Vers une durée personnalisée du traitement anti-plaquettaire?

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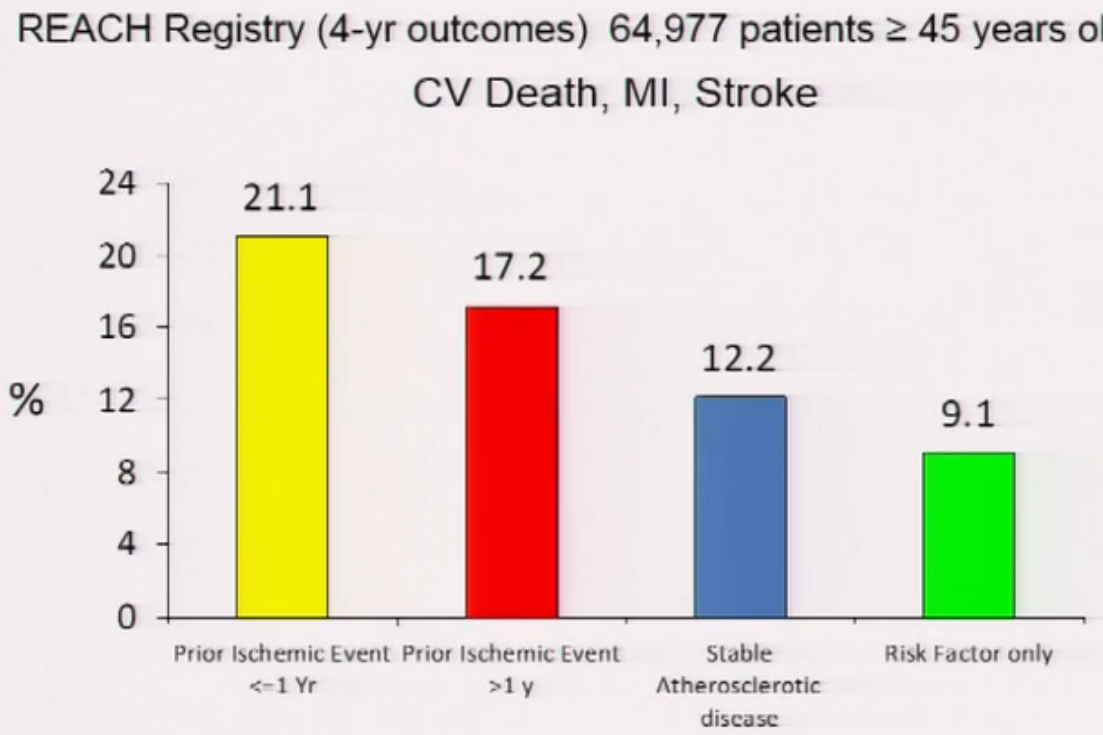
Disclosures

- Lecture fees from AstraZeneca, Sanofi
- Consulting fees from AstraZeneca, Daiichi-Sankyo

Quel est l'objectif de la DAPT post-PCI ?

1. Prévenir la thrombose de stent
2. Prévenir les récidives ischémiques cardiologiques/neurologiques/périphériques

Patients with prior MI remain at high risk for ischemic events



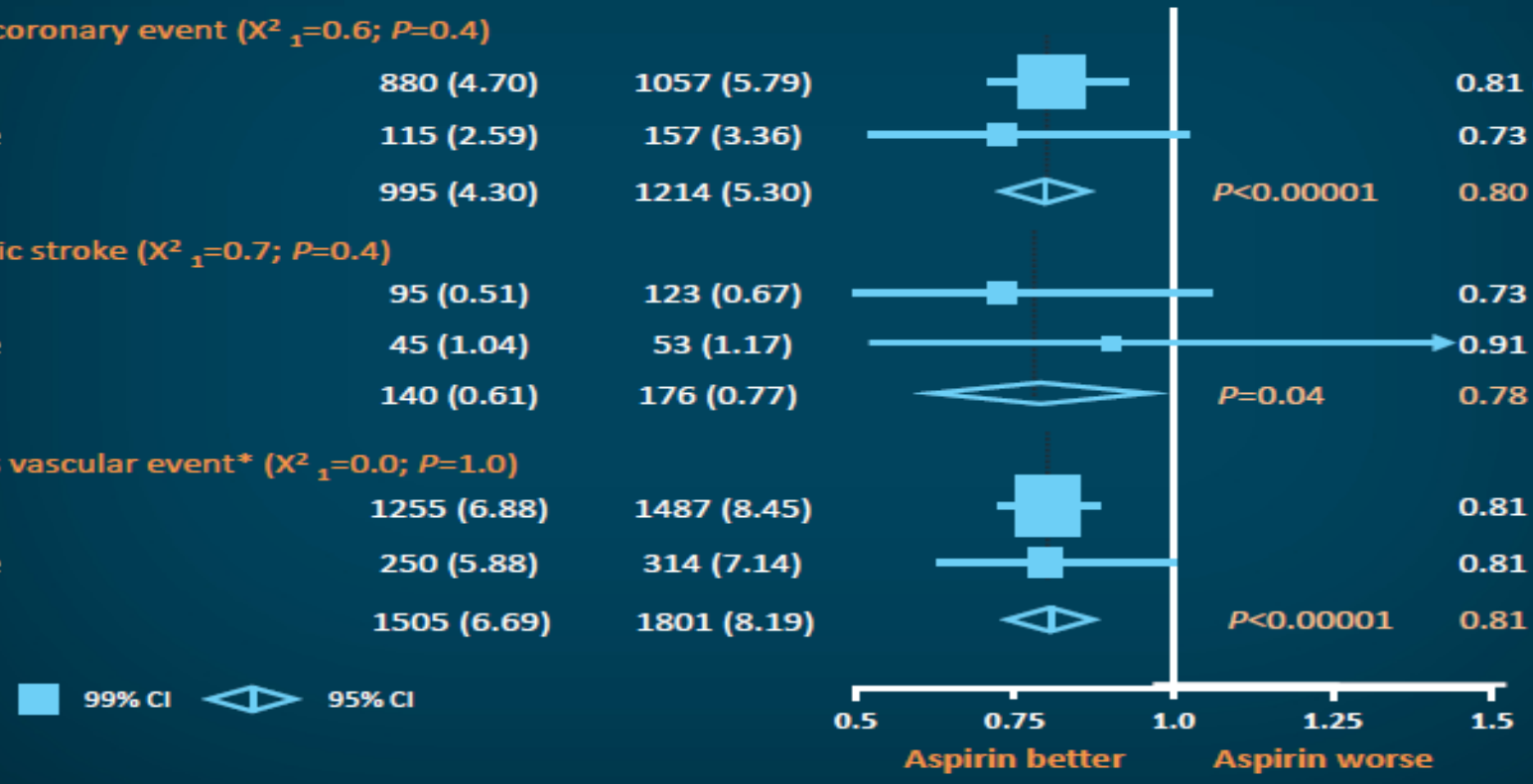
Bhatt et al. JAMA 2010; 304:1350-7

D’où venons-nous ?

Aspirin in Primary and Secondary Prevention

Meta-analyses of 16 secondary prevention trials (n = 17,000)

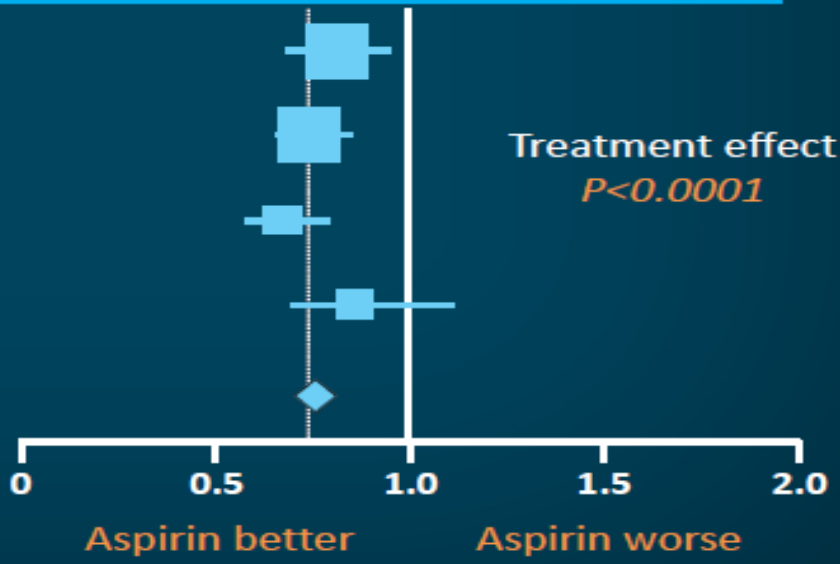
Events per year	Aspirin	Control	RR (CI)
Major coronary event (X^2_1=0.6; P=0.4)			
Male	880 (4.70)	1057 (5.79)	0.81 (0.72–0.92)
Female	115 (2.59)	157 (3.36)	0.73 (0.51–1.03)
Total	995 (4.30)	1214 (5.30)	P<0.00001 0.80 (0.73–0.88)
Ischemic stroke (X^2_1=0.7; P=0.4)			
Male	95 (0.51)	123 (0.67)	0.73 (0.50–1.06)
Female	45 (1.04)	53 (1.17)	0.91 (0.52–1.57)
Total	140 (0.61)	176 (0.77)	P=0.04 0.78 (0.61–0.99)
Serious vascular event* (X^2_1=0.0; P=1.0)			
Male	1255 (6.88)	1487 (8.45)	0.81 (0.73–0.90)
Female	250 (5.88)	314 (7.14)	0.81 (0.64–1.02)
Total	1505 (6.69)	1801 (8.19)	P<0.00001 0.81 (0.75–0.87)



Antithrombotic Trialists' Collaboration. *Lancet.* 2009;373(9678):1849-1860.

Efficacy of Aspirin at Various Doses in Reducing Vascular Events in High-risk Patients (Death from Vascular Causes, MI, or Stroke)

Aspirin (mg daily)	No. of Trials	% Odds Reduction
500–1500	34	19
160–325	19	26
75–150	12	32
<75	3	13
Any aspirin	65	23

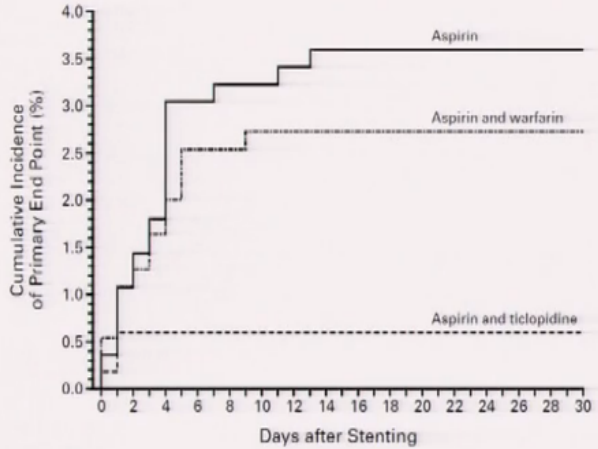


Antithrombotic Trialists' Collaboration. *BMJ.* 2002;324:71-86.

Les débuts de la DAPT

Antithrombotic therapy after coronary stenting

1653 patients (1772 lesions) with successful stent implantation

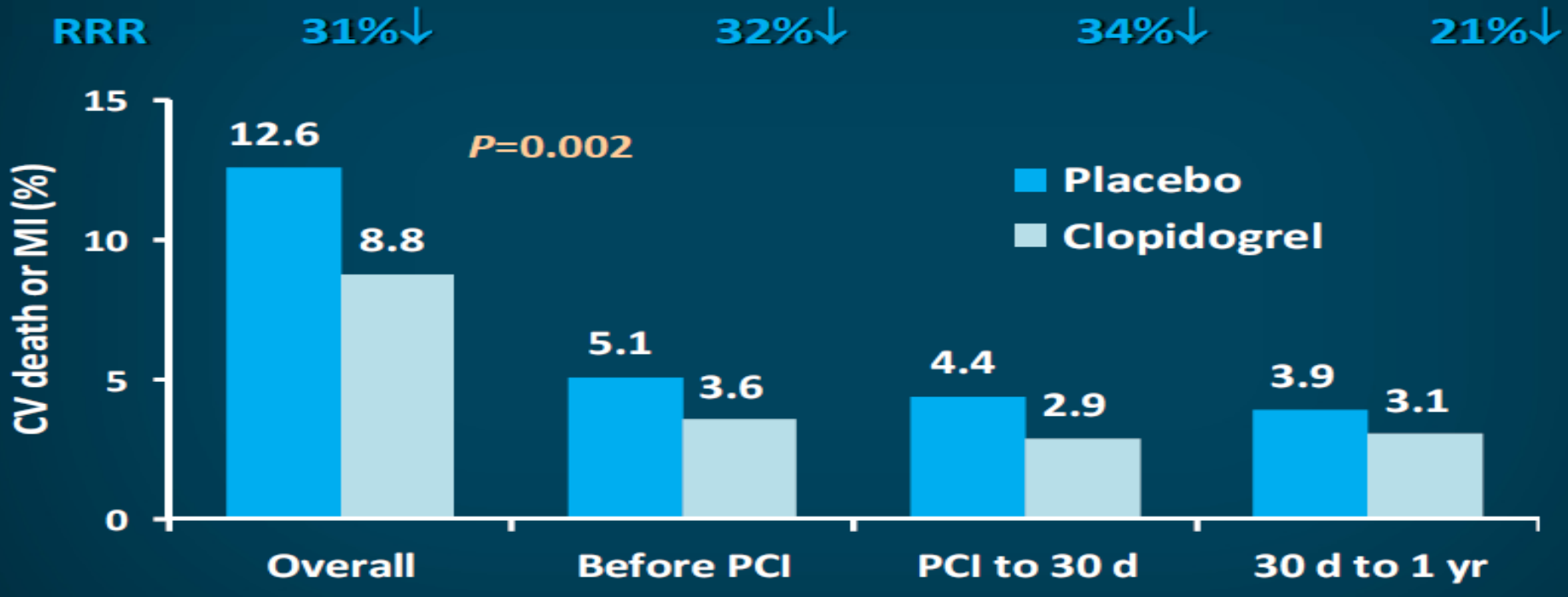


"Antithrombotic drugs are used after coronary-artery stenting to prevent stent thrombosis... After coronary stenting, aspirin and ticlopidine should be considered for the prevention of the serious complication of stent thrombosis"

Leon et al. NEJM 1998

PCI-CURE

CV Death or MI at Various Intervals



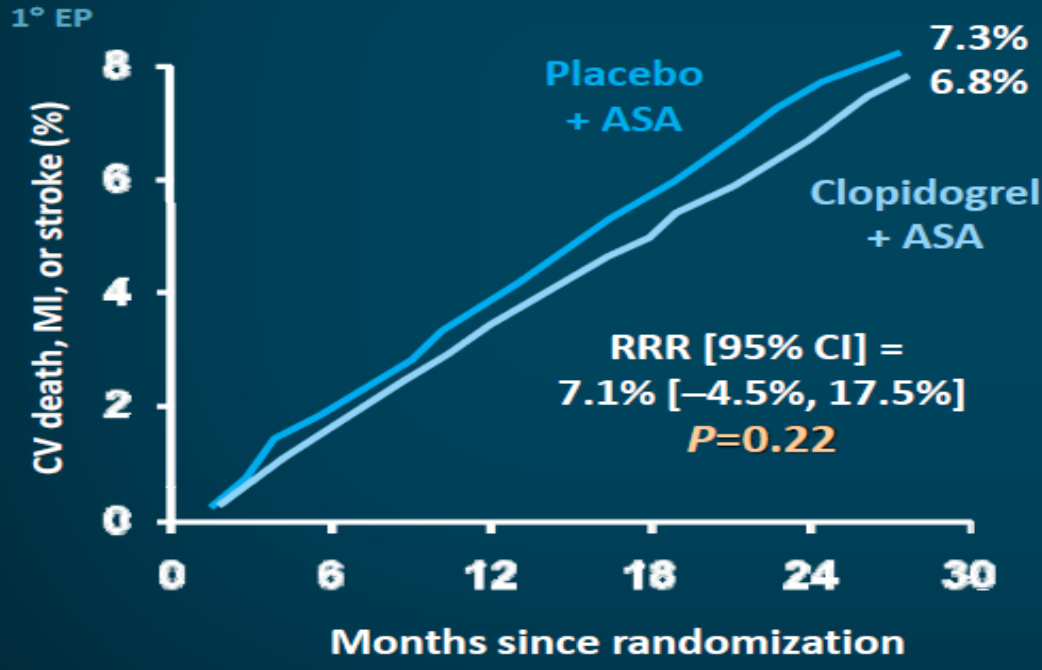
CV = cardiovascular; MI = myocardial infarction; PCI = percutaneous coronary intervention; d = day; yr = year; RRR = relative risk reduction.

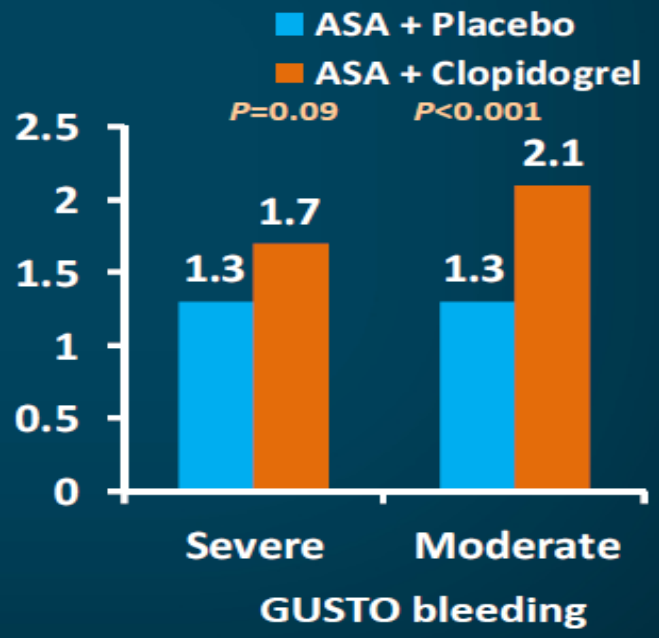
Adapted from Mehta SR et al. *Lancet.* 2001;358(9281):527-533.

CHARISMA

Long-term clopidogrel for 1° or 2° prevention

15,603 pts age >45 yrs. with either clinically evident CV ds. or multiple risk factors were treated with aspirin (75–162 mg/d), randomized to clopidogrel 75 mg/d vs. placebo, and followed for a median of 28 months





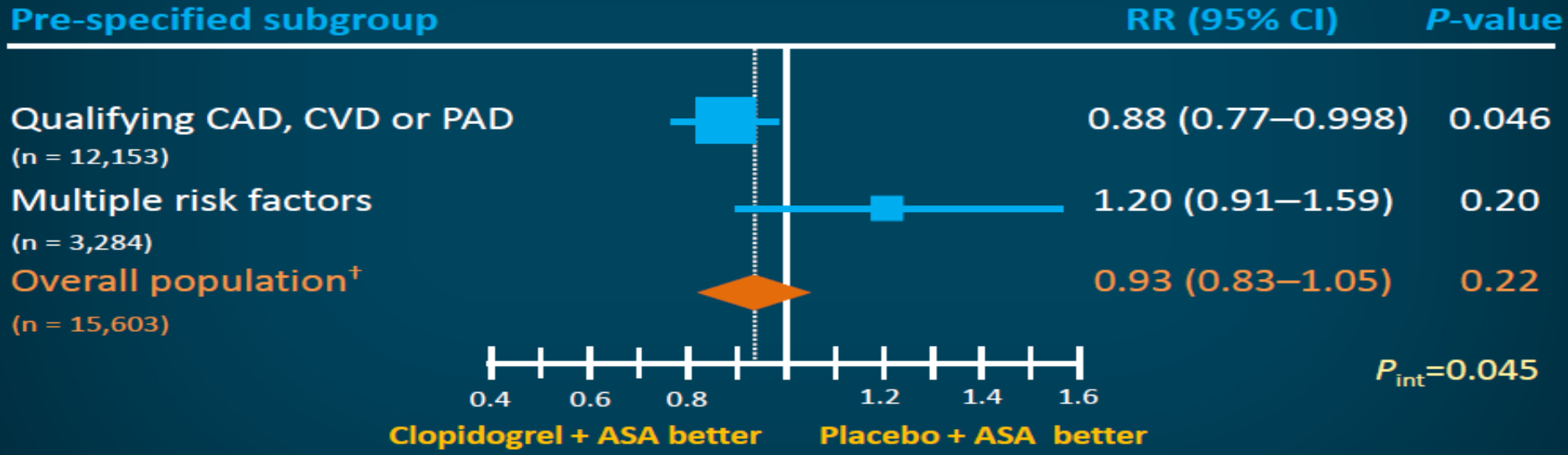
ASA = aspirin; RRR = relative risk reduction; CV = cardiovascular; MI = myocardial infarction.

Bhatt DK et al. *N Engl J Med.* 2006;354:1706-1717.

CHARISMA

Long-term clopidogrel for 1° or 2° prevention

15,603 pts age >45 yrs with either clinically evident CV ds. or multiple risk factors were treated with aspirin (75–162 mg/d), randomized to clopidogrel 75 mg/d vs. placebo, and followed for a median of 28 months



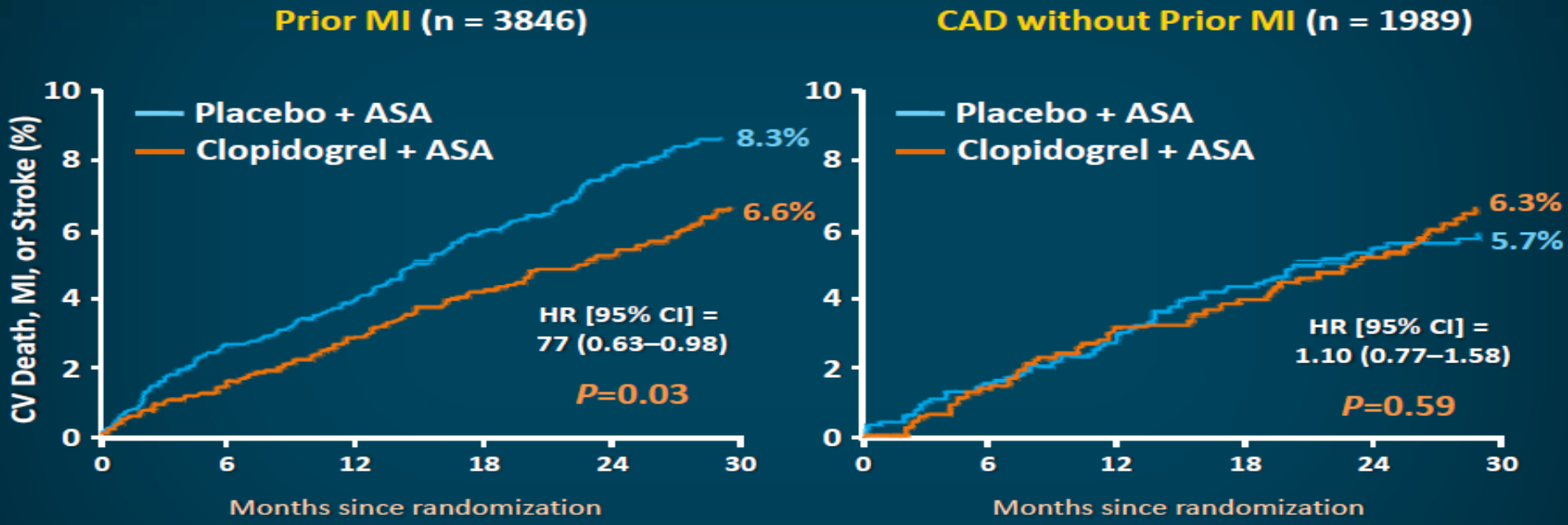
†166 patients did not meet any of the main inclusion criteria

CAD = coronary artery disease; CVD = coronary vascular disease; PAD = peripheral arterial disease; RR = relative reduction.

Bhatt DL et al. *N Engl J Med.* 2006;354:1706-1717.

CHARISMA

(5835 patients had CAD)

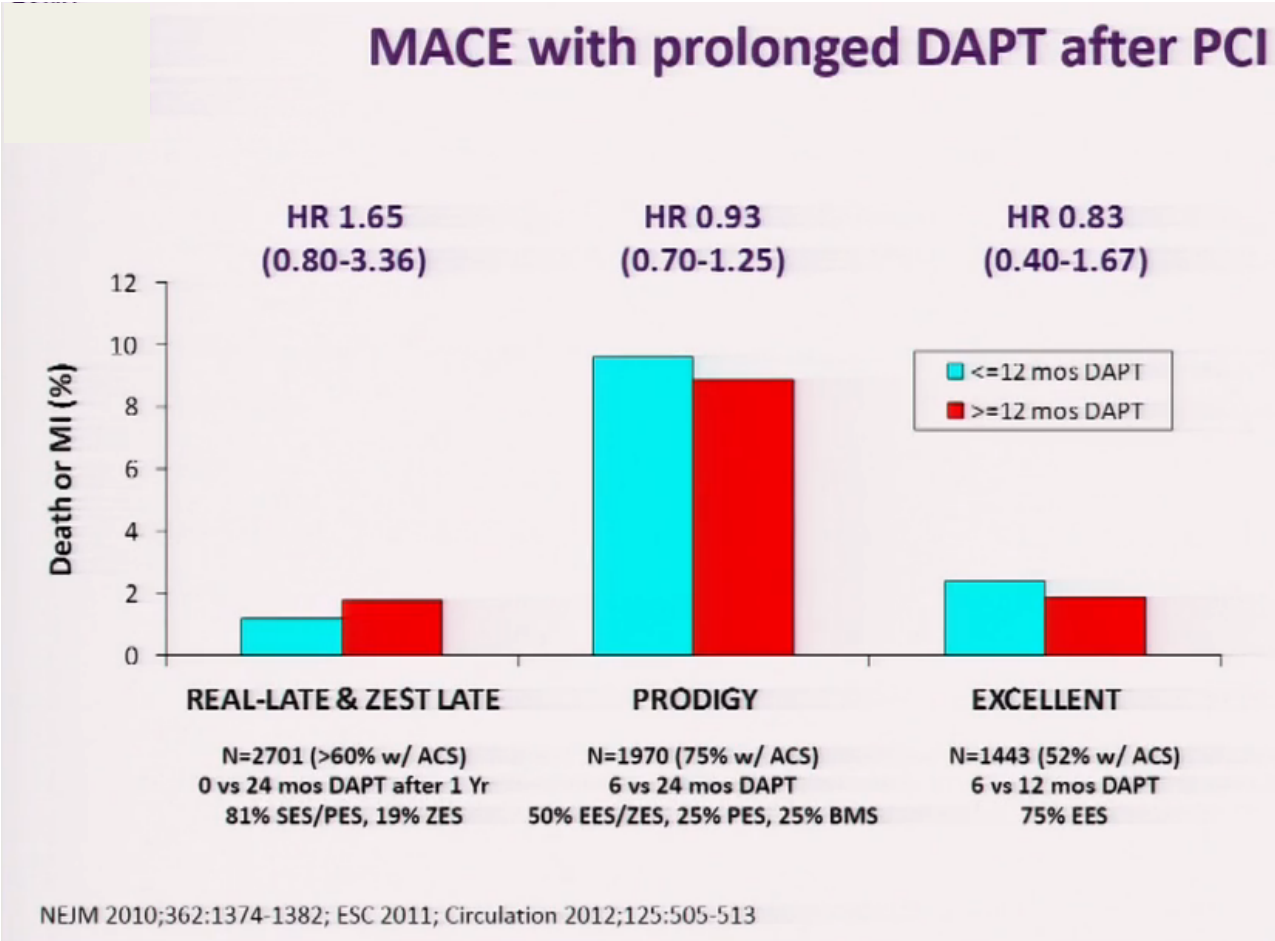


Median time from MI to randomization = 23.6 months

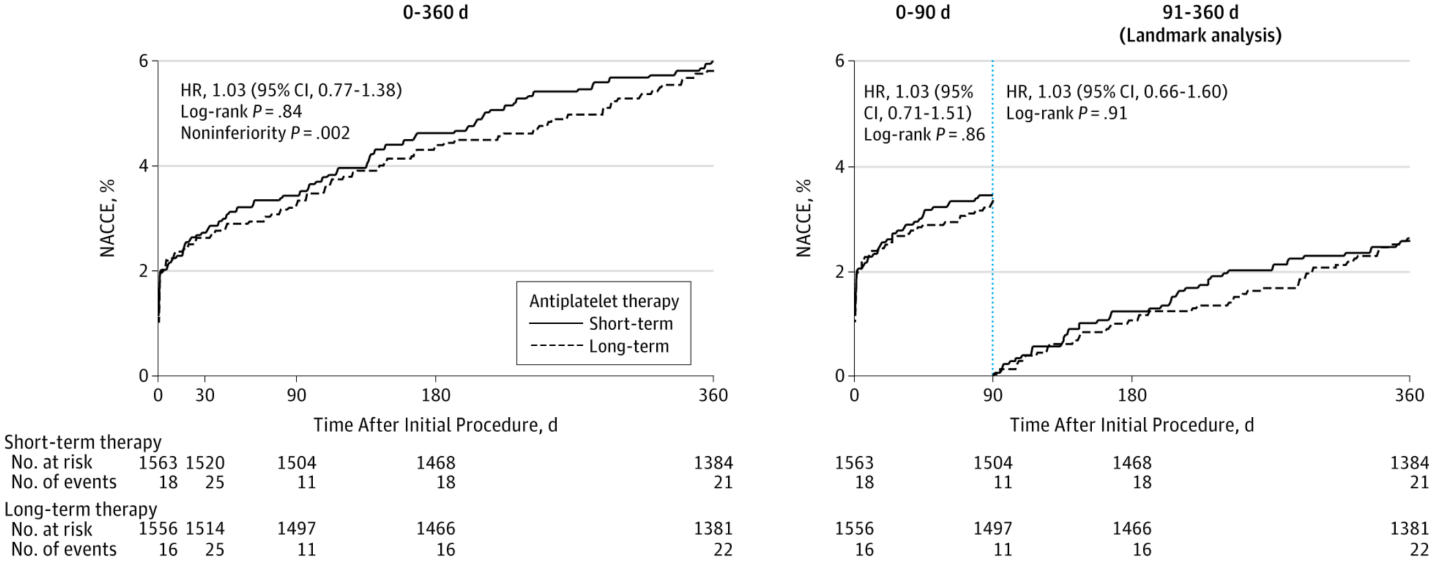
CV = cardiovascular; MI = myocardial infarction; ASA = aspirin; CAD = coronary artery disease.

Bhatt DL et al. *J Am Coll Cardiol*. 2007;49:1982-1988.

Les essais sur la durée de la DAPT



OPTIMIZE-trial: 3-12 mois



Short-term therapy					
No. at risk	1563	1520	1504	1468	1384
No. of events	18	25	11	18	21
Long-term therapy					
No. at risk	1556	1514	1497	1466	1381
No. of events	16	25	11	16	22

1563	1504	1468	1384	
18	11	18	21	
1556	1497	1466	1381	
16	11	16	22	

Fères JAMA 2015

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 4, 2014 VOL. 371 NO. 23

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*

Population (n= 10,000)

- Une population hétérogène…

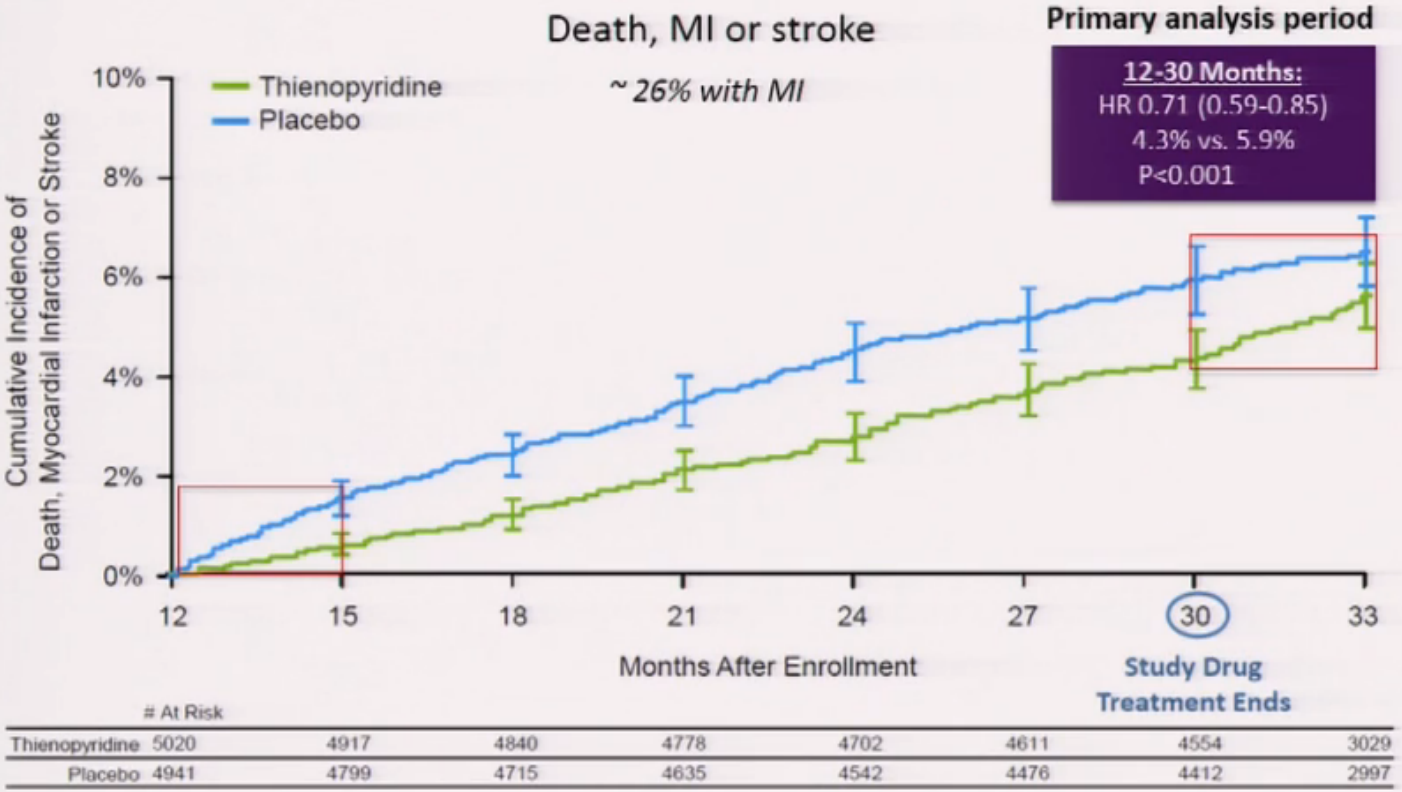
Indication for PCI — no. (%)		
STEMI	534 (10.6)	511 (10.3)
NSTEMI	776 (15.5)	767 (15.5)
Unstable angina¶	838 (16.7)	825 (16.7)
Stable angina	1882 (37.5)	1870 (37.8)
Other	990 (19.7)	968 (19.6)
Type of drug-eluting stent at index procedure — no. (%)		
Everolimus-eluting	2345 (46.7)	2358 (47.7)
Paclitaxel-eluting	1350 (26.9)	1316 (26.6)
Zotarolimus-eluting	642 (12.8)	622 (12.6)
Sirolimus-eluting	577 (11.5)	541 (10.9)
>1 type	106 (2.1)	104 (2.1)

- 55% des bénéfices observés ne sont pas en rapport avec les ST

- Surcroit d'évènement dans les 3 mois suivants l'arrêt de la DAPT

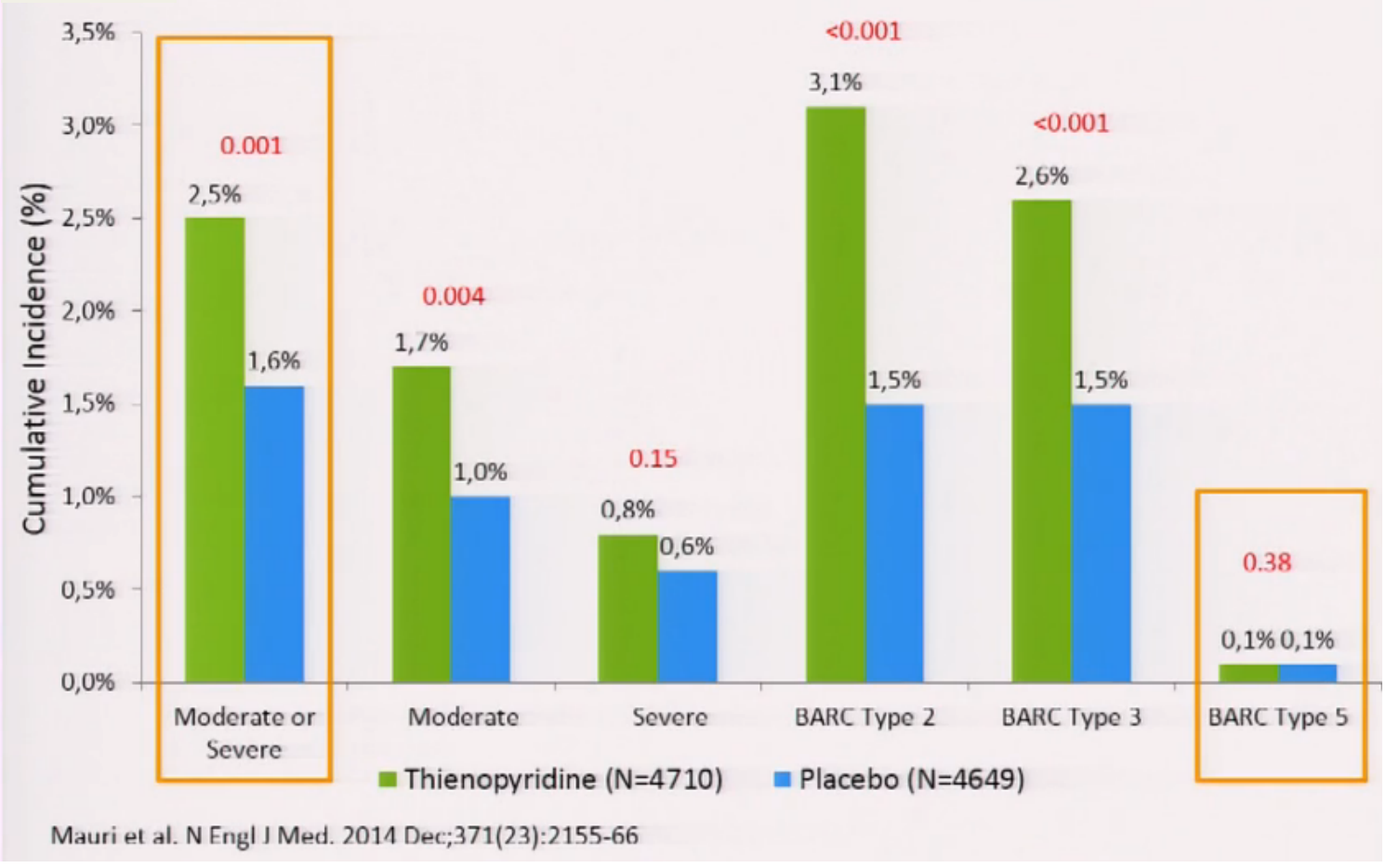
=> L'ARRET EST UN PROCESSUS ACTIF

DAPT: Continuation or withdrawal of thienopyridine 12 months after coronary stenting



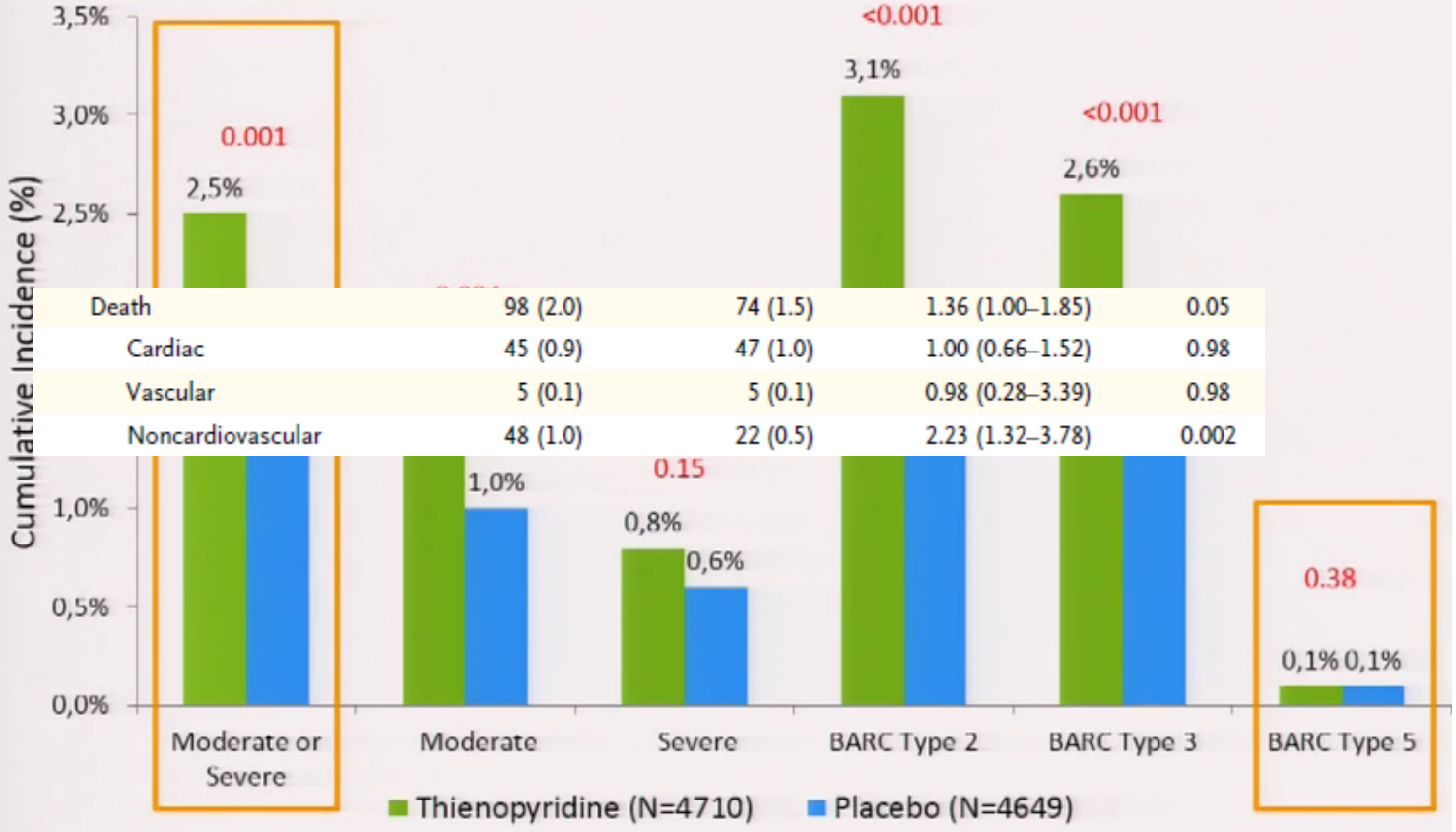
Mauri et al. NEJM 2014

DAPT: Primary safety end point (moderate or severe bleeding) 12-30 months



Mauri et al. N Engl J Med. 2014 Dec;371(23):2155-66

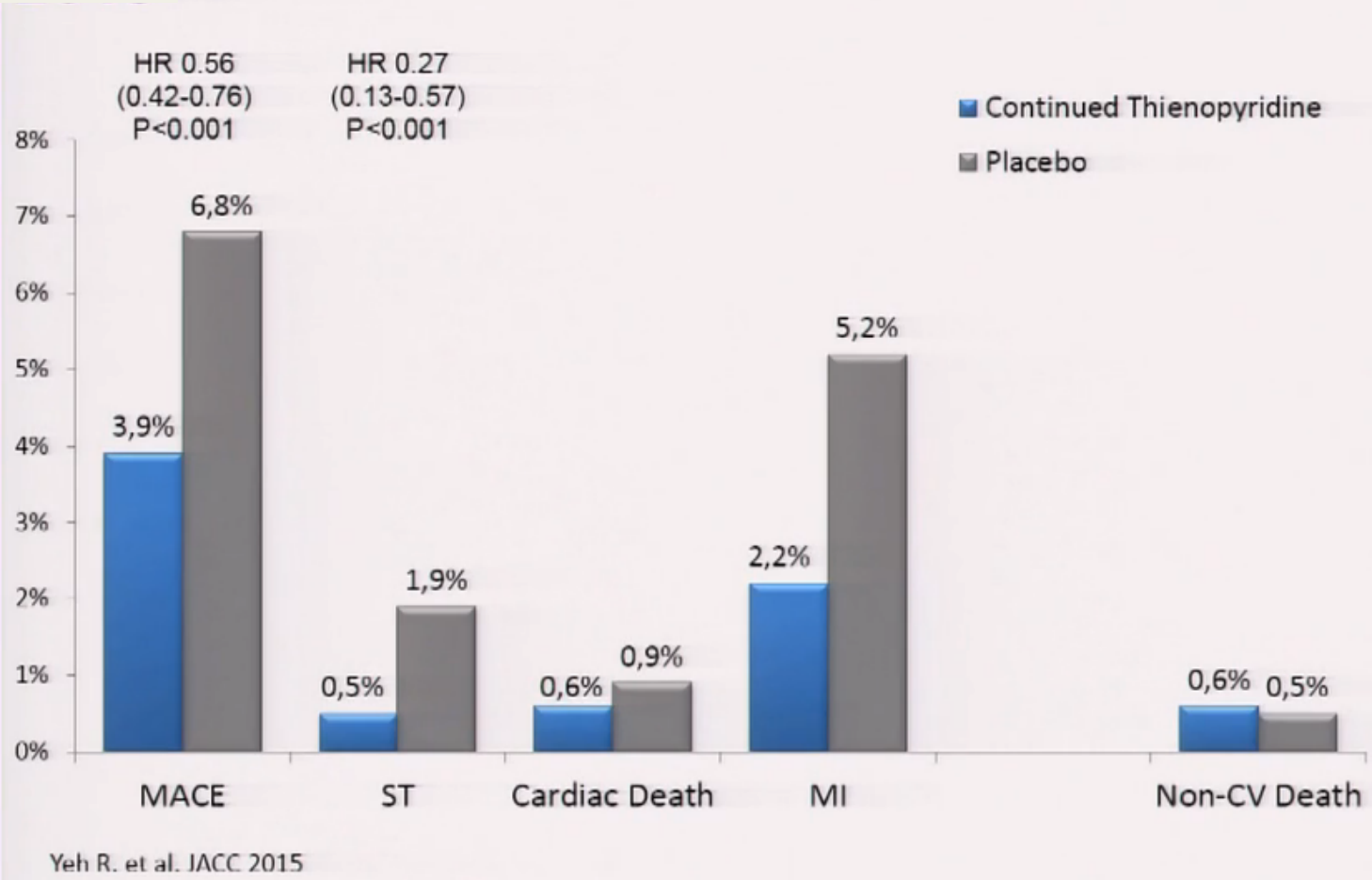
DAPT: Primary safety end point (moderate or severe bleeding) 12-30 months



Death	98 (2.0)	74 (1.5)	1.36 (1.00–1.85)	0.05
Cardiac	45 (0.9)	47 (1.0)	1.00 (0.66–1.52)	0.98
Vascular	5 (0.1)	5 (0.1)	0.98 (0.28–3.39)	0.98
Noncardiovascular	48 (1.0)	22 (0.5)	2.23 (1.32–3.78)	0.002

Mauri et al. N Engl J Med. 2014 Dec;371(23):2155-66

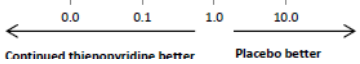
Treatment Effect in ACS Patients



Yeh R. et al. JACC 2015

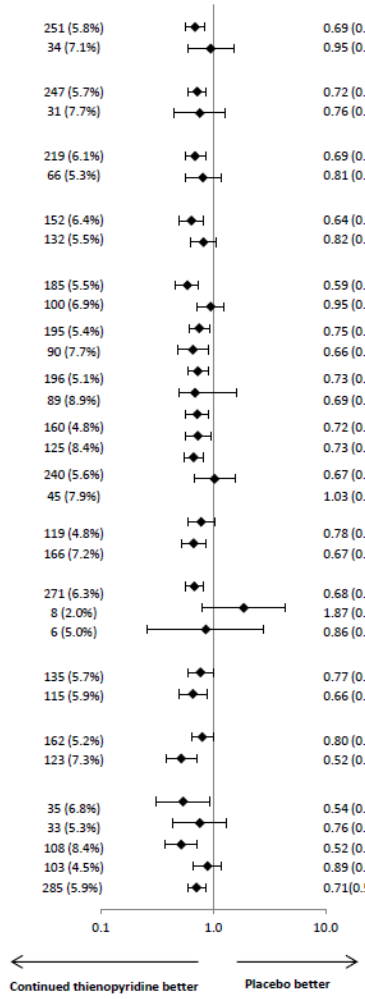
DAPT: ST selon sous-groupes

Factor	N	Continued Thienopyridine N (%)	Placebo N (%)	HR and 95% CI	HR[2] and 95% CI	P Value for Interaction
Age						0.84
< 75 Years	N=8929	18 (0.4%)	61 (1.4%)		0.29 (0.17,0.49)	
>= 75 Years	N=1032	1 (0.2%)	4 (0.8%)		0.23 (0.03,2.06)	
Race						0.34
White	N=8908	16 (0.4%)	58 (1.3%)		0.27 (0.16,0.47)	
Non-White	N=857	3 (0.7%)	5 (1.3%)		0.57 (0.14,2.40)	
Sex						0.04
Male	N=7435	12 (0.3%)	55 (1.5%)		0.21 (0.11,0.39)	
Female	N=2526	7 (0.6%)	10 (0.8%)		0.73 (0.28,1.91)	
BMI						0.54
< Median	N=4931	10 (0.4%)	38 (1.6%)		0.25 (0.13,0.51)	
>= Median	N=4943	9 (0.4%)	26 (1.1%)		0.35 (0.16,0.74)	
Medical History						
No diabetes	N=6924	10 (0.3%)	49 (1.5%)		0.20 (0.10,0.40)	0.08
Diabetes	N=3037	9 (0.6%)	16 (1.1%)		0.53 (0.23,1.20)	
No Current Tobacco Use	N=7529	13 (0.4%)	36 (1.0%)		0.35 (0.19,0.67)	0.31
Current Tobacco Use	N=2432	6 (0.5%)	29 (2.5%)		0.20 (0.08,0.49)	
No Prior MI	N=7843	14 (0.4%)	47 (1.2%)		0.30 (0.16,0.54)	0.80
Prior MI	N=2118	5 (0.5%)	18 (1.8%)		0.26 (0.10,0.69)	
No Prior PCI	N=6914	7 (0.2%)	37 (1.1%)		0.18 (0.08,0.41)	0.12
Prior PCI	N=3047	12 (0.8%)	28 (1.9%)		0.42 (0.22,0.84)	
No Prior CABG	N=8812	15 (0.4%)	55 (1.3%)		0.27 (0.15,0.47)	0.52
Prior CABG	N=1149	4 (0.7%)	10 (1.8%)		0.41 (0.13,1.30)	
Clinical or Lesion RF for ST						
No Clinical or Lesion RFs for ST	N=5162	7 (0.3%)	25 (1.0%)		0.27 (0.12,0.63)	0.89
Any Clinical or Lesion RF for ST	N=4799	12 (0.5%)	40 (1.7%)		0.29 (0.15,0.56)	
Region						1.00
North America	N=8918	19 (0.4%)	62 (1.4%)		0.30 (0.18,0.50)	
European Union	N=807	0 (0.0%)	2 (0.5%)		-(-,-)	
Australia/New Zealand	N=236	0 (0.0%)	1 (0.8%)		-(-,-)	
Aspirin Dose at Randomization						0.17
≤ 100 mg	N=4825	7 (0.3%)	34 (1.5%)		0.20 (0.09,0.46)	
> 100 mg	N=4036	12 (0.6%)	27 (1.4%)		0.43 (0.22,0.84)	
Thienopyridine Type						0.54
Clopiodogrel	N=6500	9 (0.3%)	27 (0.9%)		0.33 (0.16,0.71)	
Prasugrel	N=3461	10 (0.6%)	38 (2.3%)		0.24 (0.12,0.50)	
DES type						0.76
Sirolimus	N=1118	0 (0.0%)	4 (0.8%)		-(-,-)	
Zotarolimus†	N=1264	2 (0.3%)	5 (0.8%)		0.39 (0.08,2.00)	
Paclitaxel	N=2666	10 (0.8%)	38 (3.0%)		0.25 (0.13,0.51)	
Everolimus	N=4703	6 (0.3%)	16 (0.7%)		0.38 (0.15,0.97)	
Overall	**N=9961**	19 (0.4%)	65 (1.4%)		0.29 (0.17, 0.48)	

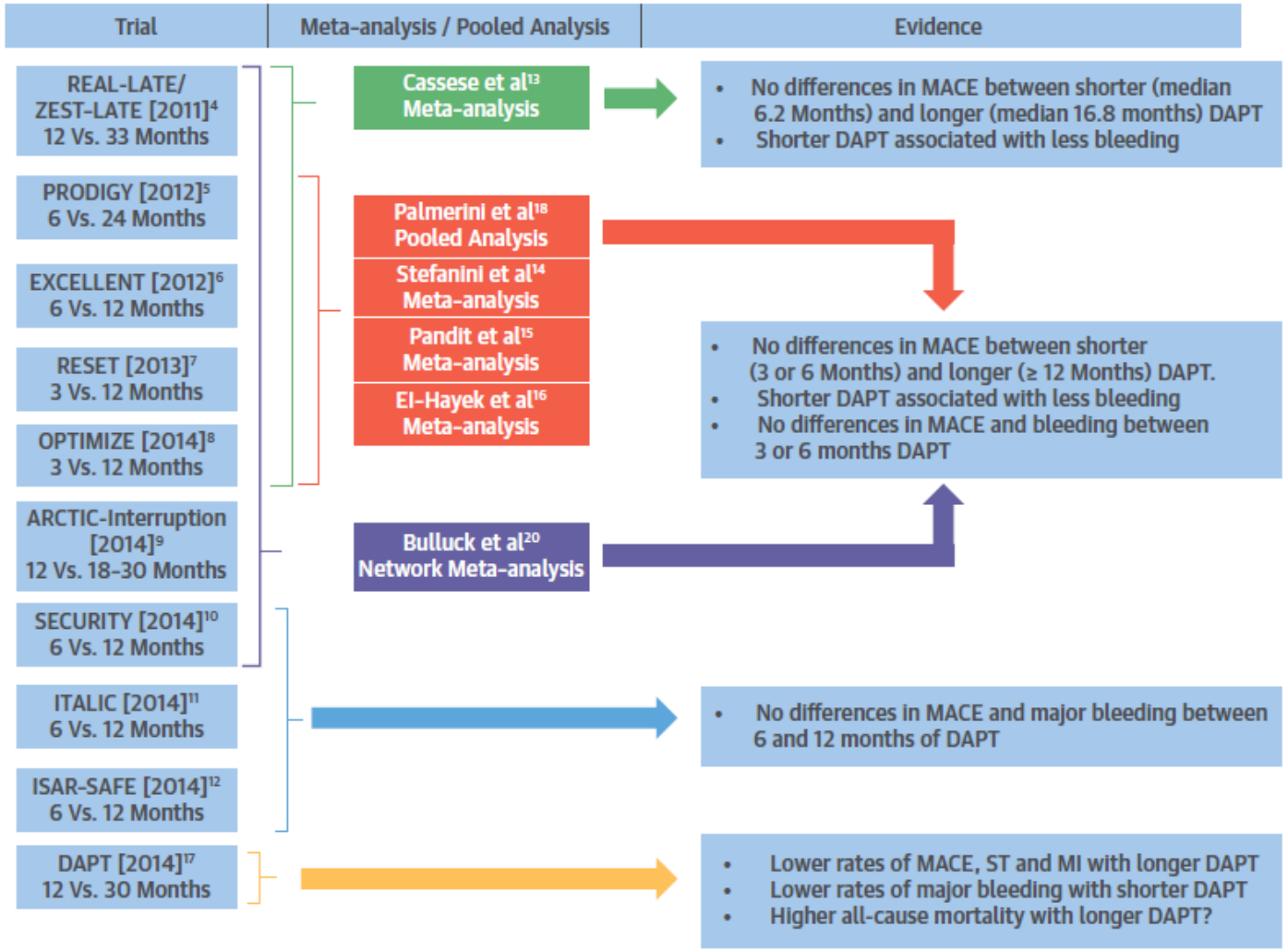


DAPT: MACCE selon sous-groupes

Factor	N	Continued Thienopyridine N (%)	Placebo N (%)	HR and 95% CI	HR[2] and 95% CI	P Value for Interaction
Age						0.22
< 75 Years	N=8929	176 (4.0%)	251 (5.8%)		0.69 (0.57,0.83)	
>= 75 Years	N=1032	35 (6.8%)	34 (7.1%)		0.95 (0.59,1.52)	
Race						0.84
White	N=8908	181 (4.2%)	247 (5.7%)		0.72 (0.59,0.87)	
Non-White	N=857	25 (6.0%)	31 (7.7%)		0.76 (0.45,1.28)	
Sex						0.46
Male	N=7435	159 (4.3%)	219 (6.1%)		0.69 (0.56,0.85)	
Female	N=2526	52 (4.4%)	66 (5.3%)		0.81 (0.56,1.17)	
BMI						0.17
< Median	N=4931	102 (4.2%)	152 (6.4%)		0.64 (0.50,0.82)	
>= Median	N=4943	108 (4.5%)	132 (5.5%)		0.82 (0.63,1.05)	
Medical History						
No diabetes	N=6924	110 (3.3%)	185 (5.5%)		0.59 (0.46,0.74)	0.01
Diabetes	N=3037	101 (6.7%)	100 (6.9%)		0.95 (0.72,1.25)	
No Current Tobacco Use	N=7529	150 (4.1%)	195 (5.4%)		0.75 (0.61,0.93)	0.52
Current Tobacco Use	N=2432	61 (5.2%)	90 (7.7%)		0.66 (0.48,0.91)	
No Prior MI	N=7843	144 (3.8%)	196 (5.1%)		0.73 (0.59,0.90)	0.77
Prior MI	N=2118	67 (6.3%)	89 (8.9%)		0.69 (0.50,0.94)	
No Prior PCI	N=6914	118 (3.5%)	160 (4.8%)		0.72 (0.56,0.91)	0.93
Prior PCI	N=3047	93 (6.3%)	125 (8.4%)		0.73 (0.56,0.95)	
No Prior CABG	N=8812	165 (3.8%)	240 (5.6%)		0.67 (0.55,0.81)	0.06
Prior CABG	N=1149	46 (8.3%)	45 (7.9%)		1.03 (0.68,1.56)	
Clinical or Lesion RF for ST						
No Clinical or Lesion RFs for ST	N=5162	96 (3.8%)	119 (4.8%)		0.78 (0.60,1.03)	0.41
Any Clinical or Lesion RF for ST	N=4799	115 (4.9%)	166 (7.2%)		0.67 (0.53,0.86)	
Region						0.08
North America	N=8918	191 (4.4%)	271 (6.3%)		0.68 (0.57,0.82)	
European Union	N=807	15 (3.8%)	8 (2.0%)		1.87 (0.79,4.41)	
Australia/New Zealand	N=236	5 (4.3%)	6 (5.0%)		0.86 (0.26,2.82)	
Aspirin Dose at Randomization						0.43
≤ 100 mg	N=4825	106 (4.5%)	135 (5.7%)		0.77 (0.60,1.00)	
> 100 mg	N=4036	80 (4.0%)	115 (5.9%)		0.66 (0.50,0.88)	
Thienopyridine Type						0.03
Clopiodogrel	N=6500	143 (4.5%)	162 (5.2%)		0.80 (0.64,1.01)	
Prasugrel	N=3461	68 (4.0%)	123 (7.3%)		0.52 (0.38,0.71)	
DES type						0.048
Sirolimus	N=1118	23 (4.2%)	35 (6.8%)		0.54 (0.31,0.93)	
Zotarolimus†	N=1264	25 (4.0%)	33 (5.3%)		0.76 (0.44,1.30)	
Paclitaxel	N=2666	59 (4.5%)	108 (8.4%)		0.52 (0.37,0.71)	
Everolimus	N=4703	97 (4.3%)	103 (4.5%)		0.89 (0.67,1.18)	
Overall	**N=9961**	211 (4.3%)	285 (5.9%)		0.71(0.59, 0.85)	

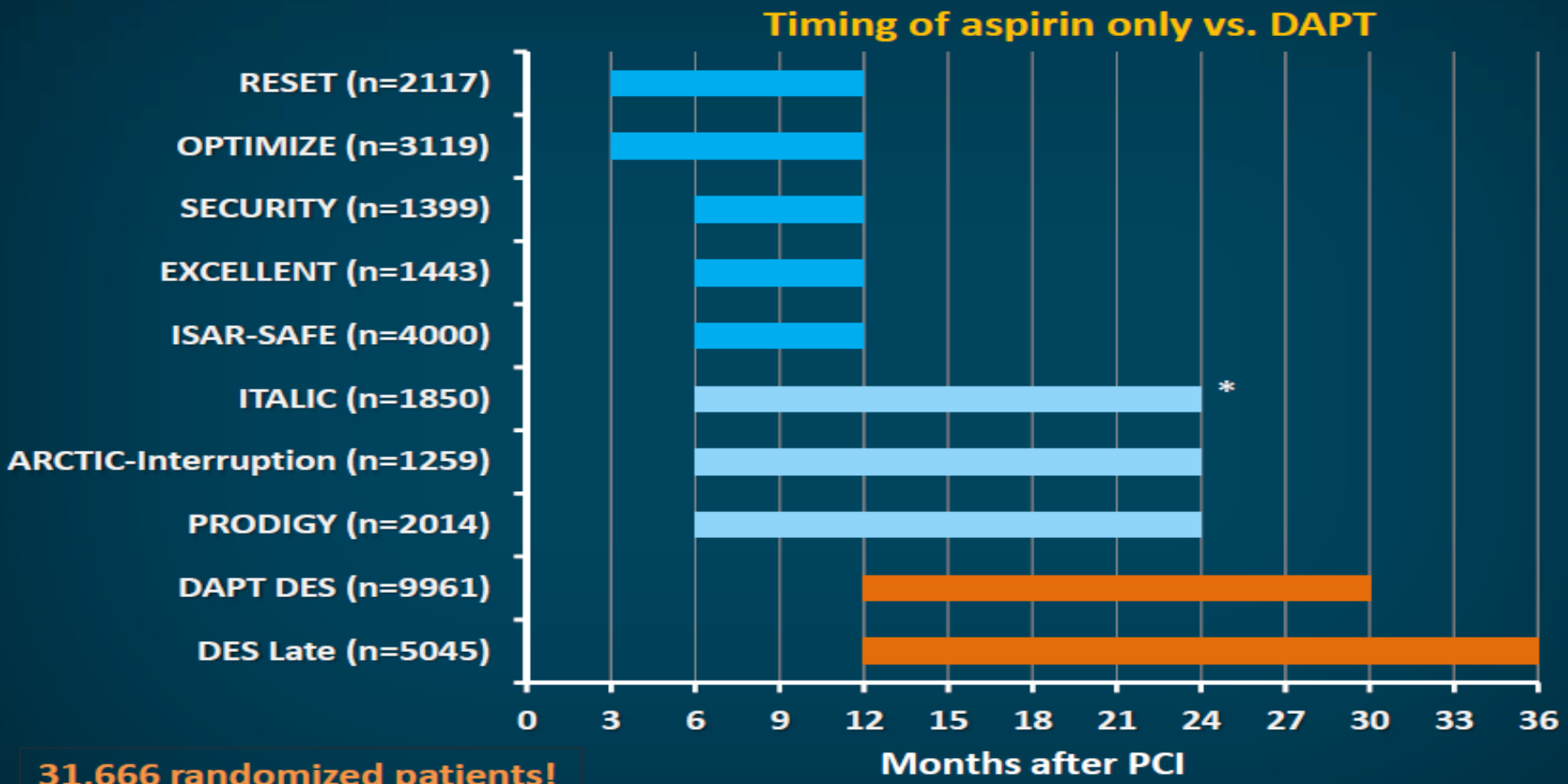


Méta-analyse…



Mehran R. JACC 2015

10 Trials of DAPT Duration after DES



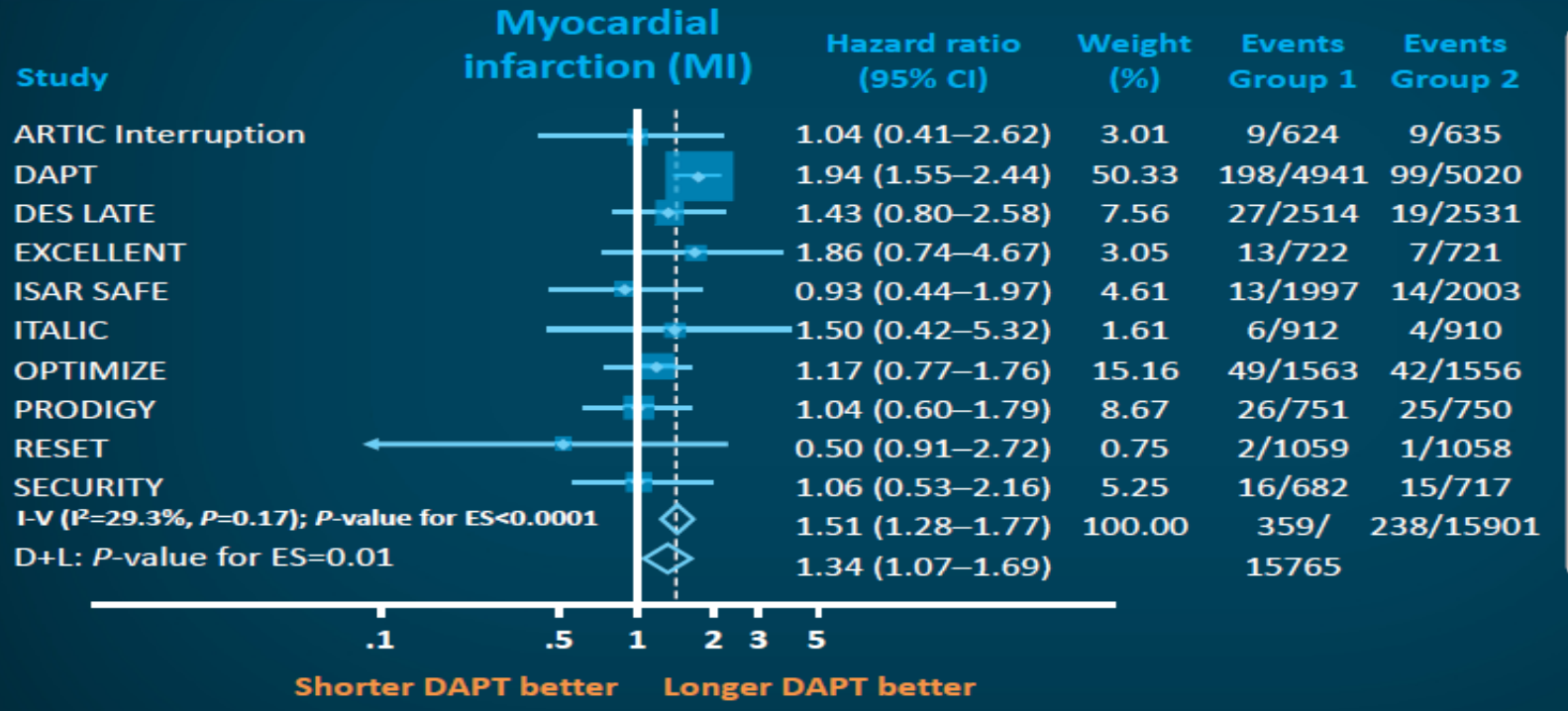
31,666 randomized patients!

*Primary endpoint at 12 months

Palmerini T et al. *Lancet.* 2015; Epub ahead of print.

Mortality with Extended-Duration DAPT After DES: MI – A Pairwise and Bayesian Network

Meta-Analysis of 10 RCTs and 31,666 Patients

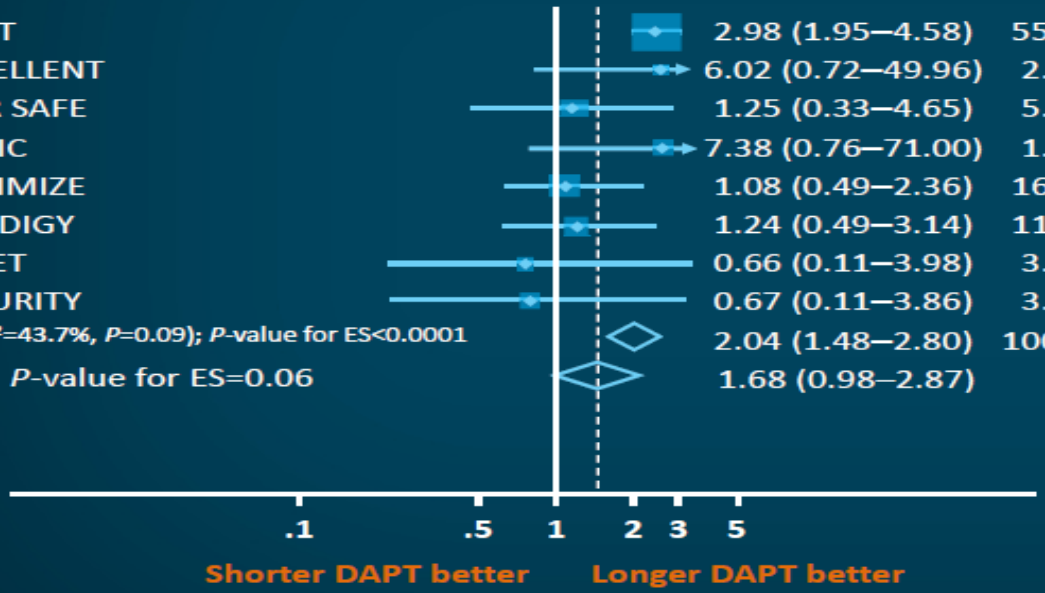


25% ⬇ MI with prolonged DAPT (P=0.01)

DAPT = dual antiplatelet therapy; DES = drug-eluting stent; ES = effect size.

Palmerini T et al. *Lancet*. 2015;Epub ahead of print.

Mortality with Extended-Duration DAPT After DES: Stent Thrombosis

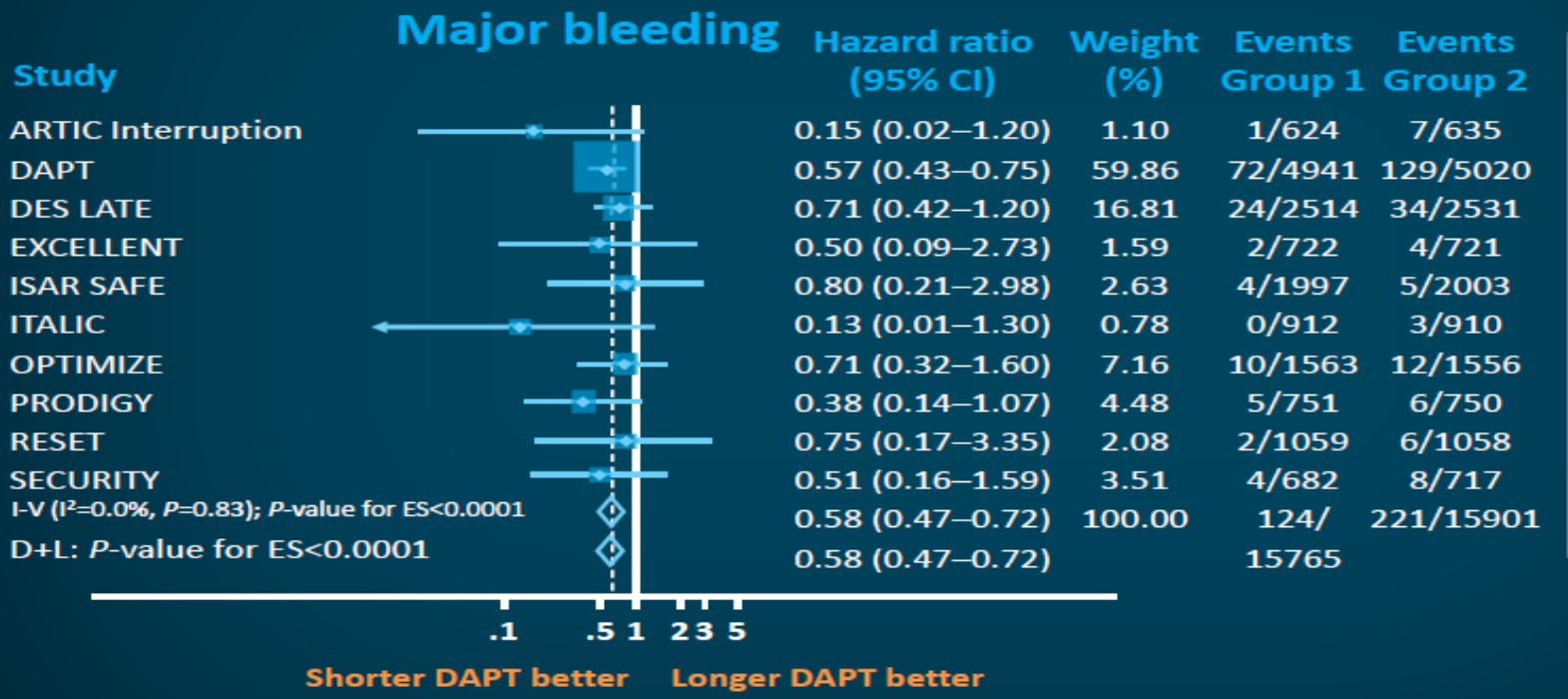


41% ↓ Stent thrombosis with prolonged DAPT (P=0.06)

DAPT = dual antiplatelet therapy; DES = drug-eluting stent; ES-effect size.

Palmerini T et al. *Lancet*. 2015;Epub ahead of print.

Mortality with Extended-Duration DAPT After DES: Major Bleeding

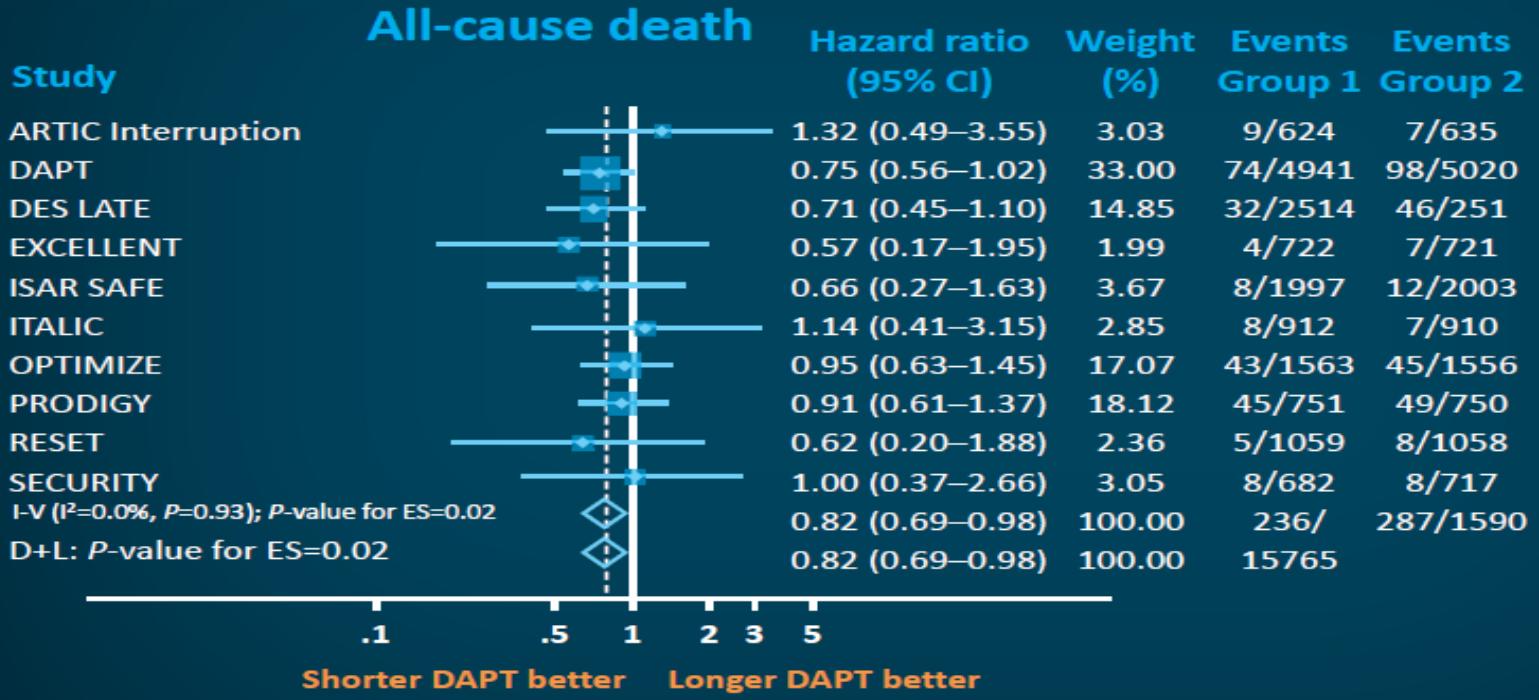


72% ↑ Bleeding with prolonged DAPT (*P*=0.0001)

DAPT = dual antiplatelet therapy; DES = drug-eluting stent; ES-effect size.

Palmerini T et al. *Lancet.* 2015;Epub ahead of print.

Mortality with Extended-Duration DAPT After DES: All-cause Death

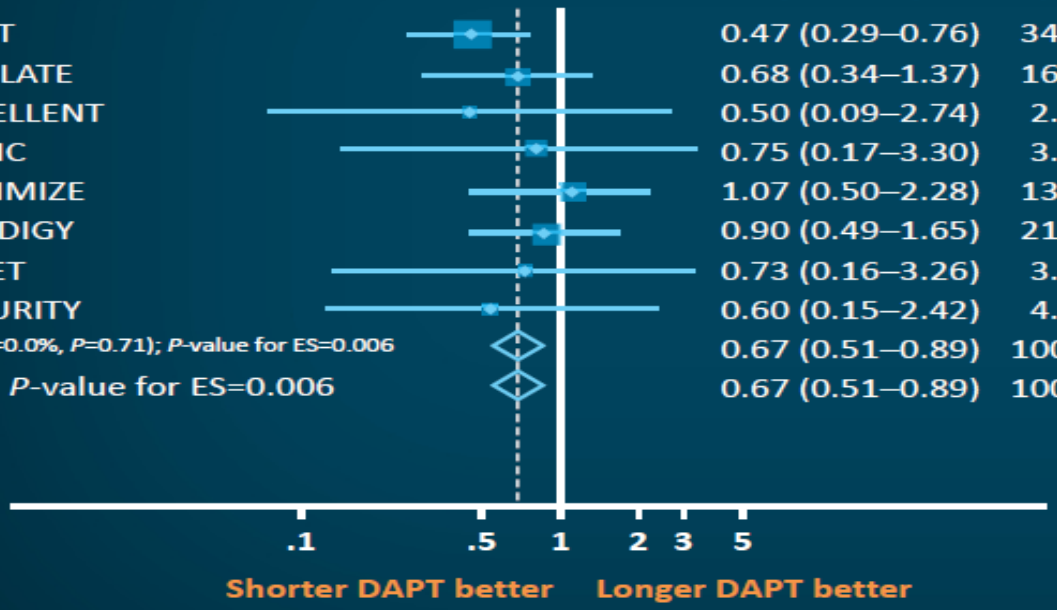


22% ↑ All-cause mortality with prolonged DAPT (*P*=0.02)

DAPT = dual antiplatelet therapy; DES = drug-eluting stent; ES-effect size.

Palmerini T et al. *Lancet*. 2015;Epub ahead of print.

Mortality with Extended-Duration DAPT After DES: Non-cardiac Death



Study	Hazard Ratio (95% CI)	Weight (%)	Events Group 1	Events Group 2
DAPT	0.47 (0.29–0.76)	34.27	22/4941	48/5020
DES LATE	0.68 (0.34–1.37)	16.38	13/2514	19/2531
EXCELLENT	0.50 (0.09–2.74)	2.73	2/722	4/721
ITALIC	0.75 (0.17–3.30)	3.62	3/912	4/910
OPTIMIZE	1.07 (0.50–2.28)	13.82	14/1563	13/1556
PRODIGY	0.90 (0.49–1.65)	21.58	20/751	22/750
RESET	0.73 (0.16–3.26)	3.50	3/1059	4/1058
SECURITY	0.60 (0.15–2.42)	4.11	3/682	5/717
I-V (I^2=0.0%, *P*=0.71); *P*-value for ES=0.006	0.67 (0.51–0.89)	100.00	80/	119/13263
D+L: *P*-value for ES=0.006	0.67 (0.51–0.89)	100.00	13144	

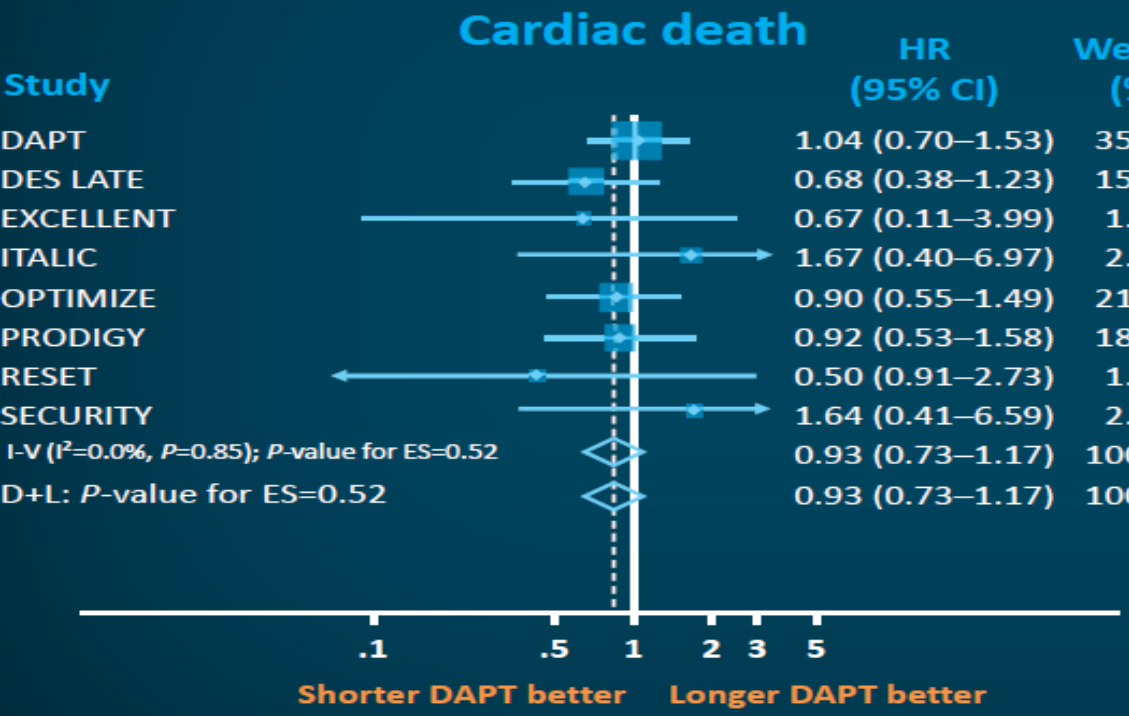
49% ↑ Non-cardiac mortality with prolonged DAPT (*P*=0.006)

DAPT = dual antiplatelet therapy; DES = drug-eluting stent; ES-effect size.

Palmerini T et al. *Lancet.* 2015;Epub ahead of print.

Mortality with Extended Duration DAPT After DES: Cardiac Death

Meta-Analysis of 10 RCTs and 31,666 Pts

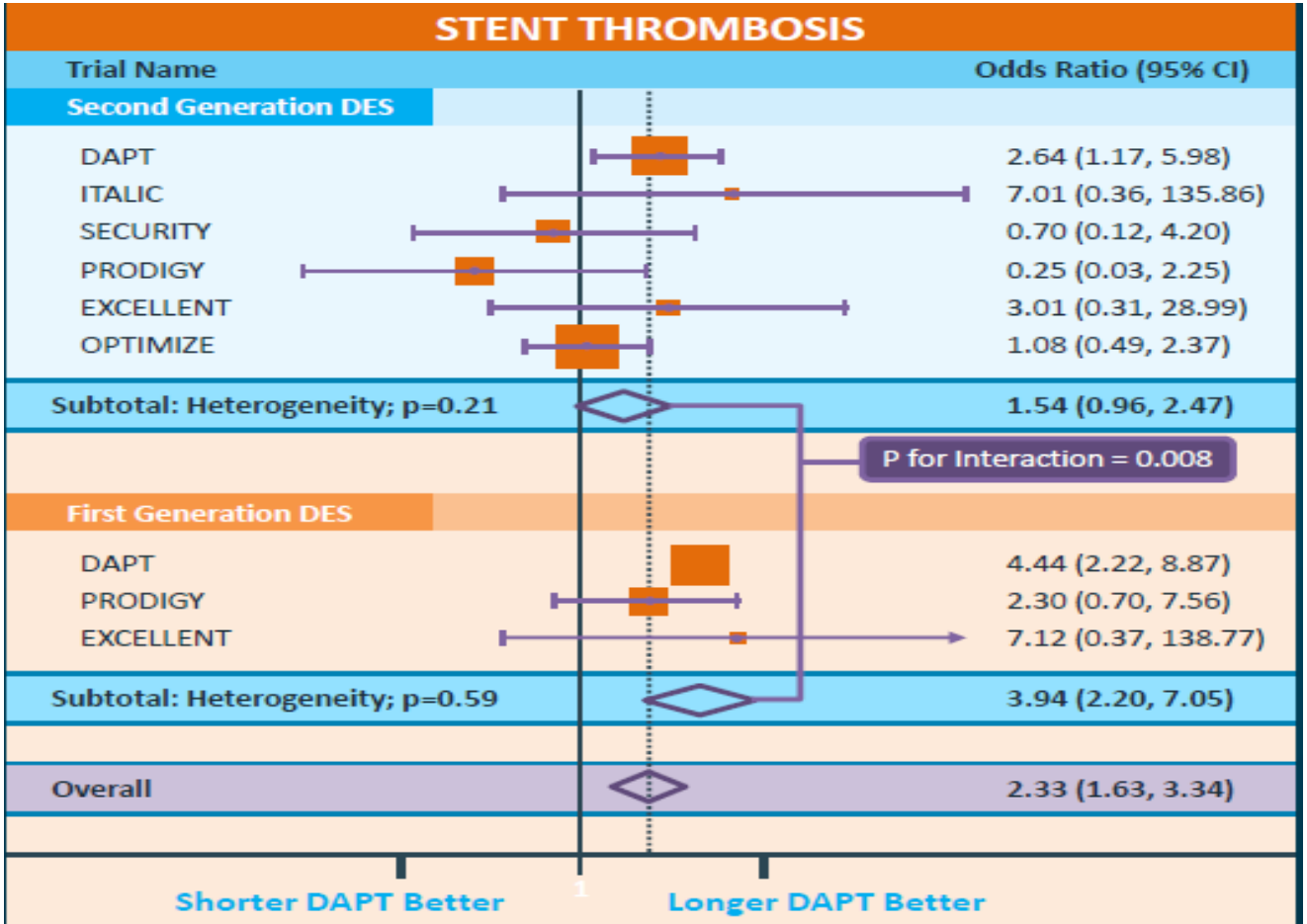


8% ↑ cardiac mortality with prolonged DAPT (*P*=NS)

DAPT = dual antiplatelet therapy; DES = drug-eluting stent; ES-effect size.

Palmerini T et al. *Lancet.* 2015;Epub ahead of print.

DAPT prolongée et type de DES

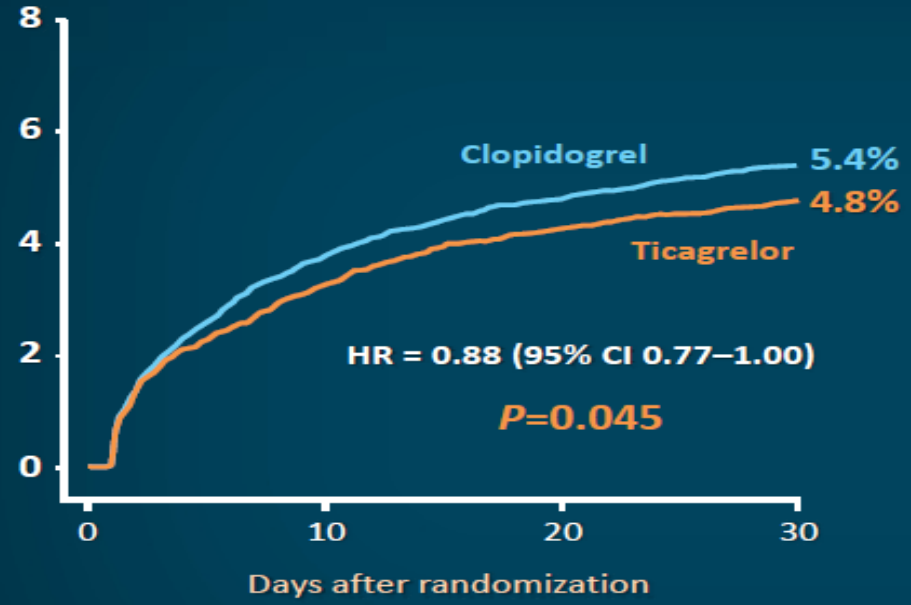


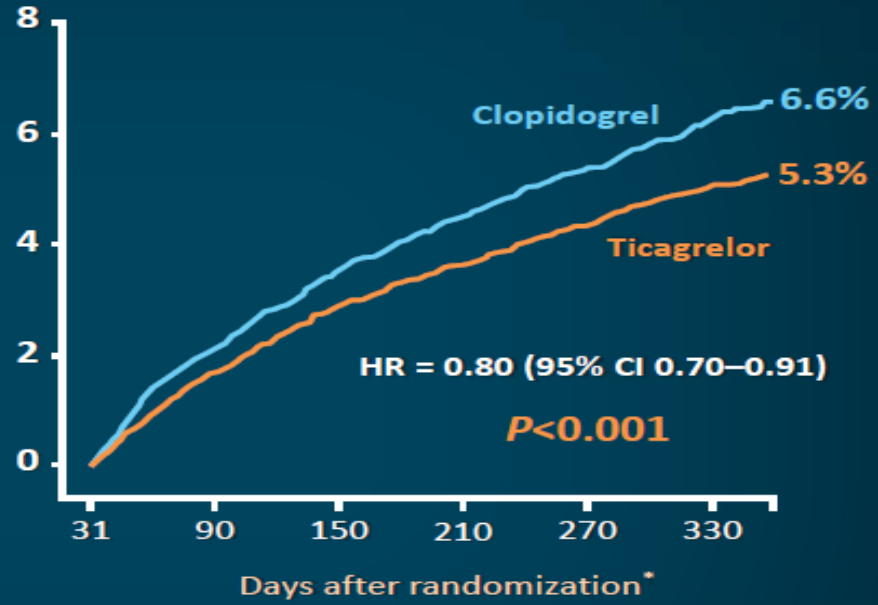
Giustino G et al.
JACC2015; 65:1298-1310

Quid des nouveaux AAP ?

Primary Efficacy Endpoint

(Composite of CV Death, MI or Stroke)





No. at risk										
Ticagrelor	9,333	8,942	8,827	8,763	8,673	8,543	8,397	7,028	6,480	4,822
Clopidogrel	9,291	8,875	8,763	8,688	8,688	8,437	8,286	6,945	6,379	4,751

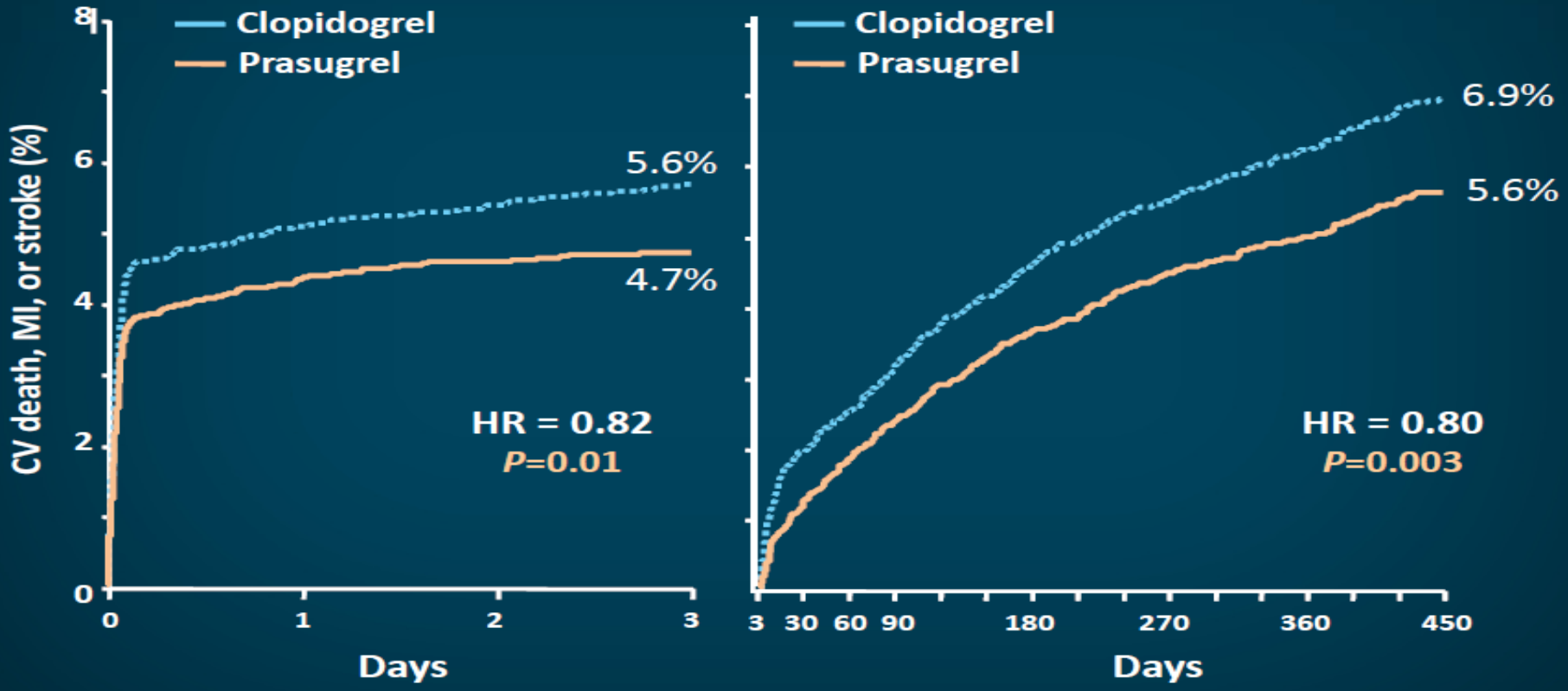
*Excludes patients with any primary event during the first 30 days

CV = cardiovascular; MI = myocardial infarction.

Wallentin L et al. *N Engl J Med.* 2009;361:1045-1057.

TRITON-TIMI-38

Timing of benefit (landmark analysis)



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

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

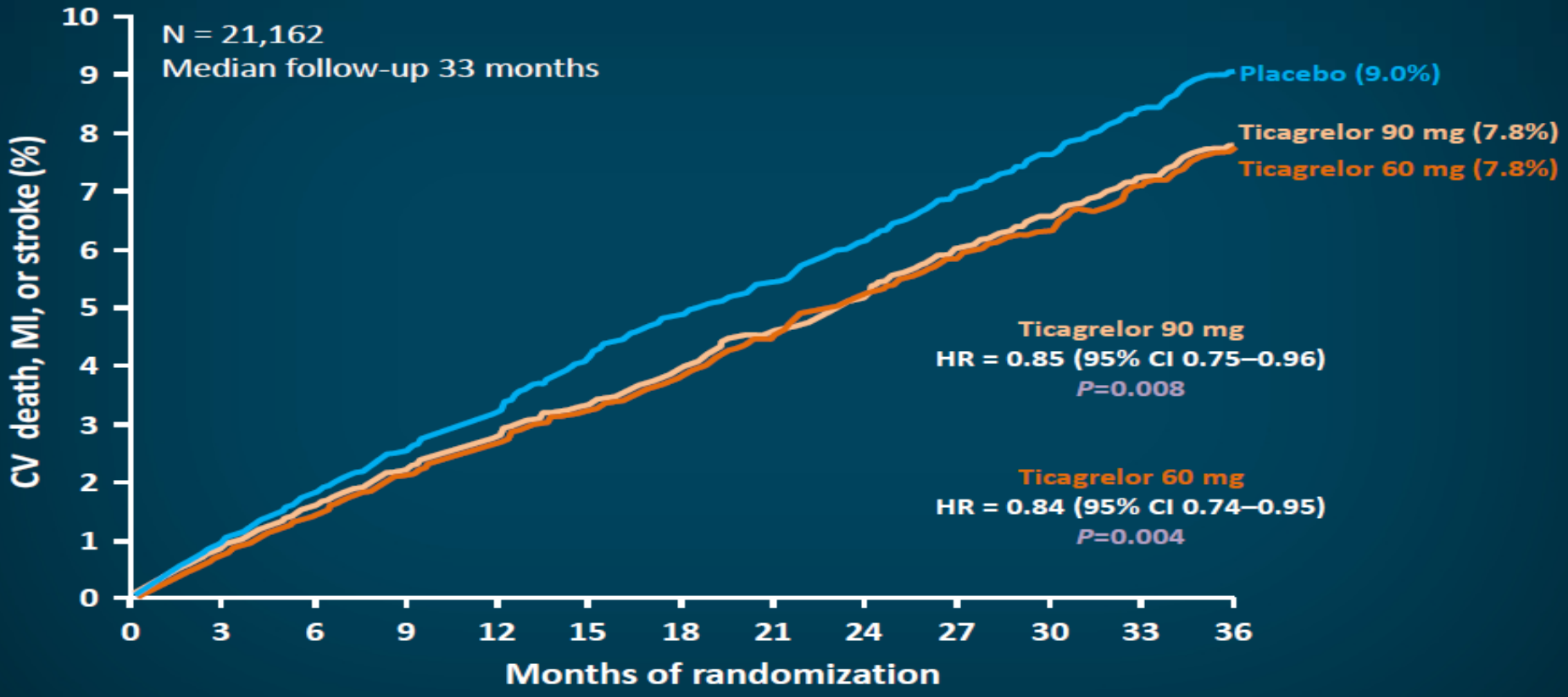
Ticagrelor 90 mg bid (N = 7050)	**Ticagrelor** 60 mg bid (N = 7045)	**Placebo** 60 mg bid (N = 7067)

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	3 patients	6 patients	1 patient

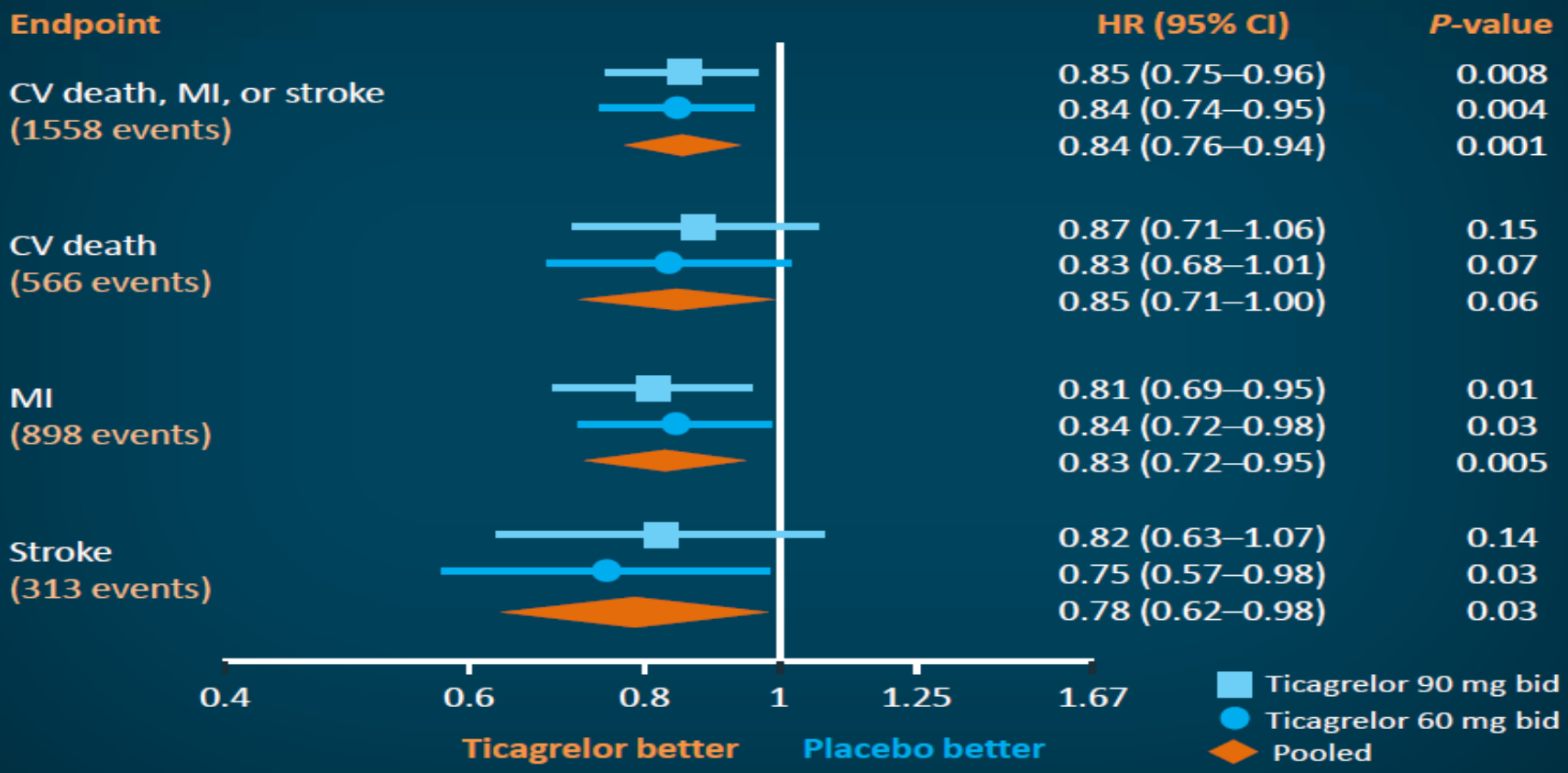
Bonaca MP et al. *N Engl J Med.* 2015:Epub ahead of print.

PEGASUS: Primary Endpoint



Bonaca MP et al. *N Engl J Med.* 2015:Epub ahead of print.

PEGASUS: Primary Endpoint Components



Bonaca MP et al. *N Engl J Med.* 2015:Epub ahead of print.

PEGASUS: Bleeding Endpoints

Endpoint	Ticagrelor 90 mg bid (n = 6988)	Ticagrelor 60 mg bid (n = 6958)	Placebo (n = 6996)	Ticagrelor 90 mg vs. placebo		Ticagrelor 60 mg vs. placebo	
				HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
TIMI major (primary Endponts)	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	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
Bleeding requiring transfusion	122 (2.43)	105 (2.09)	37 (0.72)	3.75 (2.59–5.42)	<0.001	3.08 (2.12–4.48)	<0.001
Bleeding leading to study-drug d/c	453 (7.81)	354 (6.15)	86 (1.50)	5.79 (4.60–7.29)	<0.001	4.40 (3.48–5.57)	<0.001
Fatal bleeding or nonfatal ICH	32 (0.63)	33 (0.71)	30 (0.60)	1.22 (0.74–2.01)	0.43	1.20 (0.73–1.97)	0.47
- ICH	29 (0.56)	28 (0.61)	23 (0.47)	1.44 (0.83–2.49)	0.19	1.33 (0.77–2.31)	0.31
- Hemorrhagic stroke	4 (0.07)	8 (0.19)	9 (0.19)	0.51 (0.61–1.64)	0.26	0.97 (0.37–2.51)	0.94
- Fatal bleeding	6 (0.11)	11 (0.25)	12 (0.26)	0.58 (0.22–1.54)	0.27	1.00 (0.44–2.27)	1.00

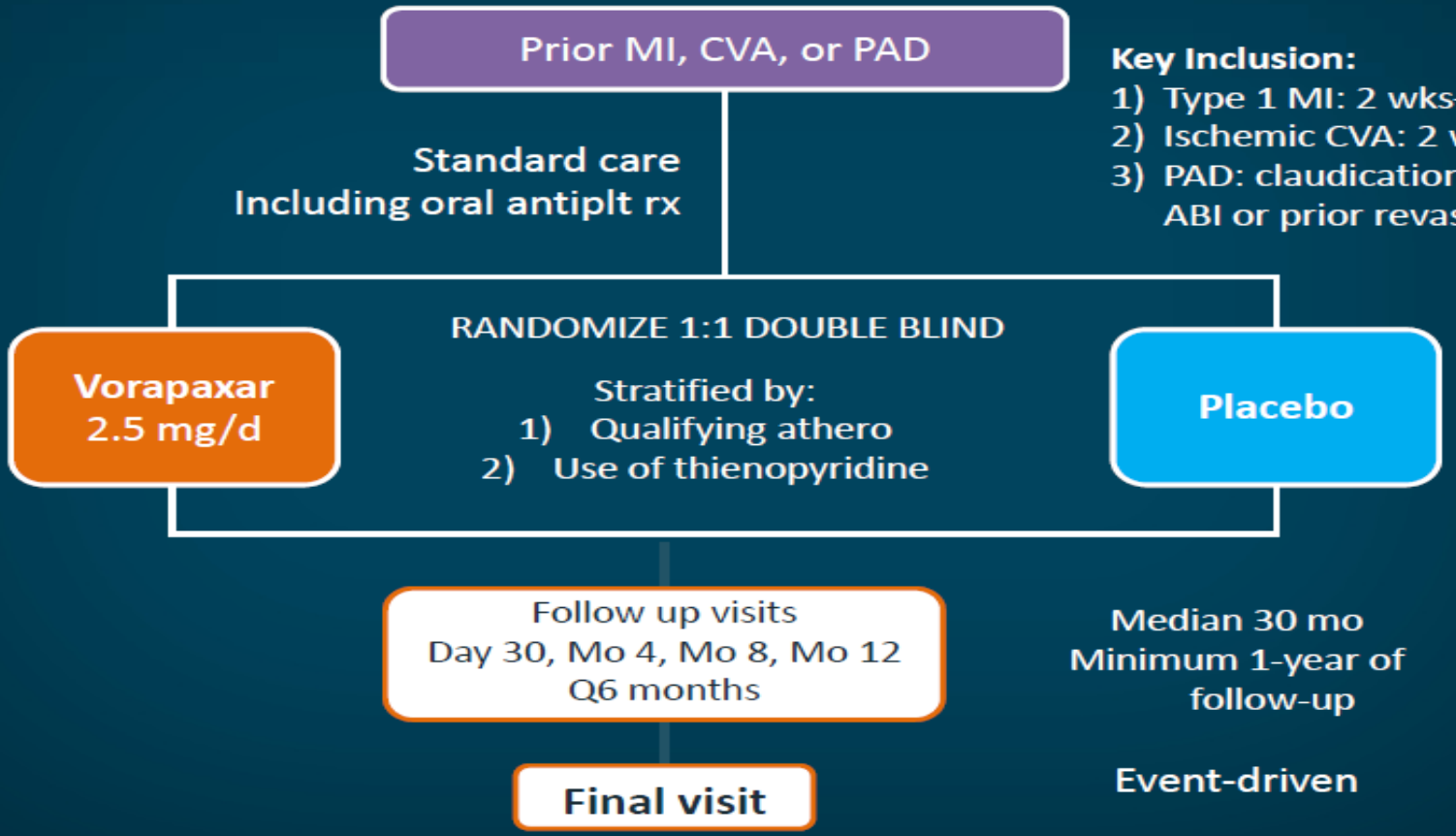
Bonaca MP et al. *N Engl J Med.* 2015:Epub ahead of print.

Et le Vorapaxar…

- Inhibiteur du récepteur plaquettaire de la thrombine
- Demi-vie > 100 heures

TRA-2P TIMI 50

Trial Design (n = 26,449)



Morrow DA et al. *N Engl J Med.* 2012;366:1404–1413.

TRA-2P TIMI 50

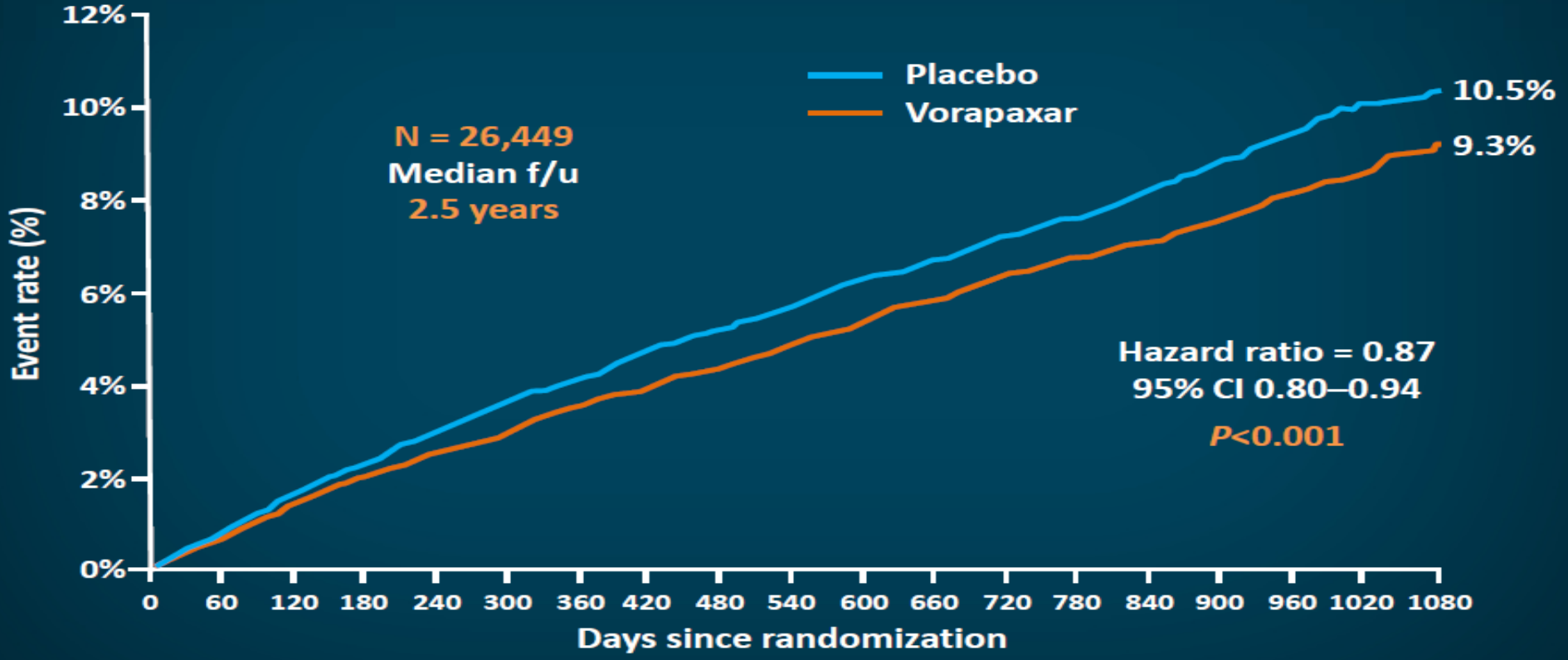
Background Therapy

		Placebo (N = 13,224)	Vorapaxar (N=13,225)
Antiplatelet therapy, %		>99% of thienopyridine used was clopidogrel	
Qualifying MI	Aspirin	98	98
(n =17,779)	Thienopyridine	78 (77% DAPT)	78
PAD	Aspirin	88	88
(n = 3787)	Thienopyridine	37 (28% DAPT)	37
Stroke	Aspirin	81	81
(n = 4883)	Thienopyridine	24 (8% DAPT)	24
	Dipyridamole	19	20
Other medications at enrollment (%)			
Lipid-lowering agent		92	91
ACEI or ARB		75	74
Beta-blocker (qualifying MI)		84	84

Morrow DA et al. *N Engl J Med.* 2012;366:1404–1413.

TRA-2P TIMI 50

Primary Efficacy: CV Death, MI, or Stroke



Morrow DA et al. *N Engl J Med.* 2012;366:1404–1413.

TRA-2P TIMI 50

Efficacy Endpoints

3-year KM rate (%)	Placebo (N = 13,224)	Vorapaxar (N = 13,225)	HR	*P*-value
CV death, MI, stroke	10.5	9.3	0.87	<0.001
- CV death	3.0	2.7	0.89	0.15
- MI	6.1	5.2	0.83	0.001
- Any stroke	2.8	2.8	0.97	0.73
- Ischemic stoke	2.6	2.2	0.85	0.06
Urgent coronary revascularization	2.6	2.5	0.88	0.11
CVD, MI, stroke, UCR, vascular hospitalization	14.7	13.1	0.87	<0.001
All-cause mortality	5.3	5.0	0.95	0.41

CV = cardiovascular; MI = myocardial infarction; CVD= cardiovascular disease; UCR =urgent coronary revascularization.

Morrow DA et al. *N Engl J Med.* 2012;366:1404–1413.

TRA-2P TIMI 50

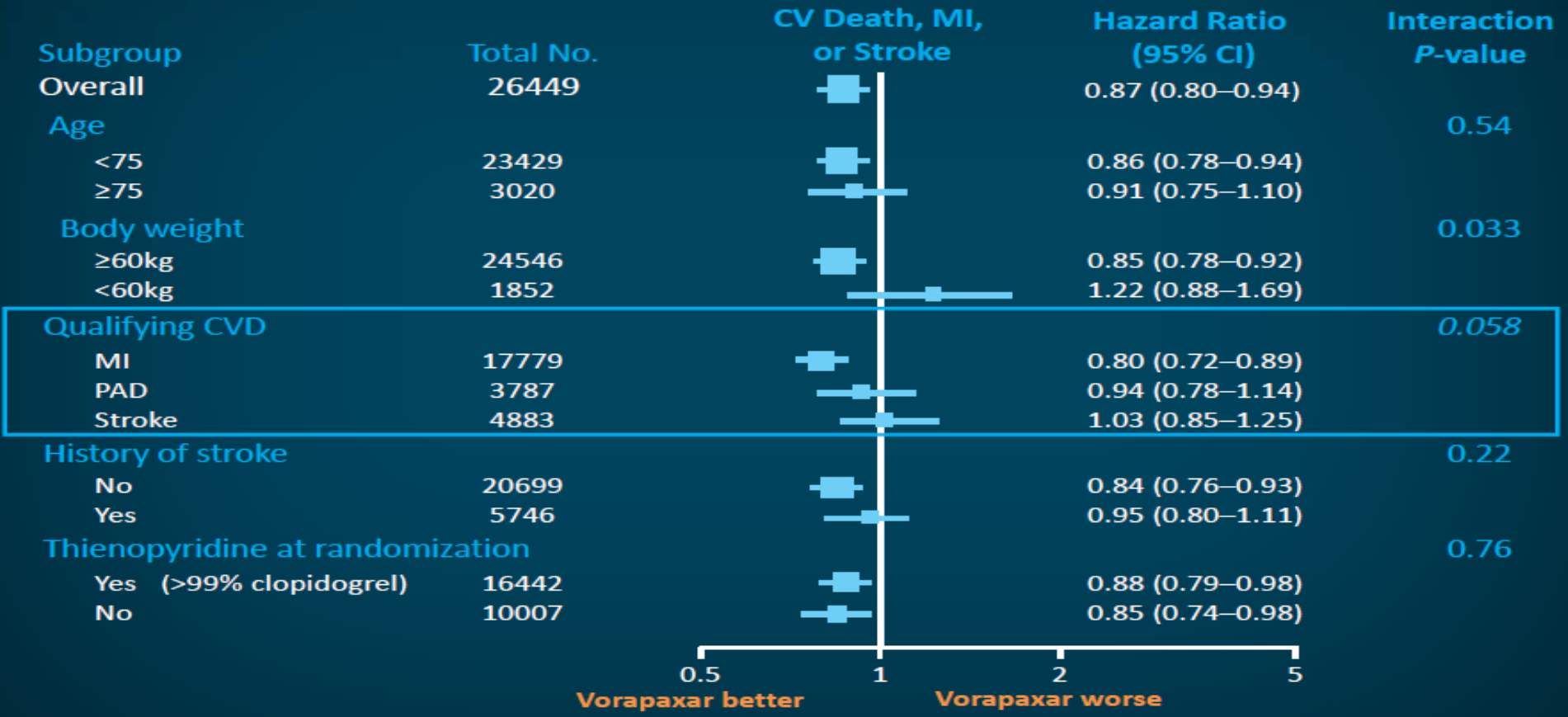
Bleeding Endpoints at 3 Years

	Placebo (N = 13,166)	Vorapaxar (N = 13,186)	HR (95% CI)	*P*-value
GUSTO moderate or severe	267 (2.5%)	438 (4.2%)	1.66 (1.43–1.93)	<0.001
- Severe	123 (1.2%)	176 (1.7%)	1.44 (1.15–1.82)	0.002
- Moderate	151 (1.4%)	271 (2.6%)	1.82 (1.49–2.22)	<0.001
TIMI clinically significant	1241 (11.1%)	1759 (15.8%)	1.46 (1.36–1.57)	<0.001
- Major	209 (1.9%)	298 (2.9%)	1.44 (1.21–1.72)	<0.001
- Non-CABG-related	198 (1.8%)	287 (2.8%)	1.46 (1.22–1.75)	<0.001
- CABG-related	10 (6.1%)	11 (7.6%)	1.13 (0.48–2.66)	0.79
- Minor	44 (0.6%)	108 (1.5%)	2.47 (1.74–3.51)	<0.001
Fatal bleeding	20 (0.2%)	29 (0.3%)	1.46 (0.82–2.58)	0.19
Intracranial hemorrhage	53 (0.5%)	102 (1.0%)	1.94 (1.39–2.70)	<0.001

Scirica BM et al. *Lancet*. 2012;380(9850):1317-1324.

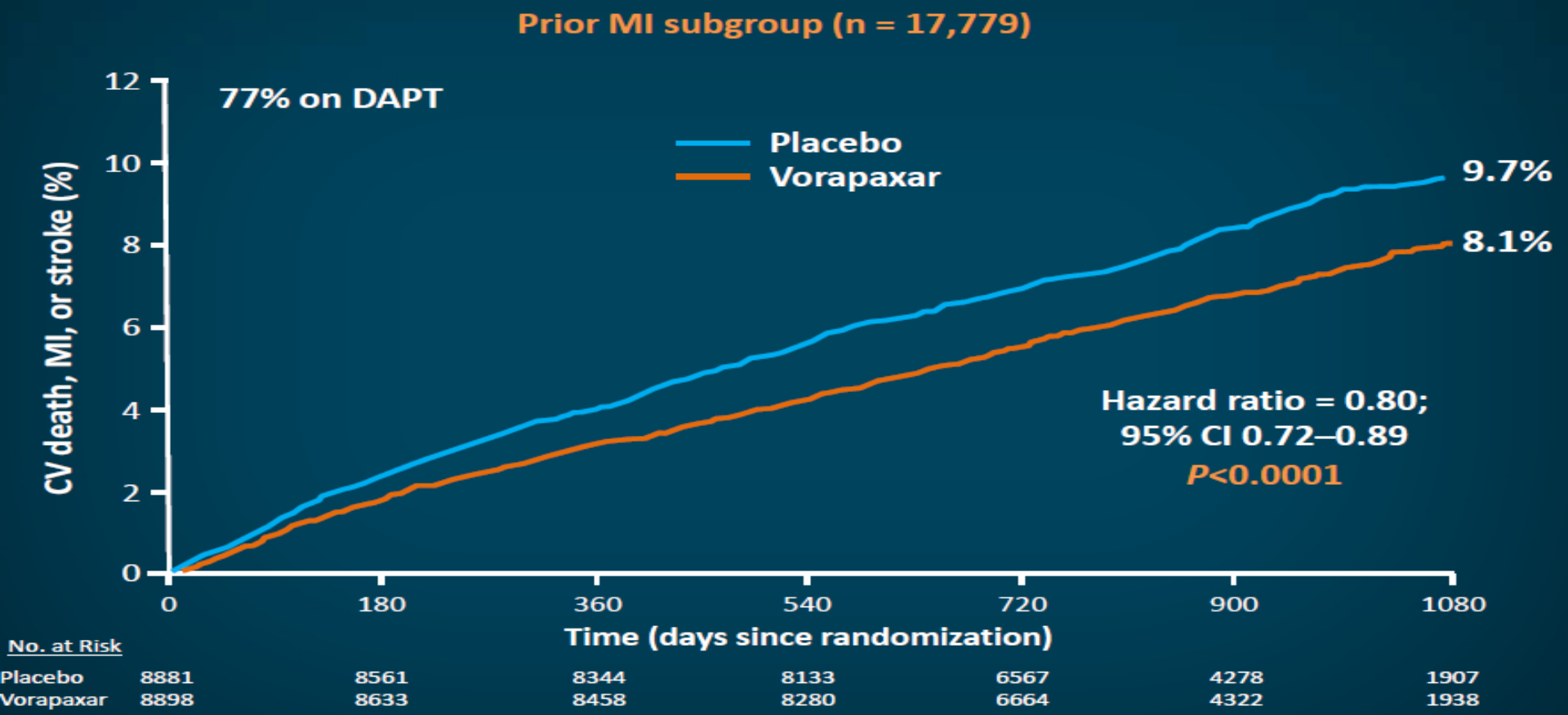
TRA-2P TIMI 50

Primary Efficacy: CV Death, MI, or Stroke



Morrow DA et al. *N Engl J Med.* 2012;366:1404-1413.

TRA 2P-TIMI 50 Trial: CV Death, MI, or Stroke



Scirica BM et al. *Lancet*. 2012;380:1317-1324.

TRA 2P-TIMI 50 Trial

Prior MI Subgroup (n = 17,779): 3-year Efficacy Rates

	Placebo (n = 8881)	Vorapaxar (n = 8898)	HR (95% CI)	*P*-value
CV death, MI, stroke	750 (9.7%)	610 (8.1%)	0.80 (0.72–0.89)	<0.0001
CV death, MI, stroke, or urgent coronary revascularization	956 (12.1%)	809 (10.5%)	0.83 (0.76–0.92)	0.0001
CV death or MI	665 (8.6%)	545 (7.2%)	0.81 (0.72–0.91)	0.0003
CV death	177 (2.4%)	150 (2.0%)	0.84 (0.68–1.05)	0.12
MI	541 (7.0%)	433 (5.7%)	0.79 (0.70–0.90)	0.0003
All-cause mortality	293 (4.0%)	273 (3.7%)	0.92 (0.78–1.09)	0.35
Any stroke	120 (1.6%)	93 (1.3%)	0.77 (0.59–1.01)	0.06
Ischemic stroke	106 (1.4%)	70 (1.0%)	0.66 (0.48–0.89)	0.006
Urgent coronary revascularization	272 (3.3%)	273 (3.7%)	0.86 (0.73–1.03)	0.10
CV death, MI, stroke, urgent coronary revascularization, or ischemia leading to admission to hospital	1051 (13.2%)	915 (11.7%)	0.86 (0.79–0.94)	0.0007

Scirica BM et al. *Lancet*. 2012;380:1317-1324

TRA 2P-TIMI 50 Trial

Prior MI Subgroup (n = 17,779): 3-year Bleeding Rates

	Placebo (n = 8881)	Vorapaxar (n = 8898)	HR (95% CI)	*P*-value
GUSTO moderate or severe	151 (2.1%)	241 (3.4%)	1.61 (1.31–1.97)	<0.0001
- Severe	71 (1.0%)	86 (1.2%)	1.22 (0.89–1.67)	0.22
- Moderate	85 (1.2%)	161 (2.2%)	1.91 (1.47–2.48)	<0.0001
GUSTO mild	1432 (18.1%)	2047 (25.4%)	1.51 (1.41–1.62)	<0.0001
TIMI clinically significant	801 (10.4%)	1159 (15.1%)	1.49 (1.36–1.63)	<0.0001
- Non-CABG major	121 (1.6%)	156 (2.2%)	1.29 (1.02–1.64)	0.03
- Minor	44 (0.6%)	108 (1.5%)	2.47 (1.74–3.51)	<0.0001
- Non-CABG major or minor	162 (2.2%)	258 (3.6%)	1.60 (1.32–1.95)	<0.0001
Fatal bleeding	9 (0.1%)	14 (0.2%)	1.56 (0.67–3.60)	0.30
Intracranial hemorrhage	28 (0.4%)	43 (0.6%)	1.54 (0.96–2.48)	0.076

Scirica BM et al. Lancet. 2012;380:1317-1324.

Guideline recommendations for duration of DAPT

Society	Management	Recommended Duration
EUROPEAN SOCIETY OF CARDIOLOGY®	STEMI	Consider up to 12 months
		Strict minimum of 1 month for BMS and 6 months for DES
EUROPEAN SOCIETY OF CARDIOLOGY®	NSTEMI	At least 12 months
EUROPEAN SOCIETY OF CARDIOLOGY®	Revasc	1 Month for BMS 6 Months for DES
		May be < 6 months if at high bleeding risk and may be > 6 months if at high ischemic risk

Steg et al. ESC STEMI Guidelines 2012; Hamm et al. ESC NSTEMI Guidelines 2011;
Windecker et al. ESC Myocardial Revascularization Guidelines 2014

En conclusion…

- « One size fits all »: probably not !
- **Intérêt de la DAPT prolongée**:

- STEMI patients
- ATCD ST
- Maladie athéromateuse évoluée
- Faible risque hémorragique
- DES première génération

Conclusion

- **Bithérapie raccourcie:**

- Patient stable
- Angioplastie simple
- Maladie peu évoluée
- Dernière génération de DES
- Risque hémorragique/chirurgie


THANK YOU FOR YOUR ATTENTION
PLEASE CLAP AND DON'T ASK
TOUGH QUESTIONS