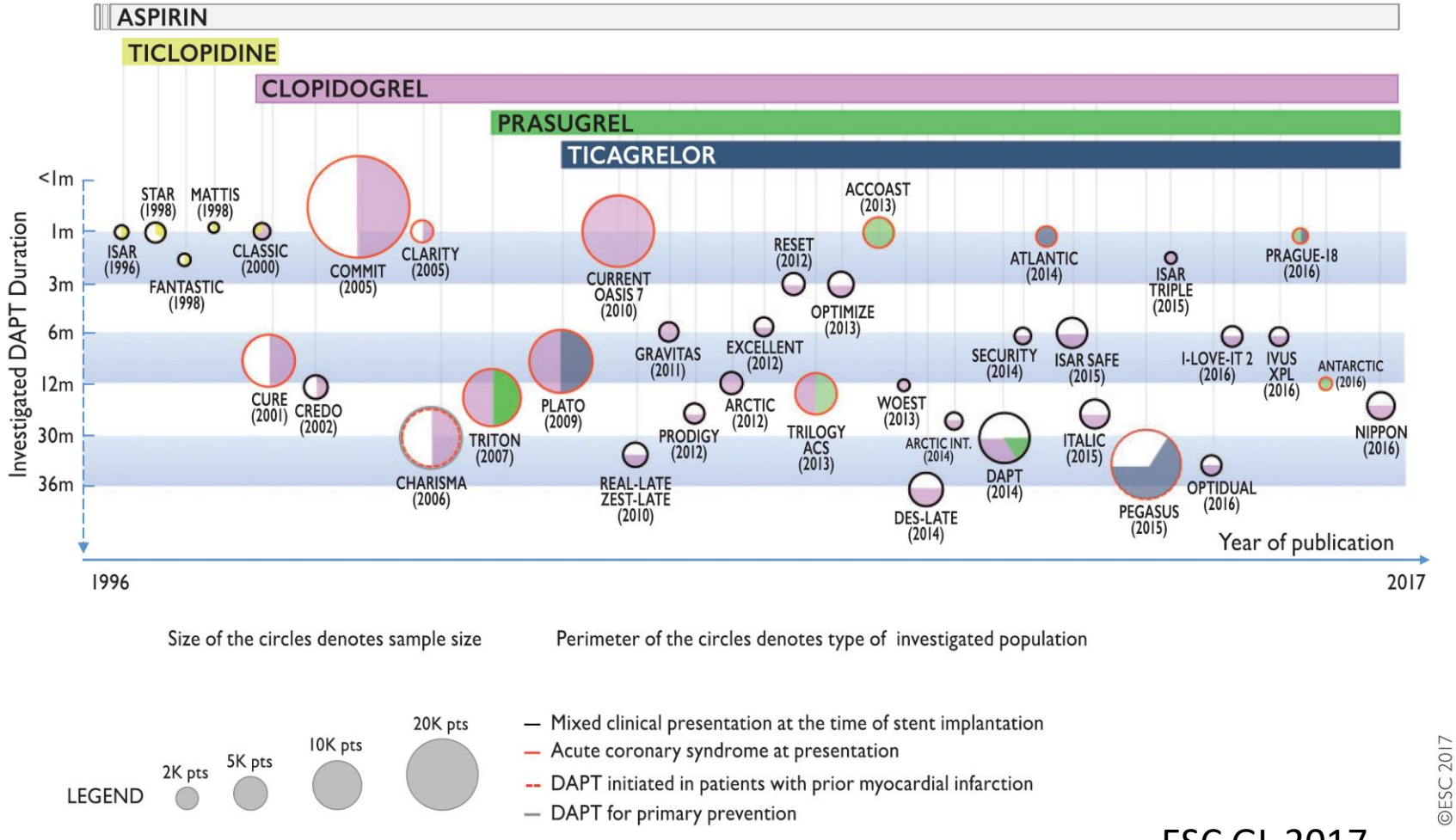
Importanza e significato della duplice terapia antiaggregante (DAPT) nelle sindromi coronariche acute

Combination therapy with 2 antiplatelet agents reduces stent thrombosis more than aspirin alone or aspirin plus warfarin - *The STARS Study*



Leon M et al. N Engl J Med 1998;339:1665–71

35 trial clinici randomizzati, con più di 225.000 pazienti inclusi, hanno stabilito la superiorità della DAPT sulla terapia anticoagulante per i pazienti sottoposti a PCI



ESC GL 2017

Durata della DAPT

- Sia gli eventi ischemici che quelli emorragici influenzano la probabilità di patologie acute cv e mortalità nei pazienti coronaropatici durante e dopo la rivascolarizzazione miocardica
- Il rischio di trombosi tardiva si è ridotto con l'uso di stent di ultima generazione
- Il rischio di sanguinamento dipende dalla durata della DAPT
- Il prolungare la DAPT oltre l'anno dopo PCI o IMA non sembra giustificato, se non in casi particolari, dal piccolo beneficio osservato nella riduzione della trombosi tardiva dello stent rispetto all'elevato rischio emorragico
- Recenti studi hanno addirittura proposto una DAPT più breve: 1-3 mesi di ASA + inibitore recettori $P2Y_{12}$, poi solo quest'ultimo

Fattori che influenzano la durata ottimale della DAPT dopo PCI e/o ACS

	Shorter time of DAPT	Longer time of DAPT
Patient-related factors 	Patients with stable CAD Patients with a history of bleeding Patients with high risk of bleeding	Patients with ACS Patients with diabetes mellitus Patients with renal dysfunction Patients with CHF Patients with previous ST Patients with PAD
Anatomy-related factors 	Short lesion Single-vessel disease	Long lesion Small vessel Bifurcation lesion Complex anatomy Left-main coronary artery
Stent-related factors 	Second-generation DES	First-generation DES Long stent Multiple stents

Eisen A, Bhatt DL. Nature Reviews Cardiology 2015

Doppia terapia antiaggregante per sindrome coronarica acuta e/o PCI in pazienti con indicazione ad anticoagulazione orale:

TRIPLA TERAPIA ANTITROMBOTICA

Doppia terapia antiaggregante per pazienti in anticoagulazione orale (triplice terapia)

Perché è utile

- Circa il 6–8% dei pz sottoposti a PCI hanno indicazione alla terapia anticoagulante a lungo termine per varie patologie quali FA, protesi valvolari meccaniche cardiache, tromboembolismo venoso

- Secondo le conoscenze attuali, in fase acuta la DAPT è necessaria per prevenire la trombosi dello stent ma non è sufficiente a prevenire lo stroke

- Viceversa, la terapia anticoagulante orale è essenziale per la prevenzione dello stroke, ma in fase acuta/subacuta non è idonea a prevenire nuovi eventi coronarici

ESC GL 2018

Doppia terapia antiaggregante per pazienti in anticoagulazione orale (triplice terapia)

Quali rischi comporta

- Paragonata alla sola terapia anticoagulante orale, l'aggiunta della DAPT a questa **aumenta le complicanze emorragiche di circa 3 volte**
- Pertanto questi pz vanno considerati ad alto rischio di sanguinamento
- Le indicazioni alla terapia anticoagulante orale vanno attentamente rivalutate
- La triplice terapia va continuata solo fino a quando viene valutata assolutamente indispensabile

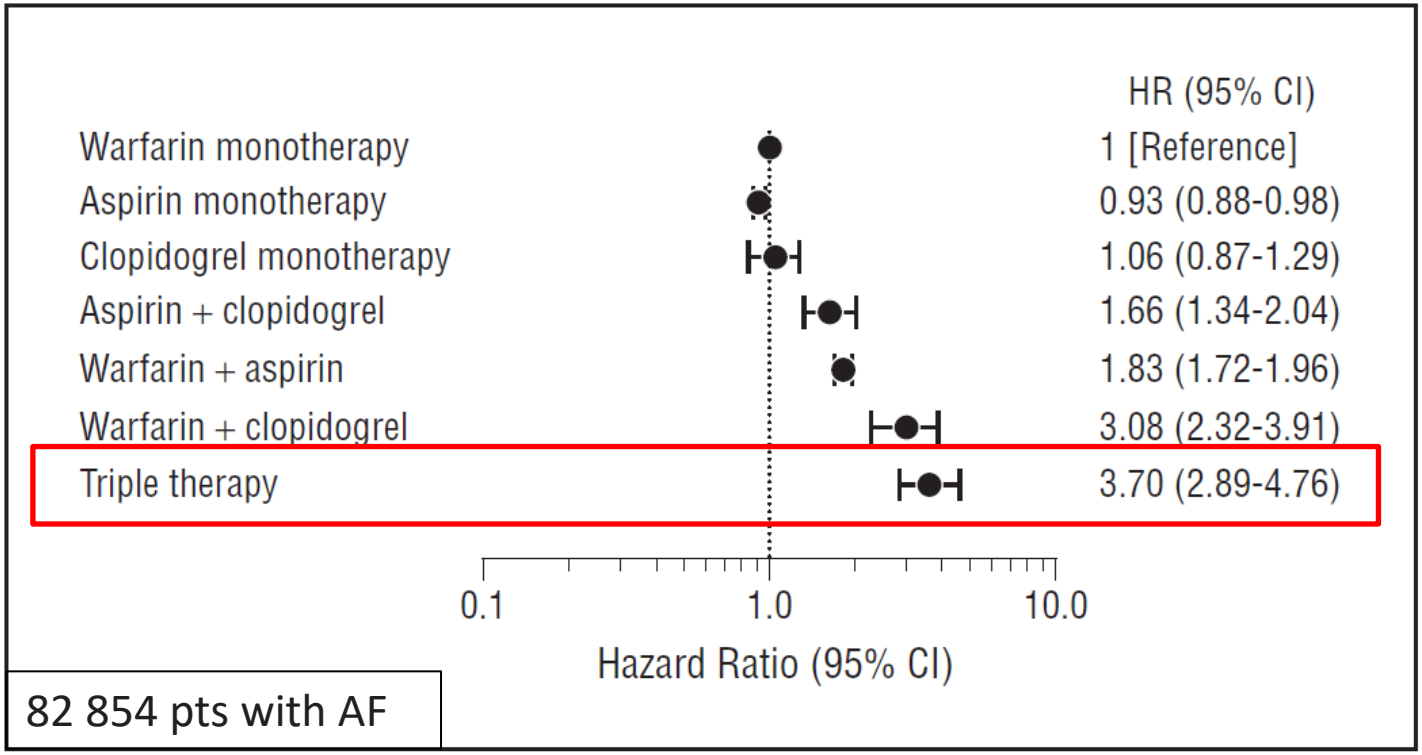
ESC GL 2018

ORIGINAL INVESTIGATION

LESS IS MORE

Risk of Bleeding With Single, Dual, or Triple Therapy With Warfarin, Aspirin, and Clopidogrel in Patients With Atrial Fibrillation

Morten L. Hansen, MD, PhD; Rikke Sørensen, MD; Mette T. Clausen, MSc Pharm; Marie Louise Fog-Petersen, MSc Pharm; Jakob Raunsø, MD; Niels Gadsbøll, MD, DMSc; Gunnar H. Gislason, MD, PhD; Fredrik Folke, MD; Søren S. Andersen, MD; Tina K. Schramm, MD; Steen Z. Abildstrøm, MD, PhD; Henrik E. Poulsen, MD, DMSc; Lars Køber, MD, DMSc; Christian Torp-Pedersen, MD, DMSc



82 854 pts with AF

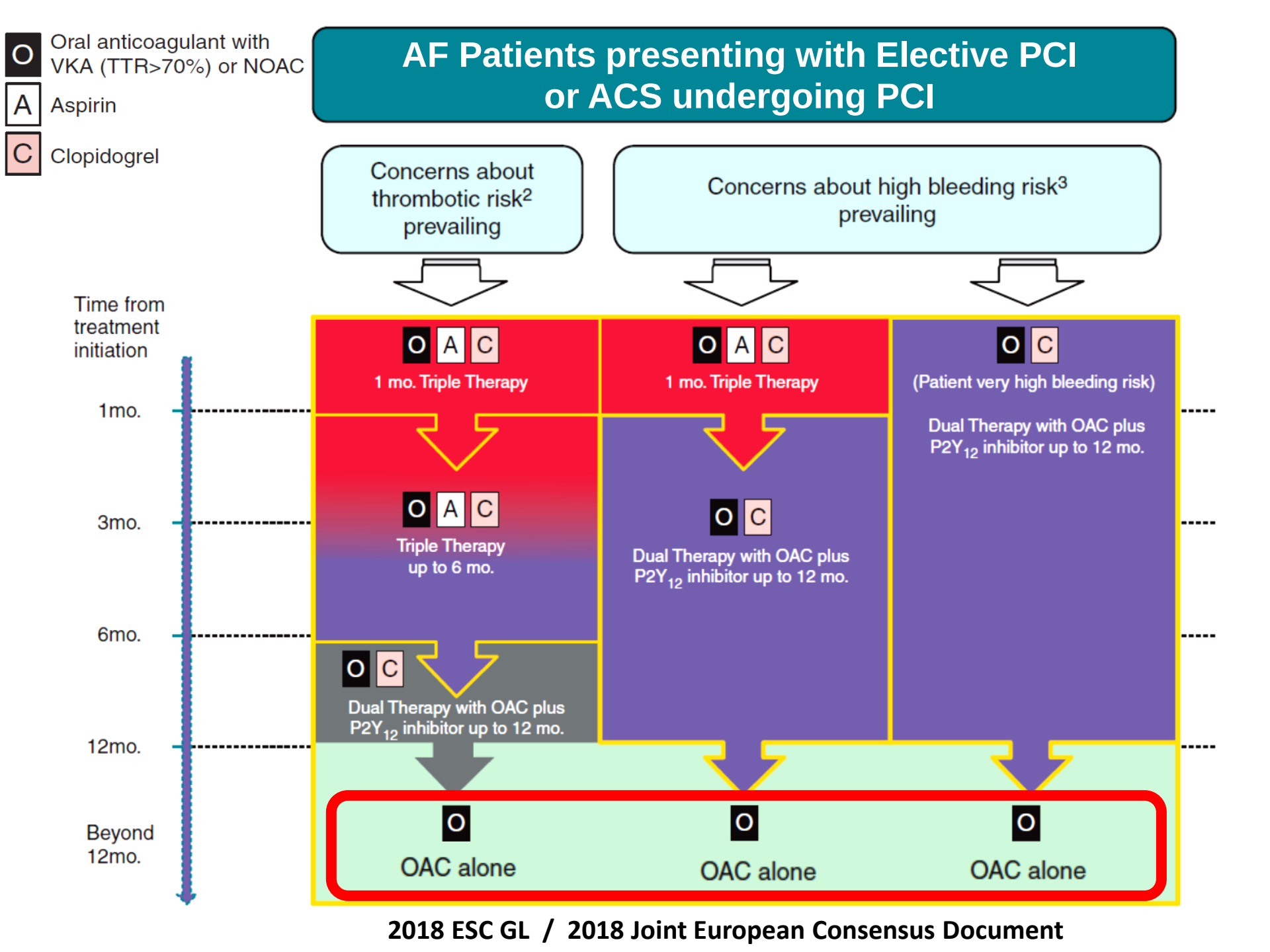
Arch Intern Med. 2010;170(16):1433-1441

ESC European Society of Cardiology

Europace (2019) **21**, 192–193
doi:10.1093/europace/euy174

EHRA CONSENSUS DOCUMENT

2018 Joint European consensus document on the management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous cardiovascular interventions: a joint consensus document of the European Heart Rhythm Association (EHRA), European Society of Cardiology Working Group on Thrombosis, European Association of Percutaneous Cardiovascular Interventions (EAPCI), and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia Society of Southern Africa (CASSA)



2018 ESC GL / 2018 Joint European Consensus Document

Sospensione della terapia antiaggregante

- I dati al riguardo non sono univoci
- Nei pz stabili e liberi da eventi, viene in genere consigliata la sospensione dei farmaci antiaggreganti a 1 anno dopo la procedura di stent
- Studi dimostrano che dopo tale periodo la terapia anticoagulante da sola è superiore all'aspirina, e che la TAO + aspirina non dà maggiore protezione ma è associata con un maggiore rischio emorragico

ESC GL 2018

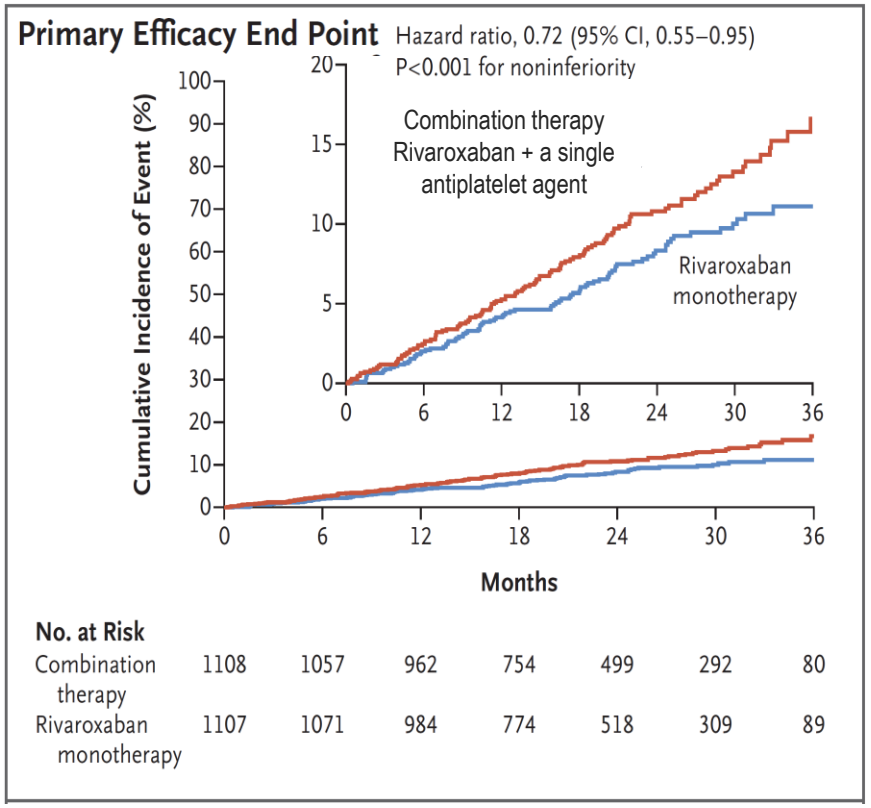
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

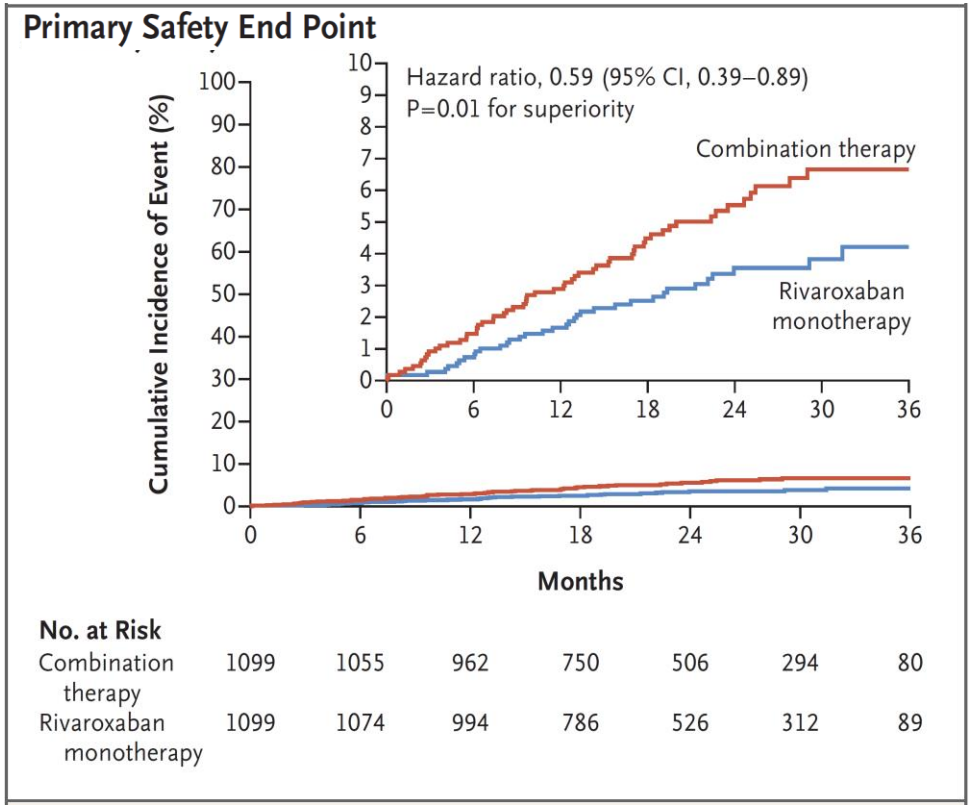
Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease

AFIRE Investigators NEJM September 19, 2019; 381:1103-1113

Stroke, systemic embolism, MI, unstable angina requiring revascularization, or death from any cause



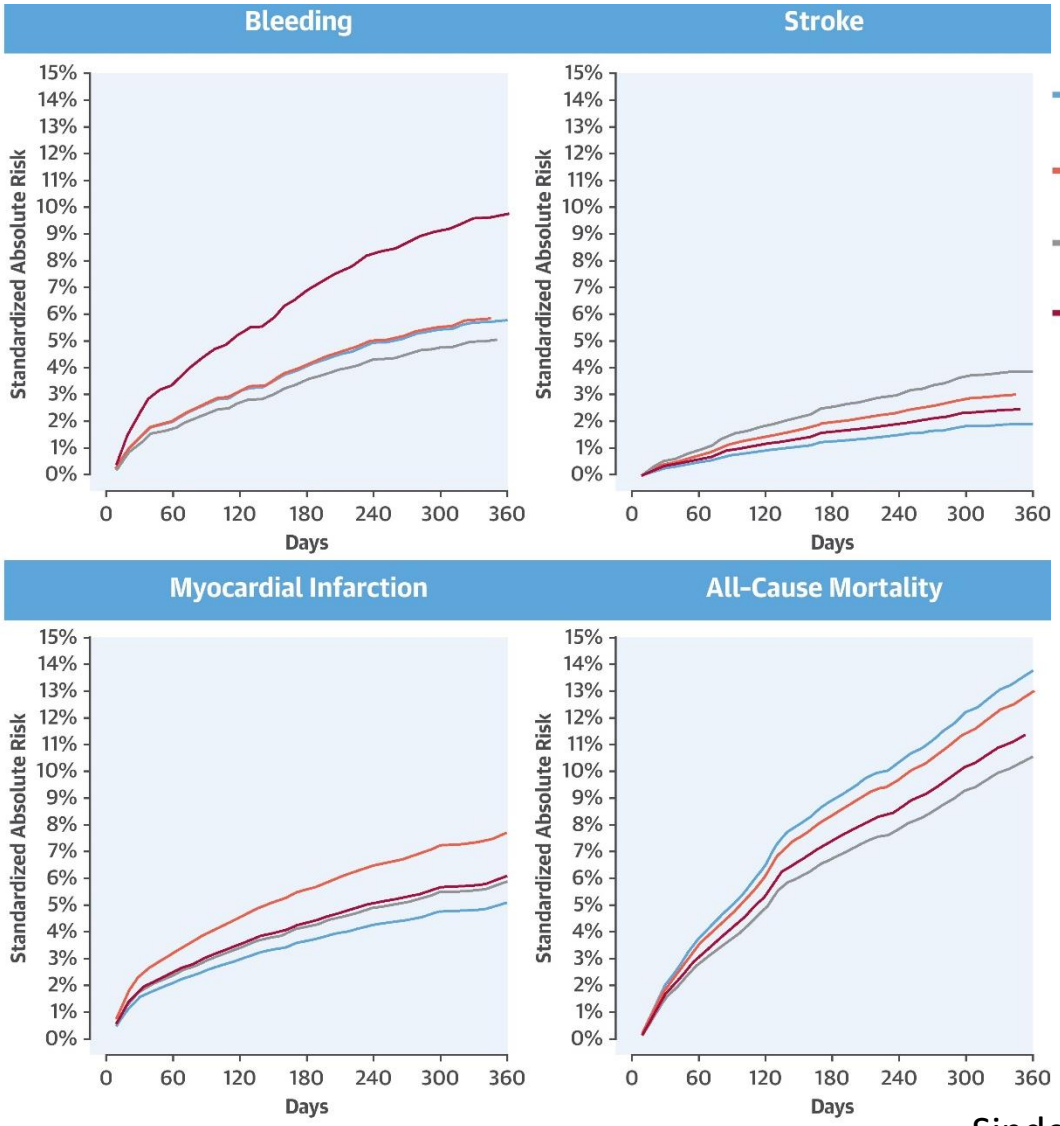
Major bleeding



RESULTS. The trial was stopped early because of increased mortality in the combination therapy group. Rivaroxaban monotherapy was noninferior for efficacy to combination therapy and superior for safety in pts with atrial fibrillation and stable coronary artery disease.

Impiego dei NOACs nella tripla e/o nella doppia terapia

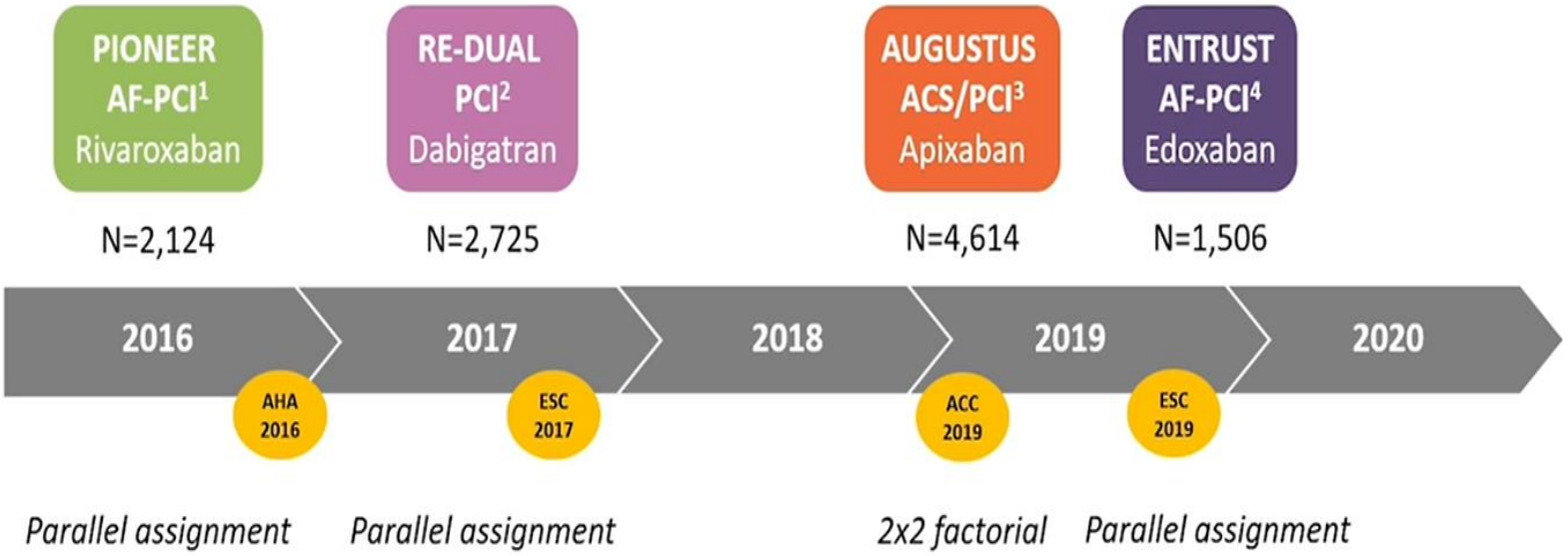
Registro Naz. Danese - Rischio di sanguinamento, stroke ischemico, MI e morte associati a terapia con DOACs vs antagonisti della vitamina K (VKA) in combinazione con ASA o clopidogrel (SAPT) o entrambi (DAPT) in pz con FA dopo MI e/o PCI



I risultati di questo studio dimostrano la maggiore sicurezza ed efficacia della terapia con DOACs rispetto a VKAs in una popolazione real-world di pazienti con FA dopo MI o PCI

Sindet-Pedersen C JACC 2018; 72(15):1790-1800

NOACs nella FA + ACS/PCI



All 4 trials are powered for safety (bleeding) and underpowered for efficacy (ischaemic endpoints)

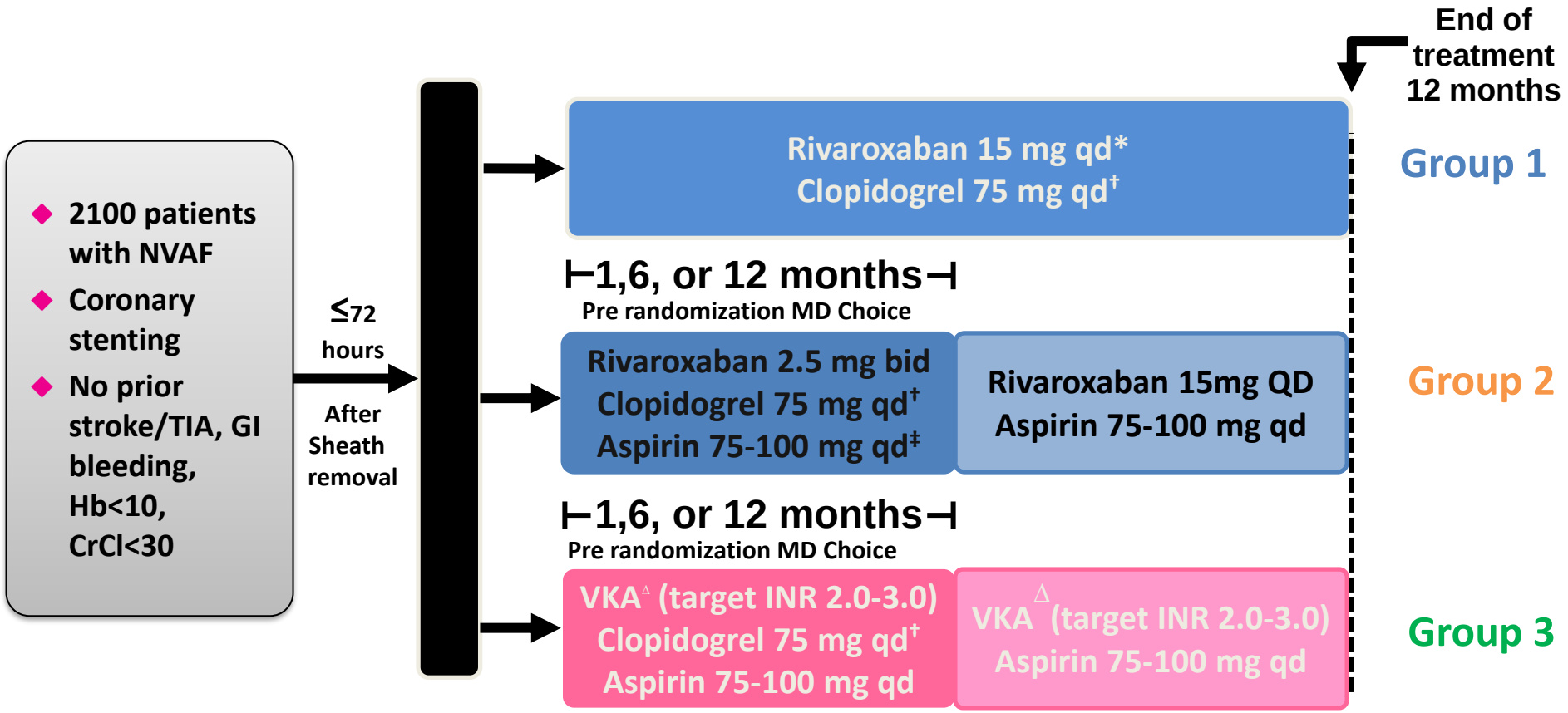
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 22, 2016 VOL. 375 NO. 25

Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI

C. Michael Gibson, M.D., Roxana Mehran, M.D., Christoph Bode, M.D., Jonathan Halperin, M.D., Freek W. Verheugt, M.D., Peter Wildgoose, Ph.D., Mary Birmingham, Pharm.D., Juliana Ianus, Ph.D., Paul Burton, M.D., Ph.D., Martin van Eickels, M.D., Serge Korjian, M.D., Yazan Daaboul, M.D., Gregory Y.H. Lip, M.D., Marc Cohen, M.D., Steen Husted, M.D., Eric D. Peterson, M.D., M.P.H., and Keith A. Fox, M.B., Ch.B.

Patients With Atrial Fibrillation Undergoing Coronary Stent Placement: PIONEER AF-PCI



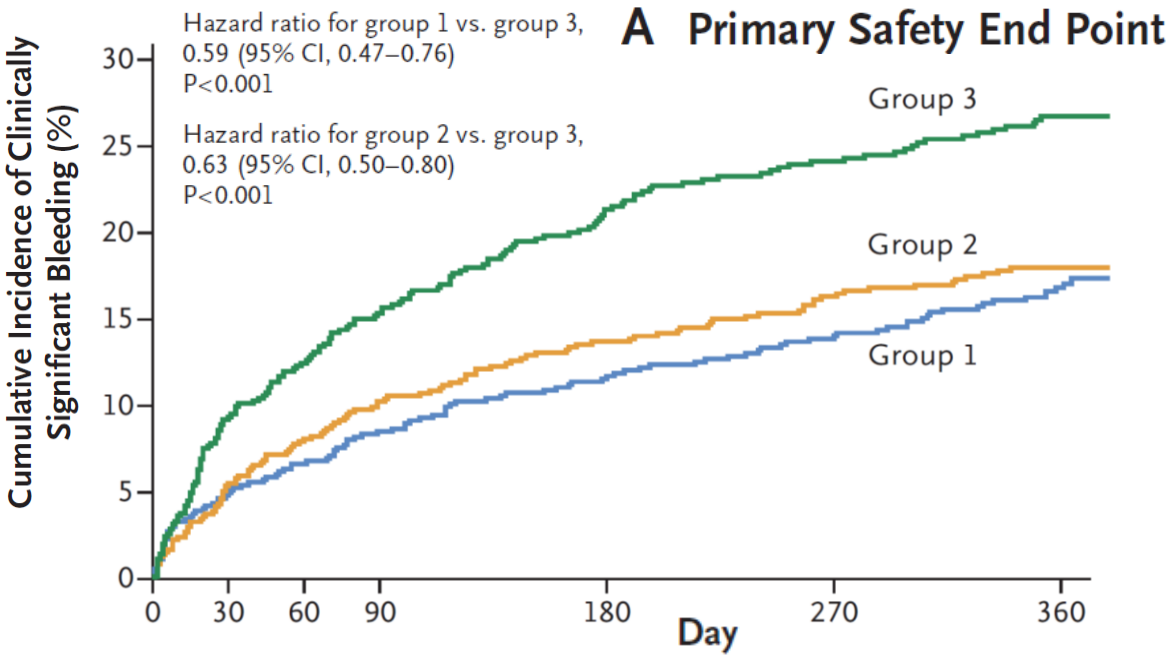
- Primary endpoint: TIMI major + minor + bleeding requiring medical attention
- Secondary endpoint: CV death, MI, and stroke (Ischemic, Hemorrhagic, or Uncertain Origin)

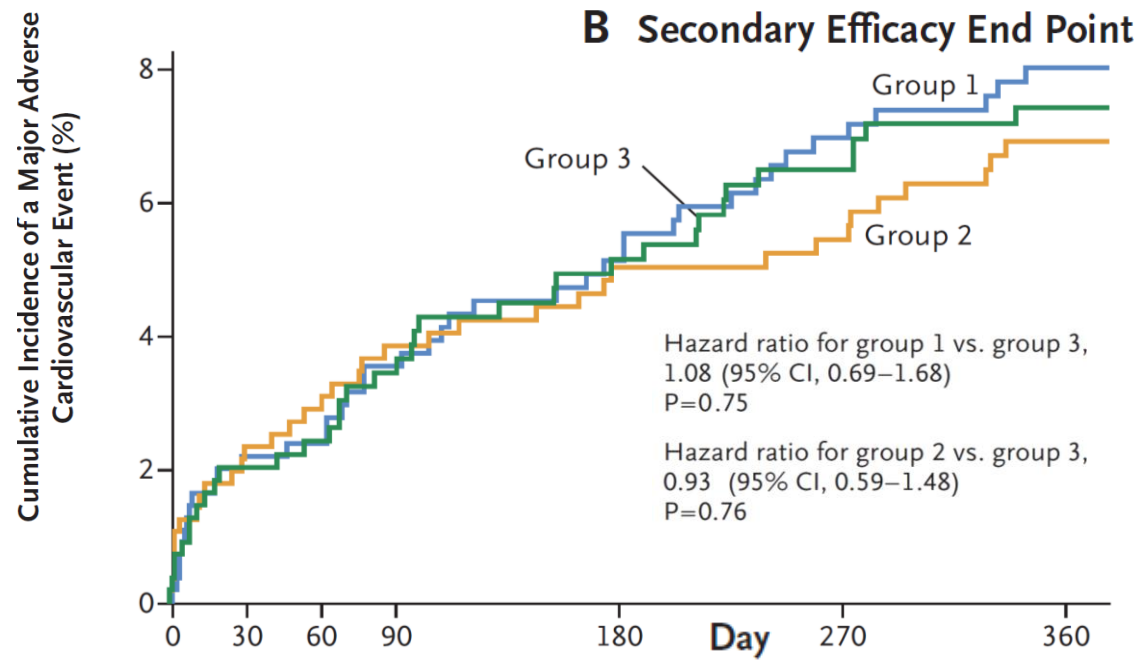
Rivaroxaban dosed at 10 mg once daily in patients with CrCl of 30 to <50 mL/min.

†Alternative $P2Y_{12}$ inhibitors: 10 mg once-daily prasugrel or 90 mg twice-daily ticagrelor.

‡Low-dose aspirin (75-100 mg/d). Δ Open label VKA

Gibson et al. NEJM 2016;375:2423-34





Group 1

rivaroxaban (15 mg once daily) plus a $P2Y_{12}$ inhibitor for 12 months

Group 2

rivaroxaban (2.5 mg twice daily) plus DAPT for 1, 6, or 12 months

Group 3

Triple therapy with a vitamin K antagonist (once daily) plus DAPT for 1, 6, or 12 months

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 19, 2017 VOL. 377 NO. 16

Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation

Christopher P. Cannon, M.D., Deepak L. Bhatt, M.D., M.P.H., Jonas Oldgren, M.D., Ph.D., Gregory Y.H. Lip, M.D., Stephen G. Ellis, M.D., Takeshi Kimura, M.D., Michael Maeng, M.D., Ph.D., Bela Merkely, M.D., Uwe Zeymer, M.D., Savion Gropper, M.D., Ph.D., Matias Nordaby, M.D., Eva Kleine, M.Sc., Ruth Harper, Ph.D., Jenny Manassie, B.Med.Sc., James L. Januzzi, M.D., Jurrien M. ten Berg, M.D., Ph.D., P. Gabriel Steg, M.D., and Stefan H. Hohnloser, M.D., for the RE-DUAL PCI Steering Committee and Investigators*

RE-DUAL PCI™

Study in NVAF patients undergoing PCI

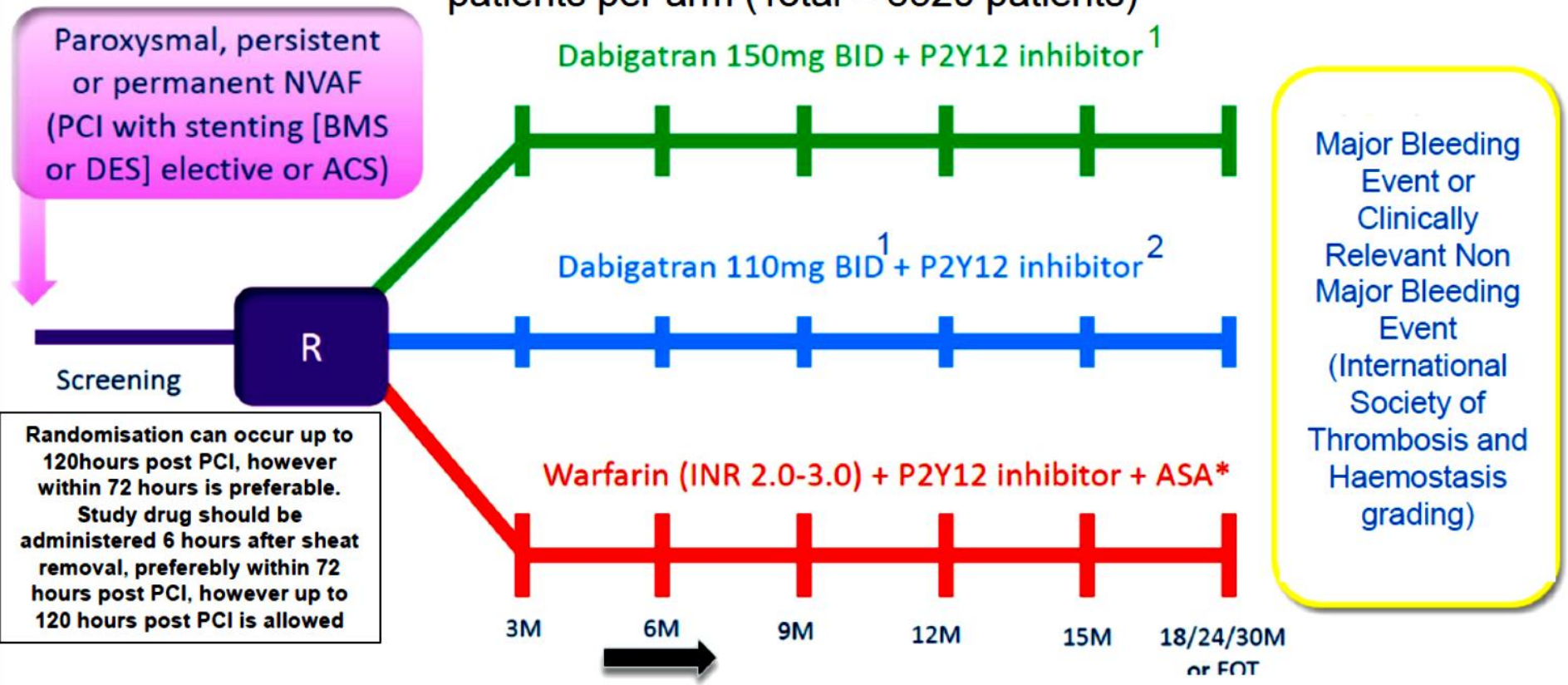
2725 patients with AF who had undergone PCI assigned to triple therapy with warfarin plus a $P2Y_{12}$ inhibitor (clopidogrel or ticagrelor) and aspirin (for 1 to 3 months) (triple-therapy group) or dual therapy with dabigatran (110 mg or 150 mg twice daily) plus a $P2Y_{12}$ inhibitor (clopidogrel or ticagrelor) and no aspirin (110-mg and 150-mg dual-therapy groups).

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

RE-DUAL PCI™

Study in NVAF patients undergoing PCI

Worldwide event-driven trial with 2840 patients per arm (Total = 8520 patients)



[1] Clopidogrel or ticagrelor can be discontinued or switched to ASA (≤100mg QD) from month 12, at investigator discretion

[2] ASA will be discontinued in patients randomized to receive warfarin at 1 month (BMS) and 3 months (DES)

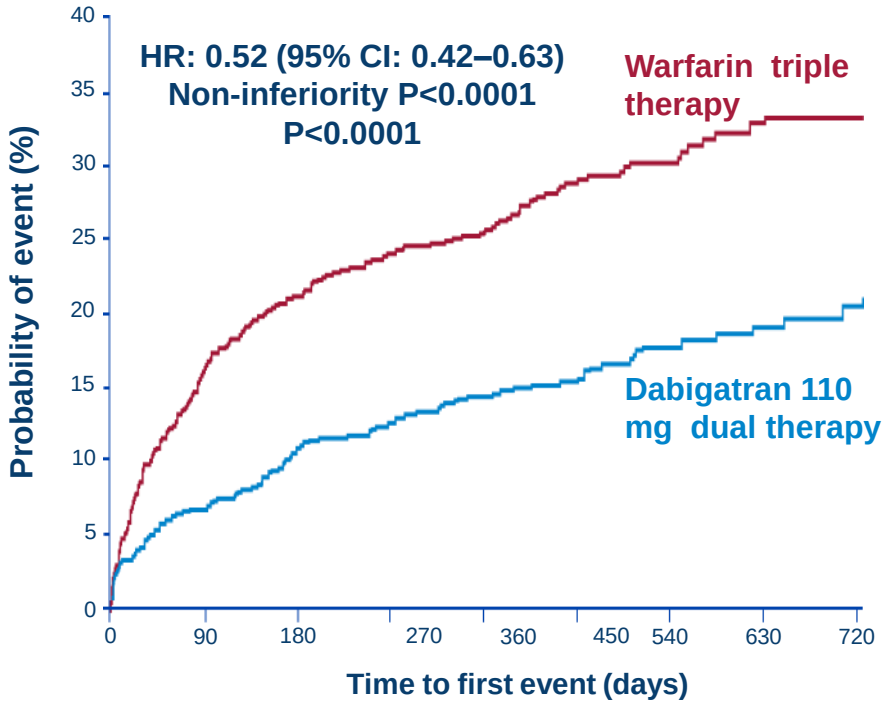
* Patients aged ≥80 years outside of the US will only be randomized to dabigatran etexilate 110mg bid or warfarin

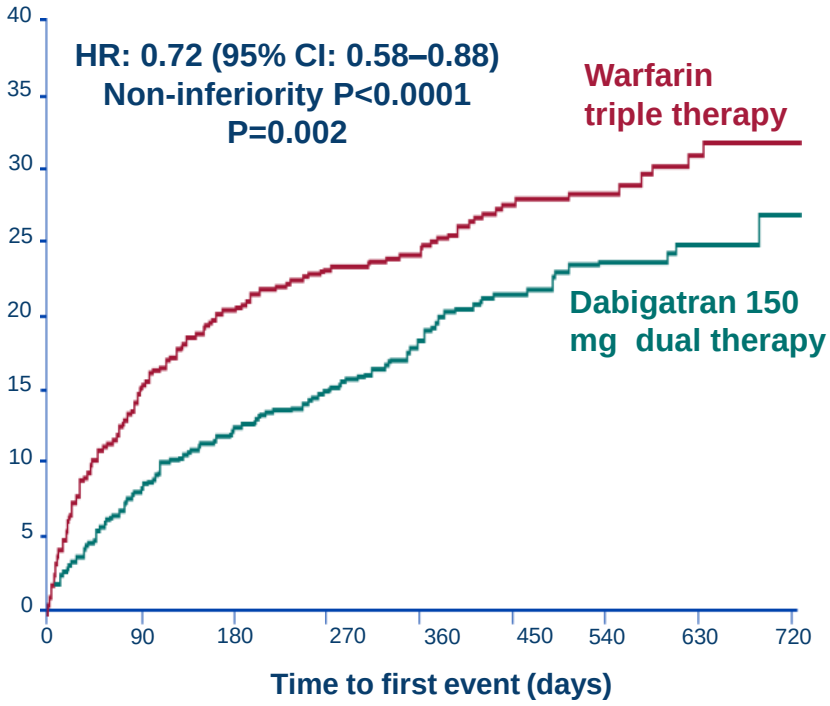
Cannon CP et al. NEJM 2017;377:1513-24

RE-DUAL PCI™

Study in NVAF patients undergoing PCI

Primary Endpoint: Time to first ISTH major or clinically relevant non-major bleeding event





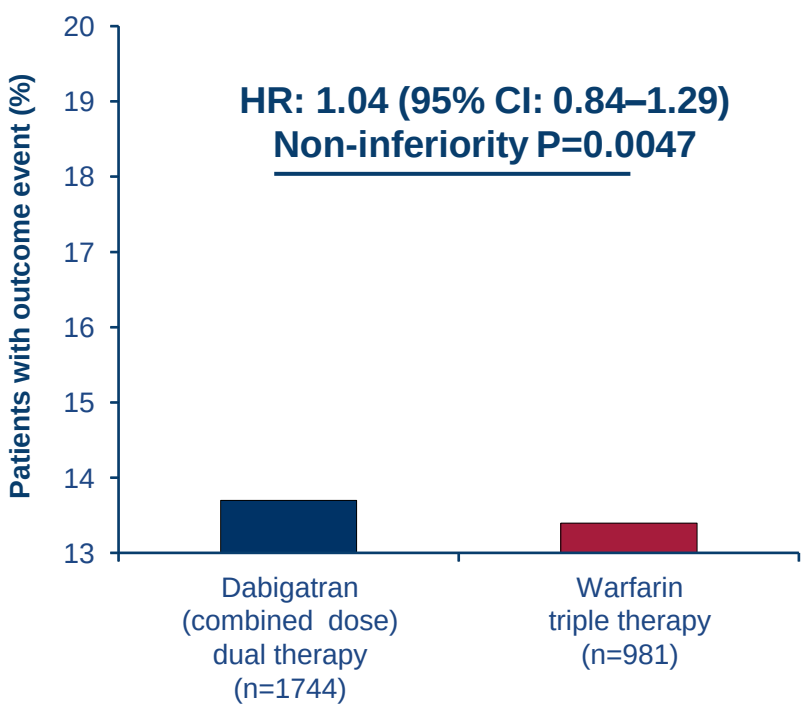
Full analysis set presented. HRs and Wald CIs from Cox proportional-hazard model. For the dabigatran 110 mg vs warfarin comparison, the model is stratified by age, non-elderly vs elderly (<70 or ≥70 in Japan and <80 or ≥80 years old elsewhere). For the dabigatran 150 mg vs warfarin comparison, an unstratified model is used, elderly patients outside the USA are excluded. Non-inferiority P value is one sided (alpha=0.025). Wald two-sided P value from (stratified) Cox proportional-hazard model (alpha=0.05)

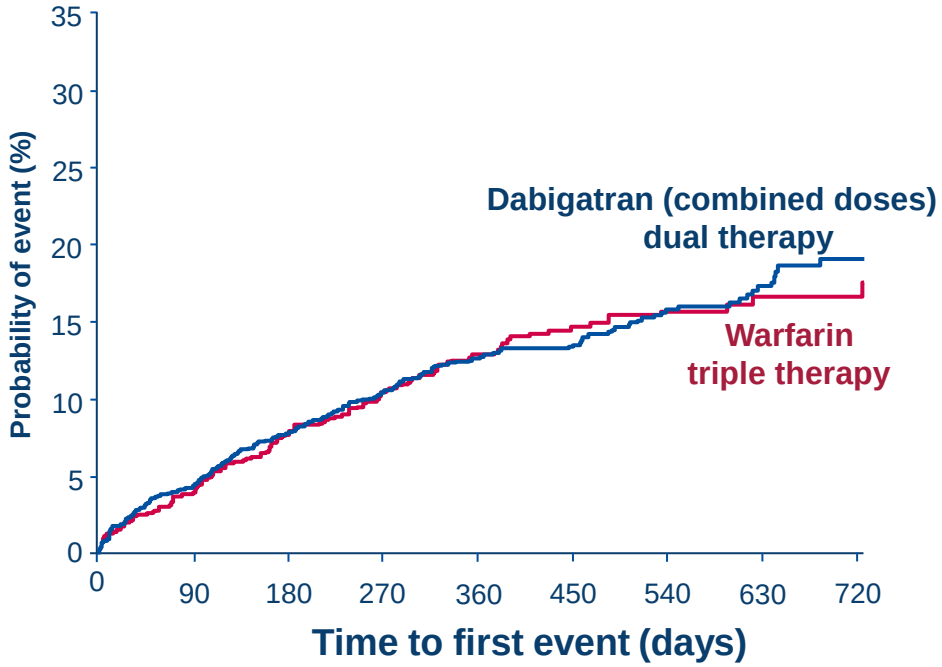
Cannon CP et al. NEJM 2017;377:1513-24

RE-DUAL PCI™

Study in NVAF patients undergoing PCI

Time to death or thromboembolic event or unplanned revascularization





Non-inferiority P value is one sided (alpha=0.025). Results presented are Step 3 of hierarchical testing procedure, testing non-inferiority of dabigatran dual therapy (combined doses) to warfarin triple therapy in death or thromboembolic event and unplanned revascularization

Cannon CP et al. NEJM 2017;377:1513-24

The NEW ENGLAND JOURNAL of MEDICINE

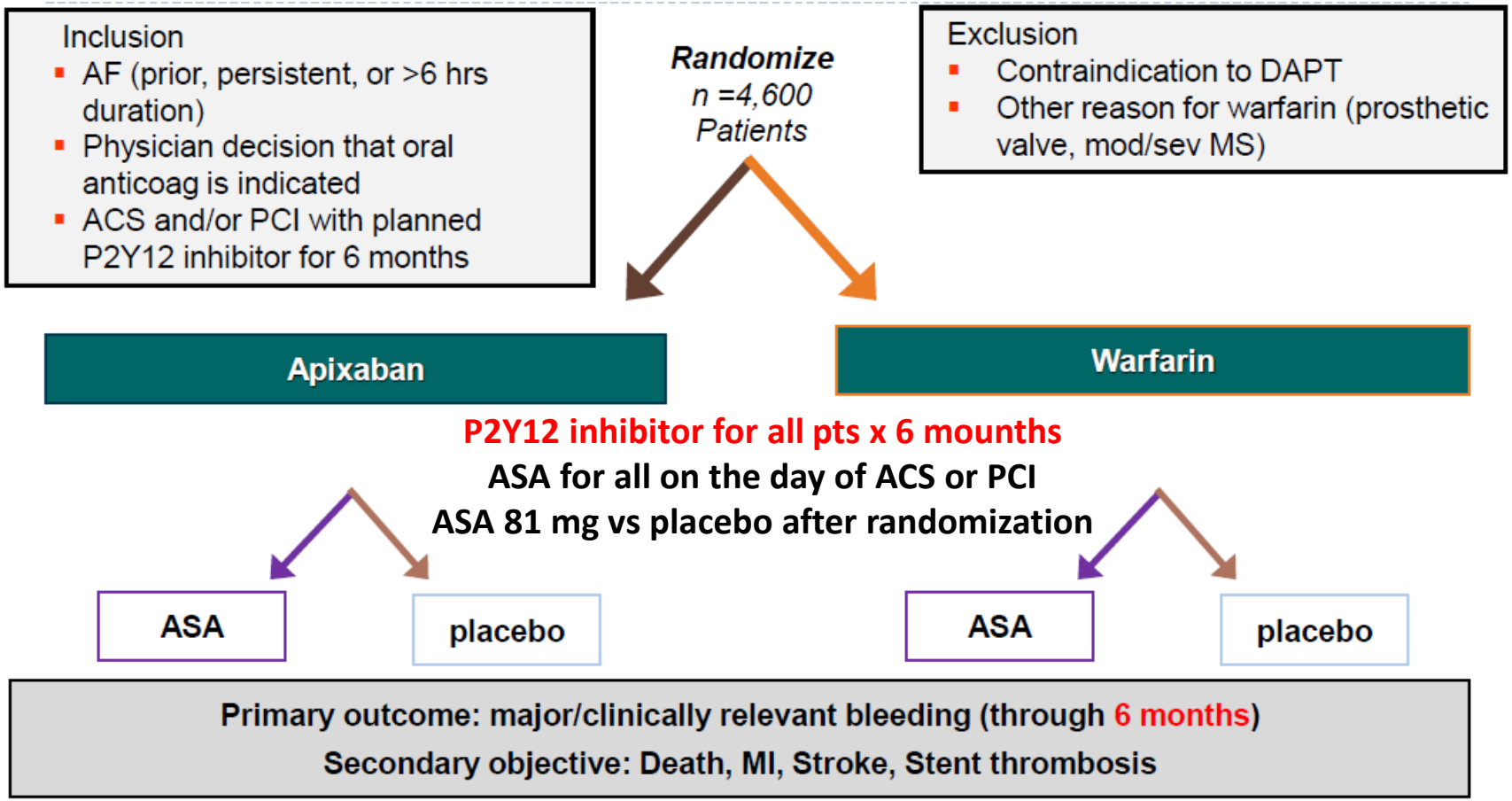
ORIGINAL ARTICLE

Antithrombotic Therapy after Acute Coronary Syndrome or PCI in Atrial Fibrillation

Renato D. Lopes, M.D., Ph.D., Gretchen Heizer, M.S., Ronald Aronson, M.D., Amit N. Vora, M.D., M.P.H., Tyler Massaro, Ph.D., Roxana Mehran, M.D., Shaun G. Goodman, M.D., Stephan Windecker, M.D., Harald Darius, M.D., Jia Li, Ph.D., Oleg Averkov, M.D., Ph.D., M. Cecilia Bahit, M.D., Otavio Berwanger, M.D., Ph.D., Andrzej Budaj, M.D., Ph.D., Ziad Hijazi, M.D., Ph.D., Alexander Parkhomenko, M.D., Ph.D., Peter Sinnaeve, M.D., Ph.D., Robert F. Storey, M.D., Holger Thiele, M.D., Dragos Vinereanu, M.D., Ph.D., Christopher B. Granger, M.D., and John H. Alexander, M.D., M.H.S., for the AUGUSTUS Investigators*

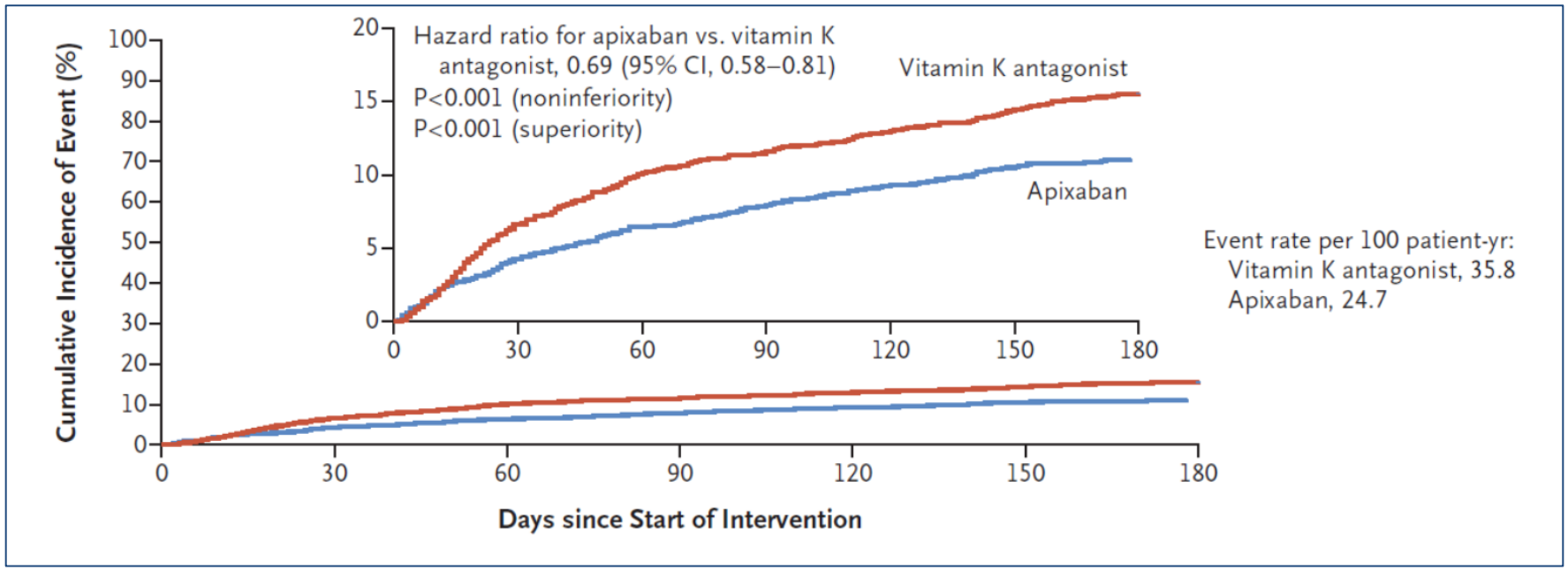
17 March 2019

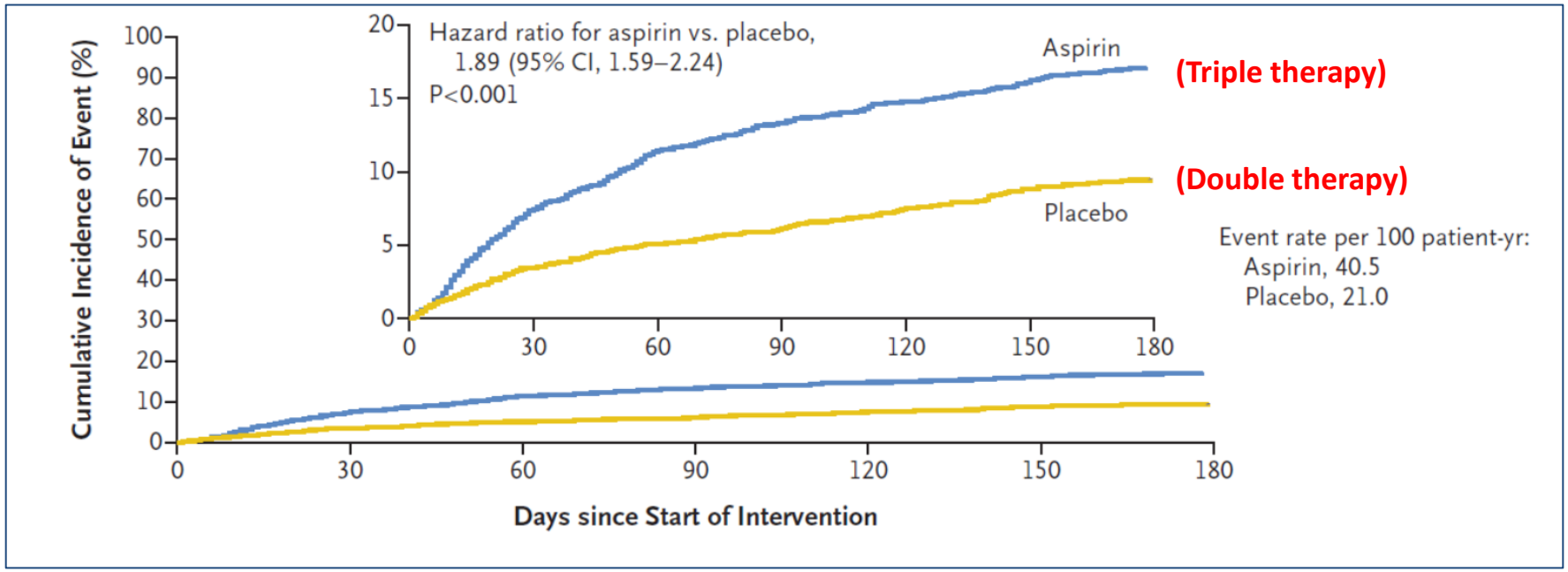
Apixaban Versus Warfarin in Patients with AF and ACS or PCI: The AUGUSTUS Trial



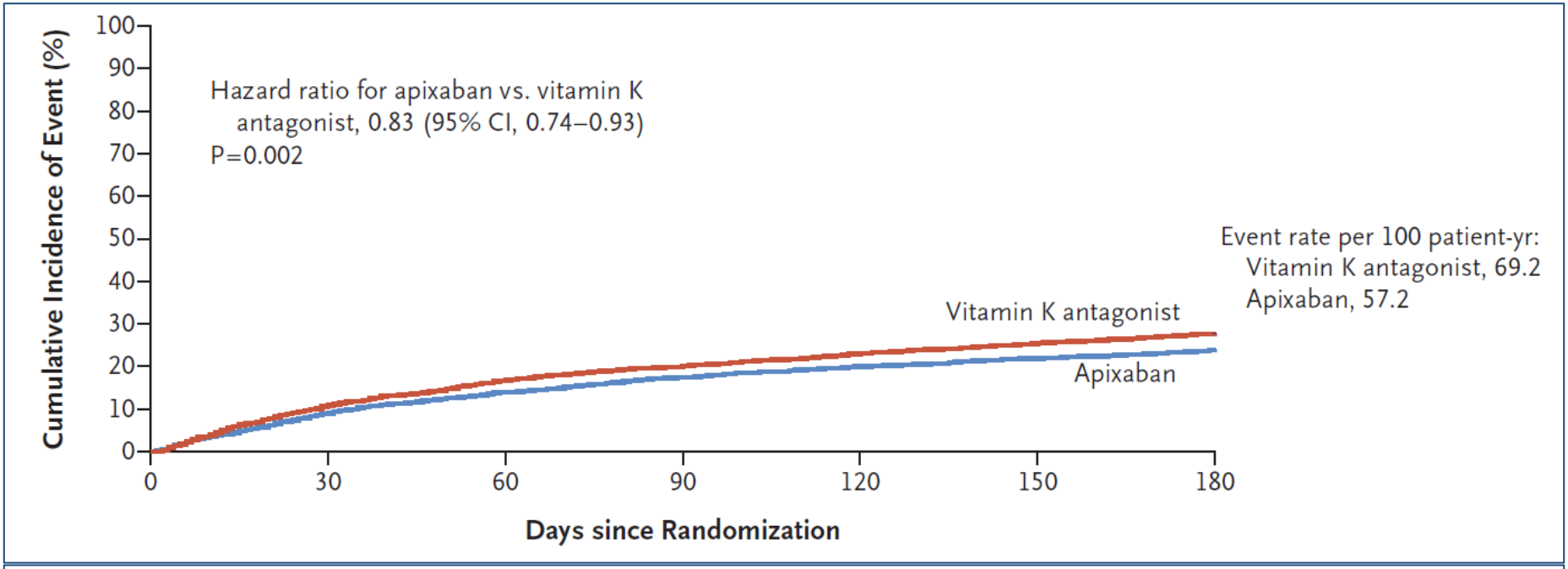
ClinicalTrials.gov Identifier: NCT02415400

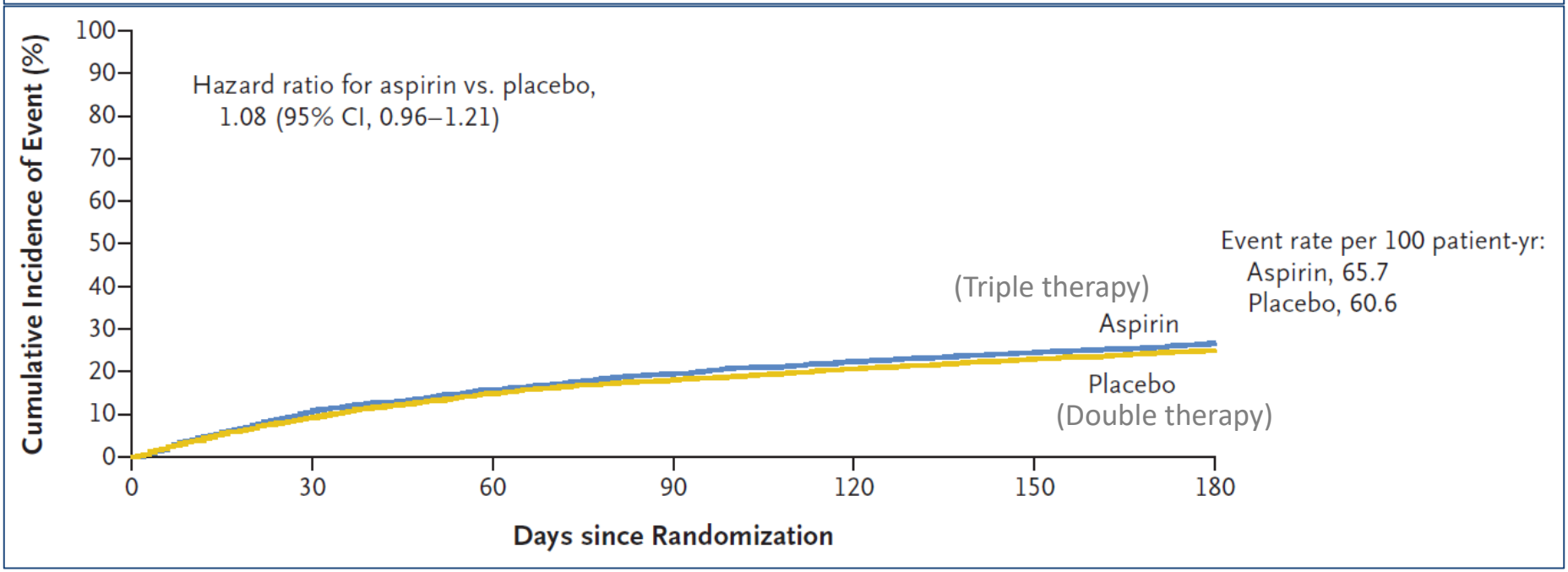
Primary outcome - major or clinically relevant nonmajor bleeding





Secondary outcome – death or hospitalization





Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial

Pascal Vranckx, Marco Valgimigli, Lars Eckardt, Jan Tijssen, Thorsten Lewalter, Giuseppe Gargiulo, Valerii Batushkin, Gianluca Campo, Zoreslava Lysak, Igor Vakaliuk, Krzysztof Milewski, Petra Laeis, Paul-Egbert Reimitz, Rüdiger Smolnik, Wolfgang Zierhut, Andreas Goette

The Lancet Published online September 3, 2019

Patients with AF requiring oral anticoagulation, had a successful PCI for stable coronary artery disease or acute coronary syndrome.

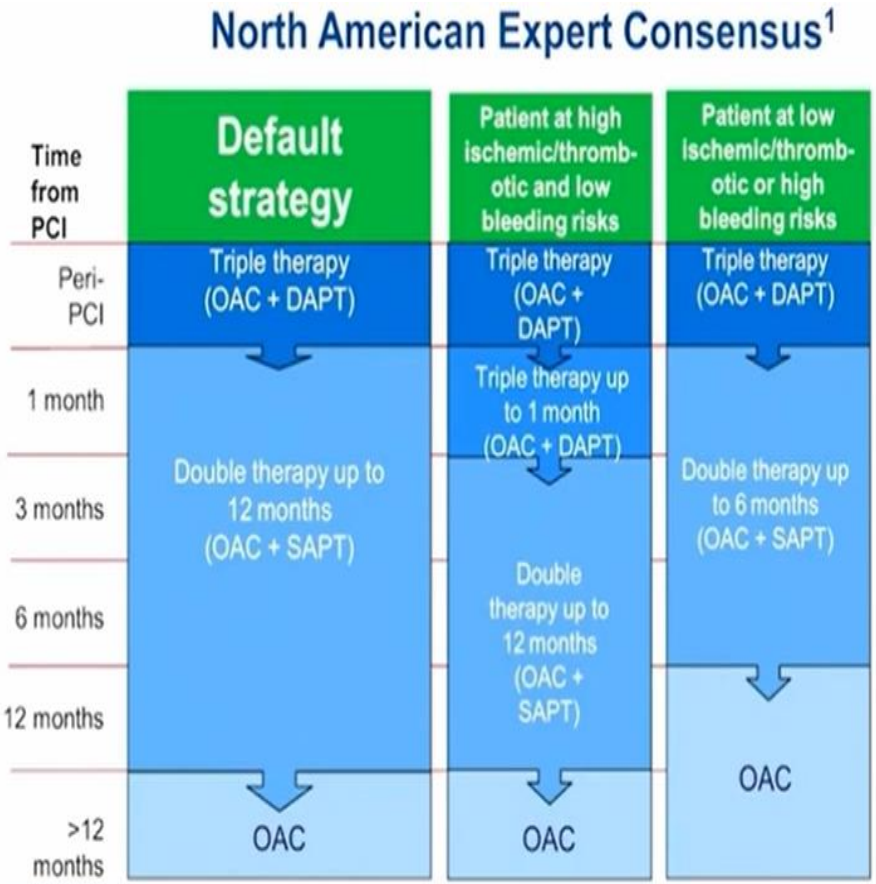
Participants were randomly assigned (1:1) from 4 h to 5 days after PCI to either edoxaban (60 or 30 mg once daily) plus a P2Y12 inhibitor for 12 months or a vitamin K antagonist (VKA) in combination with a P2Y12 inhibitor and aspirin (100 mg once daily, for 1–12 months).

	Edoxaban regimen	VKA regimen	Hazard ratio (two-sided 95% CI)	p value
Primary outcome of major or CRNM bleeding (ISTH)				
Intention-to-treat analysis				
Number of patients	751	755	..	..
Number of patients with event	128 (17%)	152 (20%)	..	..
Annualised event rate	20·7	25·6	0·83 (0·65–1·05)	Non-inferiority p=0·0010; superiority p=0·1154
On-treatment analysis				
Number of patients	746	740	..	..
Number of patients with event	124 (17%)	142 (19%)	..	..
Annualised event rate	20·7	25·5	0·84 (0·66–1·06)	Non-inferiority p=0·0016; superiority p=0·1434

Interpretation In patients with atrial fibrillation who had PCI, the edoxaban-based regimen was non-inferior for bleeding compared with the VKA-based regimen, without significant differences in ischaemic events.

The Lancet Published online September 3, 2019

Differenze tra Raccomandazioni Americane 2018 ed Europee 2018



O Oral anticoagulation with VKA (TTR >70%) or NOAC; A ASA; C clopidogrel; GRACE, Global Registry of Acute Cardiac Events; LAD, left anterior descending; SAPT, single antiplatelet therapy; TTR, time in therapeutic range. 1. Angiolillo et al. Circulation 2018;138:527; 2. Lip et al. Europace 2018;21:192

ESC European Society of Cardiology

European Heart Journal (2019) **40**, 3757–3767
doi:10.1093/eurheartj/ehz732

Safety and efficacy outcomes of double vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of non-vitamin K antagonist oral anticoagulant-based randomized clinical trials

Giuseppe Gargiulo [1,2†], Andreas Goette[3,4,5†], Jan Tijssen[6,7], Lars Eckardt[5,8], Thorsten Lewalter[5,9], Pascal Vranckx[10‡], and Marco Valgimigli [1‡]

4 included randomized clinical trials:

- PIONEER AF-PCI
- RE-DUAL PCI
- AUGUSTUS
- ENTRUST AF-PCI

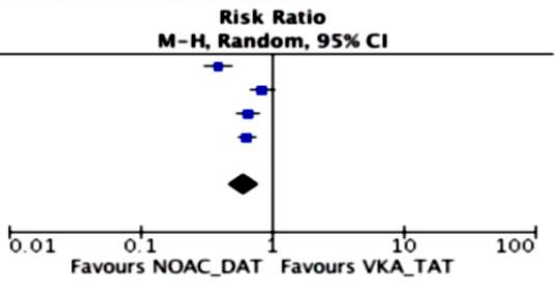
10 234 patients (DAT = 5496 vs. TAT = 4738)

A

ISTH MAJOR OR CLINICALLY RELEVANT NONMAJOR BLEEDING

Study or Subgroup	NOAC_DAT Events	NOAC_DAT Total	VKA_TAT Events	VKA_TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	84	1143	210	1123	23.7%	0.39 [0.31, 0.50]
ENTRUST AF-PCI	128	751	152	755	24.7%	0.85 [0.68, 1.05]
PIONEER AF-PCI	117	696	178	697	24.8%	0.66 [0.53, 0.81]
RE-DUAL PCI	305	1744	264	981	26.8%	0.65 [0.56, 0.75]
Total (95% CI)		**4334**		**3556**	**100.0%**	**0.62 [0.47, 0.81]**
Total events	634		804			

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 22.84$, df = 3 (P < 0.0001); $I^2 = 87\%$
Test for overall effect: Z = 3.47 (P = 0.0005)

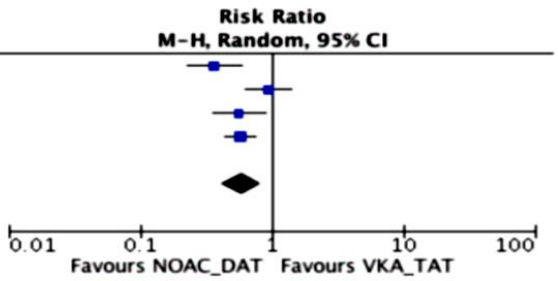


B

ISTH MAJOR BLEEDING

Study or Subgroup	NOAC_DAT Events	NOAC_DAT Total	VKA_TAT Events	VKA_TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	23	1143	62	1123	22.2%	0.36 [0.23, 0.58]
ENTRUST AF-PCI	45	751	48	755	25.2%	0.94 [0.64, 1.40]
PIONEER AF-PCI	27	696	48	697	22.6%	0.56 [0.36, 0.89]
RE-DUAL PCI	92	1744	90	981	30.0%	0.57 [0.43, 0.76]
Total (95% CI)		**4334**		**3556**	**100.0%**	**0.59 [0.41, 0.83]**
Total events	187		248			

Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 9.52$, df = 3 (P = 0.02); $I^2 = 68\%$
Test for overall effect: Z = 2.99 (P = 0.003)

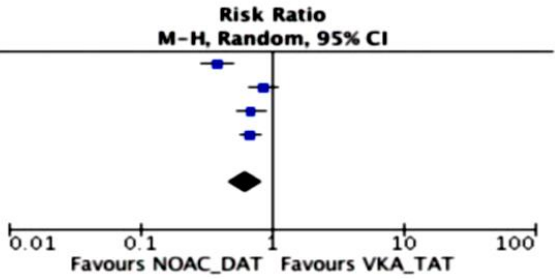


C

CLINICALLY RELEVANT NONMAJOR BLEEDING

Study or Subgroup	NOAC_DAT Events	NOAC_DAT Total	VKA_TAT Events	VKA_TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	62	1143	158	1123	23.6%	0.39 [0.29, 0.51]
ENTRUST AF-PCI	97	751	114	755	24.7%	0.86 [0.67, 1.10]
PIONEER AF-PCI	90	696	130	697	24.8%	0.69 [0.54, 0.89]
RE-DUAL PCI	213	1744	174	981	26.9%	0.69 [0.57, 0.83]
Total (95% CI)		**4334**		**3556**	**100.0%**	**0.63 [0.47, 0.85]**
Total events	462		576			

Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 18.50$, df = 3 (P = 0.0003); $I^2 = 84\%$
Test for overall effect: Z = 3.02 (P = 0.003)

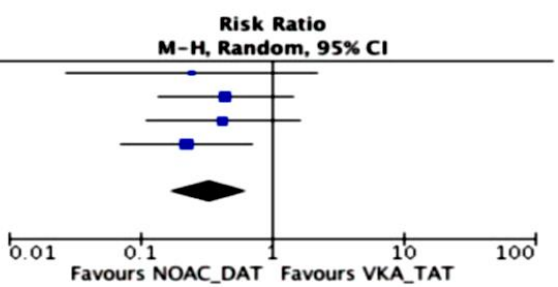


D

INTRACRANIAL HAEMORRHAGE

Study or Subgroup	NOAC_DAT Events	NOAC_DAT Total	VKA_TAT Events	VKA_TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	1	1143	4	1123	9.3%	0.25 [0.03, 2.19]
ENTRUST AF-PCI	4	751	9	755	32.5%	0.45 [0.14, 1.44]
PIONEER AF-PCI	3	696	7	697	24.6%	0.43 [0.11, 1.65]
RE-DUAL PCI	4	1744	10	981	33.5%	0.23 [0.07, 0.72]
Total (95% CI)		**4334**		**3556**	**100.0%**	**0.33 [0.17, 0.65]**
Total events	12		30			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.89$, df = 3 (P = 0.83); $I^2 = 0\%$
Test for overall effect: Z = 3.22 (P = 0.001)



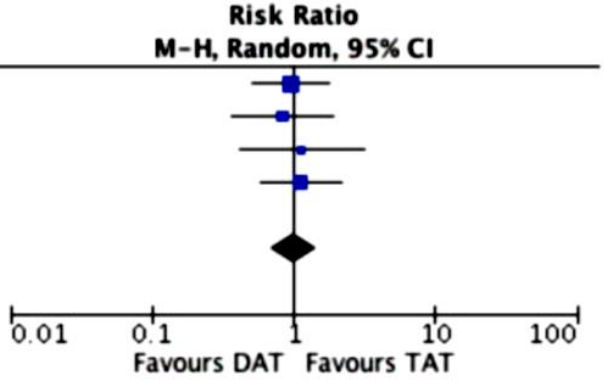
A

STROKE

Study or Subgroup	DAT Events	DAT Total	TAT Events	TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	19	2307	20	2307	35.2%	0.95 [0.51, 1.78]
ENTRUST AF-PCI	10	751	12	755	19.8%	0.84 [0.36, 1.93]
PIONEER AF-PCI	8	694	7	695	13.5%	1.14 [0.42, 3.14]
RE-DUAL PCI	26	1744	13	981	31.5%	1.13 [0.58, 2.18]
Total (95% CI)		**5496**		**4738**	**100.0%**	**1.00 [0.69, 1.45]**
Total events	63		52			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.39$, df = 3 (P = 0.94); $I^2 = 0\%$

Test for overall effect: Z = 0.01 (P = 0.99)



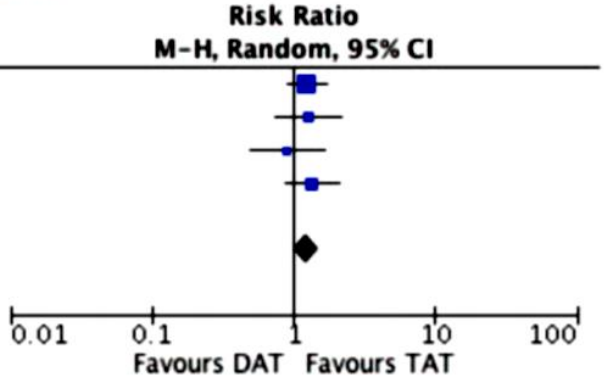
B

MYOCARDIAL INFARCTION

Study or Subgroup	DAT Events	DAT Total	TAT Events	TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	84	2307	68	2307	46.5%	1.24 [0.90, 1.69]
ENTRUST AF-PCI	29	751	23	755	15.9%	1.27 [0.74, 2.17]
PIONEER AF-PCI	19	694	21	695	12.3%	0.91 [0.49, 1.67]
RE-DUAL PCI	70	1744	29	981	25.4%	1.36 [0.89, 2.08]
Total (95% CI)		**5496**		**4738**	**100.0%**	**1.22 [0.99, 1.52]**
Total events	202		141			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.18$, df = 3 (P = 0.76); $I^2 = 0\%$

Test for overall effect: Z = 1.84 (P = 0.07)



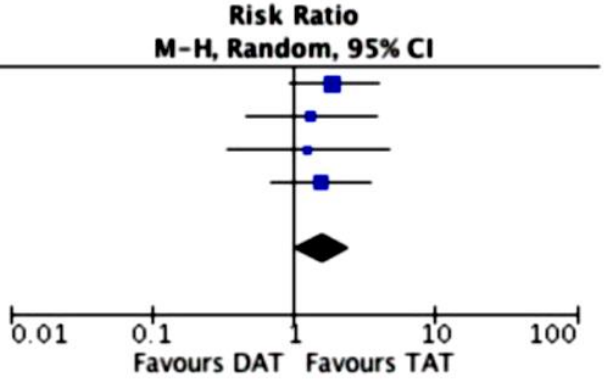
C

STENT THROMBOSIS

Study or Subgroup	DAT Events	DAT Total	TAT Events	TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	21	2307	11	2307	38.5%	1.91 [0.92, 3.95]
ENTRUST AF-PCI	8	751	6	755	18.3%	1.34 [0.47, 3.84]
PIONEER AF-PCI	5	694	4	695	11.8%	1.25 [0.34, 4.64]
RE-DUAL PCI	22	1744	8	981	31.4%	1.55 [0.69, 3.46]
Total (95% CI)		**5496**		**4738**	**100.0%**	**1.59 [1.01, 2.50]**
Total events	56		29			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.48$, df = 3 (P = 0.92); $I^2 = 0\%$

Test for overall effect: Z = 2.02 (P = 0.04)



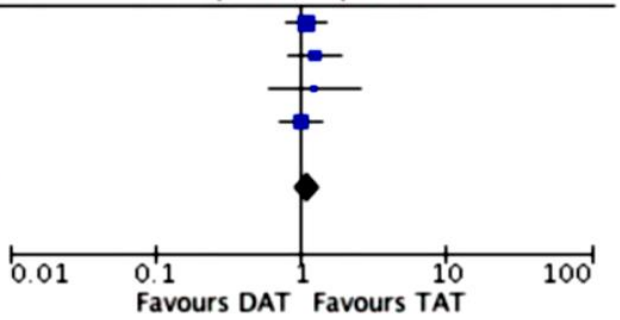
A

ALL-CAUSE DEATH

Study or Subgroup	DAT Events	DAT Total	TAT Events	TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	79	2307	72	2307	38.9%	1.10 [0.80, 1.50]
ENTRUST AF-PCI	46	751	37	755	21.6%	1.25 [0.82, 1.90]
PIONEER AF-PCI	16	694	13	695	7.3%	1.23 [0.60, 2.54]
RE-DUAL PCI	85	1744	48	981	32.2%	1.00 [0.71, 1.41]
Total (95% CI)		**5496**		**4738**	**100.0%**	**1.10 [0.91, 1.34]**
Total events	226		170			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.77$, df = 3 (P = 0.86); $I^2 = 0\%$

Test for overall effect: Z = 0.98 (P = 0.32)



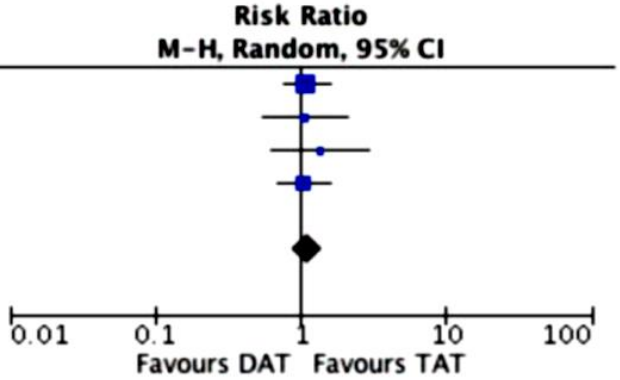
B

CARDIOVASCULAR DEATH

Study or Subgroup	DAT Events	DAT Total	TAT Events	TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	58	2307	53	2307	44.2%	1.09 [0.76, 1.58]
ENTRUST AF-PCI	17	751	16	755	13.1%	1.07 [0.54, 2.10]
PIONEER AF-PCI	15	694	11	695	10.1%	1.37 [0.63, 2.95]
RE-DUAL PCI	58	1744	31	981	32.5%	1.05 [0.69, 1.62]
Total (95% CI)		**5496**		**4738**	**100.0%**	**1.10 [0.86, 1.41]**
Total events	148		111			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.35$, df = 3 (P = 0.95); $I^2 = 0\%$

Test for overall effect: Z = 0.77 (P = 0.44)



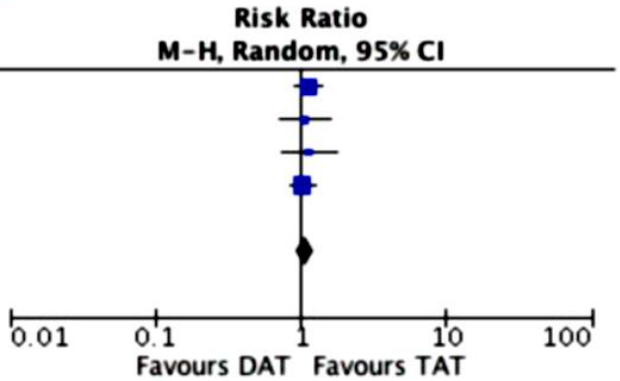
C

TRIAL-DEFINED MACE

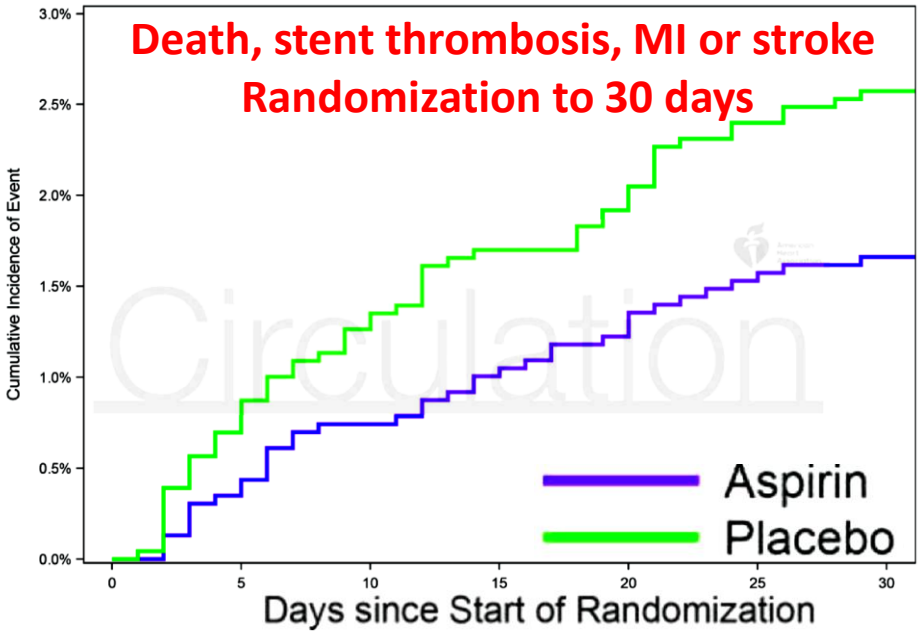
Study or Subgroup	DAT Events	DAT Total	TAT Events	TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	168	2307	149	2307	37.1%	1.13 [0.91, 1.40]
ENTRUST AF-PCI	49	751	46	755	11.1%	1.07 [0.73, 1.58]
PIONEER AF-PCI	41	694	36	695	8.9%	1.14 [0.74, 1.76]
RE-DUAL PCI	239	1744	131	981	42.9%	1.03 [0.84, 1.25]
Total (95% CI)		**5496**		**4738**	**100.0%**	**1.08 [0.95, 1.23]**
Total events	497		362			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.47$, df = 3 (P = 0.92); $I^2 = 0\%$

Test for overall effect: Z = 1.13 (P = 0.26)



Alexander JH et al The risk/benefit tradeoff of antithrombotic therapy in patients with AF early and late after an ACS or PCI: insights from Augustus_ CIRC 2020;141:1618-27



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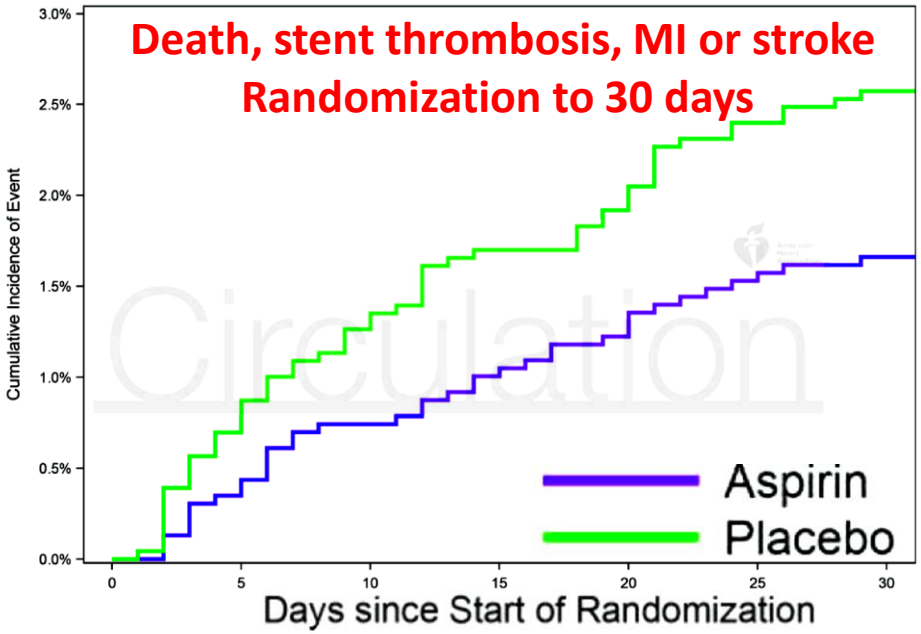

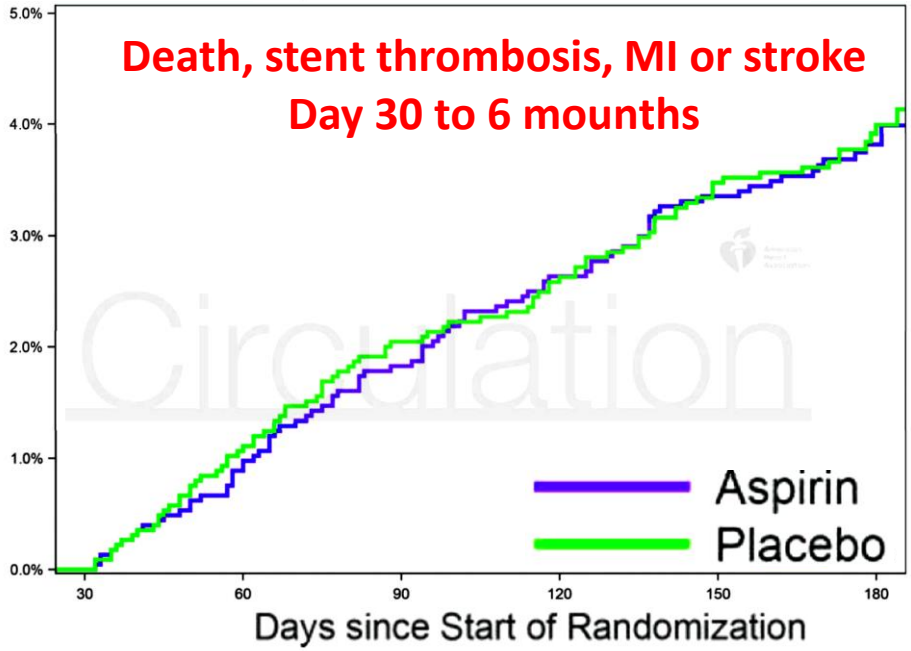

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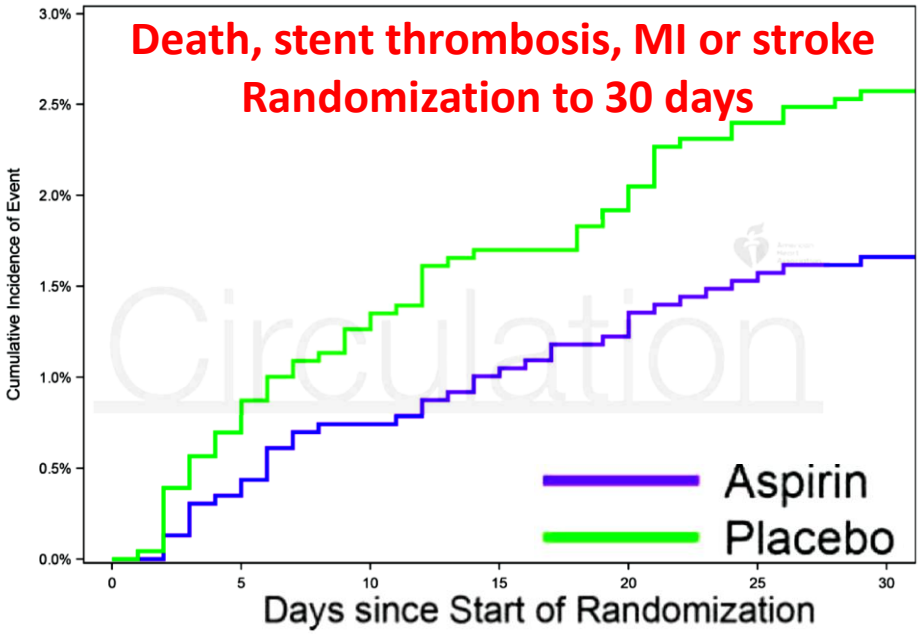

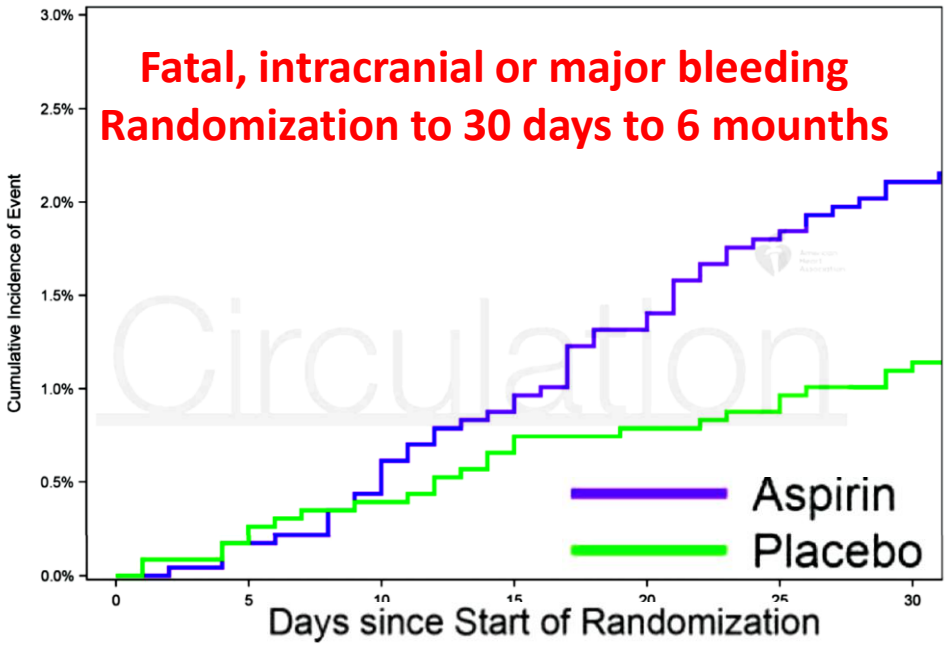

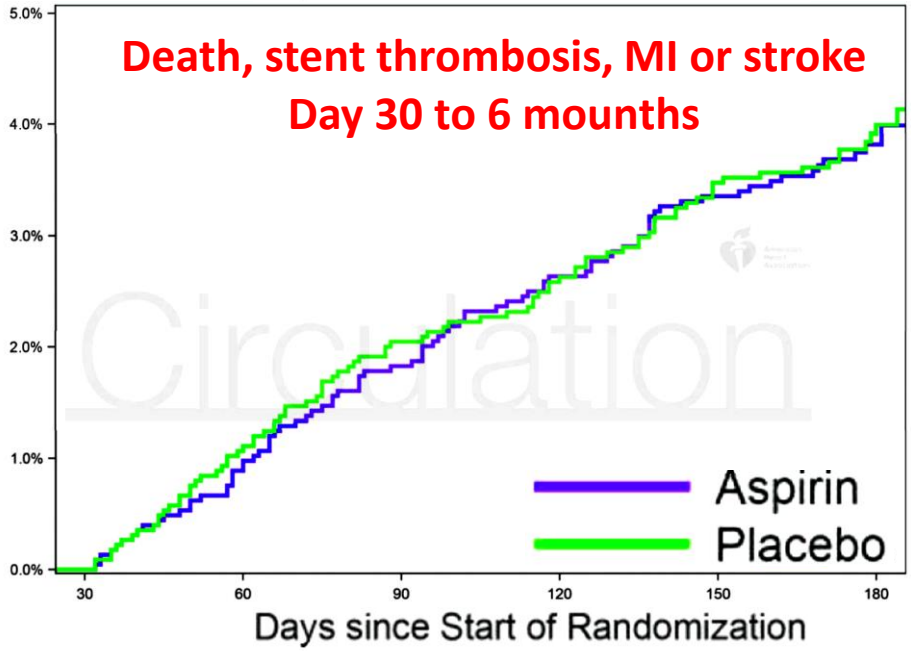

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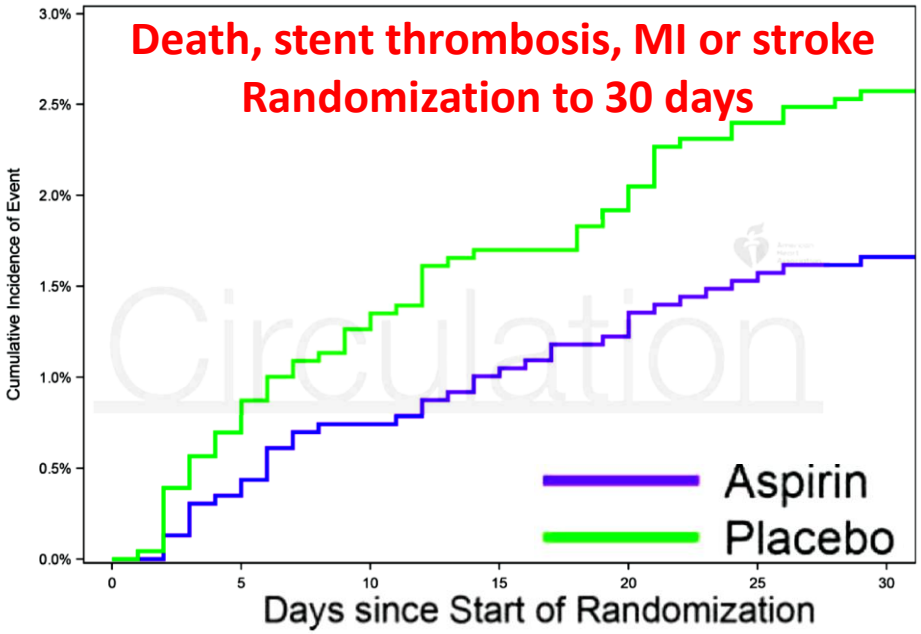
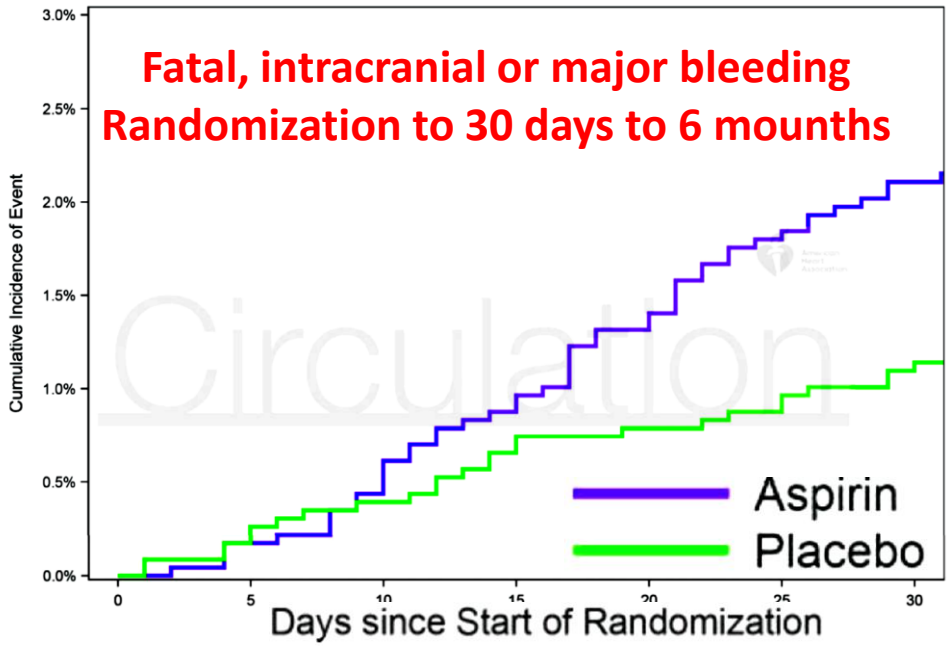
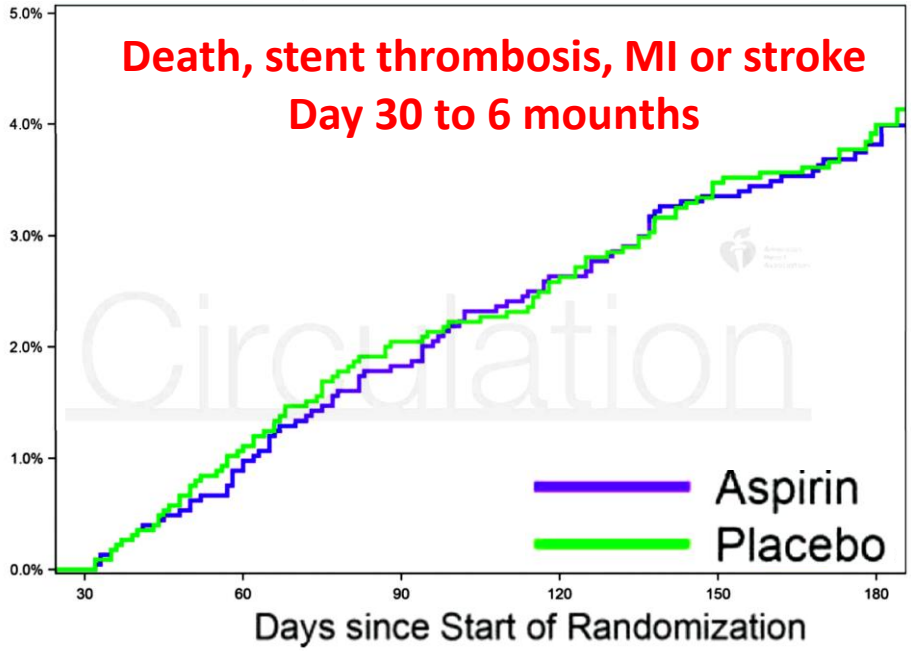
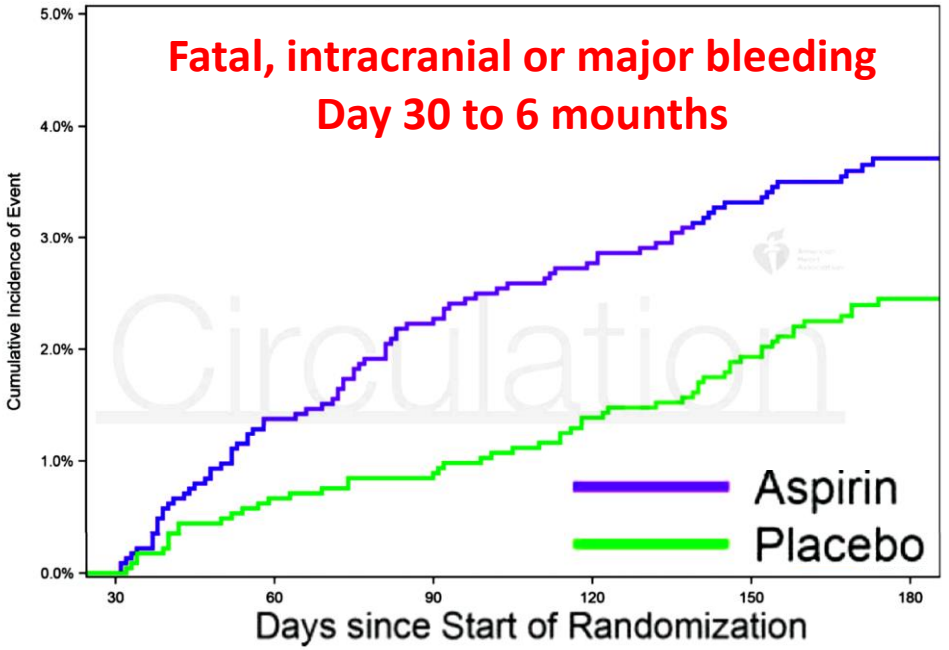
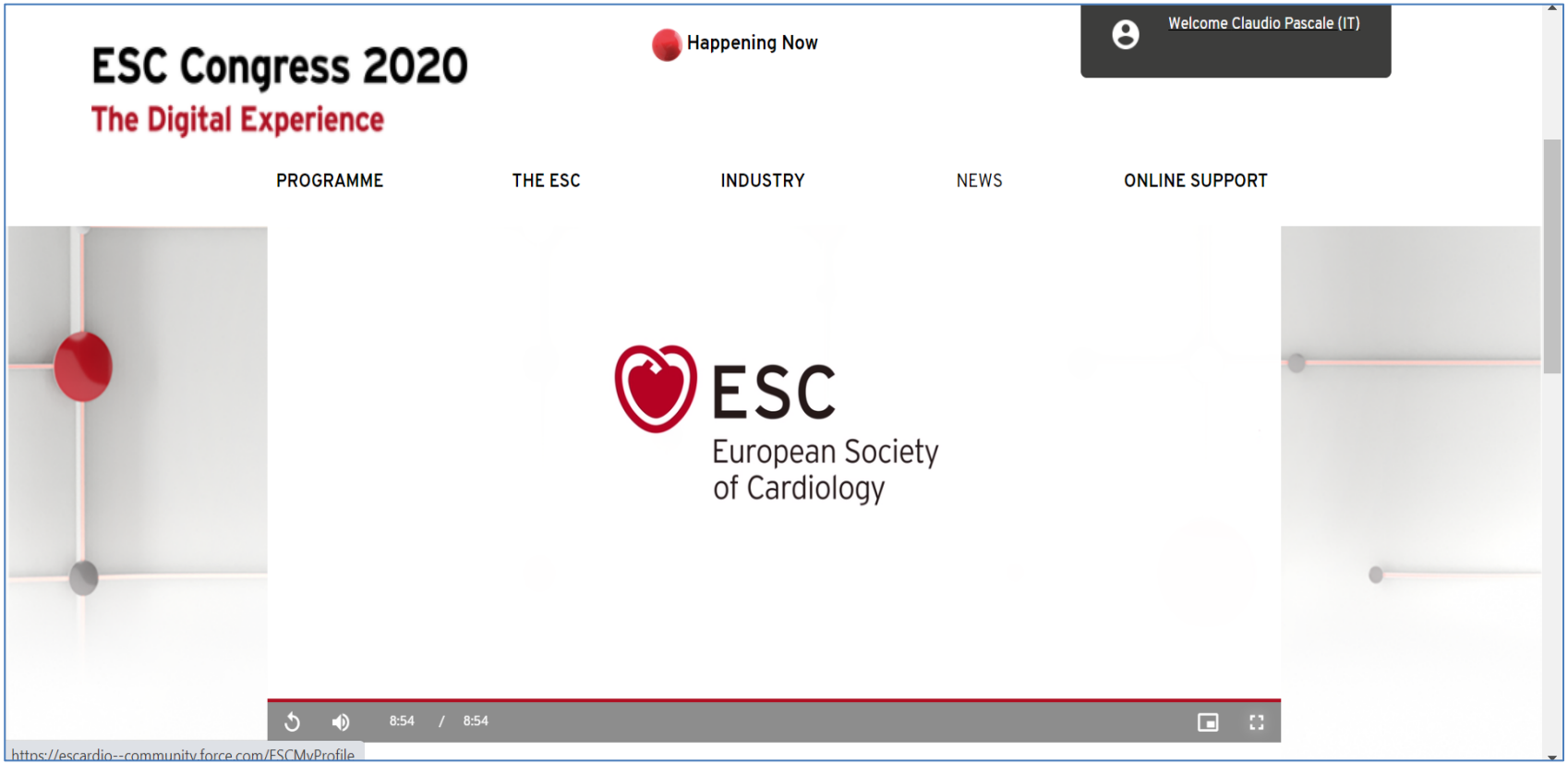








Alexander JH et al The risk/benefit tradeoff of antithrombotic therapy in patients with AF early and late after an ACS or PCI: insights from Augustus_ CIRC 2020;141:1618-27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ESC European Society of Cardiology

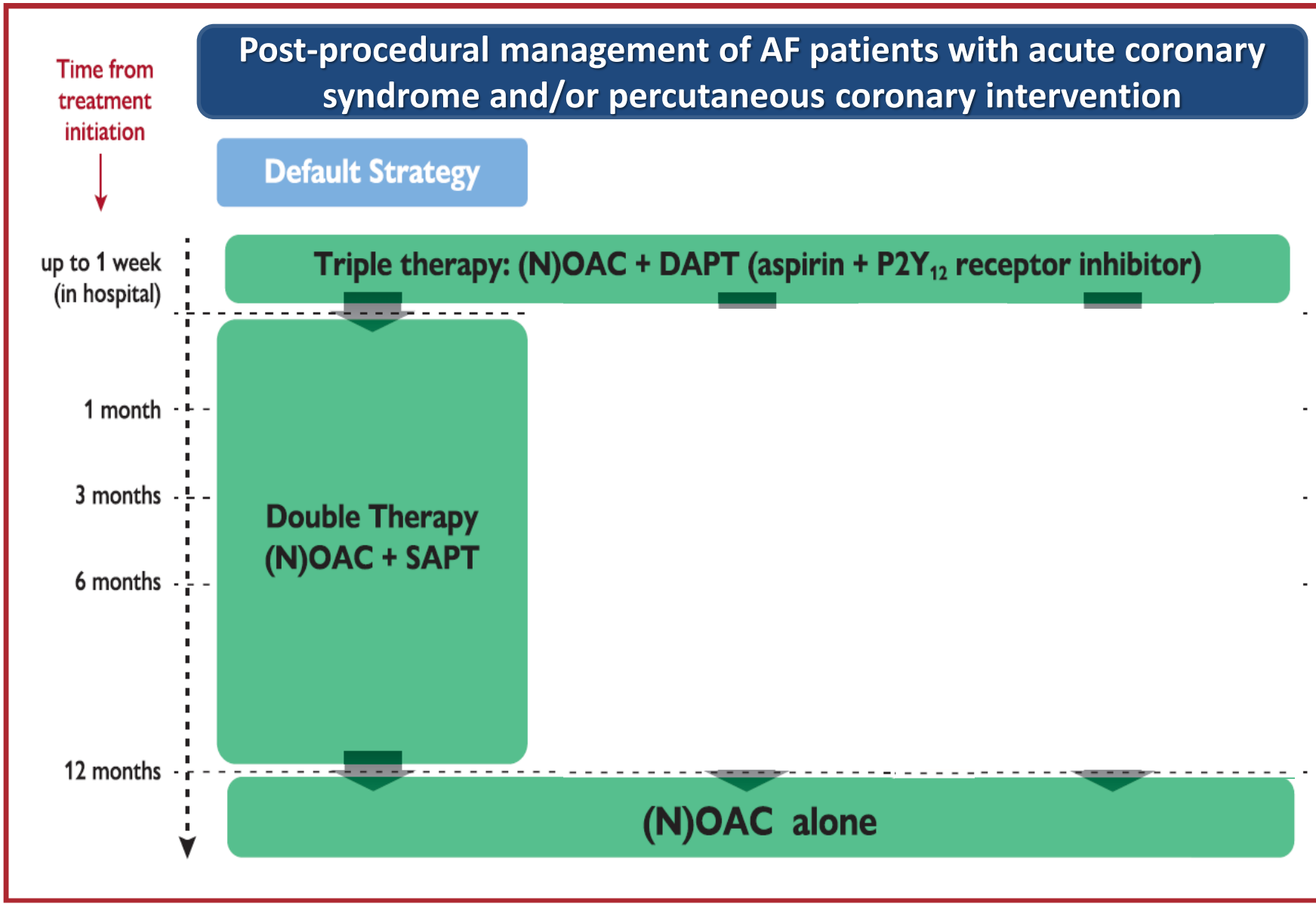
European Heart Journal (2020) **00**, 1–126
doi:10.1093/eurheartj/ehaa612

ESC GUIDELINES

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS)

The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC



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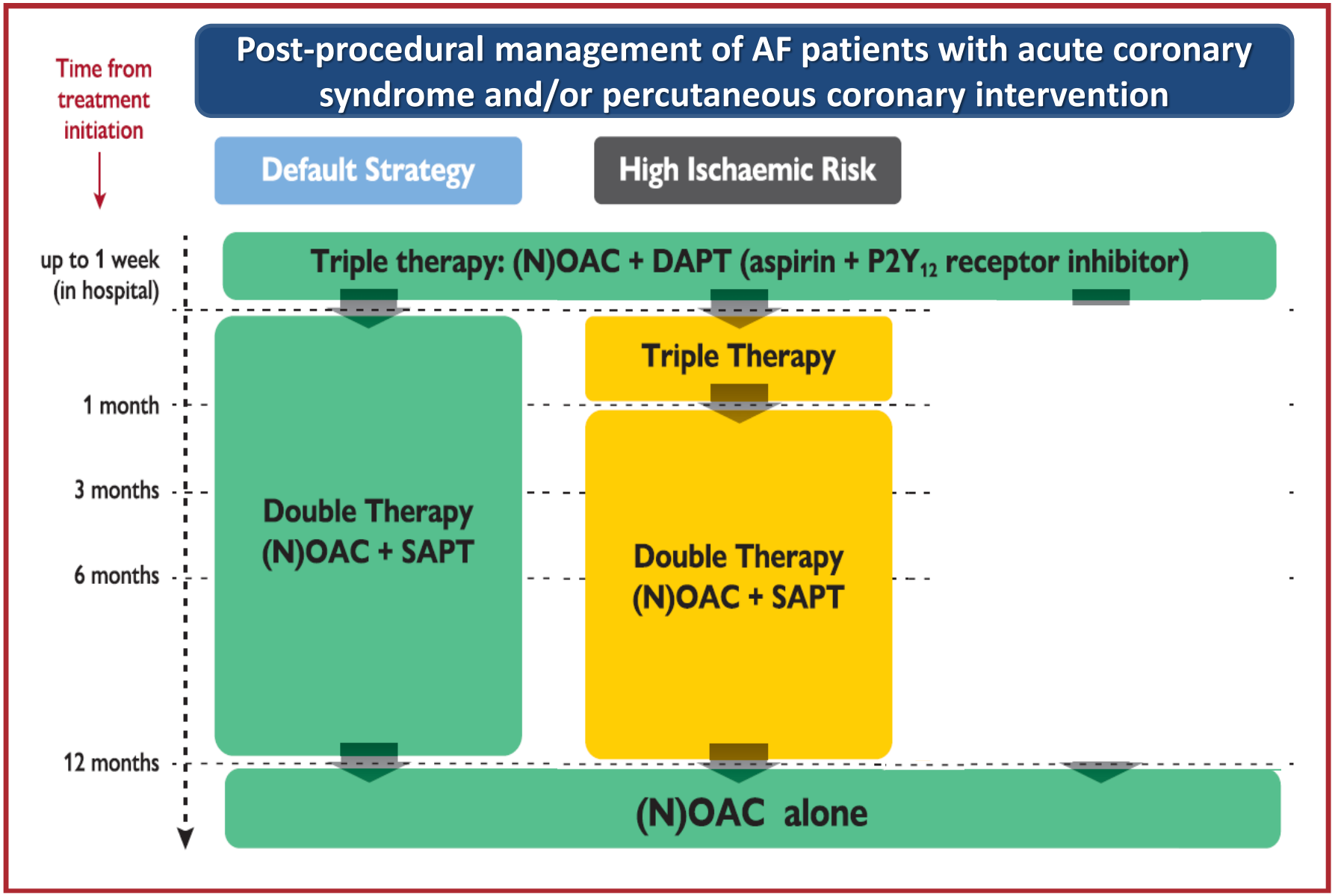
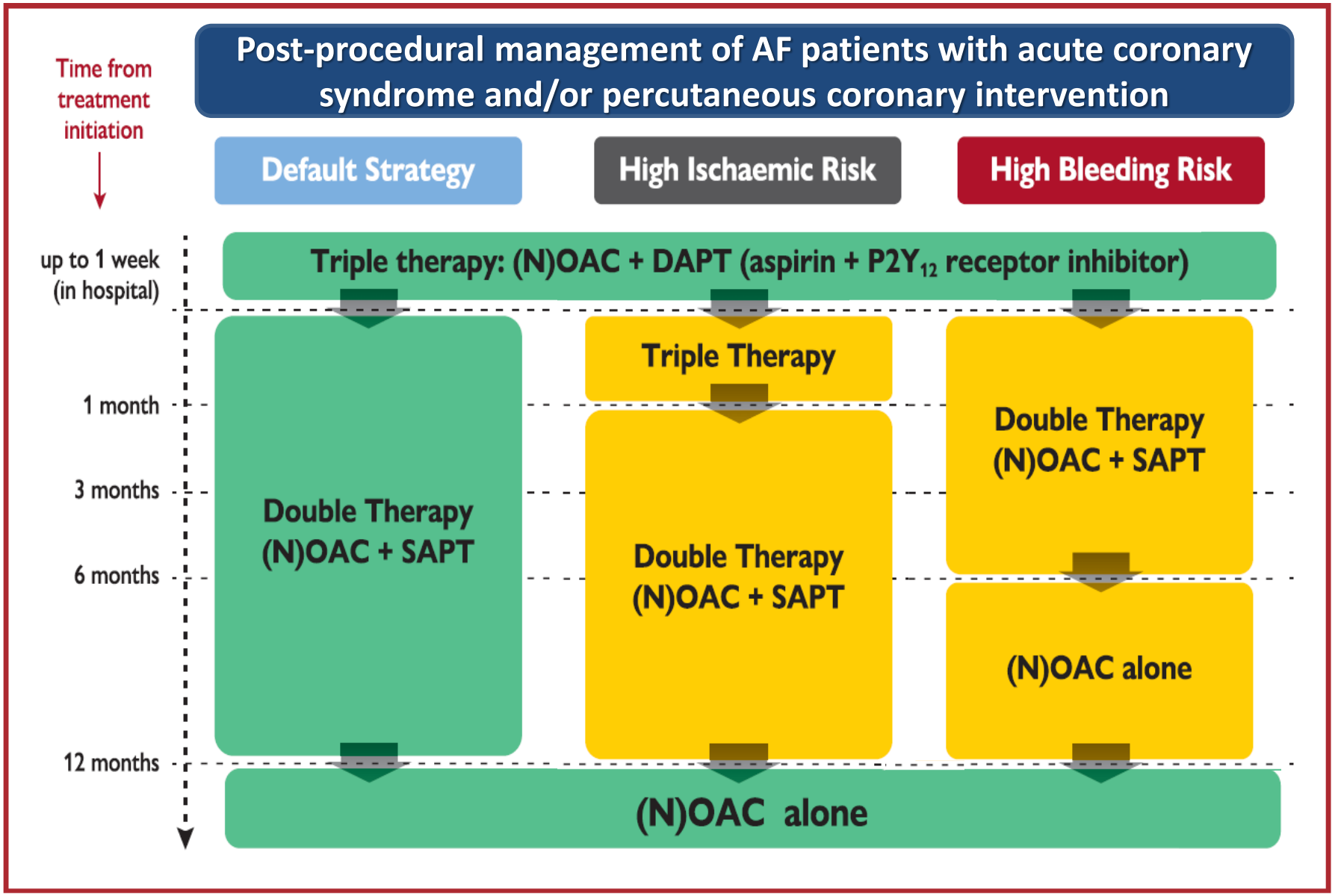


2020 FA ESC GL



2020 FA ESC GL

Conclusioni

- ✓ Non sono infrequenti pazienti con indicazione a terapia anticoagulante orale e che richiedano una duplice terapia antiaggregante per PCI in elezione o ACS, per ridurre occlusione dello stent e reinfarti
- ✓ L'impiego dei NOACs è preferibile al warfarin per il favorevole profilo di sicurezza ed efficacia
- ✓ Sono stati pubblicati vari lavori che impiegano solo una duplice terapia antitrombotica - NOACs + inibitore recettori piastrinici $P2Y_{12}$ (clopidogrel) - subito dopo la procedura o l'evento ischemico cardiaco
- ✓ Le recentissime LG ESC sulla FA hanno cambiato le indicazioni, riducendo il tempo di triplice terapia a 1 settimana e in certi casi fino al massimo di 1 mese, per continuare poi con la duplice terapia fino a 1 anno
- ✓ Oltre l'anno nella maggioranza dei casi è indicato l'uso del solo anticoagulante orale

Post-procedural management of AF patients with acute coronary syndrome and/or percutaneous coronary intervention

THROMBOTIC RISK FACTORS

- Diabetes mellitus requiring therapy
- Prior ACS/recurrent myocardial infarction
- Multivessel CAD
- Concomitant PAD
- Premature CAD (occurring at age of <45 y) or accelerated CAD (new lesion within 2 years)
- CKD (eGFR <60 mL/min)
- Clinical presentation (ACS)
- Multivessel stenting
- Complex revascularisation (left main stenting, bifurcation lesion stenting, chronic total occlusion intervention, last patent vessel stenting)
- Prior stent thrombosis on antiplatelet treatment
- Procedural factors (stent expansion, residual dissection, stent length, etc.)

BLEEDING RISK FACTORS

- Hypertension
- Abnormal renal or liver function
- Stroke or ICH history
- Bleeding history or bleeding diathesis (e.g., anaemia with haemoglobin <110 g/L)
- Labile INR (if on VKA)
- Elderly (>65 years)
- Drugs (concomitant OAC and antiplatelet therapy, NSAIDs), excessive alcohol consumption

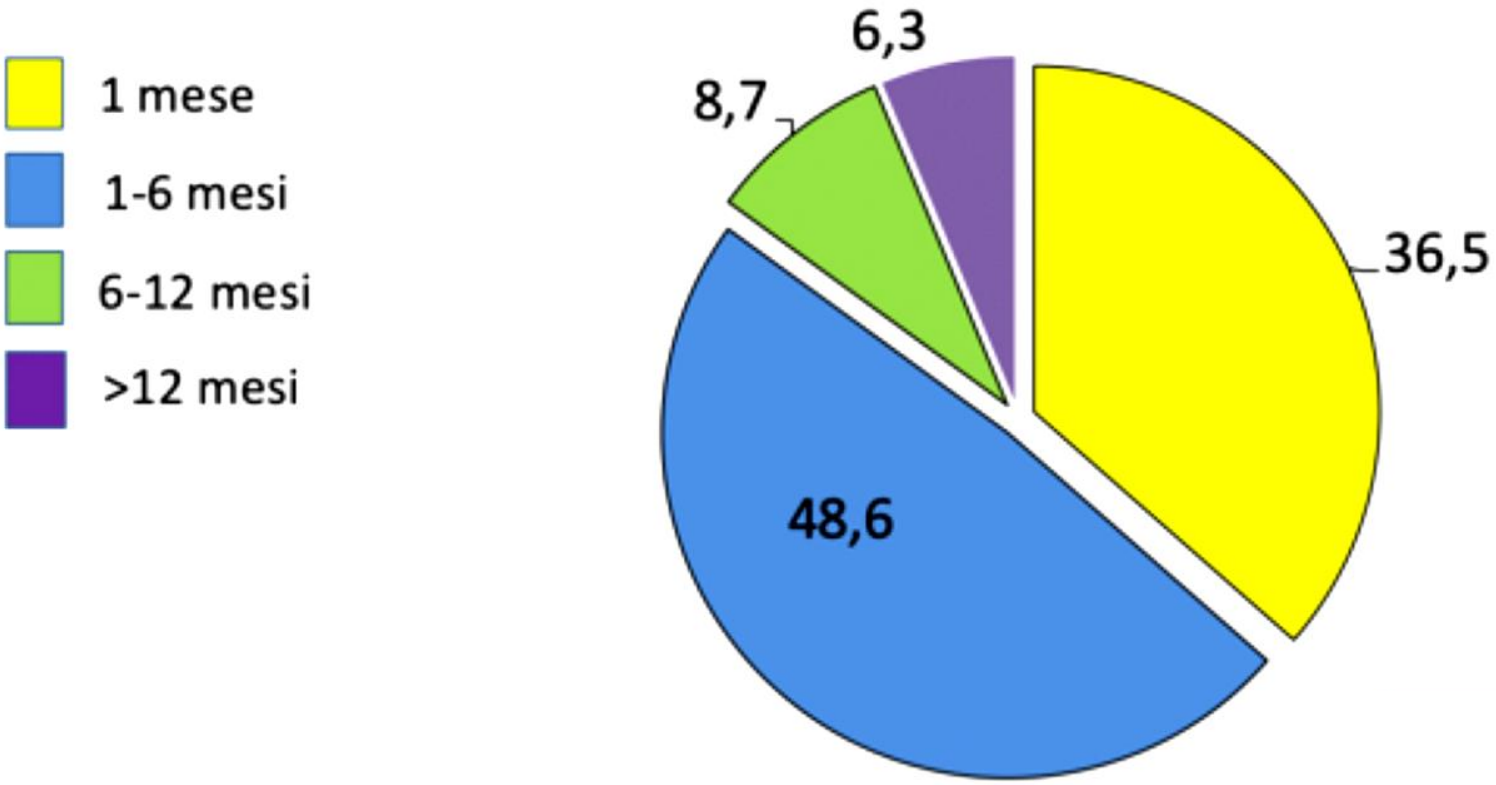
STRATEGIES TO REDUCE BLEEDING ASSOCIATED WITH PCI

- Radial artery access
- PPIs in patients taking DAPT who are at increased risk of bleeding (e.g., the elderly, dyspepsia, gastro-oesophageal reflux disease, Helicobacter pylori infection, chronic alcohol use)
- Non–administration of unfractionated heparin in patients on VKA with INR >2.5
- Pre-treatment with aspirin only, add a $P2Y_{12}$ inhibitor when coronary anatomy is known or if STEMI
- GP IIb/IIIa inhibitors only for bailout or periprocedural complications
- Shorter duration of combined antithrombotic therapy

2020 FA ESC GL

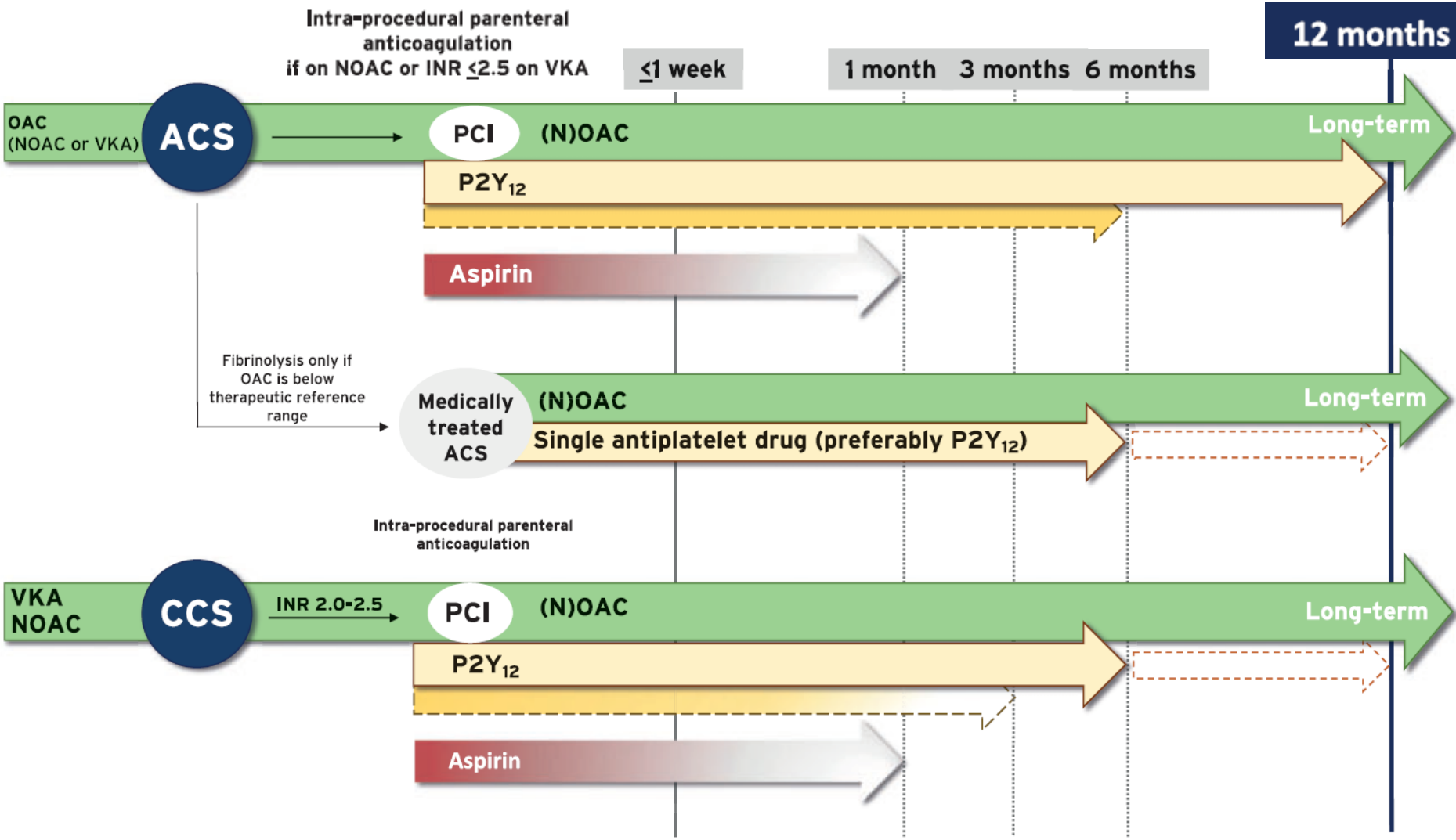
MATADOR-PCI

Studio prospettico osservazionale di ANMCO/Fondazione per il Tuo Cuore-ONLUS sulle strategie antitrombotiche attualmente impiegate nei pz affetti con FA e SCA trattati con PCI + stent



De Luca L et al. Data from the Nationwide MATADOR-PCI Registry.
Eur Heart J Cardiovasc Pharmacother 2020 Jul 11;pvaa088. doi: 10.1093/ehjcvp/pvaa088

Post-procedural management of AF patients with acute coronary syndrome and/or percutaneous coronary intervention



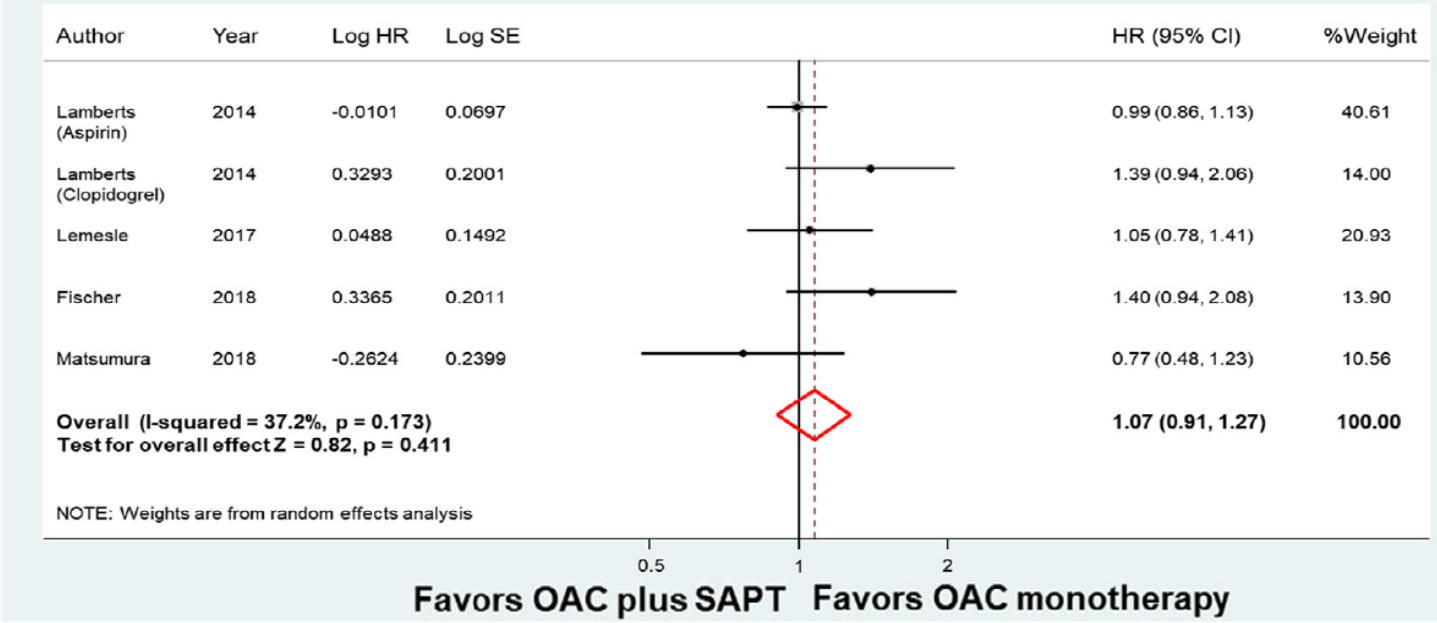
2020 FA ESC GL

Meta-Analysis of Oral Anticoagulant Monotherapy as an Antithrombotic Strategy in Patients With Stable Coronary Artery Disease and Nonvalvular Atrial Fibrillation

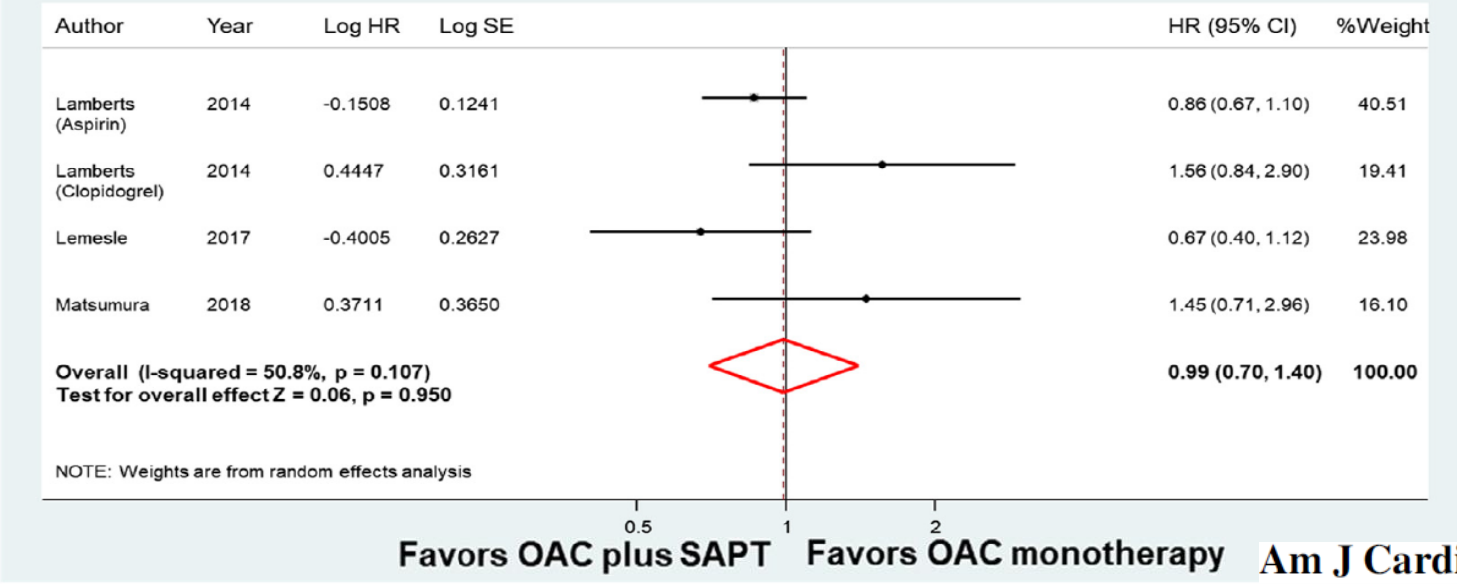
So-Ryoung Lee, MD[a,1], Tae-Min Rhee[a,1], Do-Yoon Kang, MD[b], Eue-Keun Choi, MD, PhD[a], Seil Oh, MD, PhD[a,2,*], and Gregory Y.H. Lip, MD[c,d,2,**]

Am J Cardiol 2019;124:879–885

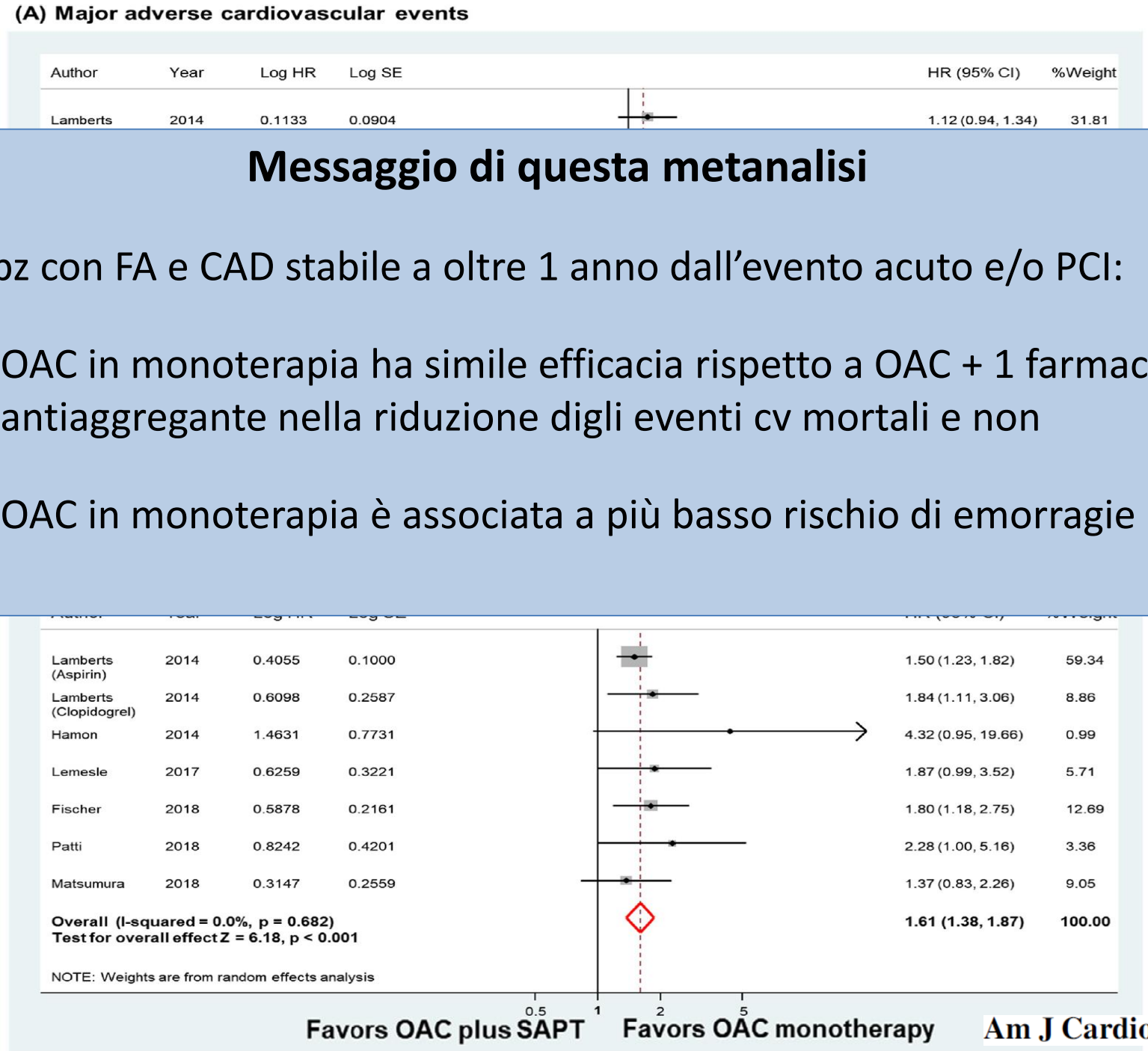
(A) All-cause death



(B) Stroke



Am J Cardiol 2019



Messaggio di questa metanalisi

In pz con FA e CAD stabile a oltre 1 anno dall'evento acuto e/o PCI:

- OAC in monoterapia ha simile efficacia rispetto a OAC + 1 farmaco antiaggregante nella riduzione digli eventi cv mortali e non
- OAC in monoterapia è associata a più basso rischio di emorragie

Am J Cardiol 2019