



A.C.C.A.

Amicale des Cardiologues de la Côte d'Azur

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LA JOURNEE D'ACTUALITESTHERAPEUTIQUES 2018

Que faire au-delà de un an ?

Dr Laurent Drogoul
Saint Laurent Du Var



Conflits d'intérêts.

Medtronic : Proctoring TAVI

Abbott : proctoring CTO

Biosensor : proctoring CTO

Recommendations

Population	ESC Guidelines	ACCF/AHA/SCAI Guidelines
Acute Coronary Syndrome (BMS or DES)	Maximum of 12 months (Class I-A) Longer durations may be considered (Class IIb-A)	At least 12 months (Class I-B) Longer durations may be considered in pts w/ DES (Class IIb-C)
Stable Ischemia and BMS	At least 1 month (Class I-A)	At least 1 month, ideally up to 12 months (Class I-B)
Stable Ischemia and DES	6 months (Class I-B)	At least 12 months (Class I-B)
Secondary Prevention	Selected patients at high ischemic risk	May be considered (Class IIb-B)

Pourquoi ce sujet ?

Tendance actuelle :

essayer de diminuer durée double AAP....

Stent actifs toutes indications...



European Heart Journal (2014) **35**, 969–978
doi:10.1093/eurheartj/eh438

FASTTRACK CLINICAL RESEARCH

Duration of dual antiplatelet treatment with clopidogrel and aspirin in patients with acute coronary syndrome

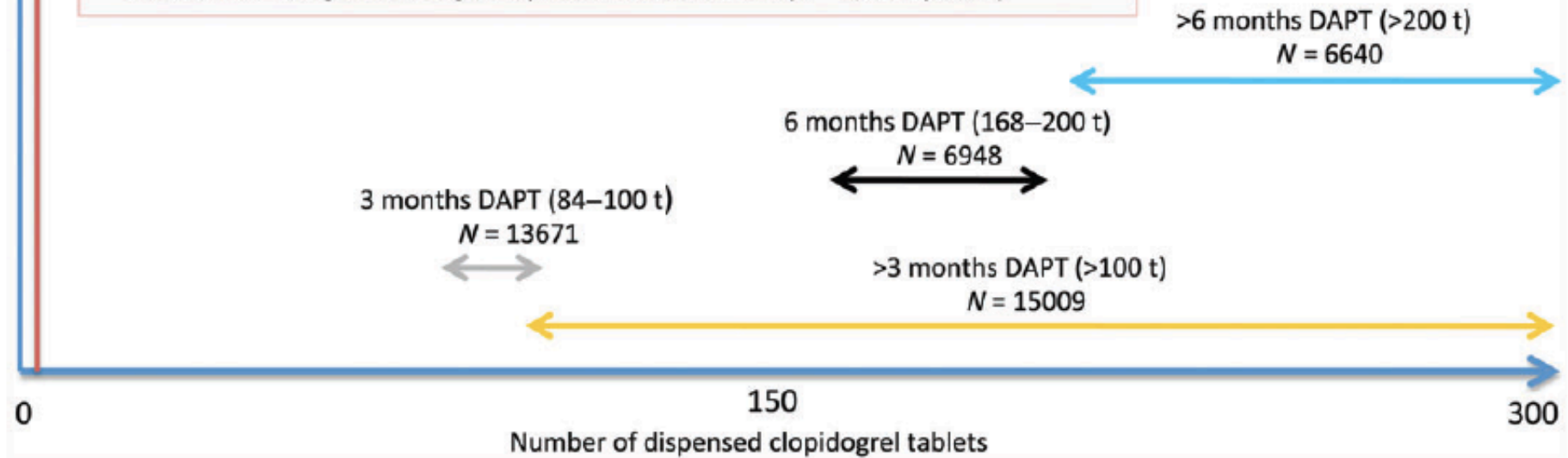
Christoph Varenhorst^{1*}, Karin Jensevik², Tomas Jernberg³, Anders Sundström⁴, Pål Hasvold^{5,6}, Claes Held¹, Bo Lagerqvist¹, and Stefan James¹

Index ACS-event

Patients with new onset NST-ASC or ST-ASC and registered in SWEDEHEART and treated with DAPT from 1 Jan 2006 to 1 July 2010 ($N = 56\,440$)

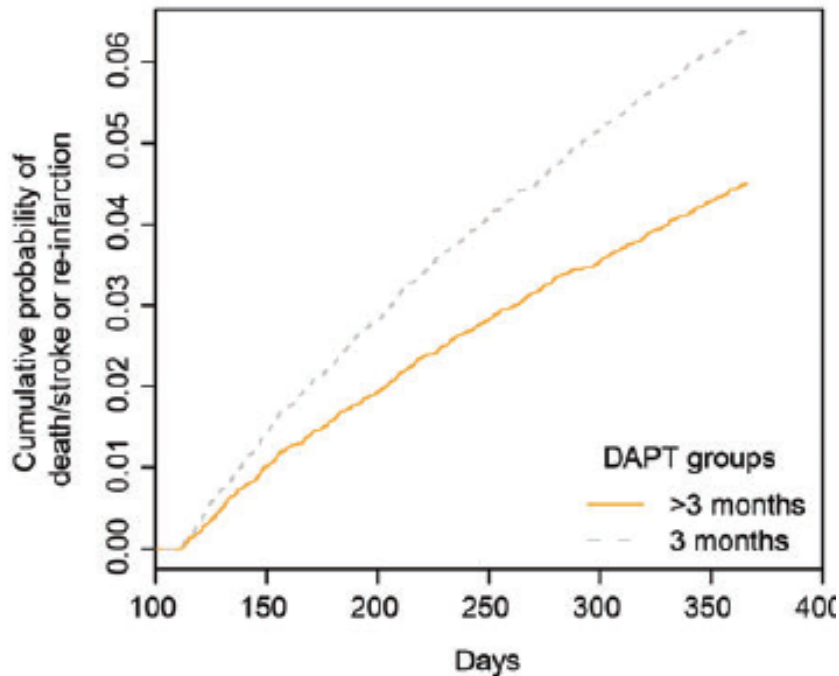
Patients excluded:

- Patients with clopidogrel use 180 days before index event ($N = 3240$)
- Patients treated with warfarin ($N = 2713$)
- Patients who did not fulfill the criteria for >3 months and 3 months DAPT ($N = 6526$) and >6 months and 6 months DAPT ($N = 30\,225$)
- Patients suffering death, re-infarction, stroke, bleeding, ST, or coronary revascularization from discharge of the index event until day 111 (for the >3 vs 3 months comparison ($N = 5677$)) or day 201 (for the >6 vs 6 months comparison ($N = 3747$))
- Patients with follow-up shorter than 1 year after index event ($N = 4775$ and 2585)
- Patients with missing values for age, body mass index or creatinine ($N = 4829$, resp, 1945)



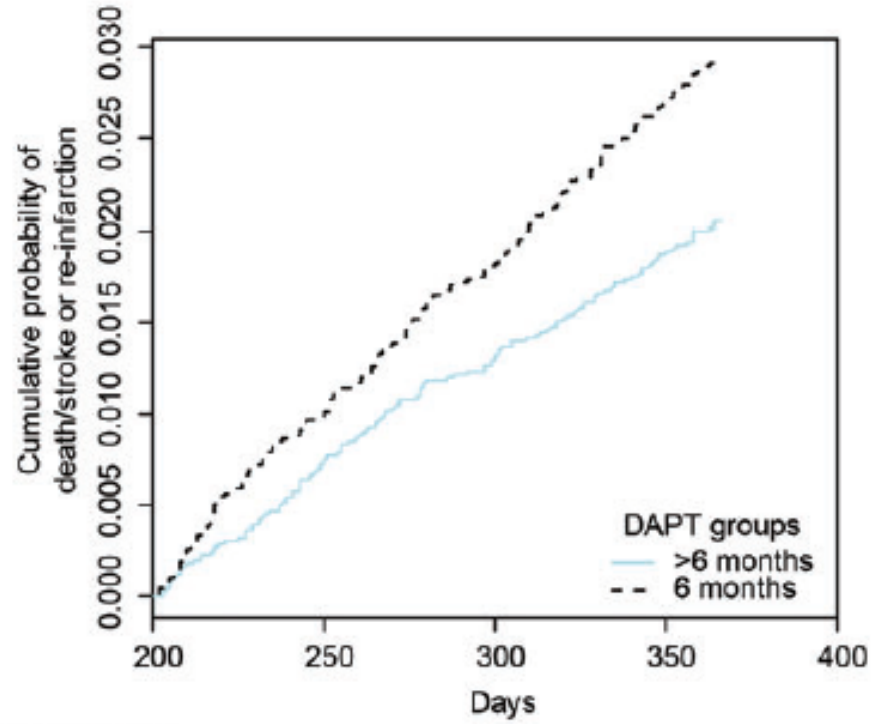
Evènements DC/AVC/IDM

3 mois vs > 3 mois



Patients at risk	
>3 months	15 009 14 619 14 297 14 031 13 830 13 656
3 months	13 671 13 365 13 040 12 795 12 589 12 429

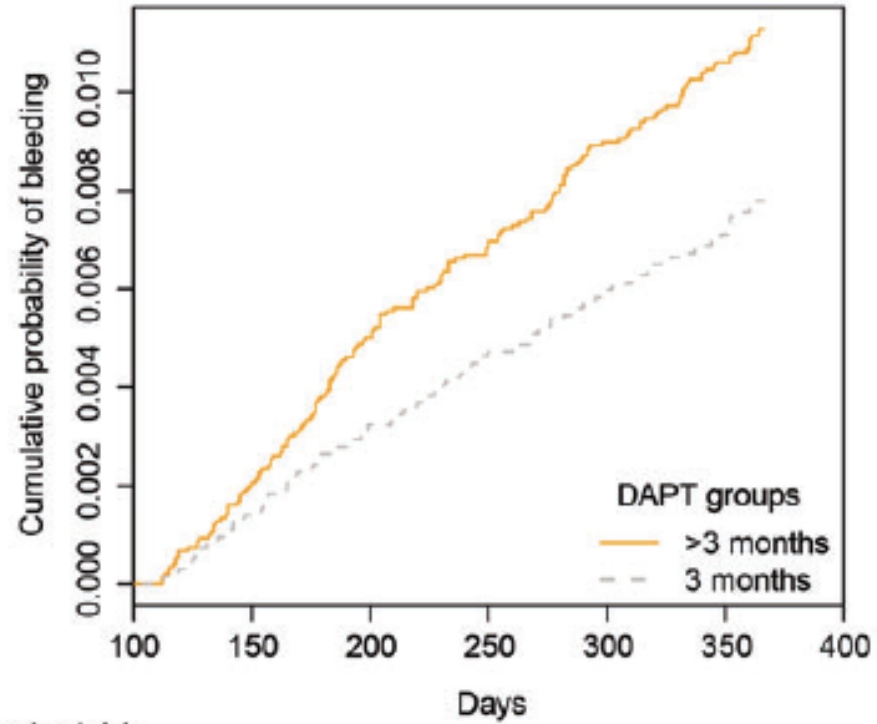
6 mois vs > 6 mois



Patients at risk	
>6 months	6640 6518 6438 6361
6 months	6948 6830 6725 6639

Saignements

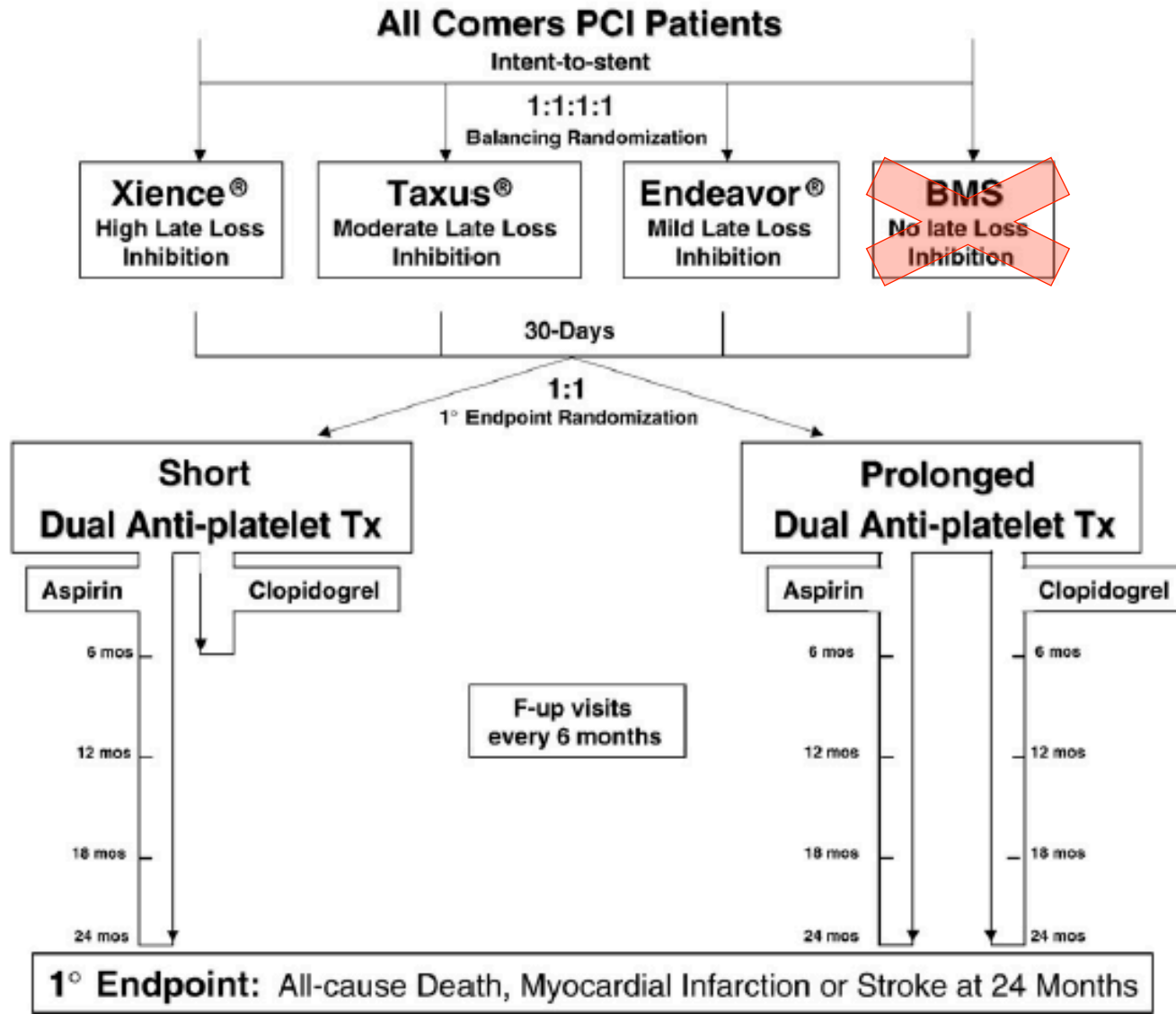
3 mois vs > 3 mois



Patients at risk						
>3 months	15 009	14 931	14 824	14 756	14 675	14 604
3 months	13 671	13 598	13 497	13 398	13 305	13 225

Randomized comparison of 6- versus 24-month clopidogrel therapy after balancing anti-intimal hyperplasia stent potency in all-comer patients undergoing percutaneous coronary intervention: Design and rationale for the PROlonging Dual-antiplatelet treatment after Grading stent-induced Intimal hyperplasia study (PRODIGY)

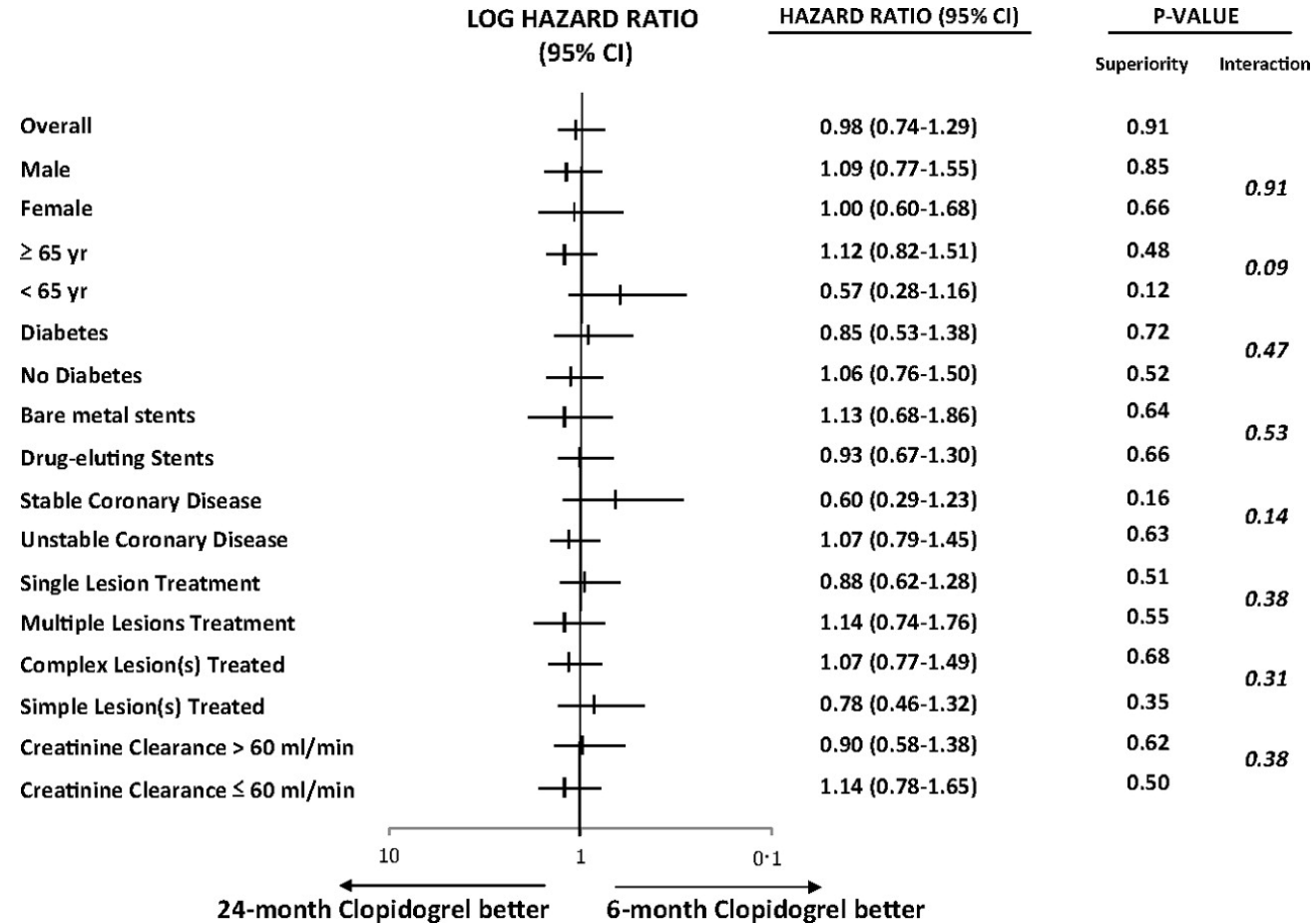
Marco Valgimigli, MD, PhD,^{a,b} Gianluca Campo, MD,^a Gianfranco Percoco, MD,^c Monia Monti, BSc,^d Fabrizio Ferrari, MD,^a Carlo Tumscitz, MD,^a Andrea Zuffi, MD,^c Federico Colombo, MD,^c Moh'd Kubbajeh, MD,^c Caterina Cavazza, MD,^a Elisa Cangiano, MD,^a Matteo Tebaldi, MD,^a Monica Minarelli, MD,^a Chiara Arcozzi, MD,^a Antonella Scalone, MD,^a Alice Frangione, MD,^c Marco Borghesi, MD,^a Jlenia Marchesini, MD,^a Giovanni Parrinello, PhD,^f and Roberto Ferrari, MD, PhD^{a,b} *Ferrara, Gussago, Valle OpPIO (Comacchio), Cotignola (RA), and Brescia, Italy*



Implanted stent type, n (%)

Bare-metal stent	246 (24.9)	246 (25.0)
Everolimus-eluting stent	248 (25.1)	245 (24.9)
Paclitaxel-eluting stent	245 (24.8)	245 (24.9)
Everolimus-eluting stent	248 (25.1)	247 (25.1)

Subgroup analyses of the primary end point.



Critères de sécurité en %	24 mois de clopidogrel	6 mois de clopidogrel	Risque relatif p
Saignement 2,3 ou 5 BARC	7,4	3,5	0,00018
Saignement 5 ou 3	3,4	1,9	0,037
Saignements 2 ou 3	6,5	3	0,00033
Saignements majeurs selon TIMI	1,6	0,6	0,041
transfusion	2,6	1,3	0,041

Donc débat en faveur longue durée DAPT mal engagé mais...



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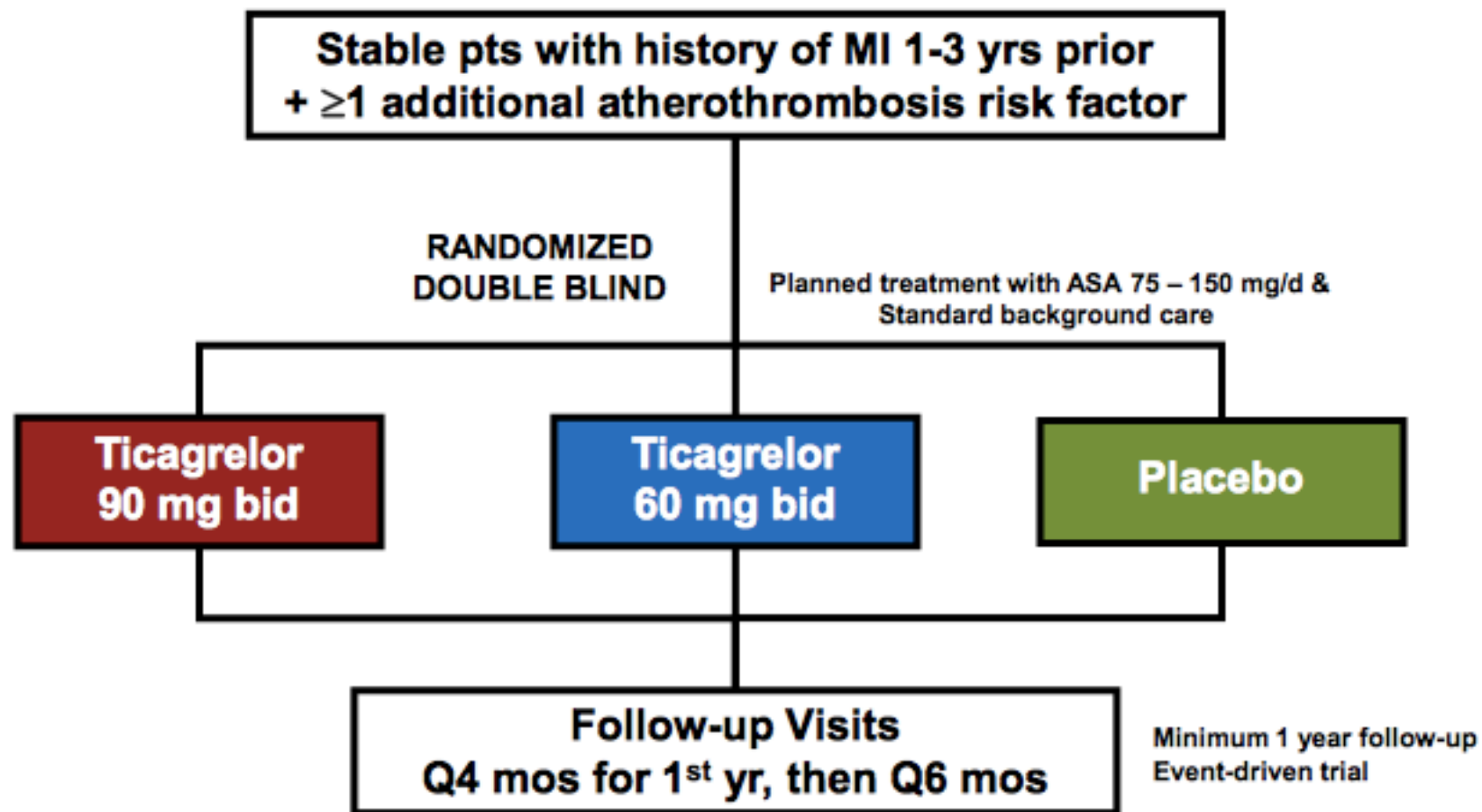
ESTABLISHED IN 1812

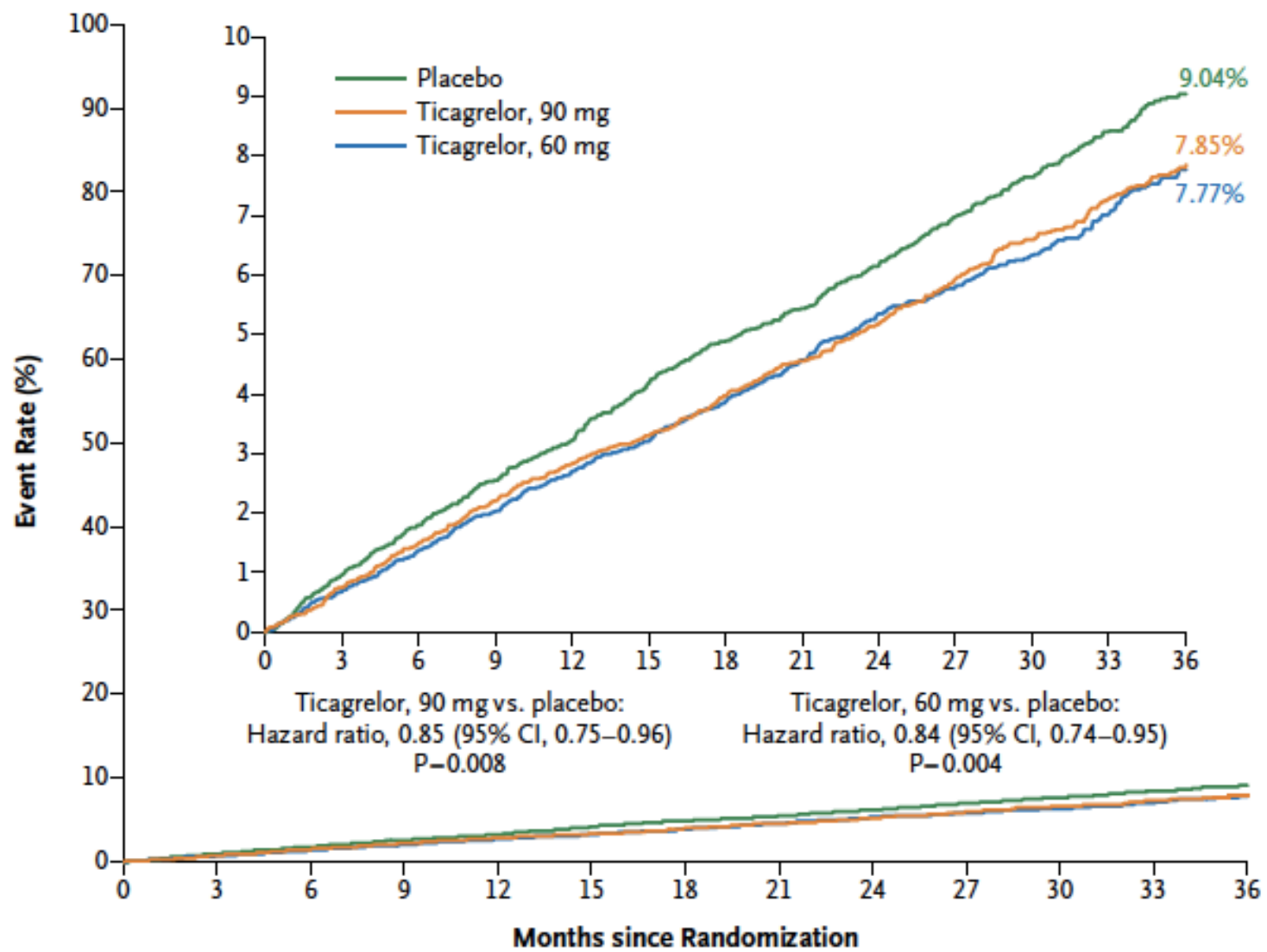
MAY 7, 2015

VOL. 372 NO. 19

Long-Term Use of Ticagrelor in Patients with Prior
Myocardial Infarction

Marc P. Bonaca, M.D., M.P.H., Deepak L. Bhatt, M.D., M.P.H., Marc Cohen, M.D., Philippe Gabriel Steg, M.D., Robert F. Storey, M.D., Eva C. Jensen, M.D., Ph.D., Giulia Magnani, M.D., Sameer Bansilal, M.D., M. Polly Fish, B.A., Kyungah Im, Ph.D., Olof Bengtsson, Ph.Lic., Ton Oude Ophuis, M.D., Ph.D., Andrzej Budaj, M.D., Ph.D., Pierre Theroux, M.D., Mikhail Ruda, M.D., Christian Hamm, M.D., Shinya Goto, M.D., Jindrich Spinar, M.D., José Carlos Nicolau, M.D., Ph.D., Robert G. Kiss, M.D., Ph.D., Sabina A. Murphy, M.P.H., Stephen D. Wiviott, M.D., Peter Held, M.D., Ph.D., Eugene Braunwald, M.D., and Marc S. Sabatine, M.D., M.P.H., for the PEGASUS-TIMI 54 Steering Committee and Investigators*





SAIGNEMENTS

End Point	Ticagrelor, 90 mg (N = 6988)	Ticagrelor, 60 mg (N = 6958)	Placebo (N = 6996)	Ticagrelor, 90 mg vs. Placebo		Ticagrelor, 60 mg vs. Placebo	
				Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
<i>number (percent)</i>							
Bleeding							
TIMI major bleeding	127 (2.60)	115 (2.30)	54 (1.06)	2.69 (1.96–3.70)	<0.001	2.32 (1.68–3.21)	<0.001
TIMI minor bleeding	66 (1.31)	55 (1.18)	18 (0.36)	4.15 (2.47–7.00)	<0.001	3.31 (1.94–5.63)	<0.001

*Comment choisir ?
DAPT à la carte*



Pierre Magnain

Selon le sexe ?

JACC: CARDIOVASCULAR INTERVENTIONS

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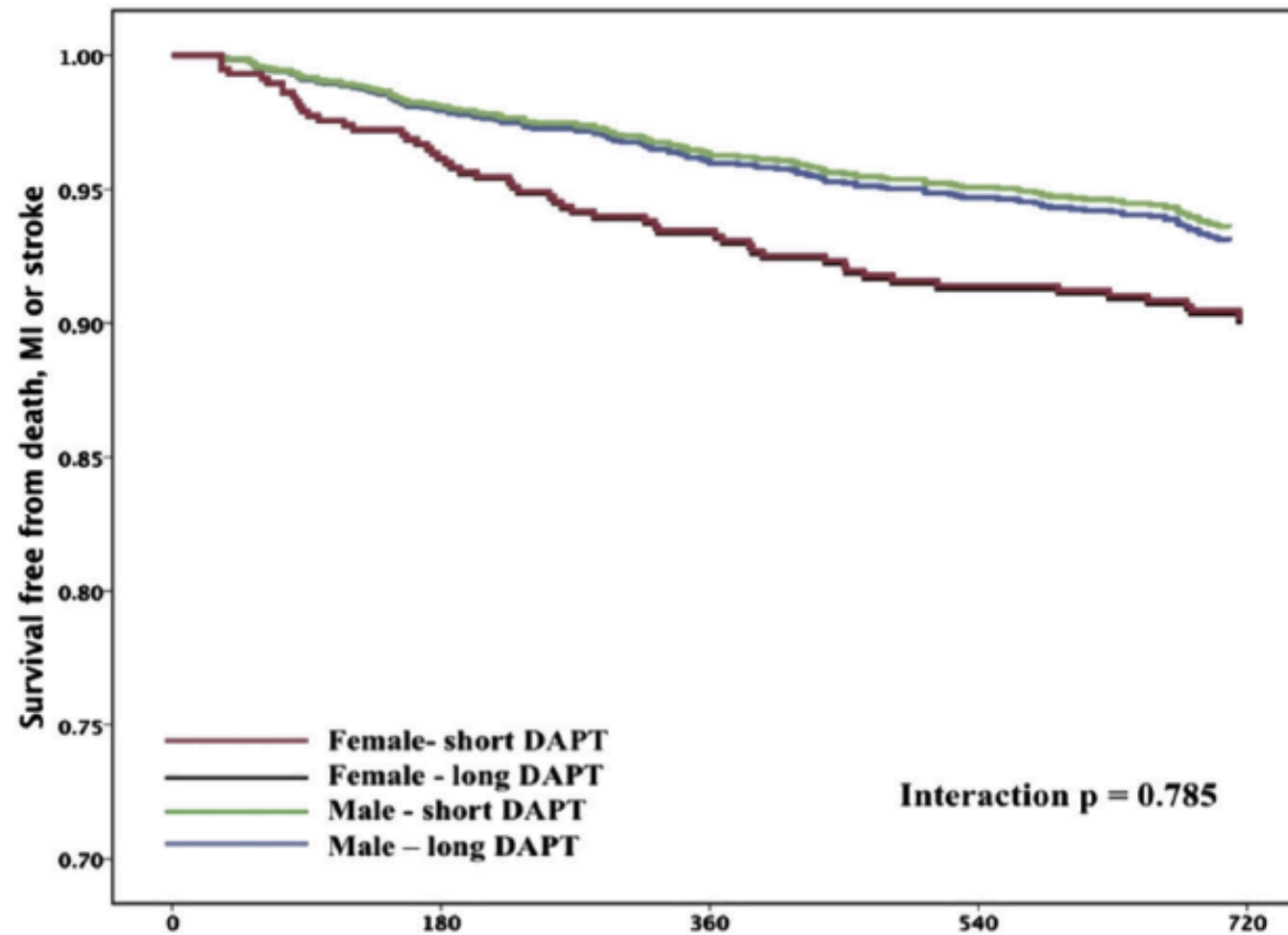
<http://dx.doi.org/10.1016/j.jcin.2016.05.046>

Impact of Sex on 2-Year Clinical Outcomes in Patients Treated With 6-Month or 24-Month Dual-Antiplatelet Therapy Duration

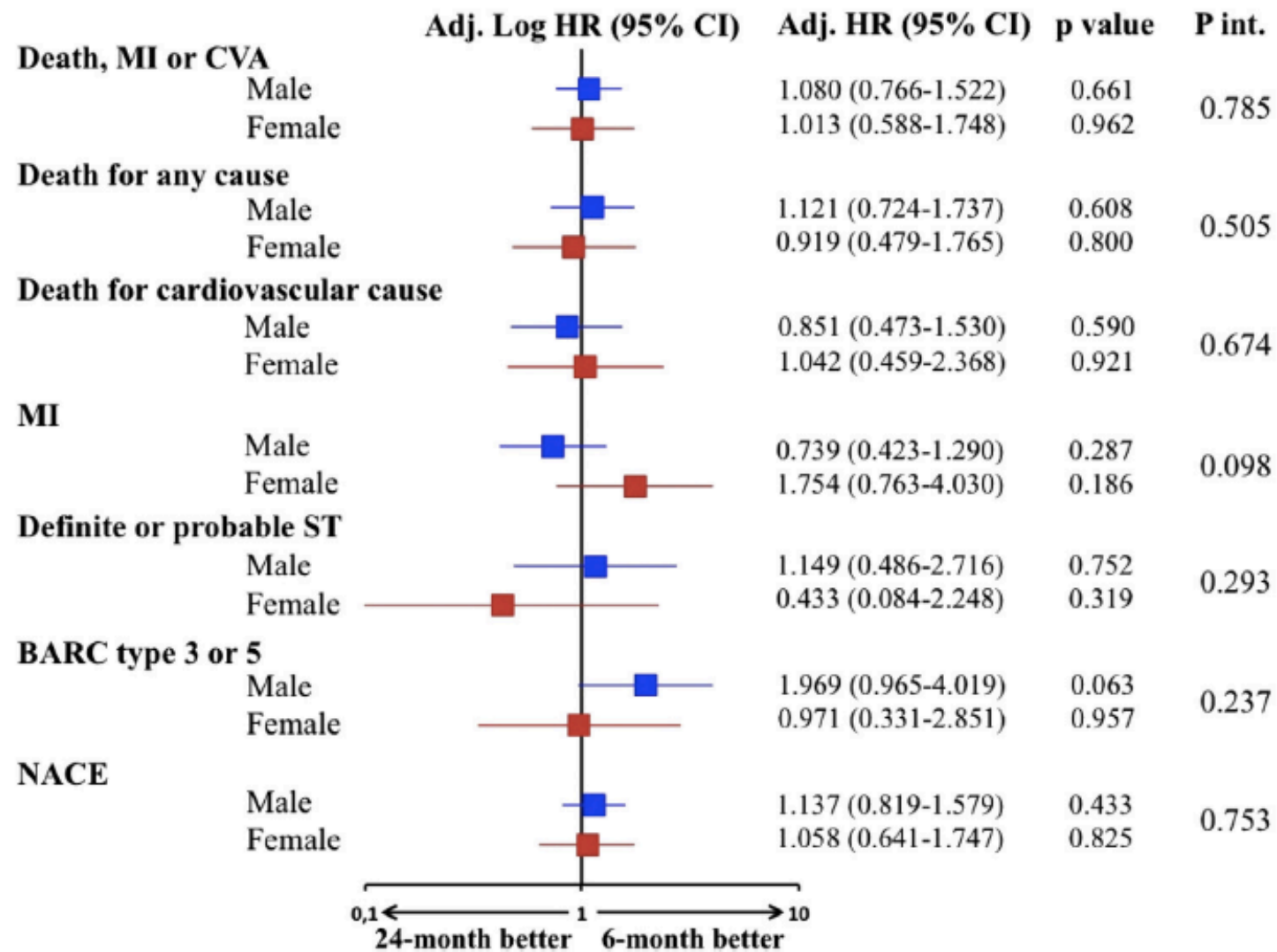
A Pre-Specified Analysis From the PRODIGY Trial



Giuseppe Gargiulo, MD,^{a,b} Sara Ariotti, MD,^{a,c} Andrea Santucci, MD,^a Raffaele Piccolo, MD,^a Andrea Baldo, MD,^a Anna Franzone, MD,^a Giulia Magnani, MD,^a Marcello Marino, MD,^a Giovanni Esposito, MD, PhD,^b Stephan Windecker, MD,^a Marco Valgimigli, MD, PhD^{a,c}



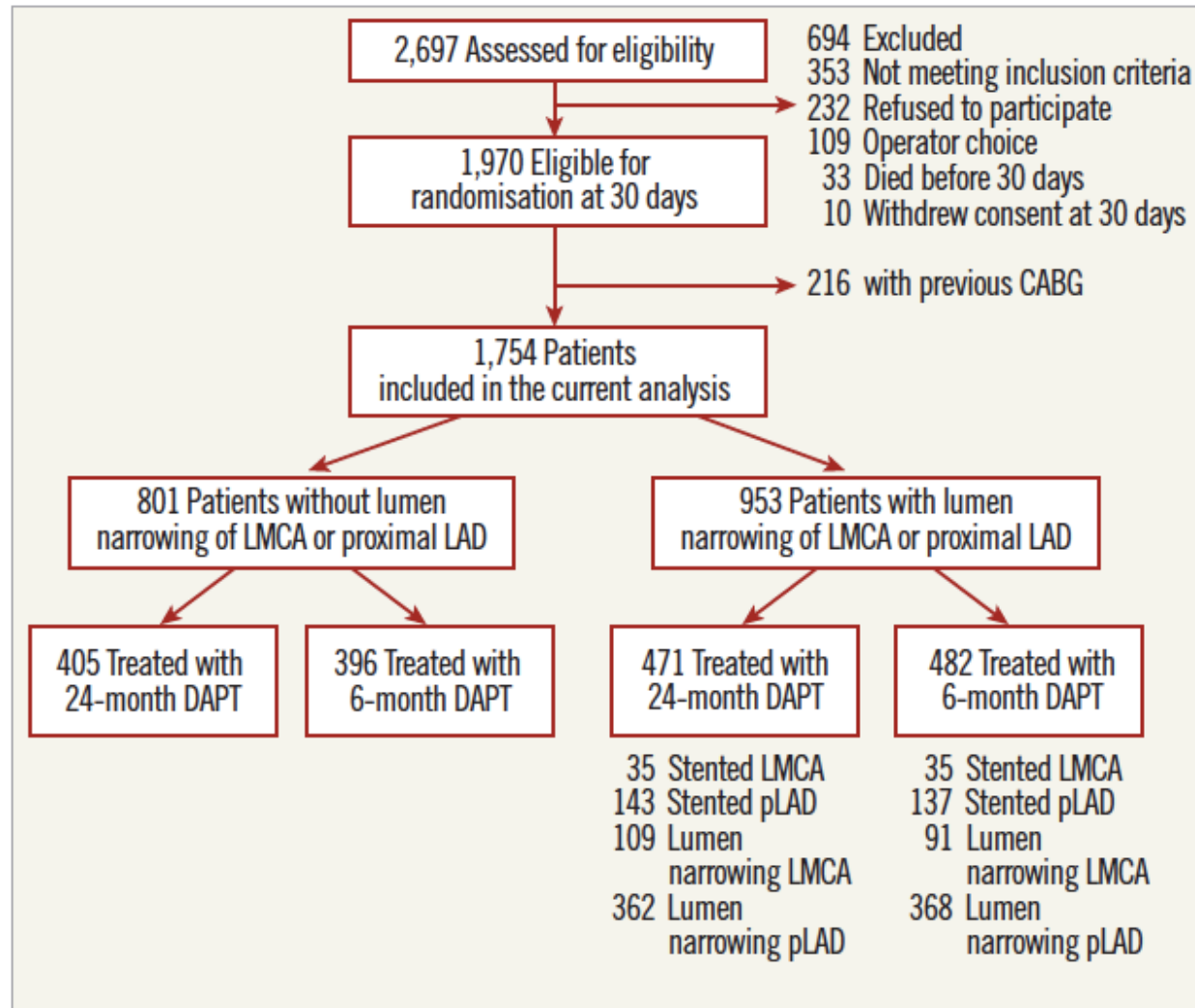
	0	180	360	540	720
Number at risk					
Female-short DAPT	236	223	220	213	206
Female-long DAPT	223	213	201	197	195
Male-short DAPT	747	724	699	689	675
Male-long DAPT	764	741	724	707	689

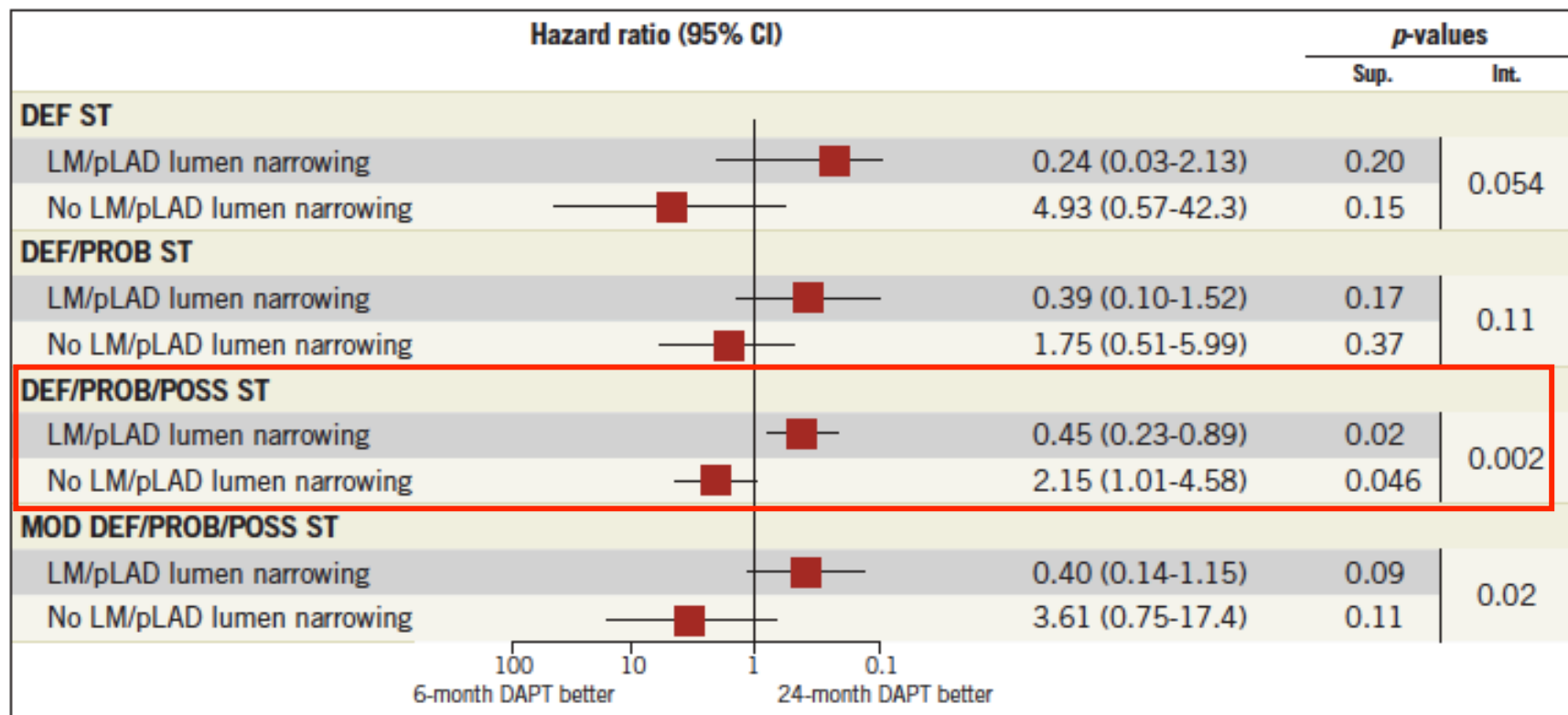


Si atteinte « pluritronculaire »?

Left main or proximal left anterior descending coronary artery disease location identifies high-risk patients deriving potentially greater benefit from prolonged dual antiplatelet therapy duration

Francesco Costa¹, MD; Marianna Adamo¹, MD; Sara Ariotti¹, MD; Giuseppe Ferrante², MD, PhD;
Eliano Pio Navarese³, MD, PhD; Sergio Leonardi⁴, MD; Hector Garcia-Garcia⁵, MD, PhD;
Pascal Vranckx⁶, MD, PhD; Marco Valgimigli^{1*}, MD, PhD



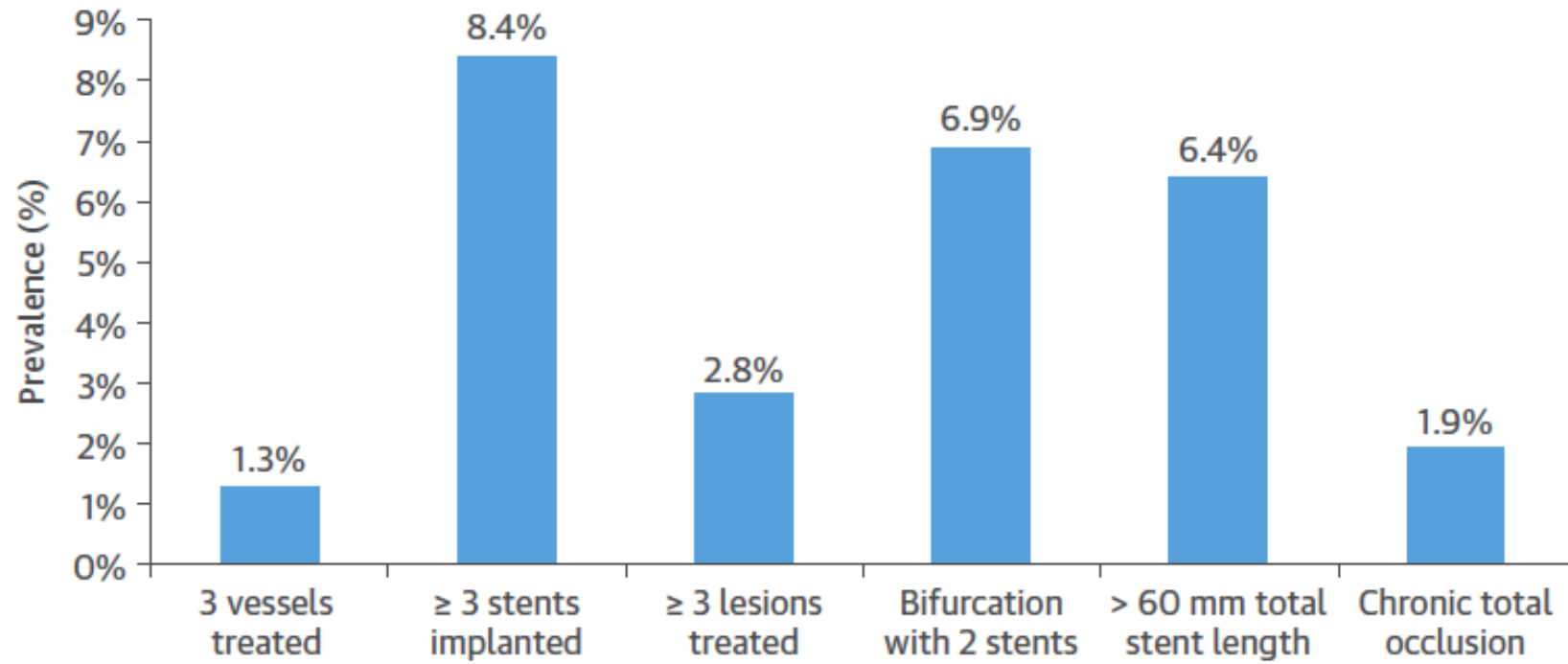


Efficacy and Safety of Dual Antiplatelet Therapy After Complex PCI



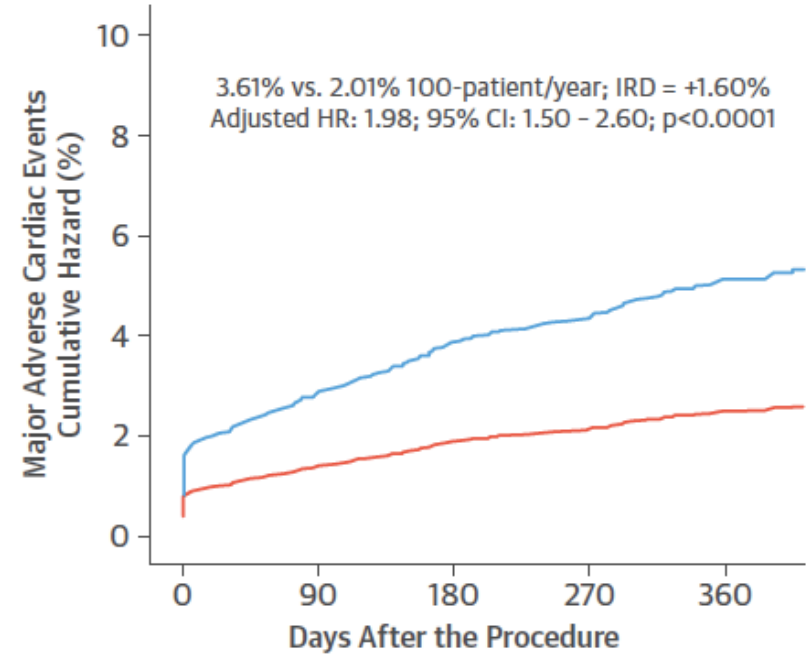
Gennaro Giustino, MD,^{a,b,c} Alaide Chieffo, MD,^c Tullio Palmerini, MD,^d Marco Valgimigli, MD, PhD,^e
Fausto Feres, MD,^f Alexandre Abizaid, MD,^f Ricardo A. Costa, MD,^f Myeong-Ki Hong, MD, PhD,^g
Byeong-Keuk Kim, MD, PhD,^g Yangsoo Jang, MD, PhD,^g Hyo-Soo Kim, MD, PhD,^h Kyung Woo Park, MD,^h
Martine Gilard, MD,ⁱ Marie-Claude Morice, MD,^j Fadi Sawaya, MD,^j Gennaro Sardella, MD,^k Philippe Genereux, MD,^{b,l}
Bjorn Redfors, MD, PhD,^b Martin B. Leon, MD,^{c,l} Deepak L. Bhatt, MD, MPH,^m Gregg W. Stone, MD,^{b,l}
Antonio Colombo, MD^c

Components of Complex PCI



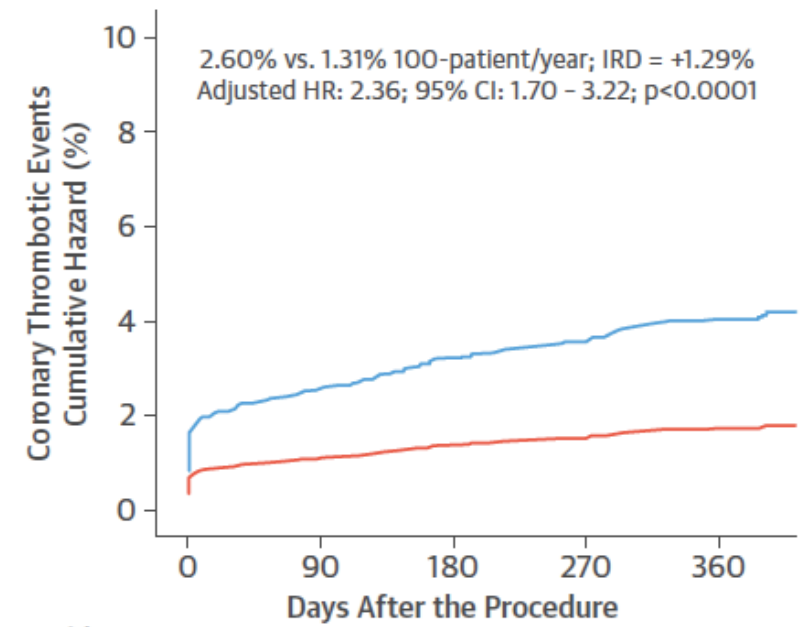
Plus d'événements Indépendamment de la durée DAPT si ATC complexe.

A



<i>Number at risk</i>		0	90	180	270	360
Non-complex PCI	Complex PCI	7870	7749	7640	7576	7031
		1642	1593	1573	1555	1361

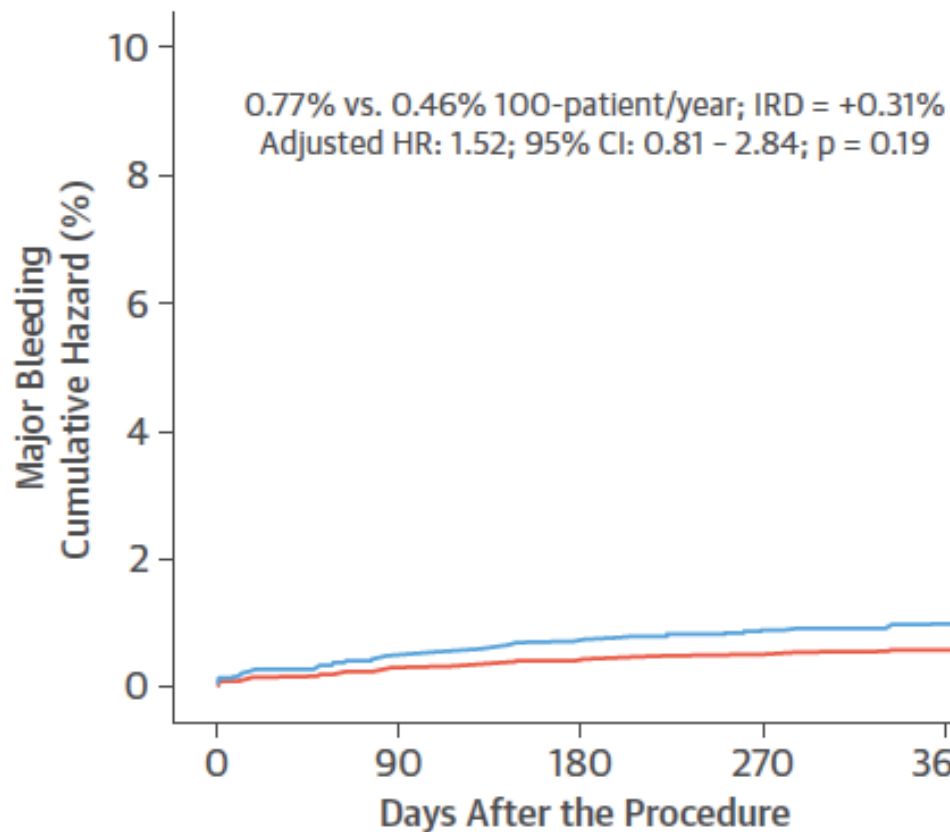
B



<i>Number at risk</i>		0	90	180	270	360
Non-complex PCI	Complex PCI	7870	7748	7645	7581	7039
		1642	1593	1573	1557	1365

— Complex PCI — Non-complex PCI

C



Number at risk

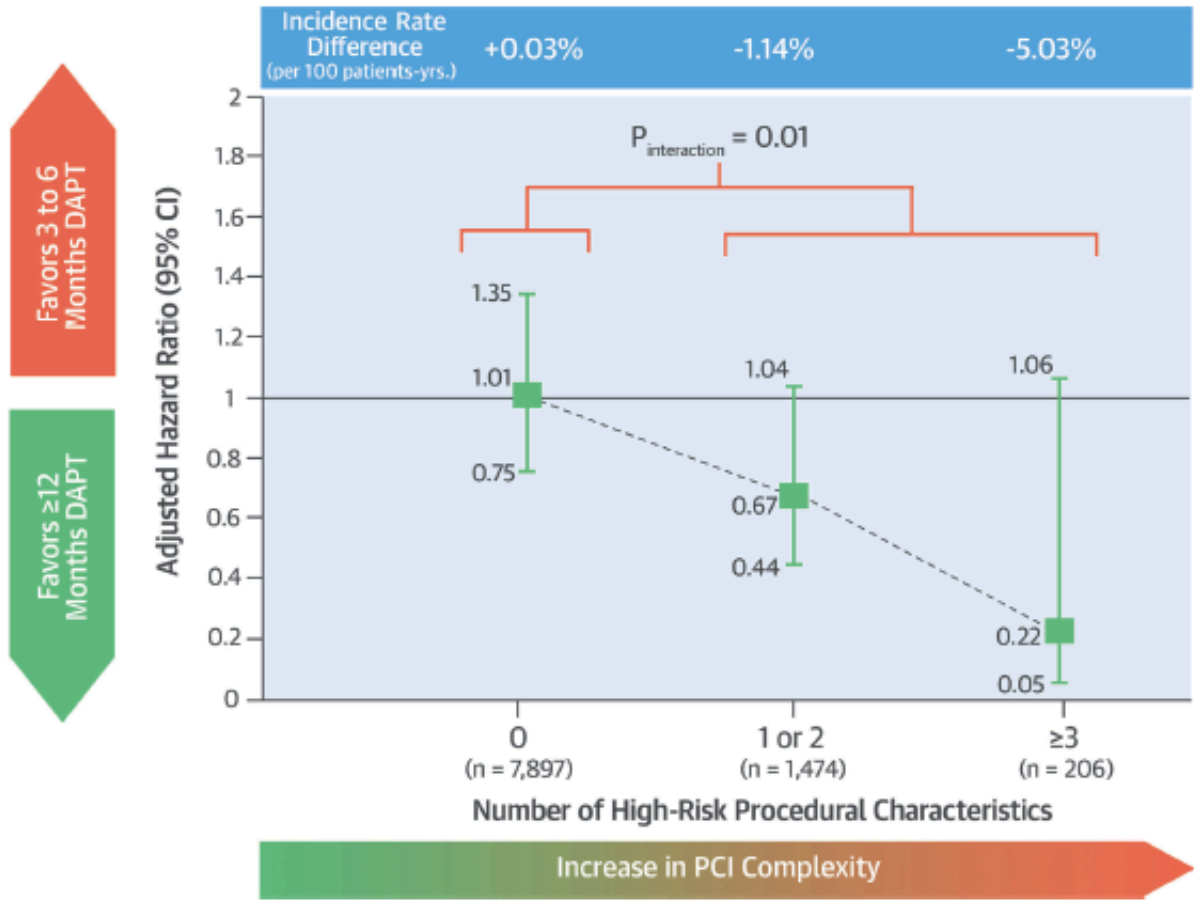
Non-complex PCI	7888	7792	7693	7625	7090
Complex PCI	1662	1627	1609	1595	1398

— Complex PCI — Non-complex PCI

Upfront DAPT Duration After Complex PCI



Effect of ≥ 12 Months Versus 3 or 6 Months DAPT on the Risk of Major Adverse Cardiac Events According to Procedural Complexity



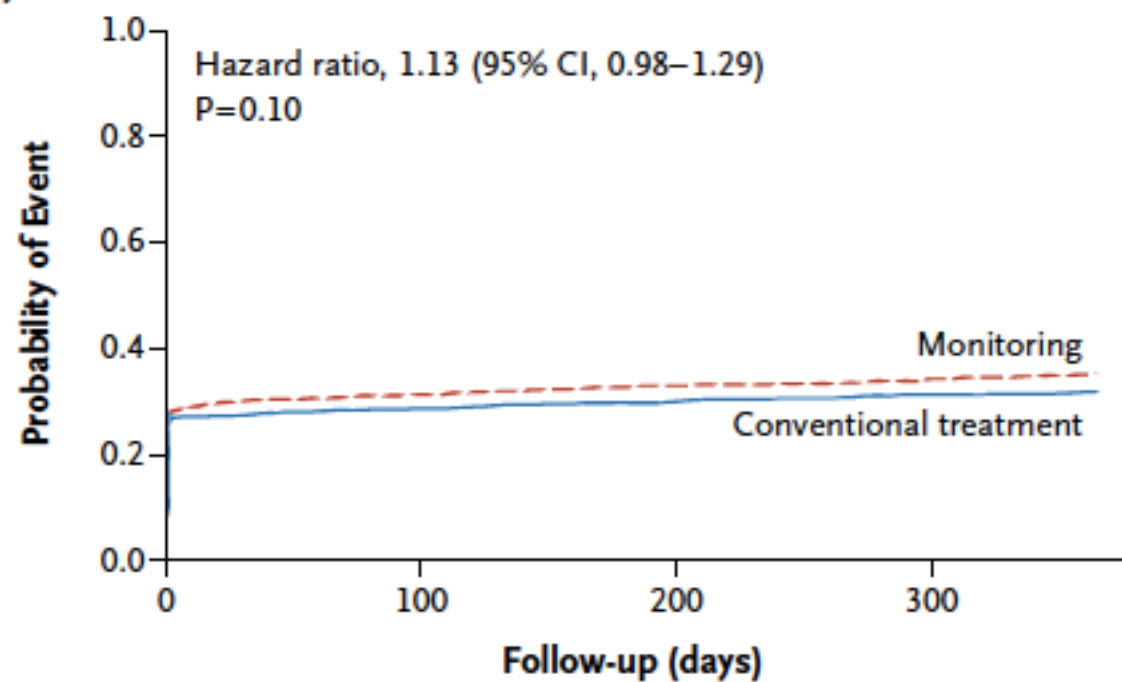
*Selon les tests de réactivité
plaquettaires ?*

ORIGINAL ARTICLE

Bedside Monitoring to Adjust Antiplatelet Therapy for Coronary Stenting

Jean-Philippe Collet, M.D., Ph.D., Thomas Cuisset, M.D., Ph.D.,
Grégoire Rangé, M.D., Guillaume Cayla, M.D., Ph.D., Simon Elhadad, M.D.,
Christophe Pouillot, M.D., Patrick Henry, M.D., Ph.D., Pascal Motreff, M.D., Ph.D.,
Didier Carrié, M.D., Ziad Boueri, M.D., Ph.D., Loic Belle, M.D.,
Eric Van Belle, M.D., Ph.D., Hélène Rousseau, Ph.D., Pierre Aubry, M.D.,
Jacques Monségu, M.D., Pierre Sabouret, M.D., Stephen A. O'Connor, M.B., B.Ch.,
Jérémy Abtan, M.D., Mathieu Kerneis, M.D., Christophe Saint-Etienne, M.D.,
Olivier Barthélémy, M.D., Farzin Beygui, M.D., Ph.D., Johanne Silvain, M.D., Ph.D.,
Eric Vicaut M.D., Ph.D., and Gilles Montalescot, M.D., Ph.D.,
for the ARCTIC Investigators*

A Primary End Point



No. at Risk

Conventional treatment	1227	835	801	767
Monitoring	1213	790	762	730

SCORES ?

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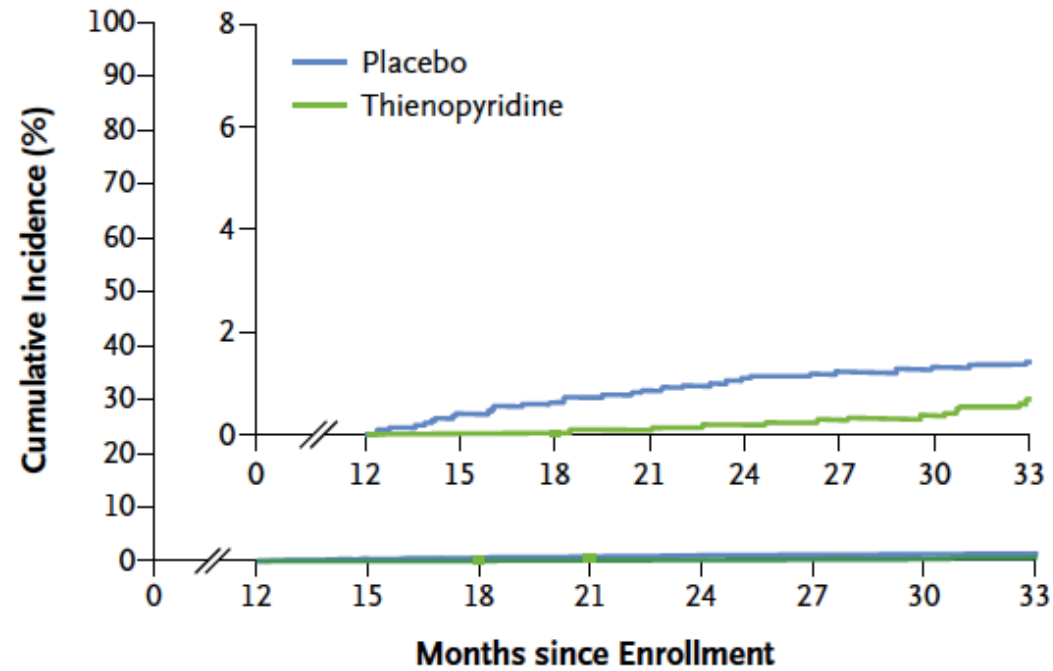
Twelve or 30 Months of Dual Antiplatelet Therapy
after Drug-Eluting Stents

Laura Mauri, M.D., Dean J. Kereiakes, M.D., Robert W. Yeh, M.D., Priscilla Driscoll-Shempp, M.B.A., Donald E. Cutlip, M.D., P. Gabriel Steg, M.D., Sharon-Lise T. Normand, Ph.D., Eugene Braunwald, M.D., Stephen D. Wiviott, M.D., David J. Cohen, M.D., David R. Holmes, Jr., M.D., Mitchell W. Krucoff, M.D., James Hermiller, M.D., Harold L. Dauerman, M.D., Daniel I. Simon, M.D., David E. Kandzari, M.D., Kirk N. Garratt, M.D., David P. Lee, M.D., Thomas K. Pow, M.D., Peter Ver Lee, M.D., Michael J. Rinaldi, M.D., and Joseph M. Massaro, Ph.D., for the DAPT Study Investigators*

Stent Thrombosis

12–30 mo Thienopyridine vs. placebo, 0.4% vs. 1.4%;
hazard ratio, 0.29; P<0.001

12–33 mo Thienopyridine vs. placebo, 0.7% vs. 1.4%;
hazard ratio, 0.45; P<0.001



No. at Risk

Thienopyridine	5020	4934	4870	4828	4765	4686	4642	3110
Placebo	4941	4845	4775	4721	4651	4603	4556	3105

Bleeding Complications	Continued Thienopyridine (N=4710)	Placebo (N=4649)	Difference	Two-Sided P Value for Difference
	<i>no. of patients (%)</i>		<i>percentage points (95% CI)</i>	
GUSTO severe or moderate†	119 (2.5)	73 (1.6)	1.0 (0.4 to 1.5)	0.001
Severe	38 (0.8)	26 (0.6)	0.2 (-0.1 to 0.6)	0.15
Moderate	81 (1.7)	48 (1.0)	0.7 (0.2 to 1.2)	0.004
BARC type 2, 3, or 5	263 (5.6)	137 (2.9)	2.6 (1.8 to 3.5)	<0.001
Type 2	145 (3.1)	72 (1.5)	1.5 (0.9 to 2.1)	<0.001
Type 3	122 (2.6)	68 (1.5)	1.1 (0.6 to 1.7)	<0.001
Type 5	7 (0.1)	4 (0.1)	0.1 (-0.1 to 0.2)	0.38

DAPT Score Utility for Risk Prediction in Patients With or Without Previous Myocardial Infarction



Dean J. Kereiakes, MD,^a Robert W. Yeh, MD,^{b,c,d} Joseph M. Massaro, PhD,^{c,e} Donald E. Cutlip, MD,^{b,c,f}
P. Gabriel Steg, MD,^{g,h,i,j} Stephen D. Wiviott, MD,^{b,k} Laura Mauri, MD,^{b,c,k} on behalf of the DAPT Study Investigators

DAPT score¹⁵

After 12 months of uneventful DAPT

Standard DAPT (12 months)

vs.

Long DAPT (30 months)

Age

≥75

65 to <75

<65

Cigarette smoking

Diabetes mellitus

MI at presentation

Prior PCI or prior MI

Paclitaxel-eluting stent

Stent diameter <3 mm

CHF or LVEF <30%

Vein graft stent

-2 pt

-1 pt

0 pt

+1 pt

+1 pt

+1 pt

+1 pt

+1 pt

+1 pt

+2 pt

+2 pt

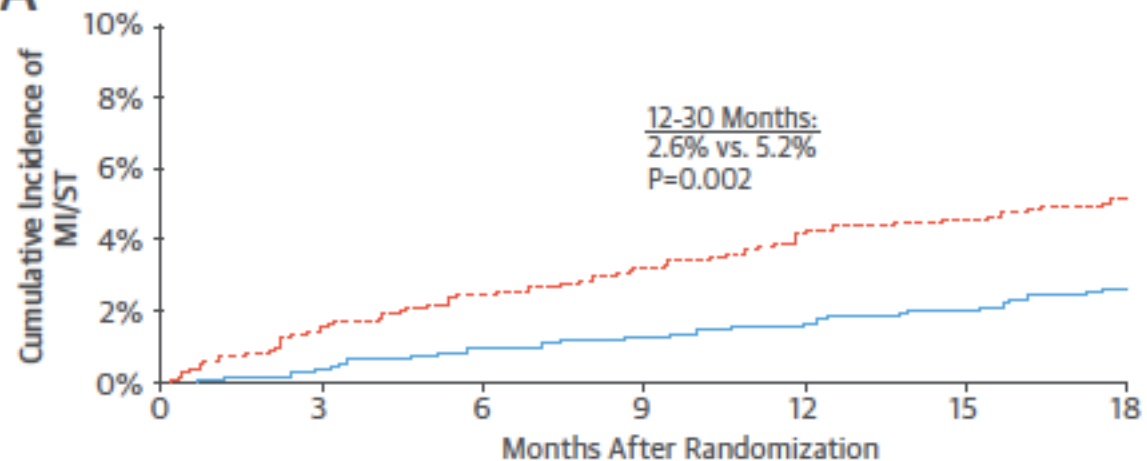
-2 to 10 points

Score ≥2 → Long DAPT

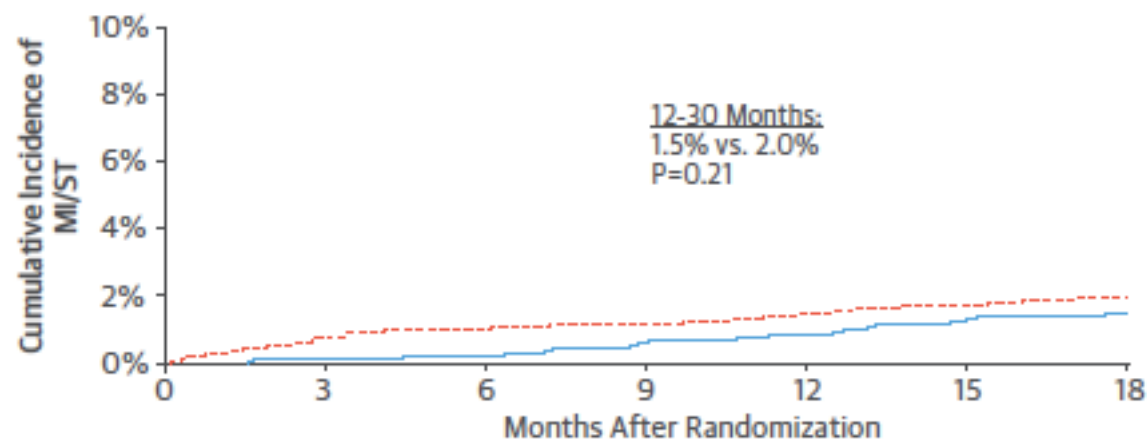
Score <2 → Standard DAPT

www.daptstudy.org

A Patients with DAPT Score ≥ 2

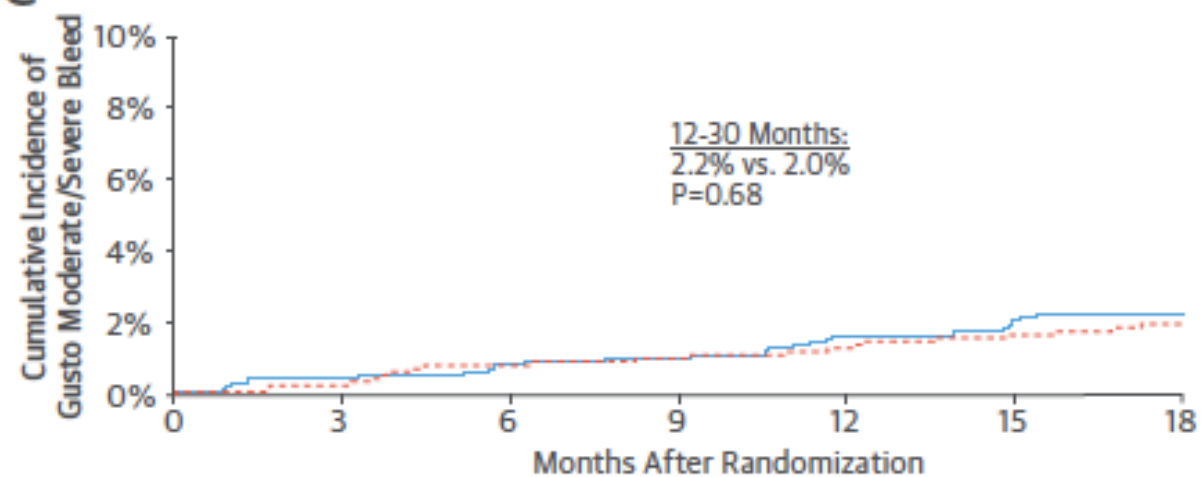


Patients with DAPT Score < 2

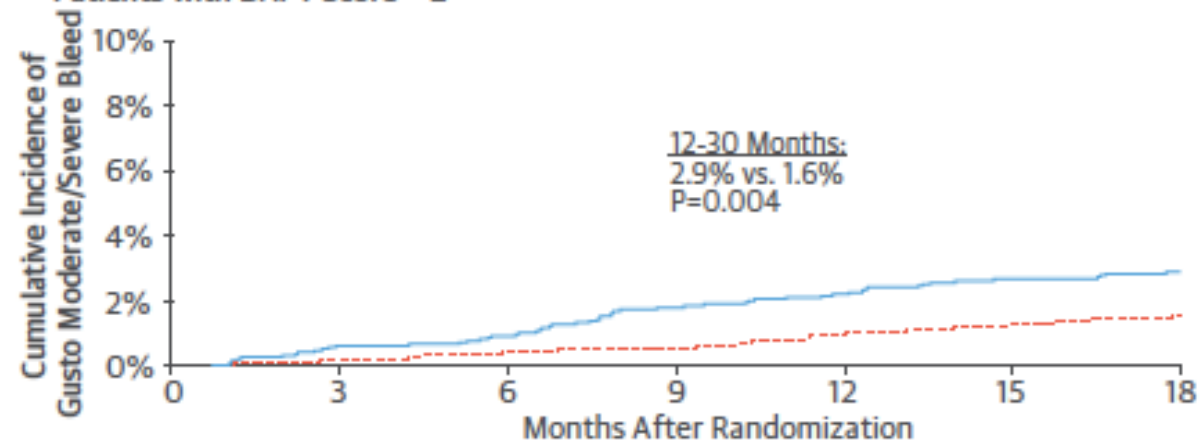


— Continued Thienopyridine - - - Placebo

C Patients with DAPT Score ≥ 2



Patients with DAPT Score < 2



— Continued Thienopyridine - - - Placebo

La génétique ?

Impact of CYP2C19 Metabolizer Status on Patients With ACS Treated With Prasugrel Versus Clopidogrel



Jacob A. Doll, MD,^a Megan L. Neely, PhD,^b Matthew T. Roe, MD, MHS,^{a,b} Paul W. Armstrong, MD,^c Harvey D. White, MB, ChB, DSc,^d Dorairaj Prabhakaran, MD, DM, MSc,^e Kenneth J. Winters, MD,^f Suman Duvvuru, PhD,^f Scott S. Sundseth, PhD,^g Joseph A. Jakubowski, PhD,^f Paul A. Gurbel, MD,^h Deepak L. Bhatt, MD, MPH,ⁱ E. Magnus Ohman, MD,^{a,b} Keith A.A. Fox, MB, ChB,^j for the TRILOGY ACS Investigators

SCA traités médicalement

A. Extensive Metabolizers (EM)

Clopidogrel (Prodrug)

Prasugrel (Prodrug)

Hepatic Metabolism
Including CYP2C19
(Alleles *1/*1,
*1/*17, or *17/*17)

C.

Active Clopidogrel
Metabolite

Platelets

Active Prasugrel
Metabolite

B. Reduced Metabolizers (RM)

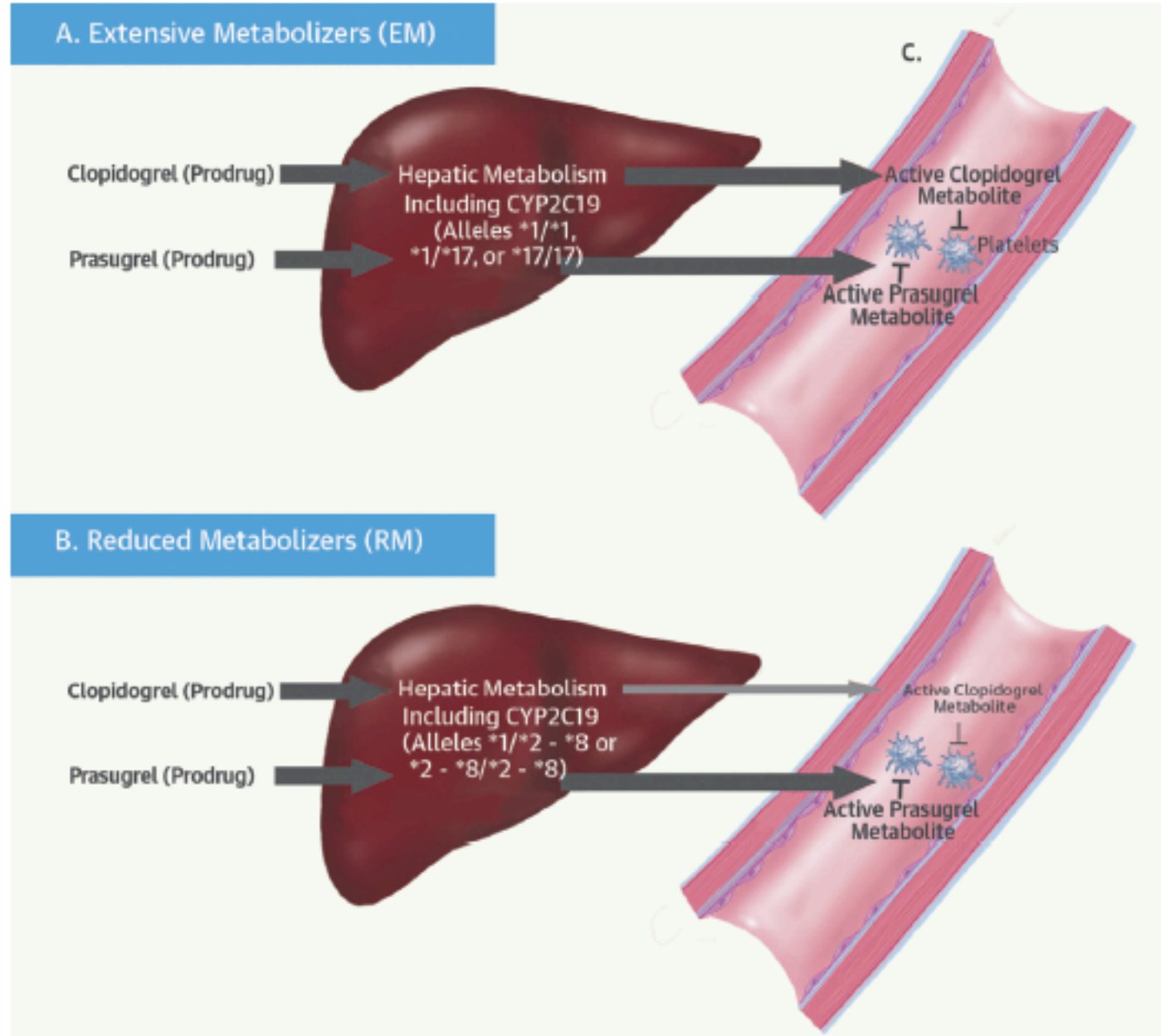
Clopidogrel (Prodrug)

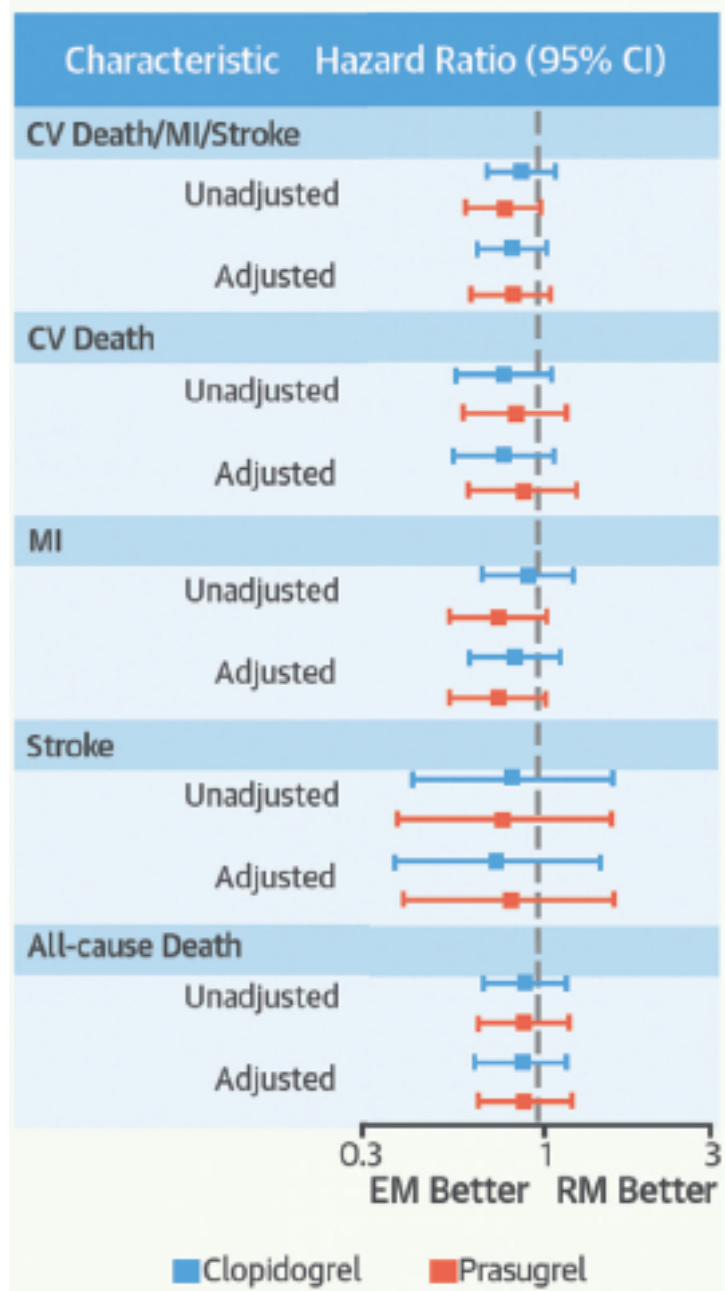
Prasugrel (Prodrug)

Hepatic Metabolism
Including CYP2C19
(Alleles *1/*2 - *8 or
*2 - *8/*2 - *8)

Active Clopidogrel
Metabolite

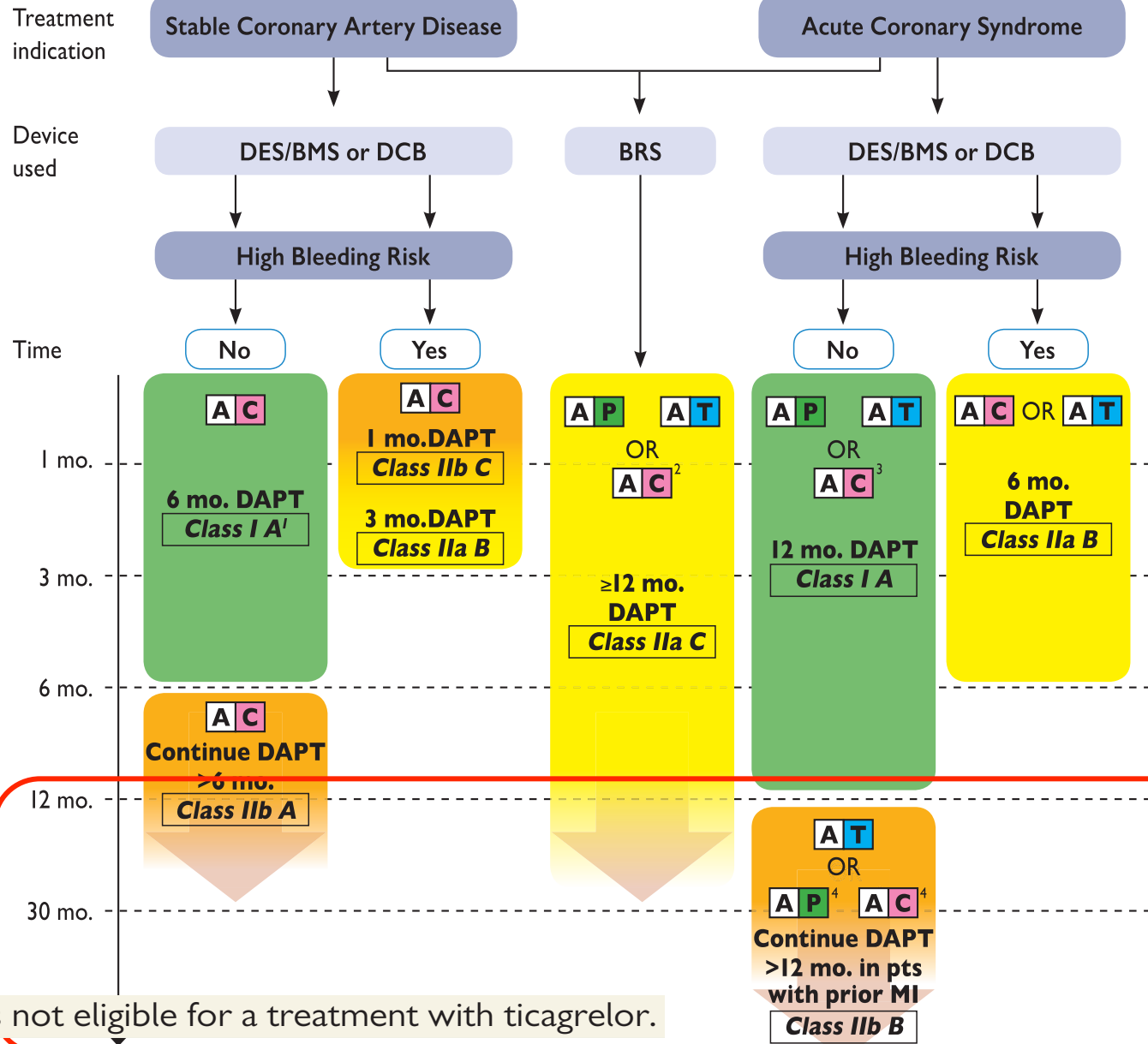
Active Prasugrel
Metabolite





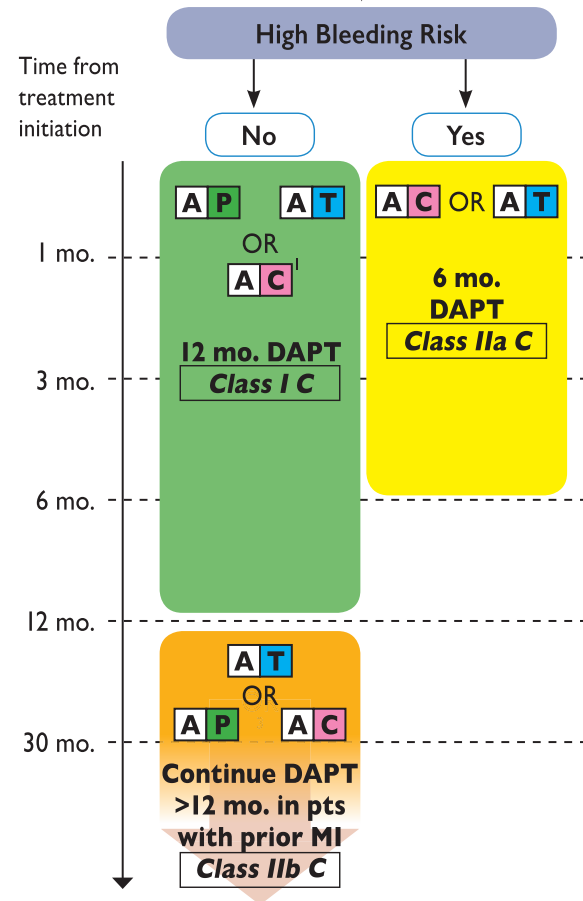
2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS

Percutaneous Coronary Intervention



⁴: If patient is not eligible for a treatment with ticagrelor.

Patients with Acute Coronary Syndrome Undergoing Coronary Artery Bypass Grafting



A = Aspirin **C** = Clopidogrel
P = Prasugrel **T** = Ticagrelor

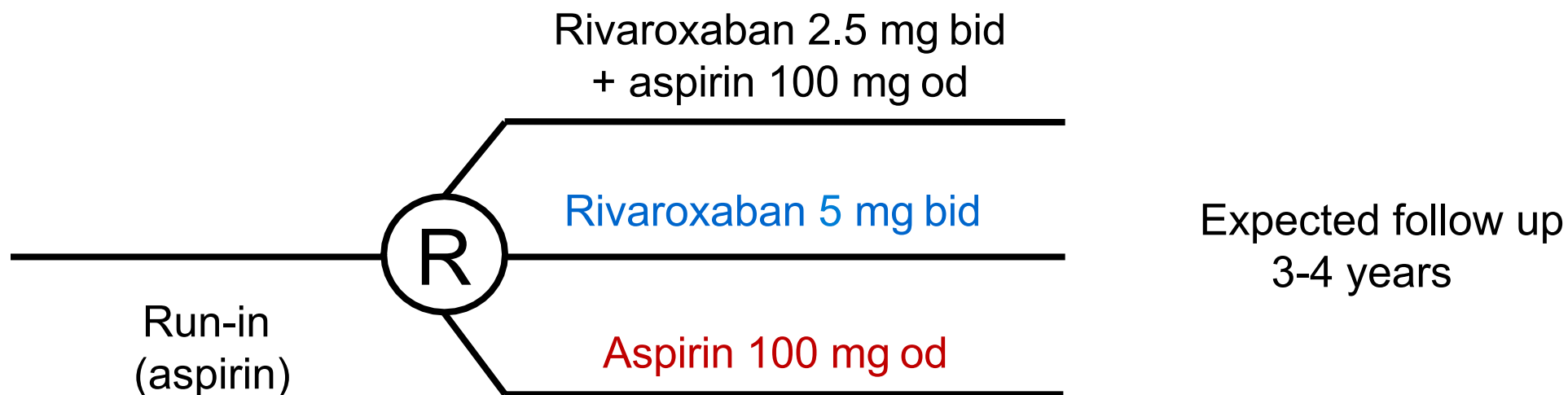
Rivaroxaban with or without aspirin in patients with stable coronary artery disease: an international, randomised, double-blind, placebo-controlled trial

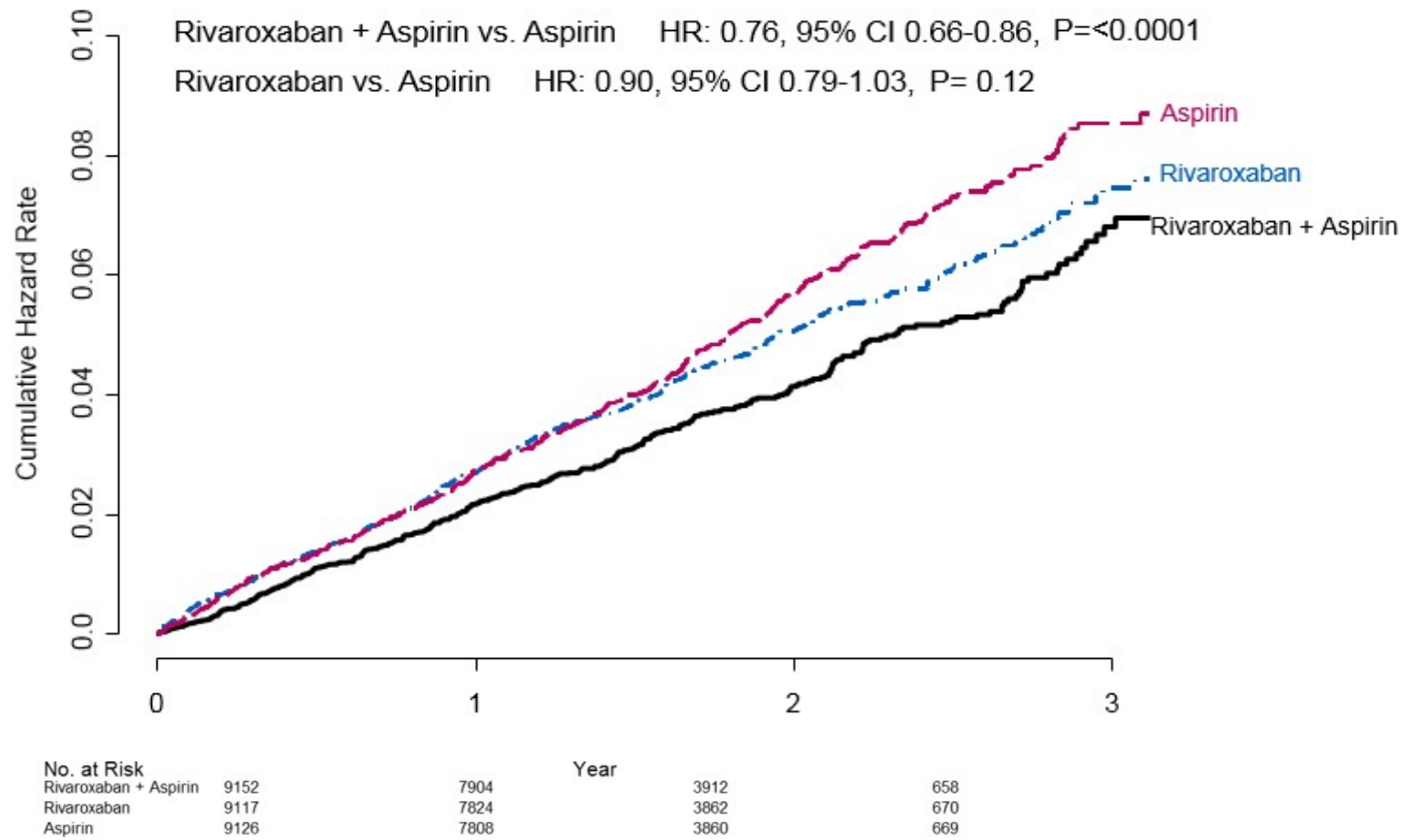


*Stuart J Connolly, John W Eikelboom, Jackie Bosch, Gilles Dagenais, Leanne Dyal, Fernando Lanas, Kaj Metsarinne, Martin O'Donnell, Anthony L Dans, Jong-Won Ha, Alexandr N Parkhomenko, Alvaro A Avezum, Eva Lonn, Liu Lisheng, Christian Torp-Pedersen, Petr Widimsky, Aldo P Maggioni, Camilo Felix, Katalin Keltai, Masatsugu Hori, Khalid Yusoff, Tomasz J Guzik, Deepak L Bhatt, Kelley R H Branch, Nancy Cook Bruns, Scott D Berkowitz, Sonia S Anand, John D Varigos, Keith A A Fox, Salim Yusuf, on behalf of the COMPASS investigators**

COMPASS design

Stable CAD or PAD
2,200 with a primary outcome event





Major bleeding

Outcome	R + A N=9,152	R N=9,117	A N=9,126	Rivaroxaban + Aspirin vs. Aspirin		Rivaroxaban vs. Aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	P	HR (95% CI)	P
Major bleeding	288 (3.1%)	255 (2.8%)	170 (1.9%)	1.70 (1.40-2.05)	<0.0001	1.51 (1.25-1.84)	<0.0001
Fatal	15 (0.2%)	14 (0.2%)	10 (0.1%)	1.49 (0.67-3.33)	0.32	1.40 (0.62-3.15)	0.41
Non fatal ICH*	21 (0.2%)	32 (0.4%)	19 (0.2%)	1.10 (0.59-2.04)	0.77	1.69 (0.96-2.98)	0.07
Non-fatal other critical organ*	42 (0.5%)	45 (0.5%)	29 (0.3%)	1.43 (0.89-2.29)	0.14	1.57 (0.98-2.50)	0.06

Outcome	R + A N=9,152	A N=9,126	Rivaroxaban + Aspirin vs. Aspirin	
	N (%)	N (%)	HR (95% CI)	P
Net clinical benefit (Primary + Severe bleeding events)	431 (4.7%)	534 (5.9%)	0.80 (0.70-0.91)	0.0005

En conclusion

Le principe de DATP « à la carte » après 1 an est acquis.

N'influencent le choix :
Le sexe
La génétique...
Les tests de réactivités

Influencent le choix :
Une atteinte athéromateuse TC ou IVA
ATC complexe
La molécule : ticagrelor/Rivaroxaban
Le score DAPT
Le risque hémorragique

