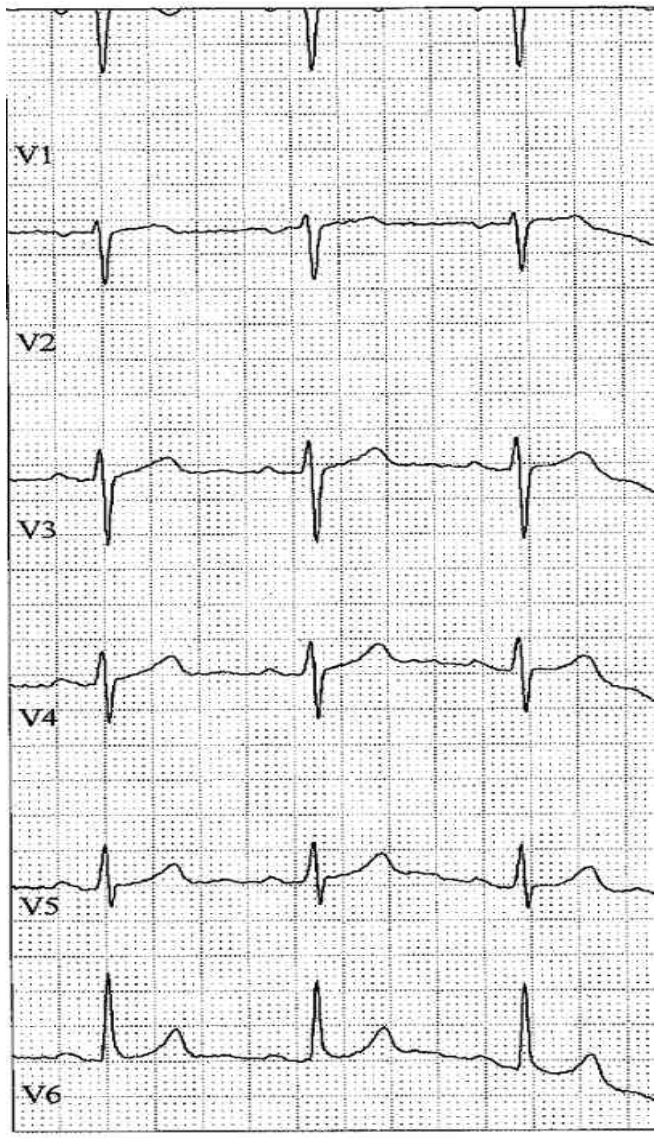
Trattamento Farmacologico Integrato per il Rischio Evitabile nella Sindrome Coronarica Cronica

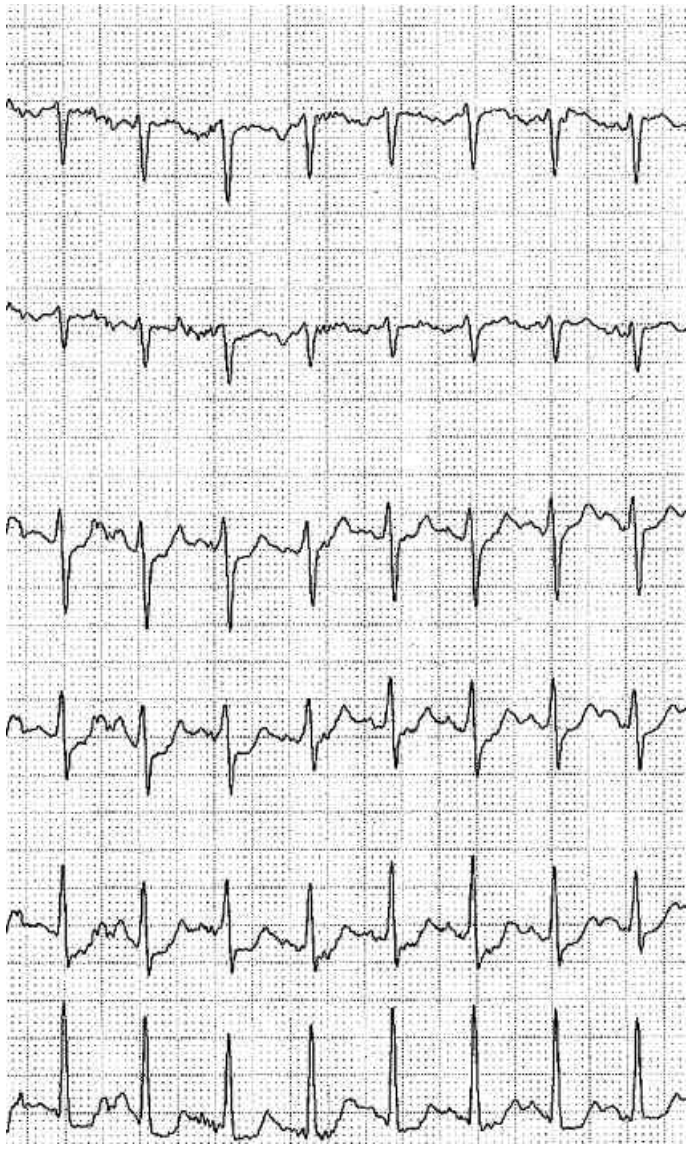
Ciro Indolfi

Presidente Società Italiana di Cardiologia

BASELINE

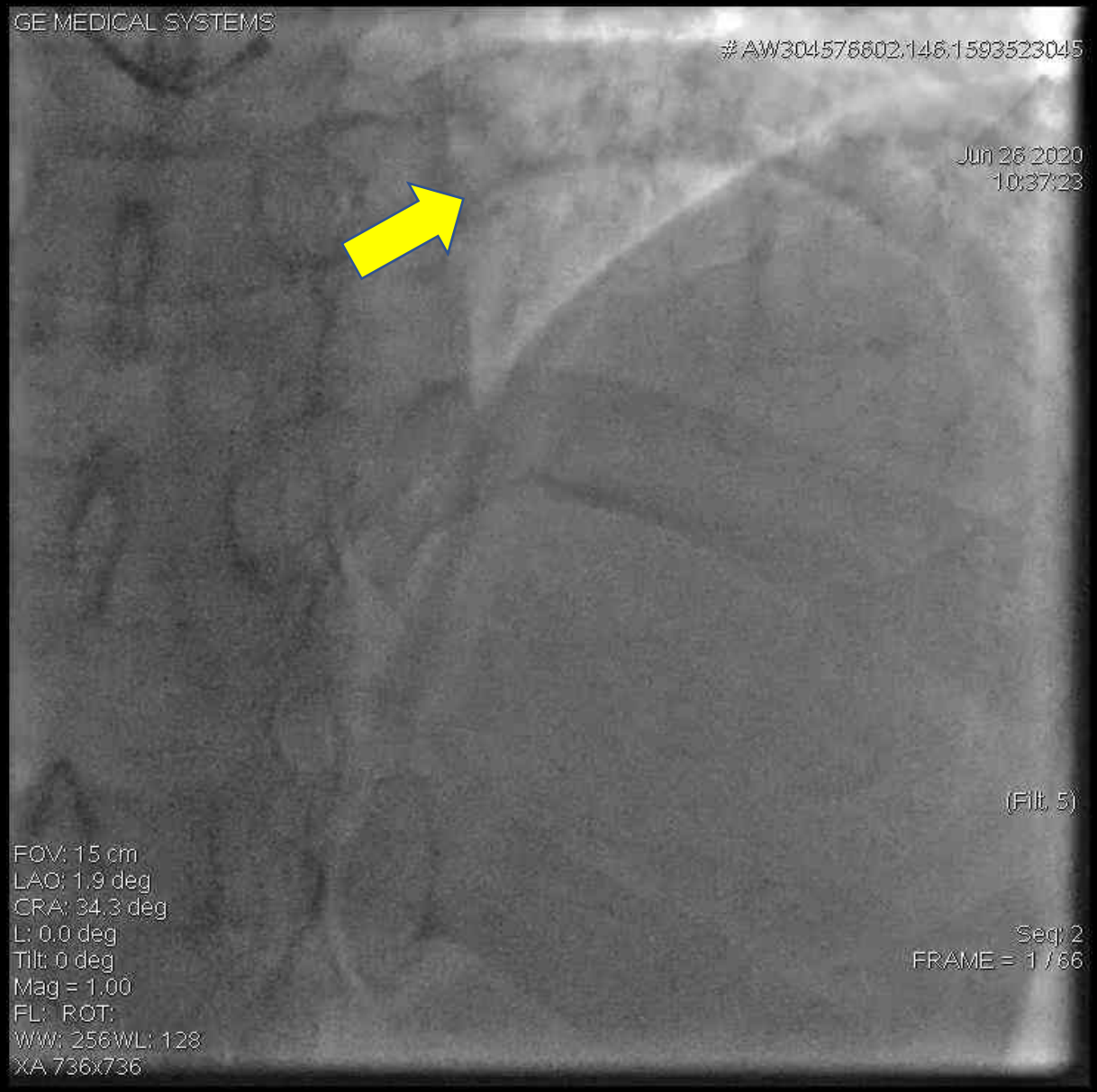


STRESS STRESS (Stage VI)



HR 140/min (88% FMT)
AP 180/95 mmHg DP 25200

Left Coronary Artery (LCA)



55 yo
75% Proximal LAD stenosis

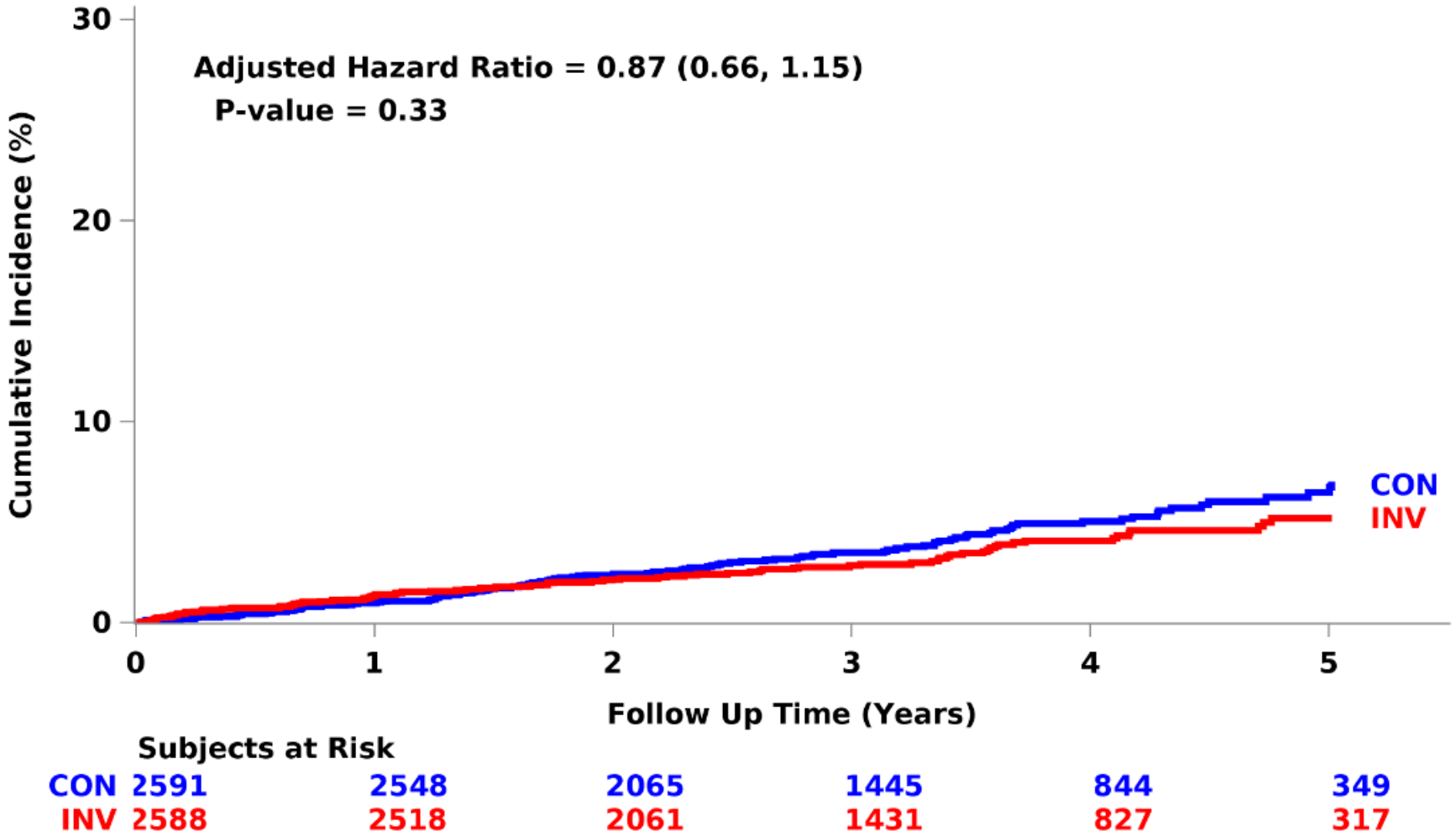
International Study Of Comparative Health Effectiveness With Medical And Invasive Approaches (ISCHEMIA):

Primary Report of Clinical Outcomes

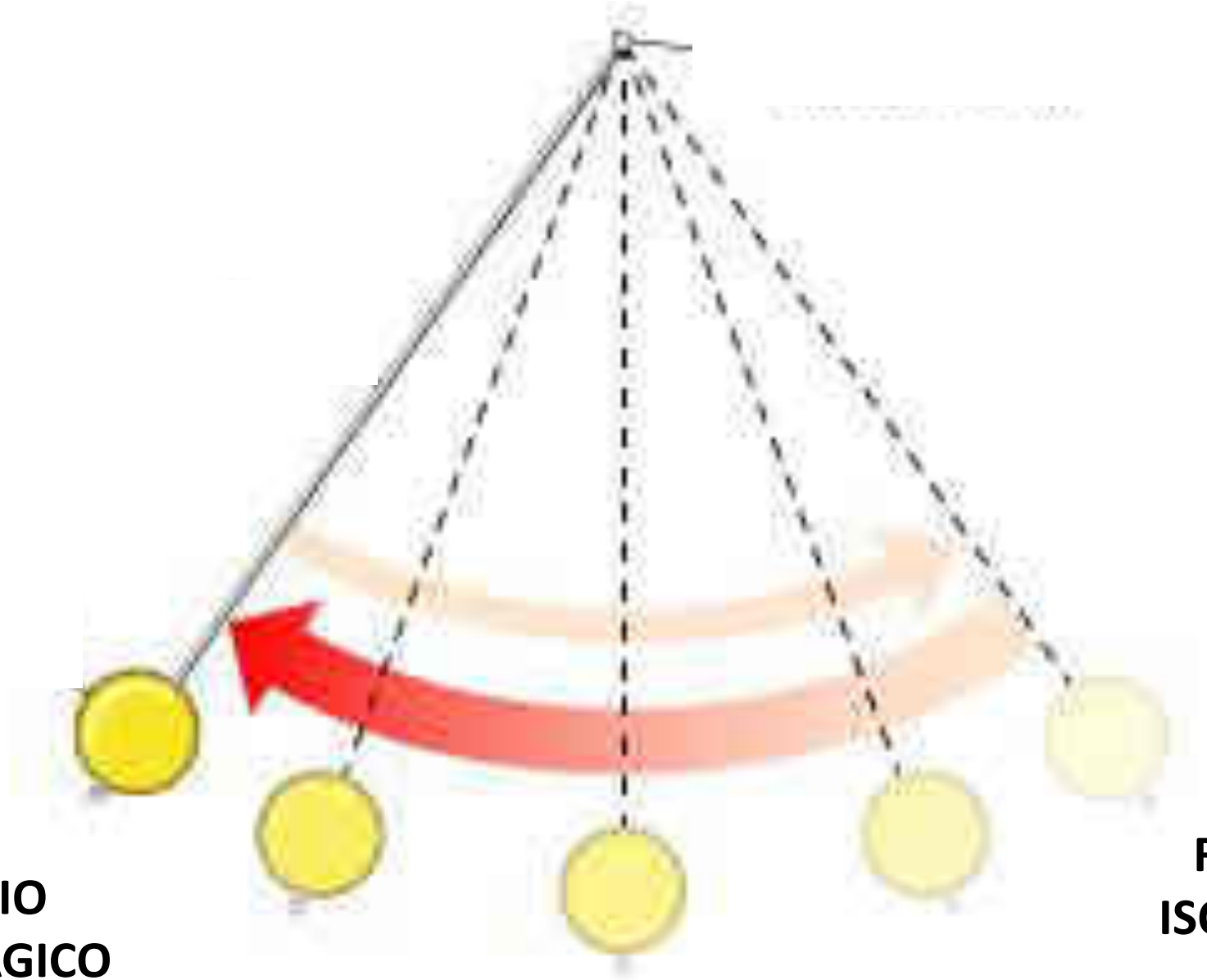
Funded by the National Heart, Lung, and Blood Institute

Judith S. Hochman, MD
NYU School of Medicine
On behalf of the ISCHEMIA Research Group

Ischemia Trial: Cardiovascular Death



IL TRATTAMENTO ANTI-TROMBOTICO



RISCHIO EMORRAGICO

RISCHIO ISCHEMICO

Dopo 12 mesi :

1 O 2 Farmaci anti-trombotici ?

PEGASUS: Randomization

Stable pts with MI 1–3 years prior + ≥1 high-risk factor

Randomized 21,162 patients

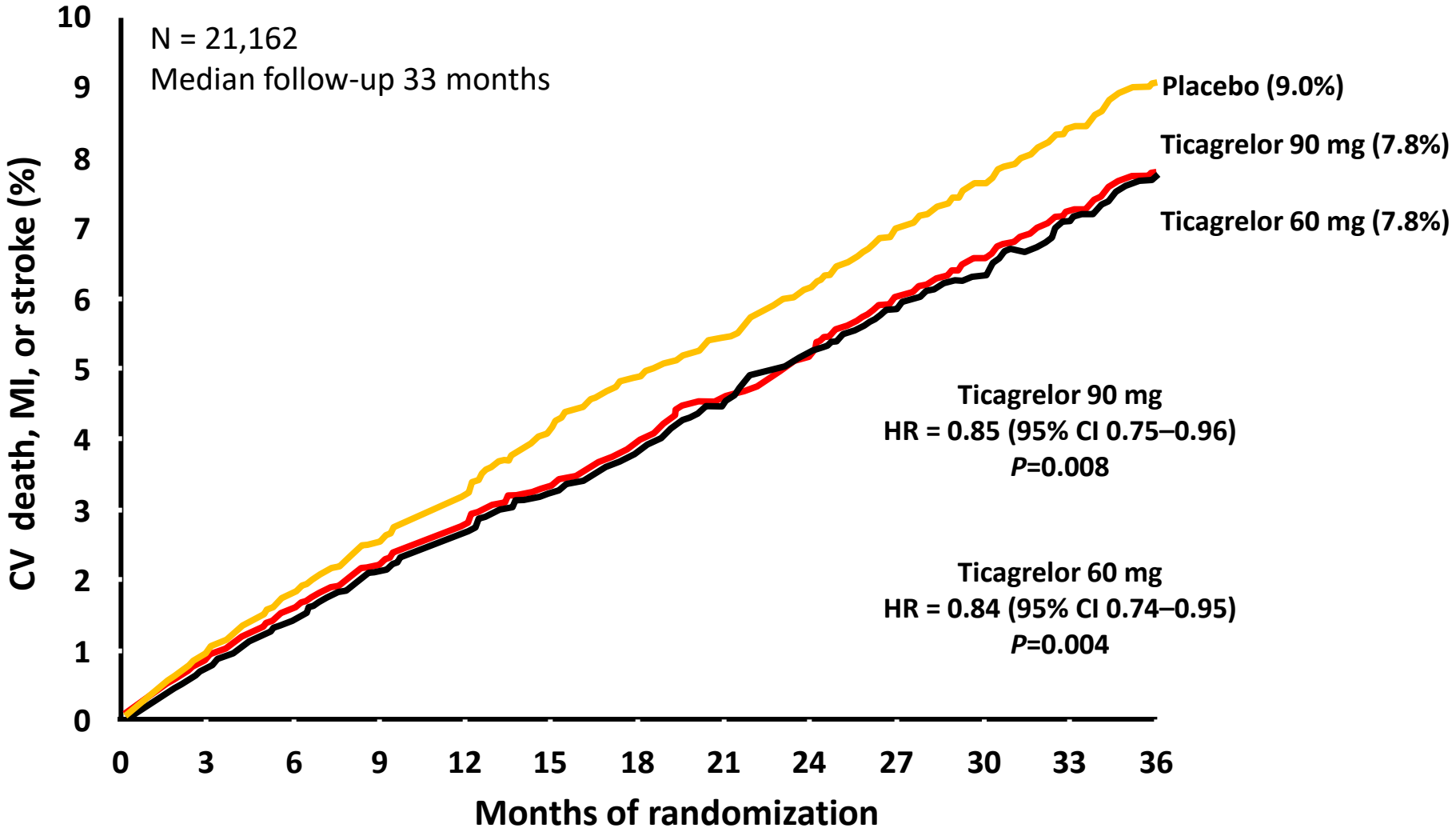
at 1161 sites in 31 countries between 10/2010–5/2013

Ticagrelor 90 mg bid (N = 7050)	**Ticagrelor** 60 mg bid (N = 7045)	**Placebo** 60 mg bid (N = 7067)

Follow-up = median 33 months (IQR 28-37)
Minimum 16 months, maximum 47 months

Premature perm. drug discontinuation	12%/year	11%/year	8%/year
Withdrew consent	0.7% total	0.7% total	0.7% total
Lost to follow-up		6 patients	1 patient

PEGASUS: Primary Endpoint

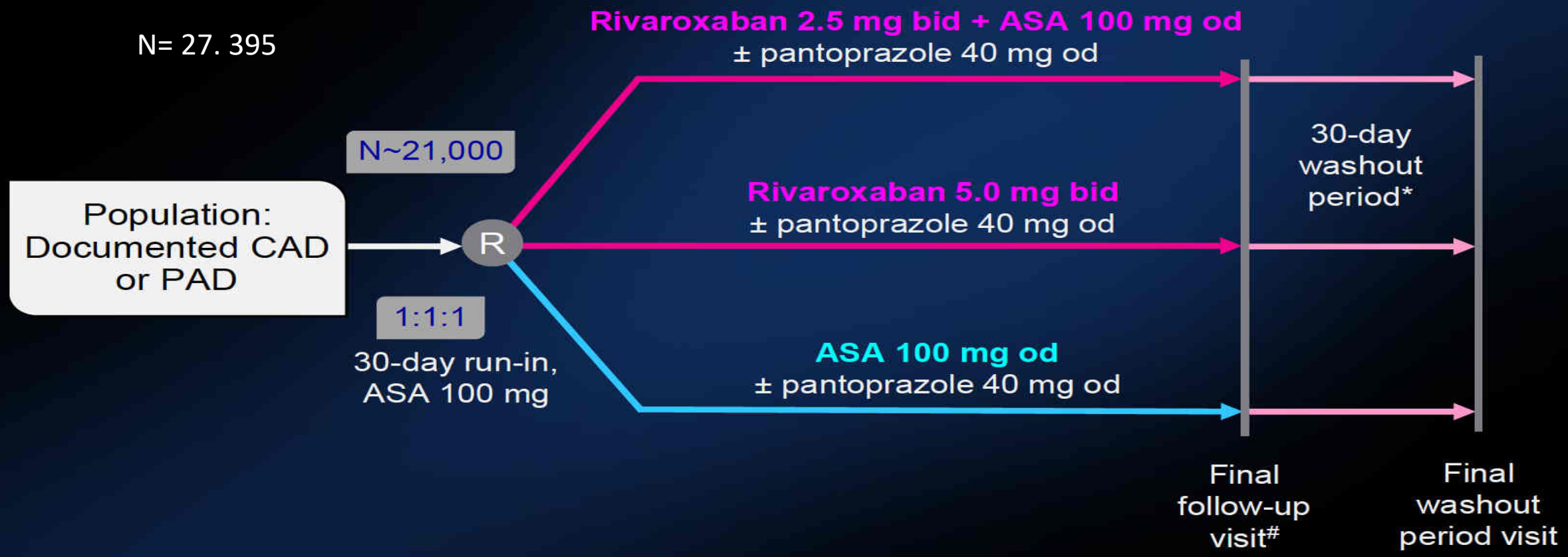


Bonaca MP et al. *N Engl J Med. 2015 May 7;372(19):1791-800*.

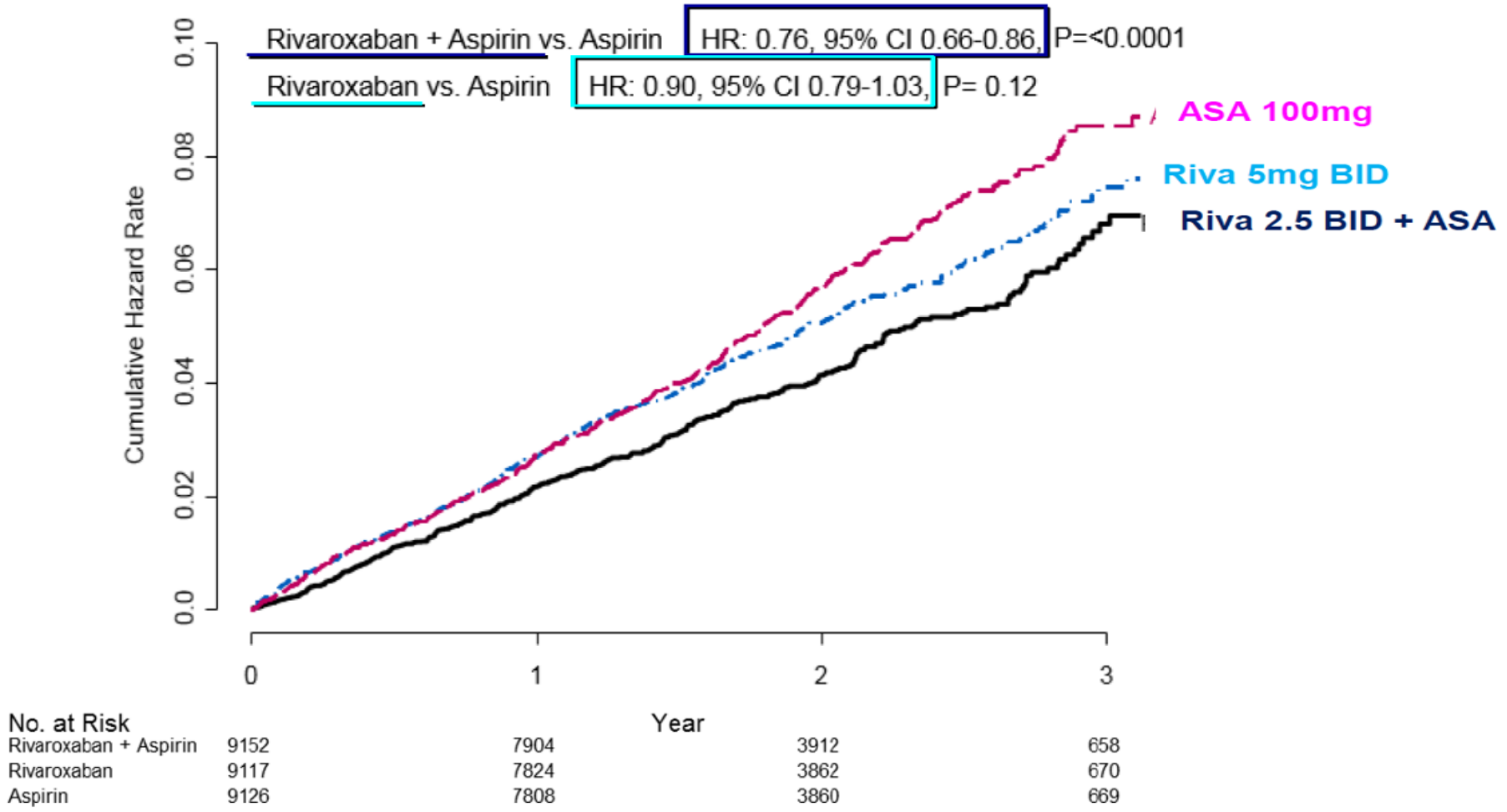
UN NUOVO PARADIGMA:
LA TERAPIA ANTICOAGULANTE PER L’ATEROTROMBOSI

COMPASS: Rivaroxaban in CAD or PAD

Objective: efficacy and safety of rivaroxaban, low-dose rivaroxaban plus ASA or ASA alone for reducing risk of MI, stroke or CV death in CAD or PAD



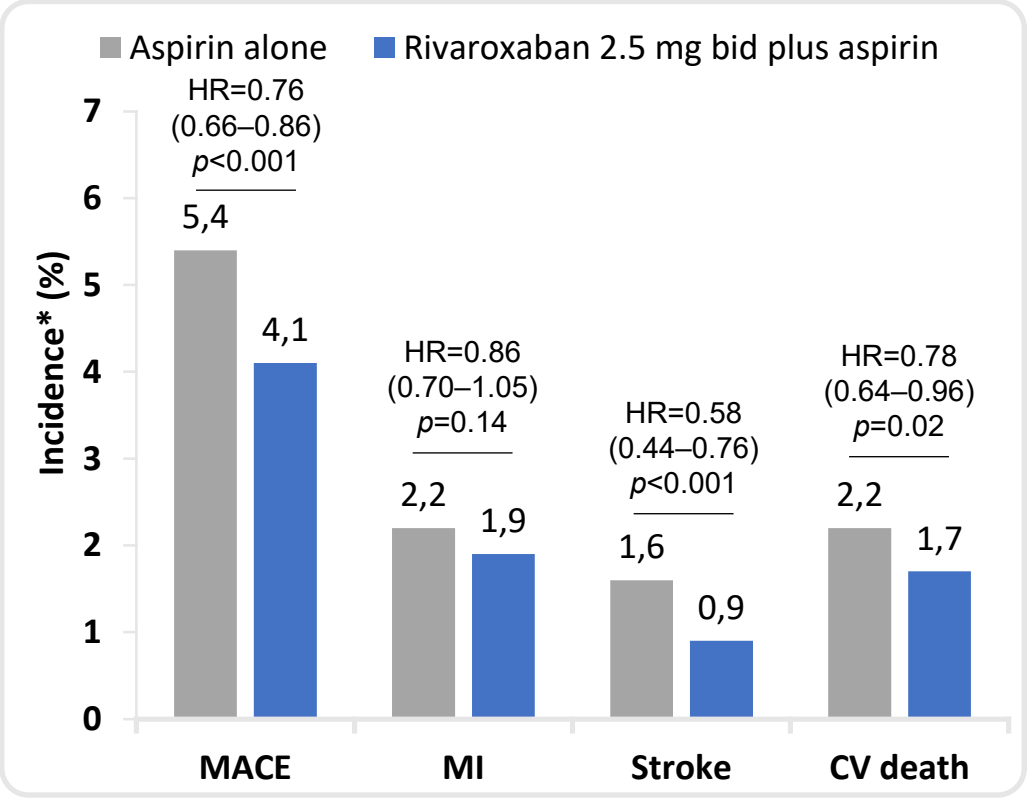
COMPASS: CV Death, Stroke, MI



Eikelboom et al. for the COMPASS investigators, *NEJM* 2017

Significant reduction of MACE (24%) with manageable bleeding risk

Major adverse cardiovascular events



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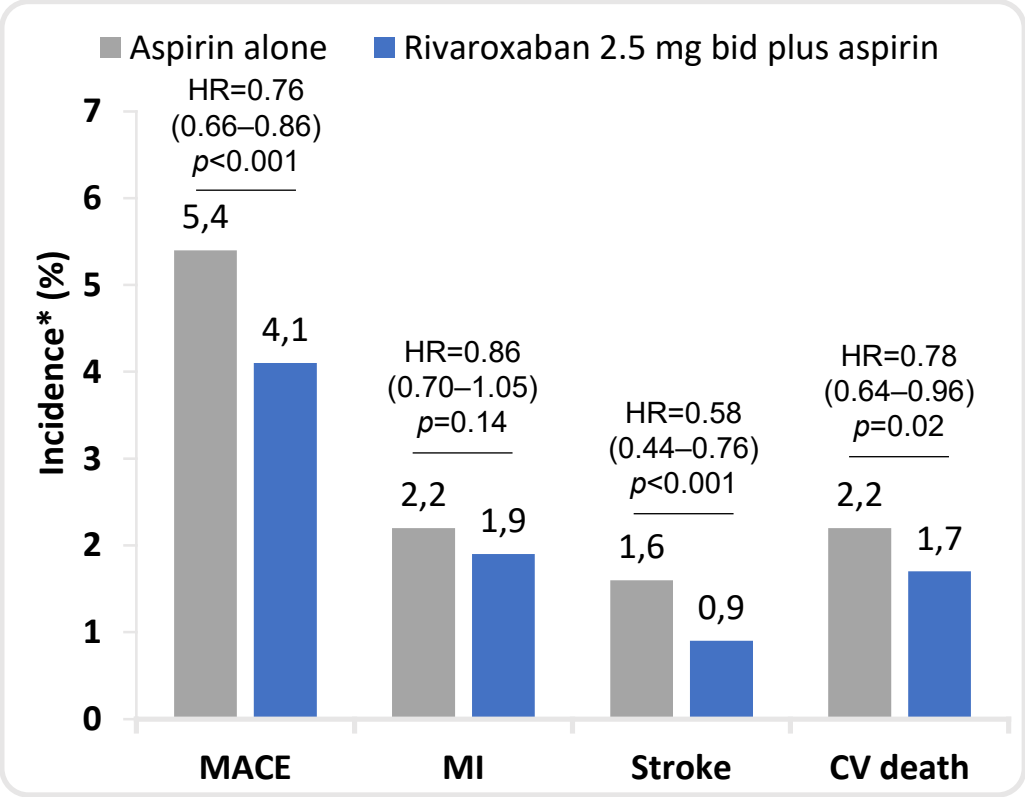
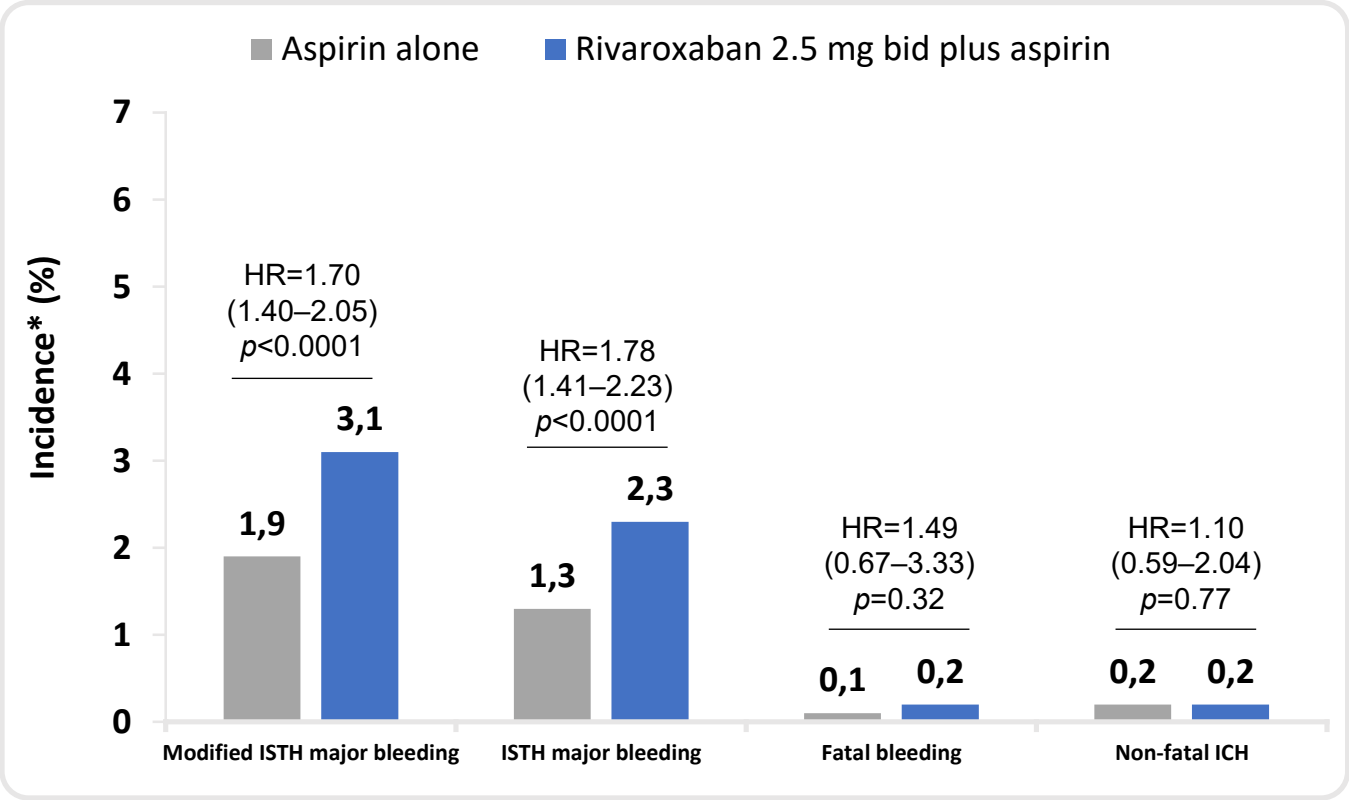


Major bleeding events

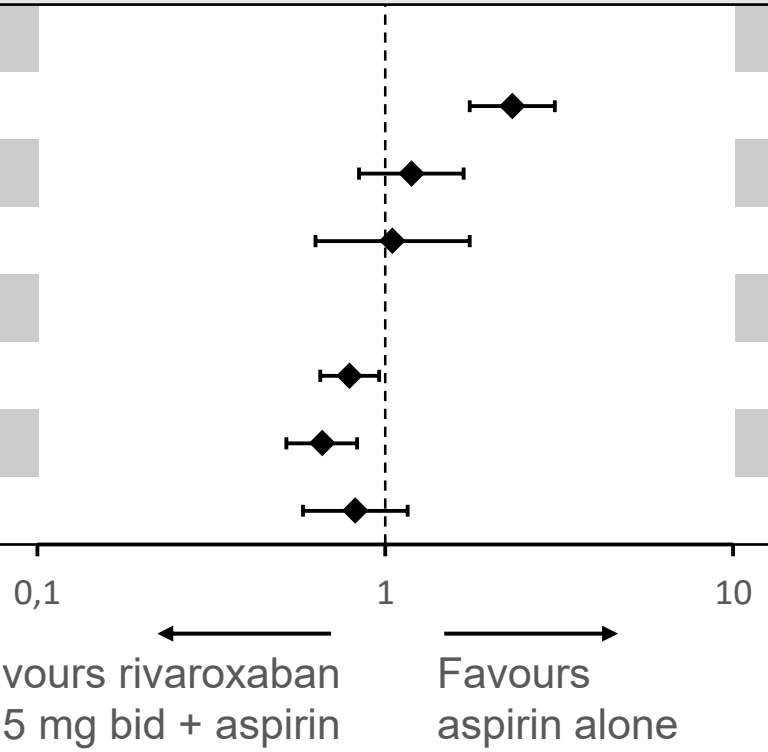


No increase in fatal, ICH, critical organ bleeding

Increased Bleeding with Rivaroxaban 2.5 mg bid Plus Aspirin Occurred Mostly in the First Year

Landmark analysis for key efficacy and safety outcomes in patients with CAD

	Rivaroxaban 2.5 mg bid + aspirin n/N (%)		Aspirin alone n/N (%)		HR (95% CI)
Major bleeding					
<1 year	163/8313	(2)	70/8261	(1)	2.32 (1.75–3.07)
1–2 years	70/7189	(1)	59/7183	(1)	1.19 (0.84–1.68)
>2 years	30/3628	(1)	29/3694	(1)	1.05 (0.63–1.75)
MACE					
<1 year	176/8313	(2)	221/8261	(3)	0.79 (0.65–0.96)
1–2 years	113/7228	(2)	169/7125	(2)	0.66 (0.52–0.83)
>2 years	58/3655	(2)	70/3621	(2)	0.82 (0.58–1.16)



Connolly SJ *et al*, *Lancet* 2018;391:205–218

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

An Important Step for Thrombocardiology

Eugene Braunwald, M.D.

New Guidelines Recommend a Second Antithrombotic for Selected Patients with Chronic Coronary Syndromes

2019 guidelines for the management of CCS

Recommendations	Class	Evidence level
Adding a **second antithrombotic drug** to aspirin for long-term secondary prevention should be considered in patients with a **high risk of ischaemic events** and without high bleeding risk	IIa	A
Adding a **second antithrombotic drug** to aspirin for long-term secondary prevention may be considered in patients with at least a **moderately increased risk of ischaemic events** and without high bleeding risk	IIb	A

High ischaemic risk defined as:

- Diffuse multivessel CAD with **at least 1** of the following:
  - Diabetes mellitus requiring medication
  - Recurrent MI
  - PAD
  - CKD with eGFR 15–59 ml/min/1.73 m^2

Moderate ischaemic risk defined as:

- **At least 1** of the following:
  - Multivessel/diffuse CAD
  - Diabetes mellitus requiring medication
  - Recurrent MI
  - PAD
  - HF
  - CKD with eGFR 15–59 ml/min/1.73 m^2

Knuuti J *et al, Eur Heart J* 2019; doi: 10.1093/eurheartj/ehz42

What Are the Options for Dual Antithrombotic Therapy in Patients with Chronic Coronary Syndromes?

Treatment options for dual antithrombotic therapy in combination with aspirin 75–100 mg od

2019 guidelines for the management of CCS

Drug option	Dose	Indication	Additional cautions
Clopidogrel	75 mg od	◆ Post-MI in patients who have tolerated DAPT for 1 year	
Prasugrel	10 mg od*	◆ Post-PCI for MI in patients who have tolerated DAPT for 1 year	Age >75 years
Rivaroxaban	2.5 mg bid	◆ Post-MI >1 year ***or*** ◆ Multivessel CAD	CrCl 15–29 ml/min
Ticagrelor	60 mg bid	◆ Post-MI in patients who have tolerated DAPT for 1 year	

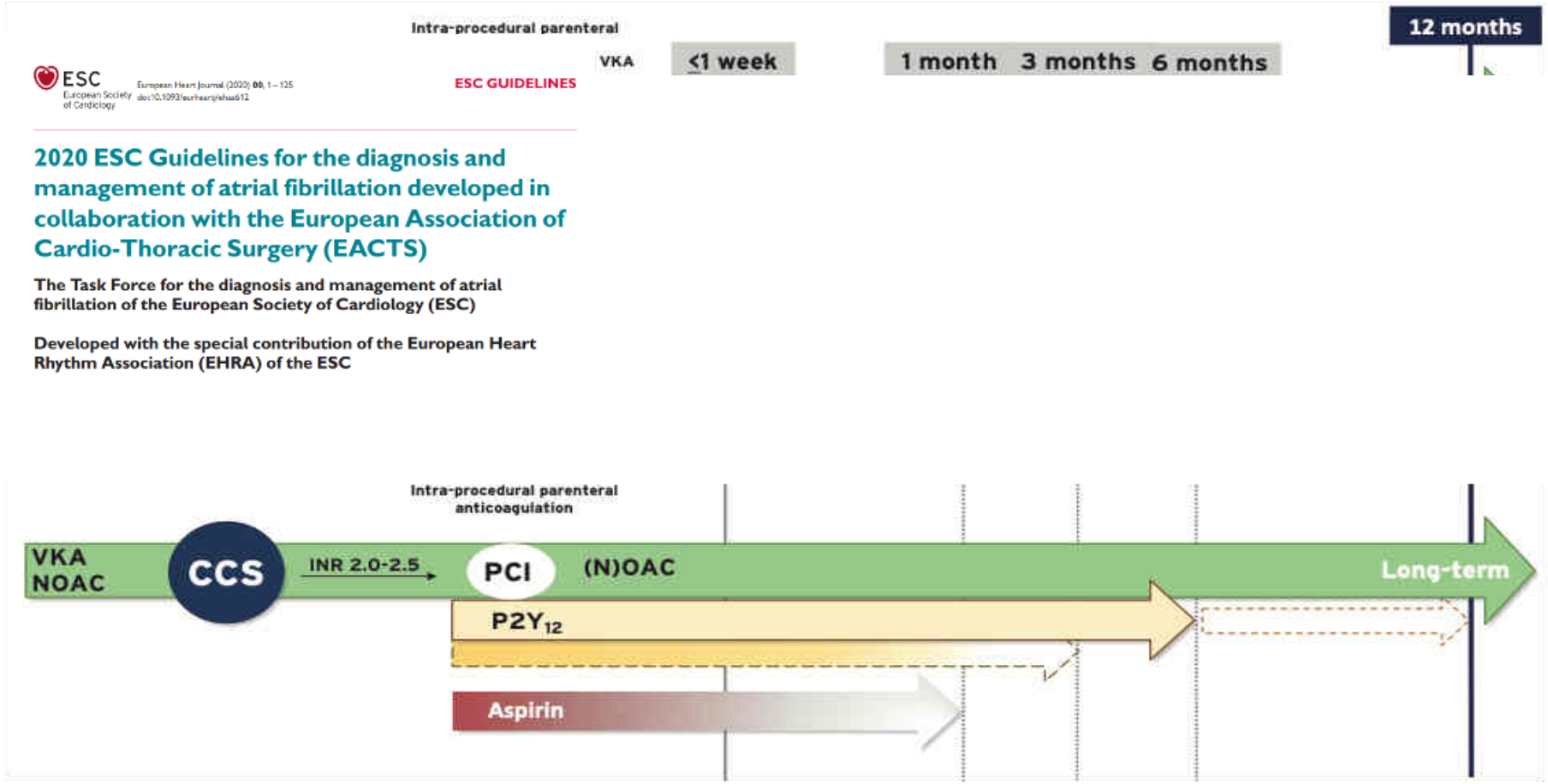
Rivaroxaban is the only option for dual antithrombotic therapy indicated in patients with CCS at high ischaemic risk with or without a prior MI

*or 5 mg od if body weight <60 kg or age >75 years

Knuuti J *et al, Eur Heart J* 2019; doi: 10.1093/eurheartj/ehz42

Post-procedural management of patients with AF and ACS/PCI (full-outlined arrows represent a default strategy; graded/dashed arrows show treatment modifications depending on individual patient's ischaemic and bleeding risks)

ESC European Society of Cardiology



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2020 ESC Guidelines for the diagnosis and management of atrial fibrillation (European Heart Journal 2020-doi/10.1093/eurheartj/ehaa612)

Stable Lesion

Vulnerable Plaque

LDL TARGET NEL PAZIENTE CON INFARTO

(O CON MALATTIA ATEROSCLEROTICA, DIABETE TIPO 1 DA PIU' DI 20 ANNI, IRC <30 ML/MIN, DIABETE CON 3 FATTORI DI RISCHIO)

<55

& RIDUZIONE ≥ 50 % DEI VALORI DI BASE

Classe I, livello A

LDL TARGET NEL PAZIENTE CON 2 SCA ENTRO 2 ANNI

<40

& RIDUZIONE ≥ 50 % DEI VALORI DI BASE

Classe IIb, livello B

COME RAGGIUNGERE QUESTI TARGETS AMBIZIOSI ?

2019 ESC/EAS Guidelines for the management of dyslipidaemias.

Intensity of lipid lowering treatment

Treatment reduction	Average LDL-C
• Moderate intensity statin	≈ 30%
• High intensity statin	≈ 50%
• High intensity statin plus ezetimibe	≈ 65%
• PCSK9 inhibitor	≈ 60%
• PCSK9 inhibitor plus high intensity statin	≈ 75%
• PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%

Conclusioni

- **L'aggiunta di un secondo farmaco antitrombotico all'aspirina per la prevenzione secondaria a lungo termine deve essere presa in considerazione nei pazienti ad alto rischio di eventi ischemici e senza elevato rischio di sanguinamento (IIA-A).**

- **L'aggiunta di un secondo farmaco antitrombotico all'aspirina per la prevenzione secondaria a lungo termine può essere presa in considerazione nei pazienti con un rischio almeno moderatamente aumentato di eventi ischemici e senza un rischio di sanguinamento elevato (IIB-A)**

- **Dopo i 12 mesi è possibile utilizzare nei pazienti ad alto rischio trombotico e basso rischio di sanguinamento post IMA il Ticagrelor 60x2 in aggiunta all'ASA (Età >65, Diabete mellito in terapia, IRC, Malattia multivasale, ulteriore IMA).**

- **Un nuovo approccio nei pazienti ad alto rischio di eventi ischemici con PAD sintomatica è la somministrazione di un anticoagulante (Rivaoxaban 2.5x2) + ASA.**

- **Nei pazienti con pregresso IMA o malattia aterosclerotica il target di LDL dovrebbe essere inferiore a 55 mg/dL o < 40 mg/dL nei pazienti che hanno avuto 2 eventi entro due anni.**

GRAZIE PER L’ATTENZIONE