Durée de la double inhibition antiplaquettaire après un syndrome coronarien aigu ou une angioplastie coronarienne

Alexis Matteau, MD, MSc, FRCPC
Cardiologue, CHUM
Centre de recherche du CHUM
Professeur adjoint de clinique, Université de Montréal
alexis.matteau@umontreal.ca

21 novembre 2015

SSVQ
Société des sciences vasculaires du Québec

CENTRE CARDIOVASCULAIRE DU CHUM

CRCHUM
CENTRE DE RECHERCHE
Centre hospitalier de l'Université de Montréal

Conflits d'intérêts

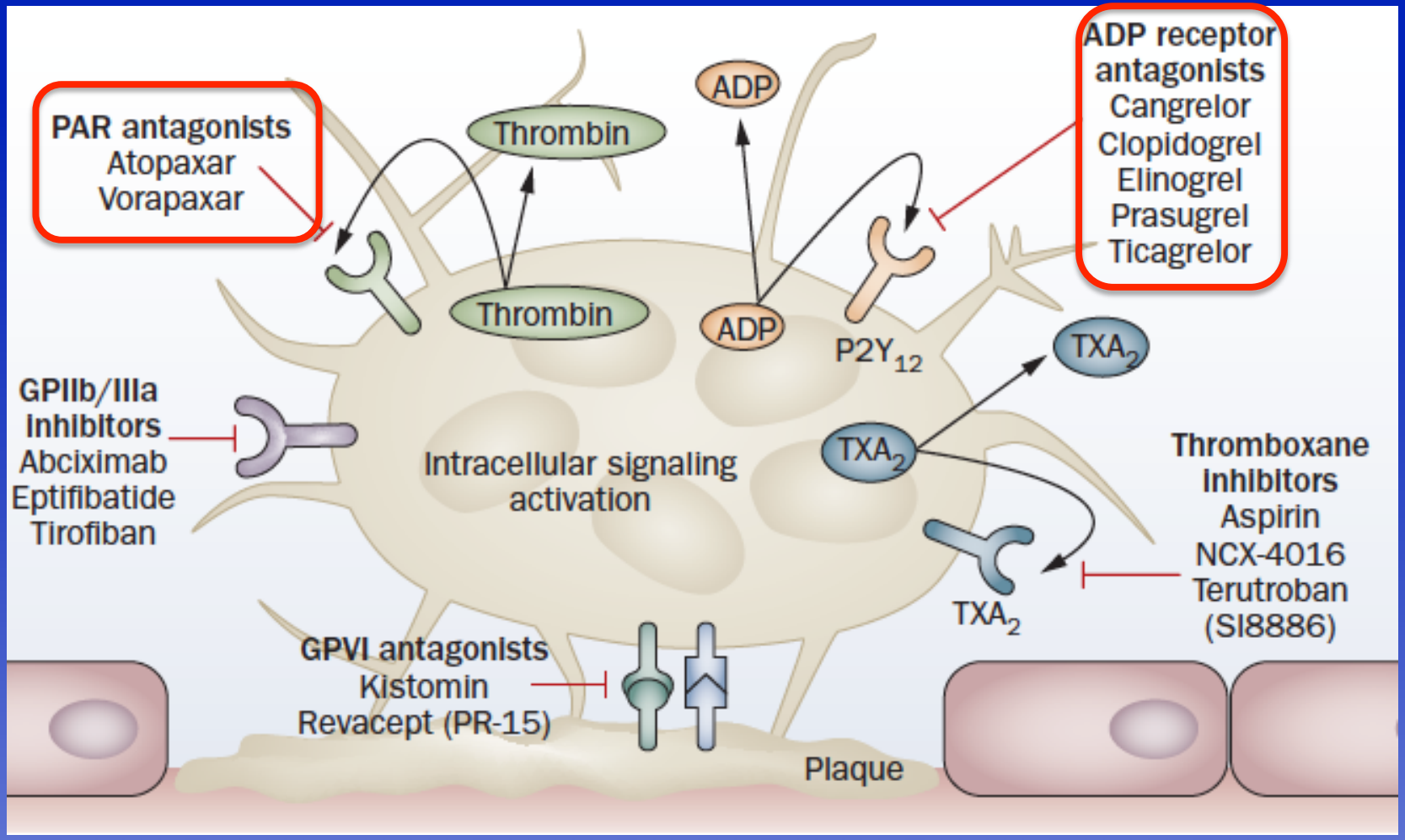
- Subvention de formation:
  - Boston Scientific
- Conférenciers:
  - Pfizer, AstraZeneca

Objectifs

1. Réviser la littérature récente concernant la durée de la double thérapie antiplaquettaire
2. Déterminer quels patients peuvent bénéficier d'une double thérapie antiplaquettaire prolongée
3. Comprendre les risques associés à la double thérapie antiplaquettaire

Le bon vieux temps…

Nouvelles thérapies



Nat Rev Cardiol 2011

Antagonistes récepteur ADP $P2Y_{12}$

	Clopidogrel	Prasugrel	Ticagrelor
Blocage récepteur	Irréversible	Irréversible	Réversible
Prodrogue	Oui	Oui	Non
$T_{1/2}$	6 heures	7 heures	8-12 heures
Administration	Die	Die	Bid
Début action	2-8 heures	30 min – 4 hres	30 min – 4 hres
Arrêt action	7 jours	7-10 jours	3-5 jours
Recommandation chirurgie	7 jours	7 jours	5 jours

Santé Canada

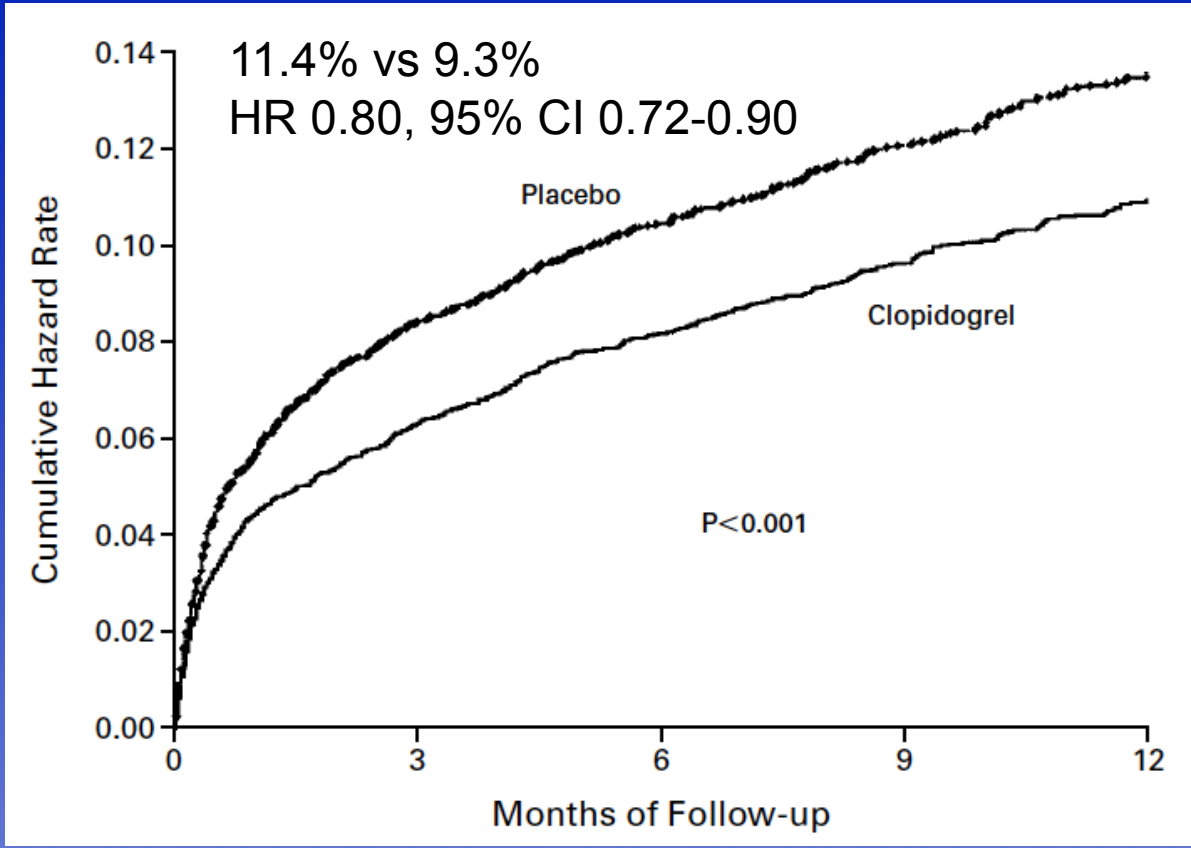
Clopidogrel	Prasugrel	Ticagrelor
Prévention secondaire -MCAS -MVAS -AVC		
Syndrome coronarien aigu (1 an) -Tx médical -PCI -PAC	Syndrome coronarien aigu (1 an) -PCI	Syndrome coronarien aigu (1 an) -Tx médical -PCI -PAC
Fibrillation auriculaire		

The New England Journal of Medicine

EFFECTS OF CLOPIDOGREL IN ADDITION TO ASPIRIN IN PATIENTS WITH ACUTE CORONARY SYNDROMES WITHOUT ST-SEGMENT ELEVATION

THE CLOPIDOGREL IN UNSTABLE ANGINA TO PREVENT RECURRENT EVENTS TRIAL INVESTIGATORS*

- 12562 patients
  - PCI: 2658 pts (21%)
  - PAC: 2072 pts (16%)
- Clopidogrel
  - 300 mg bolus
  - 75 mg die X 12 mois



N Eng J Med 2001

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 15, 2007 VOL. 357 NO. 20

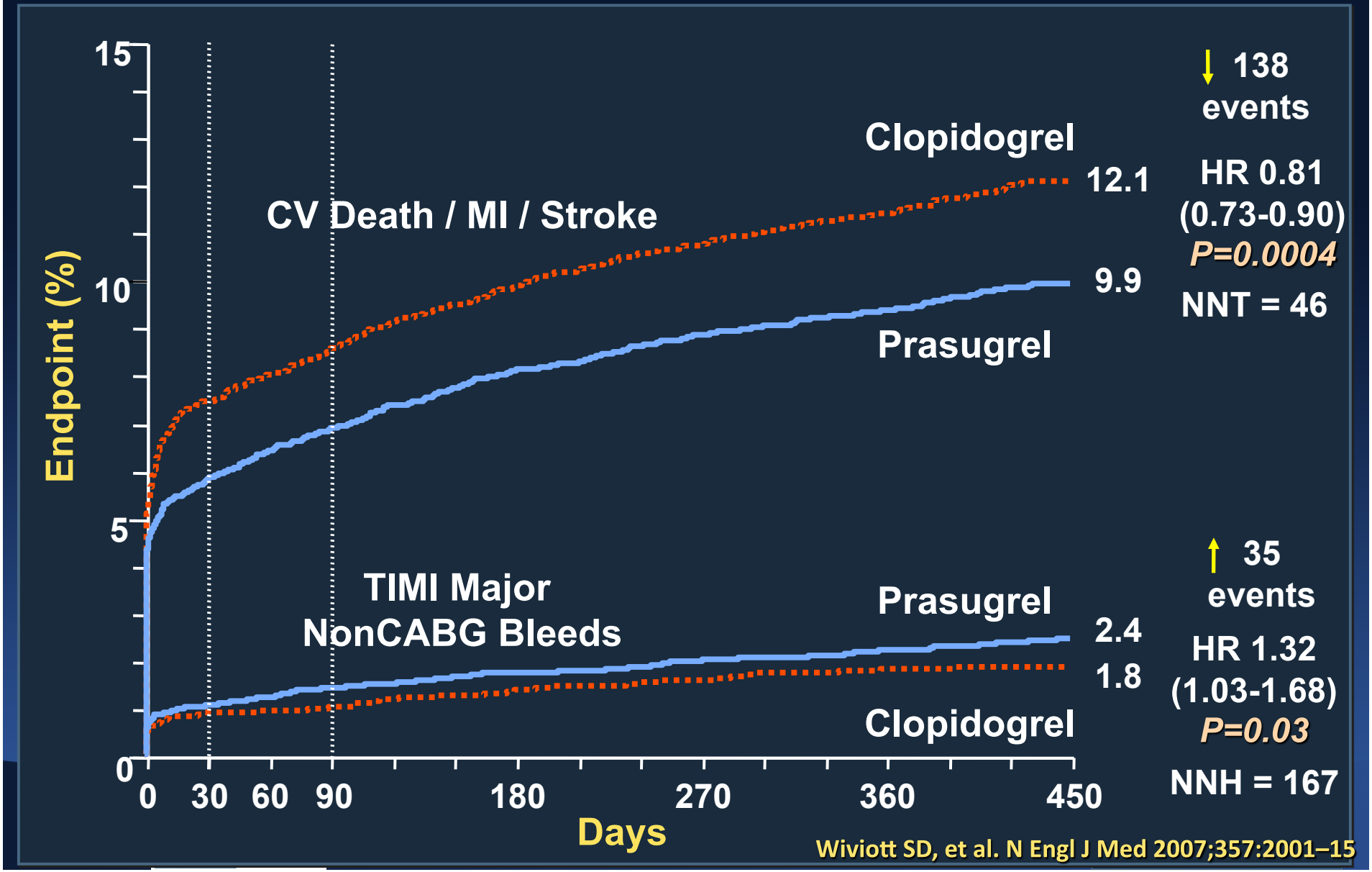
Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes

Stephen D. Wiviott, M.D., Eugene Braunwald, M.D., Carolyn H. McCabe, B.S., Gilles Montalescot, M.D., Ph.D., Witold Ruzyllo, M.D., Shmuel Gottlieb, M.D., Franz-Joseph Neumann, M.D., Diego Ardissino, M.D., Stefano De Servi, M.D., Sabina A. Murphy, M.P.H., Jeffrey Riesmeyer, M.D., Govinda Weerakkody, Ph.D., C. Michael Gibson, M.D., and Elliott M. Antman, M.D., for the TRITON–TIMI 38 Investigators*

- 13608 patients SCA et angioplastie planifiée
  - 10074 pts AI/NSTEMI
  - 3534 pts STEMI
- Administration après coronaro diagnostique, angioplastie choisie (sauf STEMI)

N Eng J Med 2007

Balance of Efficacy and Safety



Wiviott SD, et al. N Engl J Med 2007;357:2001–15

Attention…

End Point	Prasugrel (N=6741)	Clopidogrel (N=6716)	Hazard Ratio for Prasugrel (95% CI)	P Value
	no. of patients (%)			
Non–CABG-related TIMI major bleeding (key safety end point)	146 (2.4)	111 (1.8)	1.32 (1.03–1.68)	0.03
Related to instrumentation	45 (0.7)	38 (0.6)	1.18 (0.77–1.82)	0.45
Spontaneous	92 (1.6)	61 (1.1)	1.51 (1.09–2.08)	0.01
Related to trauma	9 (0.2)	12 (0.2)	0.75 (0.32–1.78)	0.51
Life-threatening†	85 (1.4)	56 (0.9)	1.52 (1.08–2.13)	0.01
Related to instrumentation	28 (0.5)	18 (0.3)	1.55 (0.86–2.81)	0.14
Spontaneous	50 (0.9)	28 (0.5)	1.78 (1.12–2.83)	0.01
Related to trauma	7 (0.1)	10 (0.2)	0.70 (0.27–1.84)	0.47
Fatal‡	21 (0.4)	5 (0.1)	4.19 (1.58–11.11)	0.002
Nonfatal	64 (1.1)	51 (0.9)	1.25 (0.87–1.81)	0.23
Intracranial	19 (0.3)	17 (0.3)	1.12 (0.58–2.15)	0.74

- ICT/AVC: Augmentation décès/IM/AVC ET saignement majeur
- Poids < 60 kg ou âge > 75 ans: Bénéfice incertain et risque de saignement

The NEW ENGLAND JOURNAL of MEDICINE

Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes

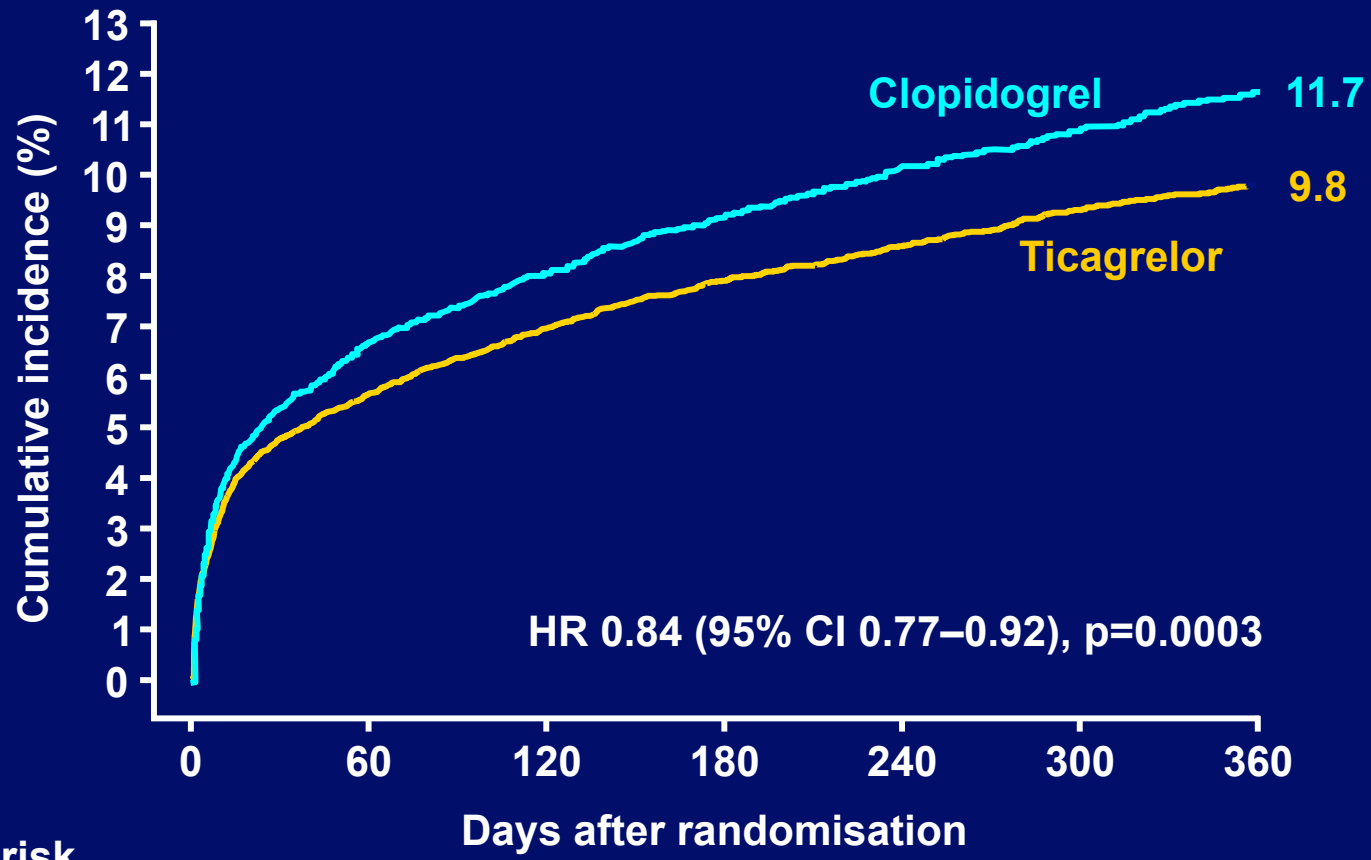
Lars Wallentin, M.D., Ph.D., Richard C. Becker, M.D., Andrzej Budaj, M.D., Ph.D., Christopher P. Cannon, M.D., Håkan Emanuelsson, M.D., Ph.D., Claes Held, M.D., Ph.D., Jay Horrow, M.D., Steen Husted, M.D., D.Sc., Stefan James, M.D., Ph.D., Hugo Katus, M.D., Kenneth W. Mahaffey, M.D., Benjamin M. Scirica, M.D., M.P.H., Allan Skene, Ph.D., Philippe Gabriel Steg, M.D., Robert F. Storey, M.D., D.M., and Robert A. Harrington, M.D., for the PLATO Investigators*

- 18624 patients SCA < 24 heures
  - 11598 pts AI/NSTEMI
  - 7026 pts STEMI
- Administration avant ou après coronaro diagnostique

N Eng J Med 2009

K-M estimate of time to first primary efficacy event (composite of CV death, MI or stroke)

PLATO



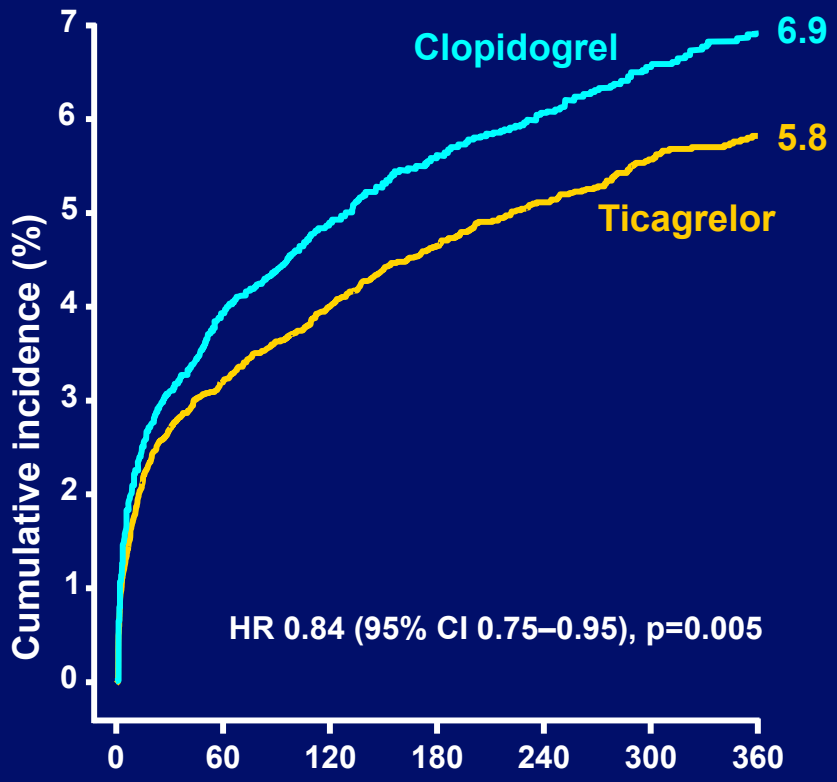
No. at risk							
Ticagrelor	9,333	8,628	8,460	8,219	6,743	5,161	4,147
Clopidogrel	9,291	8,521	8,362	8,124	6,743	5,096	4,047

K-M = Kaplan-Meier; HR = hazard ratio; CI = confidence interval

Secondary efficacy endpoints over time

PLATO

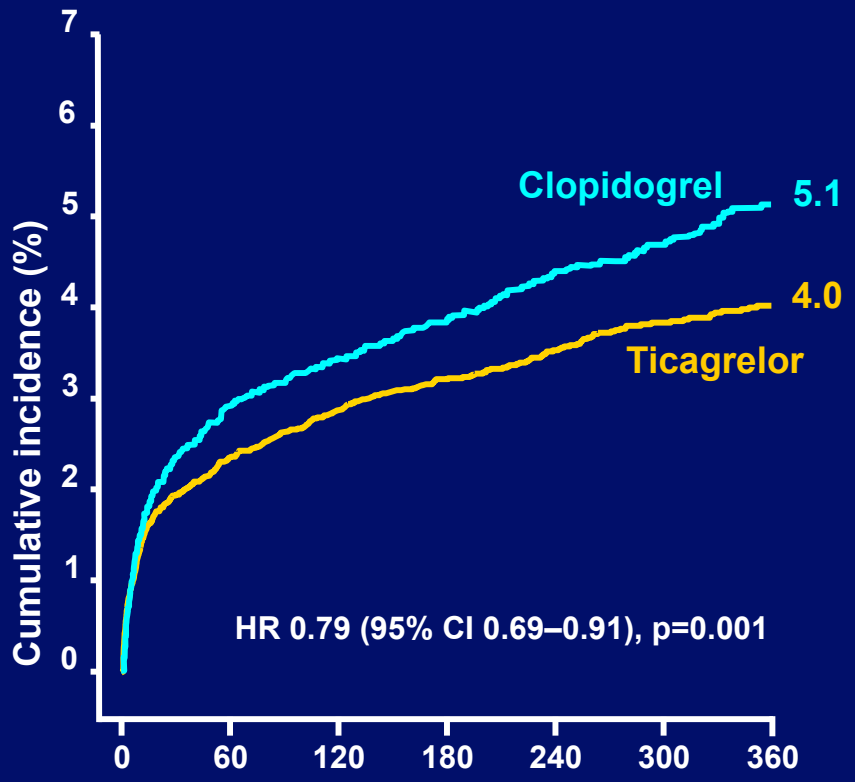
Myocardial infarction



No. at risk

Ticagrelor	9,333	8,678	8,520	8,279	6,796	5,210	4,191
Clopidogrel	9,291	8,560	8,405	8,177	6,703	5,136	4,109

Cardiovascular death

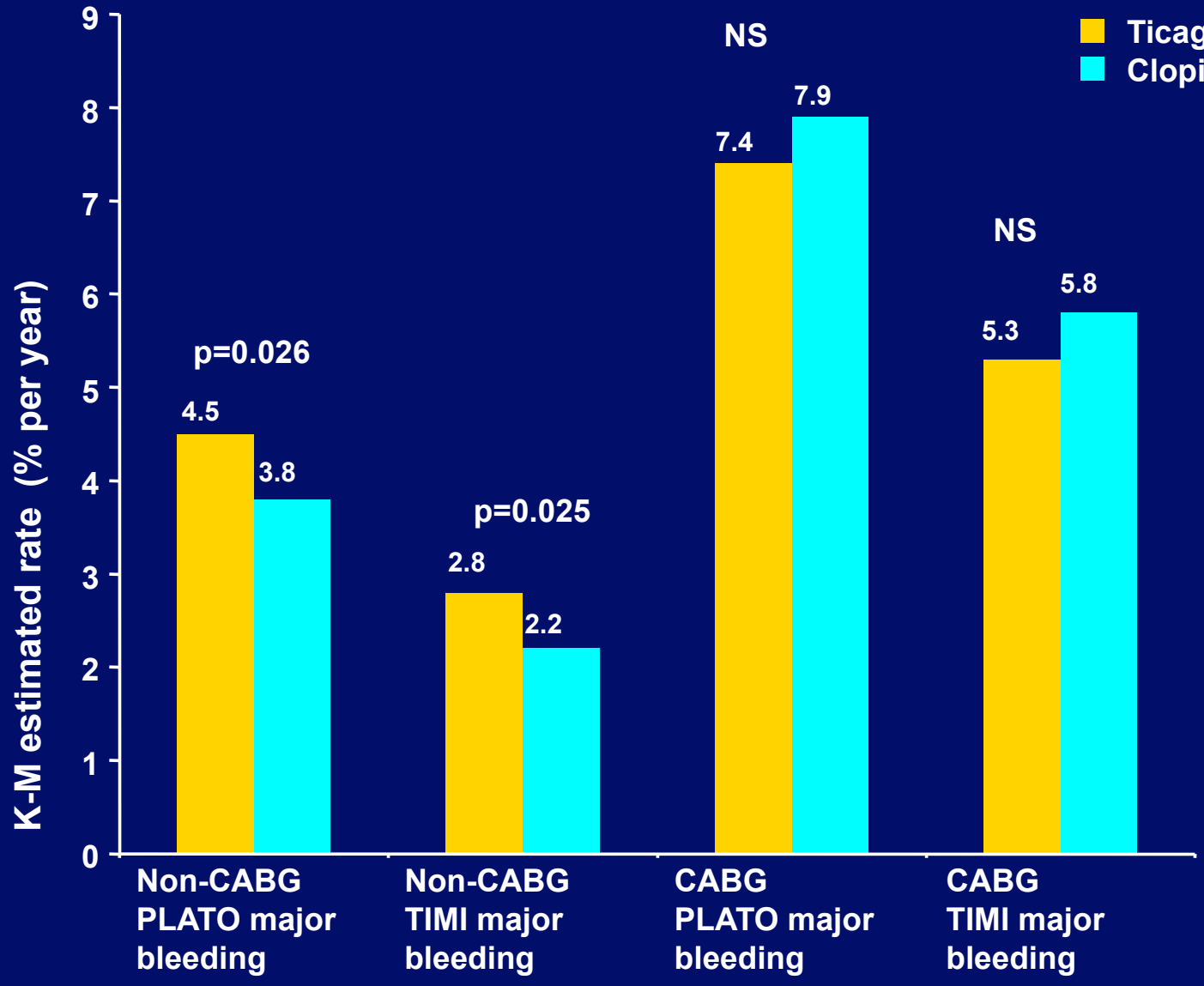


	9,333	8,294	8,822	8,626	7119	5,482	4,419
	9,291	8,865	8,780	8,589	7079	5,441	4,364

Duke Clinical Research Institute

UCR
UPPSALA CLINICAL RESEARCH CENTER

Non-CABG and CABG-related major bleeding



Canadian Journal of Cardiology 29 (2013) 1334–1345

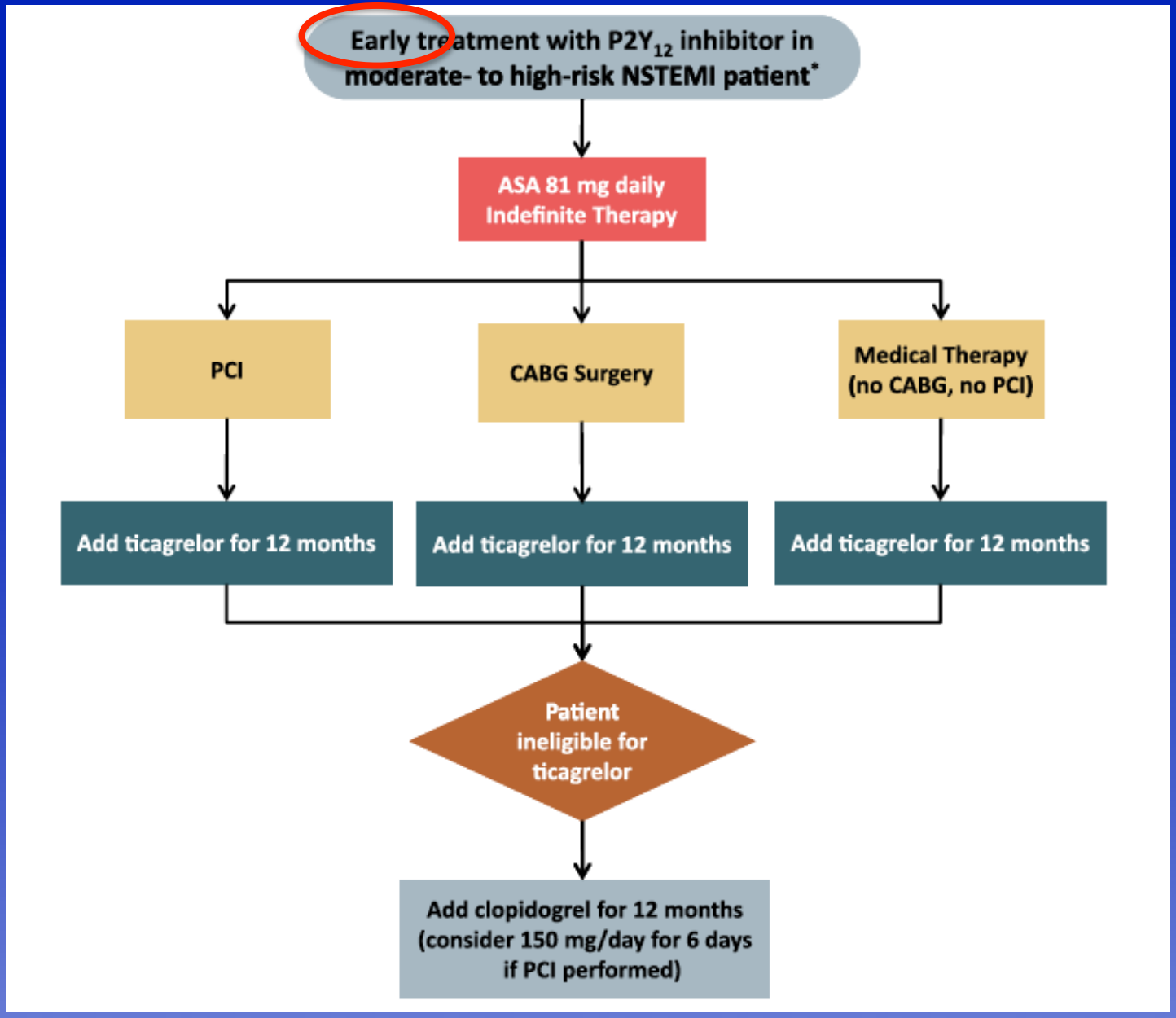
Society Guidelines

Focused 2012 Update of the Canadian Cardiovascular Society Guidelines for the Use of Antiplatelet Therapy

Jean-François Tanguay, MD, CSPQ, FRCPC, FACC, FAHA, FESC,[a] Alan D. Bell, MD, CCFP,[b] Margaret L. Ackman, BSc(Pharm), PharmD, ACPR, FCSHP,[c] Robert D.C. Bauer, MD, FRCPC, FACC,[d] Raymond Cartier, MD, FRCPC,[e] Wee-Shian Chan, MD, FRCPC,[f] James Douketis, MD, FRCPC,[g] André Roussin, MD, FRCPC,[h] Gregory Schnell, BSP, MD, FRCPC,[i] Subodh Verma, MD, PhD, FRCSC,[j] Graham Wong, MD, MPH, FRCPC, FACC,[k] and Shamir R. Mehta, MD, MSc, FRCPC, FACC, FESC[l]

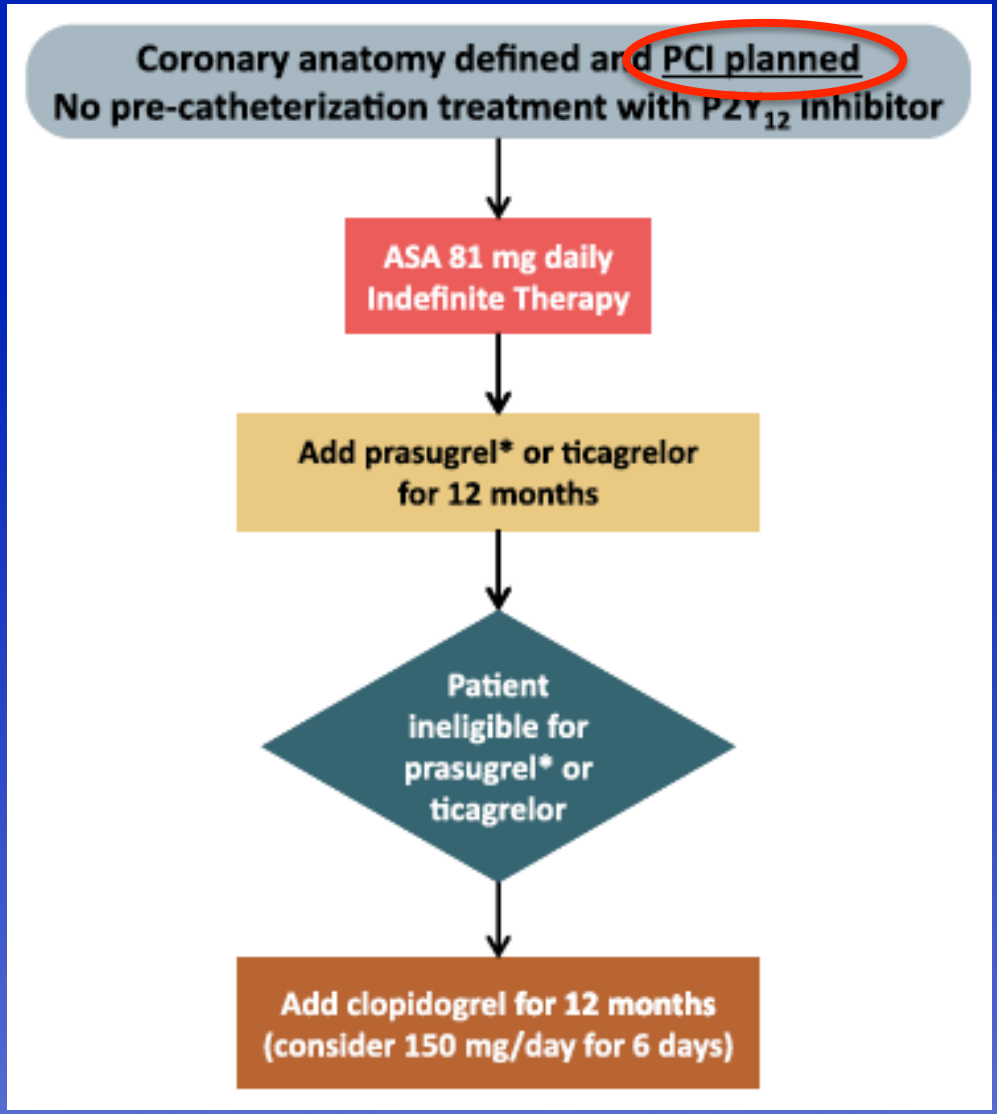
Can J Cardiol 2013

Recommandations CCS antiplaquettaires 2012



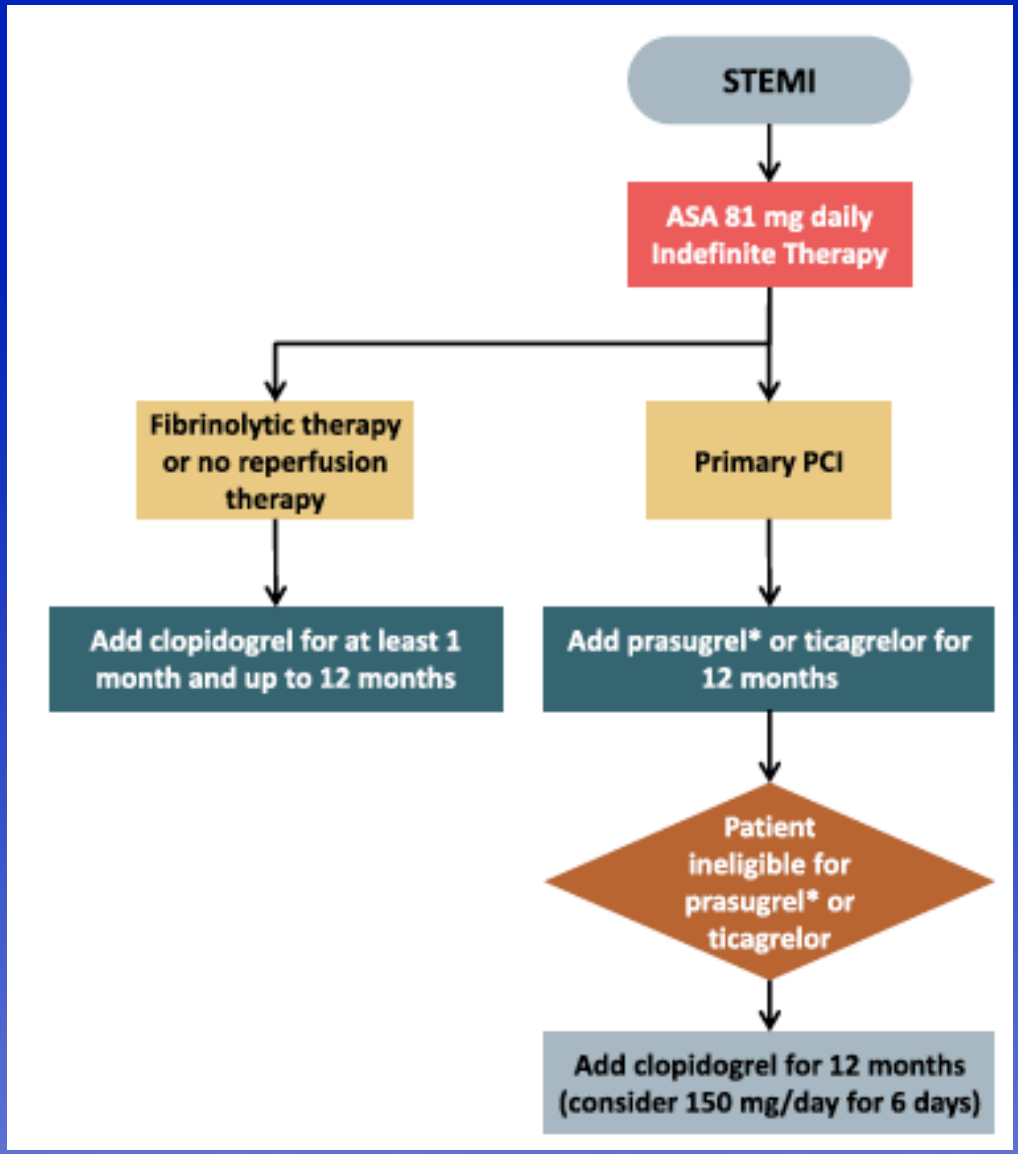
CJC 2013

Recommandations CCS antiplaquettaires 2012



CJC 2013

Recommandations CCS antiplaquettaires 2012



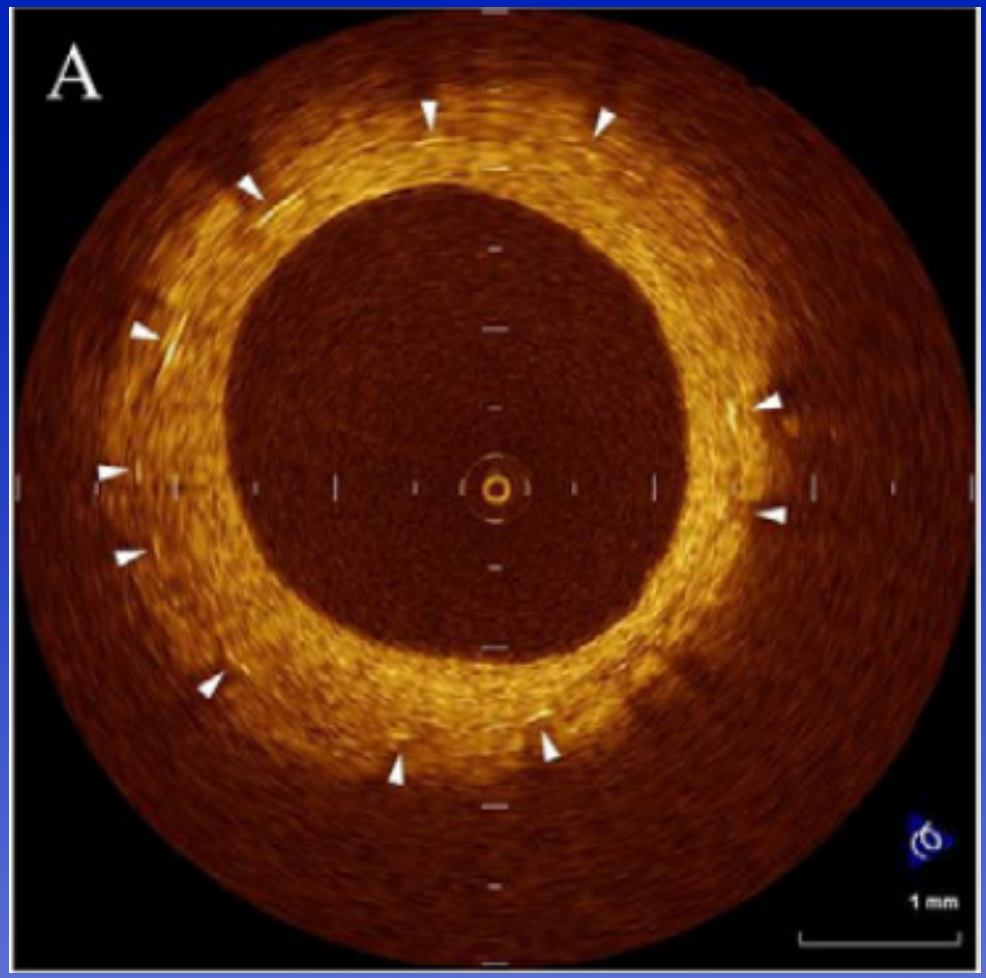
CJC 2013

Quelles sont les données après une angioplastie coronarienne avec *stent* ?

Stent non-médicamenté

- Formation d'une couche de néointima rapide
  - Durée minimale: 1 mois

  (2 semaines en cas de nécessité clinique ++)



Am Heart J 2012

Stent médicamenté

- Situation devient plus complexe…

- DES pour un SCA?
- DES pour MCAS stable?
- Durée minimale versus durée idéale?
- Matrice biorésorbable versus *stent*

Une avalanche arrive!

ARCTIC-Interruption

DES-LATE

ISAR-SAFE

ITALIC

RESET

DAPT

PEGASUS

OPTIMIZE

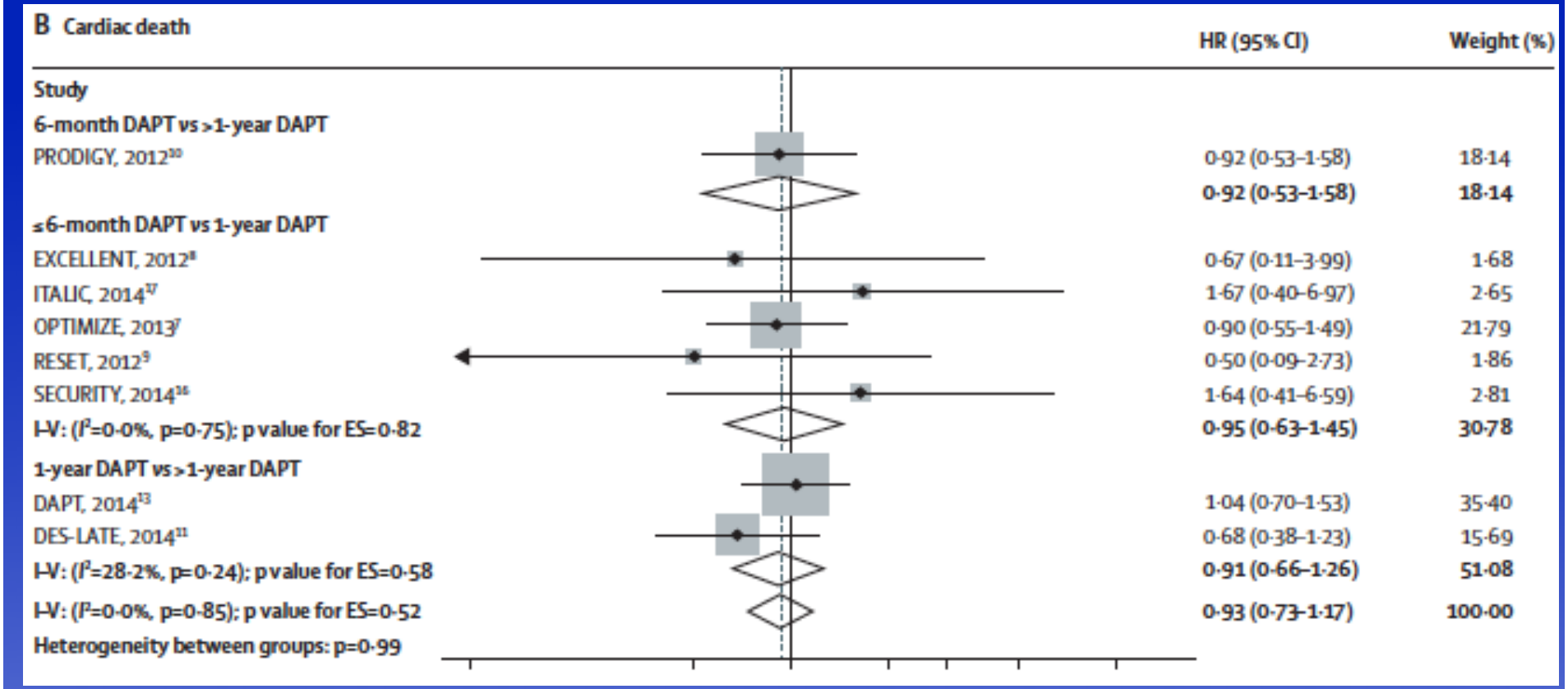
EXCELLENT

PRODIGY

SECURITY

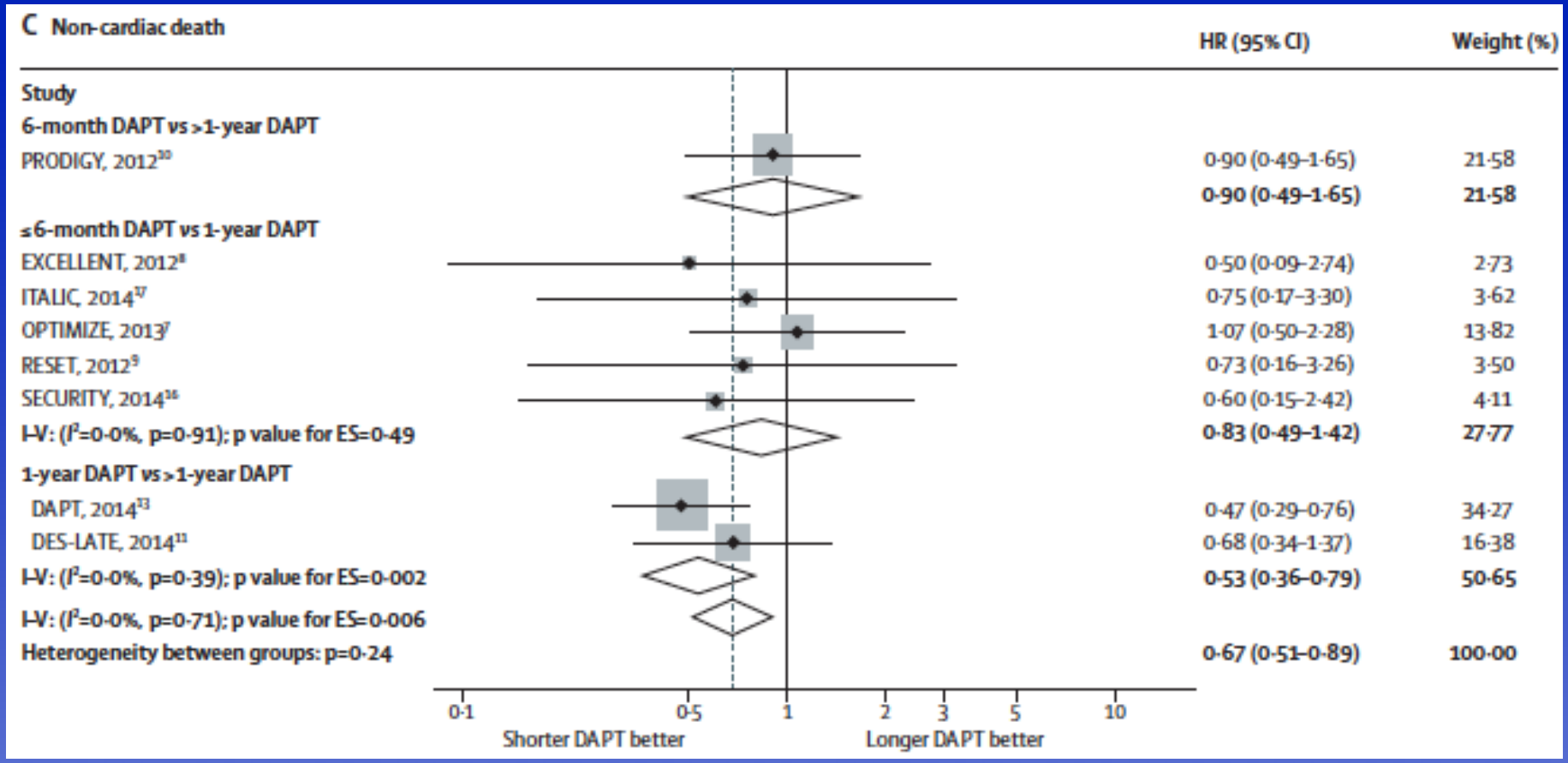
	Pub	N	Population	SCA	Durée
EXCELLENT	2012	1443	100% DES	50%	6 vs 12
PRODIGY	2012	1501	25% BMS 25%zota/25%pacli/25% evero	75%	6 vs 24
RESET	2012	2117	50% zota 50% autres DES	55%	3 vs 12
OPTIMIZE	2013	3119	100% zotarolimus	40%	3 vs 12
DES-LATE	2013	5045	100% DES	60%	12 vs 36
SECURITY	2014	1399	100% DES	40% (AI)	6 vs 12
ITALIC	2014	1894	100%DES	25%	6 vs 12
ISAR-SAFE	2014	4000	100% DES	40%	6 vs 12
ARCTIC-INTERRUPTION	2014	1259	100% DES	25%	12 vs 18-24
DAPT	2014	9961	100% DES	40%	12 vs 30

Mortalité CV similaire



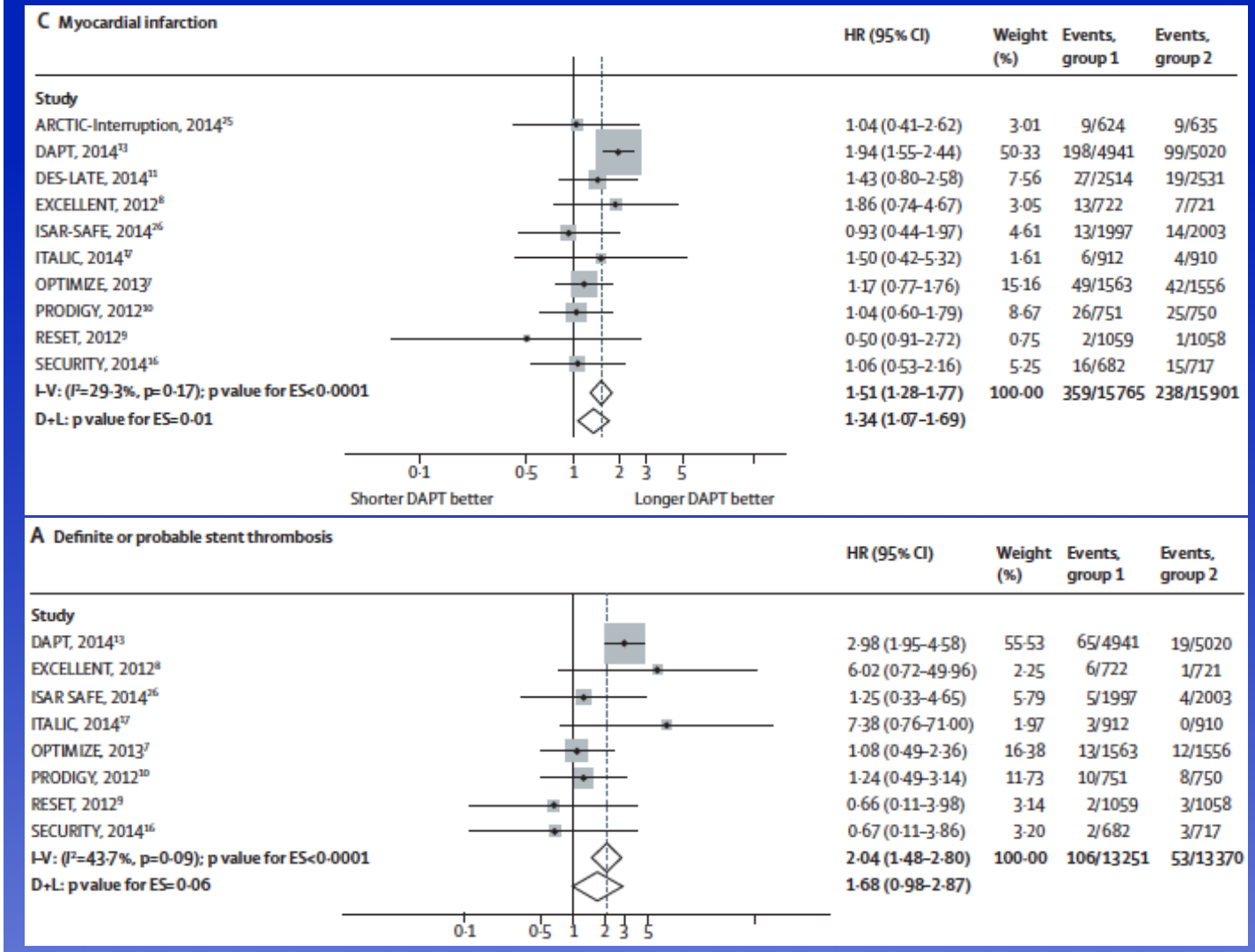
Lancet 2015

Signal au niveau de la mortalité non-cardiovascullaire

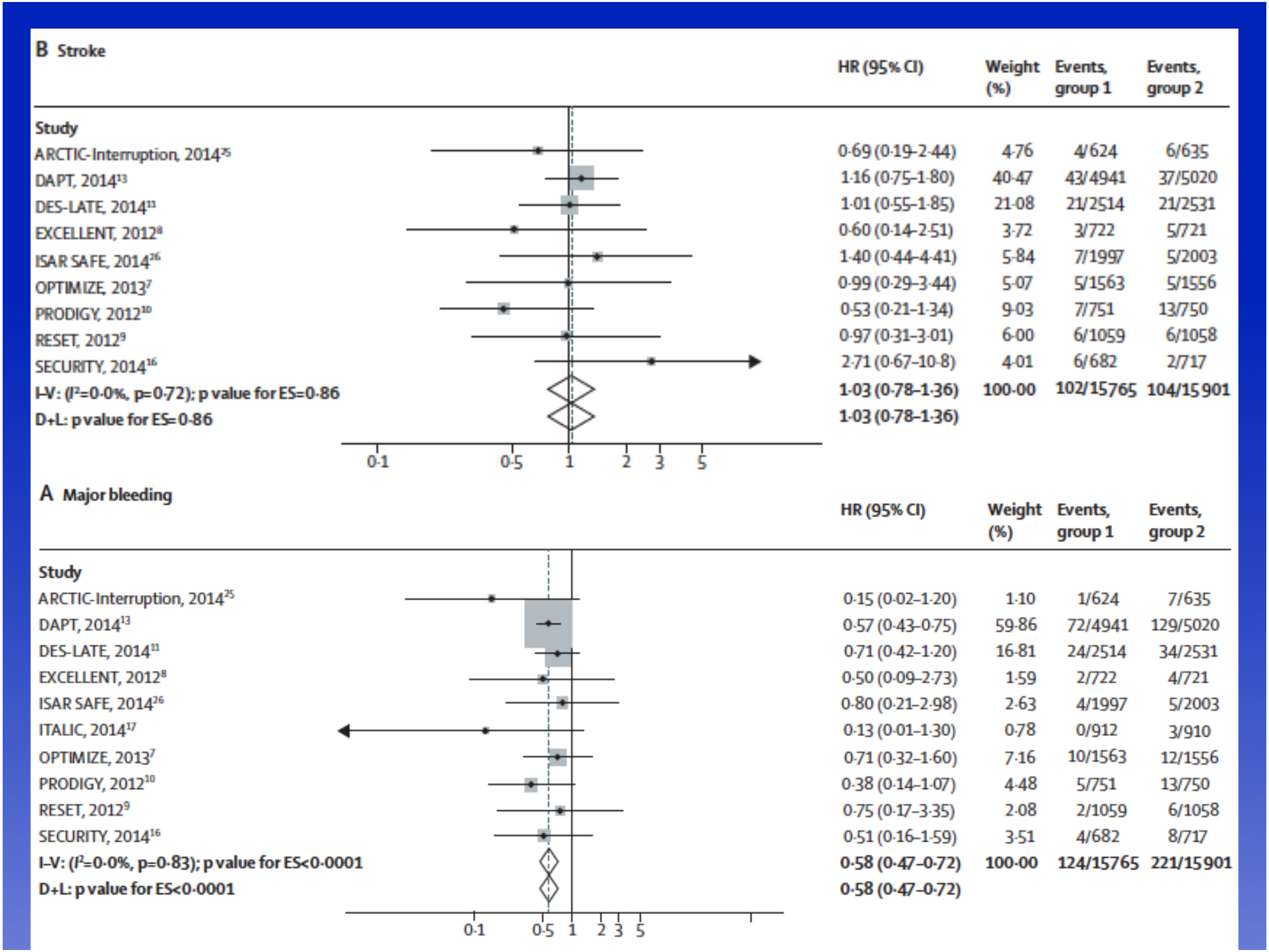


Lancet 2015

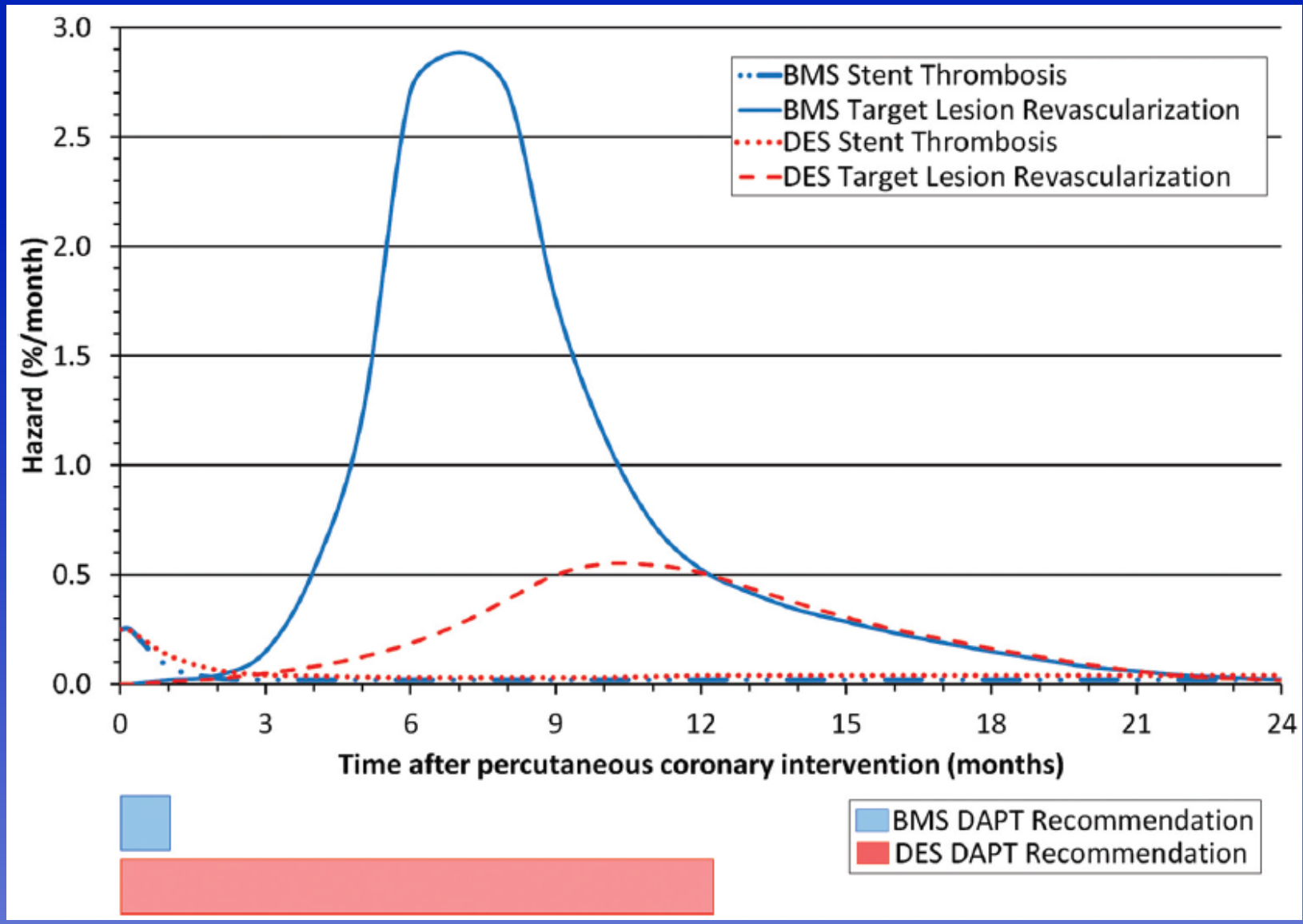
Bénéfice au niveau coronarien, mais risque associé



Lancet 2015


B Stroke
HR (95% CI)
Weight (%)
Events, group 1
Events, group 2
Study
ARCTIC-Interruption, 2014[25] 0·69 (0·19–2·44) 4·76 4/624 6/635
DAPT, 2014[13] 1·16 (0·75–1·80) 40·47 43/4941 37/5020
DES-LATE, 2014[11] 1·01 (0·55–1·85) 21·08 21/2514 21/2531
EXCELLENT, 2012[8] 0·60 (0·14–2·51) 3·72 3/722 5/721
ISAR SAFE, 2014[26] 1·40 (0·44–4·41) 5·84 7/1997 5/2003
OPTIMIZE, 2013[7] 0·99 (0·29–3·44) 5·07 5/1563 5/1556
PRODIGY, 2012[10] 0·53 (0·21–1·34) 9·03 7/751 13/750
RESET, 2012[9] 0·97 (0·31–3·01) 6·00 6/1059 6/1058
SECURITY, 2014[16] 2·71 (0·67–10·8) 4·01 6/682 2/717
I-V: (I^2=0·0%, p=0·72); p value for ES=0·86 1·03 (0·78–1·36) 100·00 102/15765 104/15901
D+L: p value for ES=0·86 1·03 (0·78–1·36)
0·1
0·5
1
2
3
5
A Major bleeding
HR (95% CI)
Weight (%)
Events, group 1
Events, group 2
Study
ARCTIC-Interruption, 2014[25] 0·15 (0·02–1·20) 1·10 1/624 7/635
DAPT, 2014[13] 0·57 (0·43–0·75) 59·86 72/4941 129/5020
DES-LATE, 2014[11] 0·71 (0·42–1·20) 16·81 24/2514 34/2531
EXCELLENT, 2012[8] 0·50 (0·09–2·73) 1·59 2/722 4/721
ISAR SAFE, 2014[26] 0·80 (0·21–2·98) 2·63 4/1997 5/2003
ITALIC, 2014[17] 0·13 (0·01–1·30) 0·78 0/912 3/910
OPTIMIZE, 2013[7] 0·71 (0·32–1·60) 7·16 10/1563 12/1556
PRODIGY, 2012[10] 0·38 (0·14–1·07) 4·48 5/751 13/750
RESET, 2012[9] 0·75 (0·17–3·35) 2·08 2/1059 6/1058
SECURITY, 2014[16] 0·51 (0·16–1·59) 3·51 4/682 8/717
I-V: (I^2=0·0%, p=0·83); p value for ES<0·0001 0·58 (0·47–0·72) 100·00 124/15765 221/15901
D+L: p value for ES<0·0001 0·58 (0·47–0·72)
0·1
0·5
1
2
3
5

Comprendre les risques



Circ 2012

De façon générale avec *stent* médicamenté

- Durée minimale sécuritaire: 3-6 mois
- Durée idéale ≠ universel
- Durée > 12 mois de routine
  - Non-recommandé

Est-ce que la double thérapie antiplaquettaire est donnée pour le *stent* ou pour le patient?

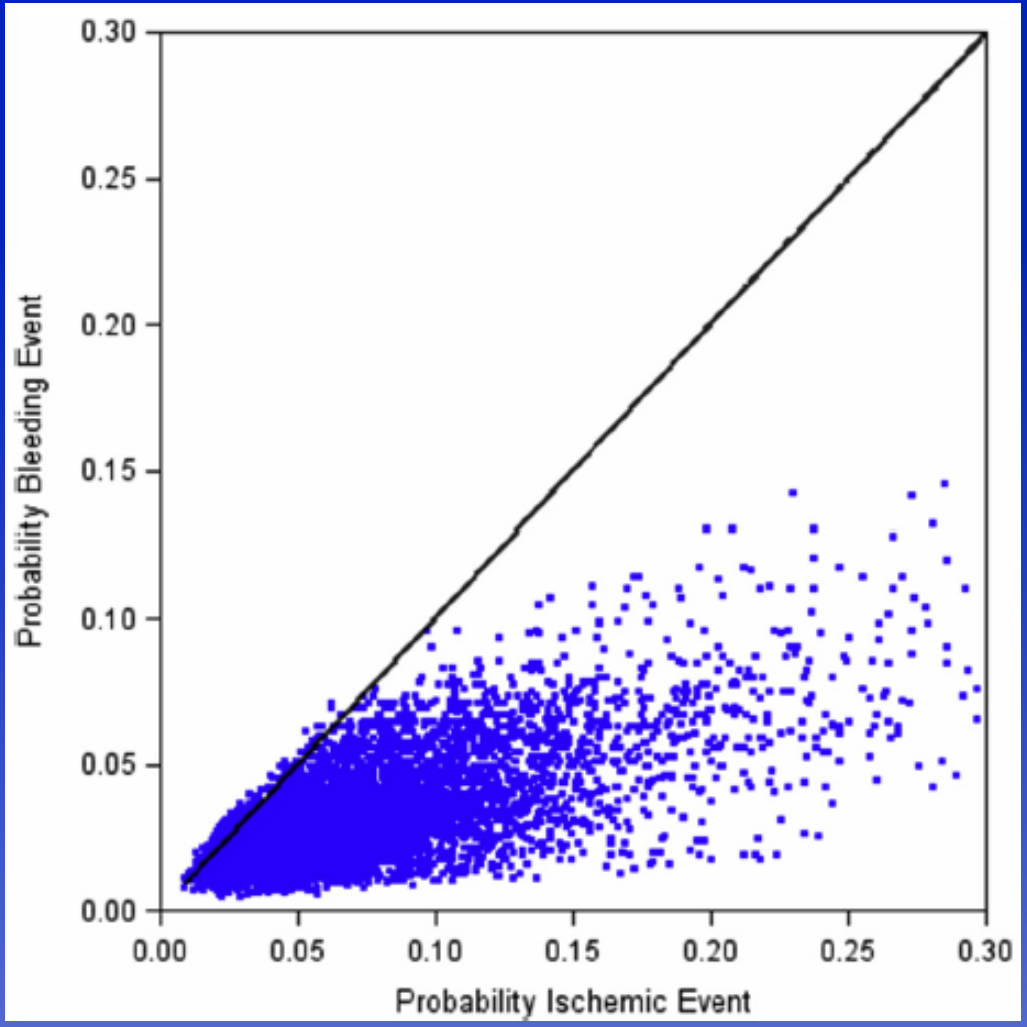
Prédiction du risque à long terme (4 ans) post-PCI

Variable	ISCHEMIC ENDPOINT		BLEEDING ENDPOINT	
	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
Age, per 10 years	1.37	1.25 – 1.50	1.38	1.22 – 1.56
Male	1.36	1.12 – 1.66	-	-
Body mass index, per kg/m^2	1.03	1.01 – 1.04	-	-
Active smoking	1.49	1.22 – 1.81	1.34	1.03 – 1.75
Diabetes mellitus	1.77	1.50 – 2.09	1.24	1.00 – 1.55
Prior myocardial infarction	1.47	1.23 – 1.76	-	-
Prior coronary artery bypass graft surgery	1.41	1.06 – 1.87	-	-
Prior congestive heart failure	1.75	1.27 – 2.39	1.73	1.15 – 2.60
Creatinine clearance, mL/min				
≥ 60	Reference	Reference	Reference	Reference
30-59	1.93	1.55 – 2.41	1.61	1.23 – 2.11
< 30	5.41	3.14 – 9.32	2.79	1.43 – 5.41
Missing	1.61	1.19 – 2.18	0.56	0.30 – 1.07
Presentation				
Stable angina	Reference	Reference	-	-
Non-ST elevation acute coronary syndrome	1.14	0.96 – 1.35		
ST elevation myocardial infarction	1.71	1.29 – 2.26		
E-ZES	0.80	0.68 – 0.93	-	-
Total stent length, per 10 mm	1.07	1.03 – 1.10	-	-

- Facteurs de risque de saignement sont aussi des facteurs de risque d'événements ischémiques

Am J Cardiol 2015

Corrélation des risques



- 97% risques ischémiques > saignements majeurs

Am J Cardiol 2015

Prévention secondaire à long terme

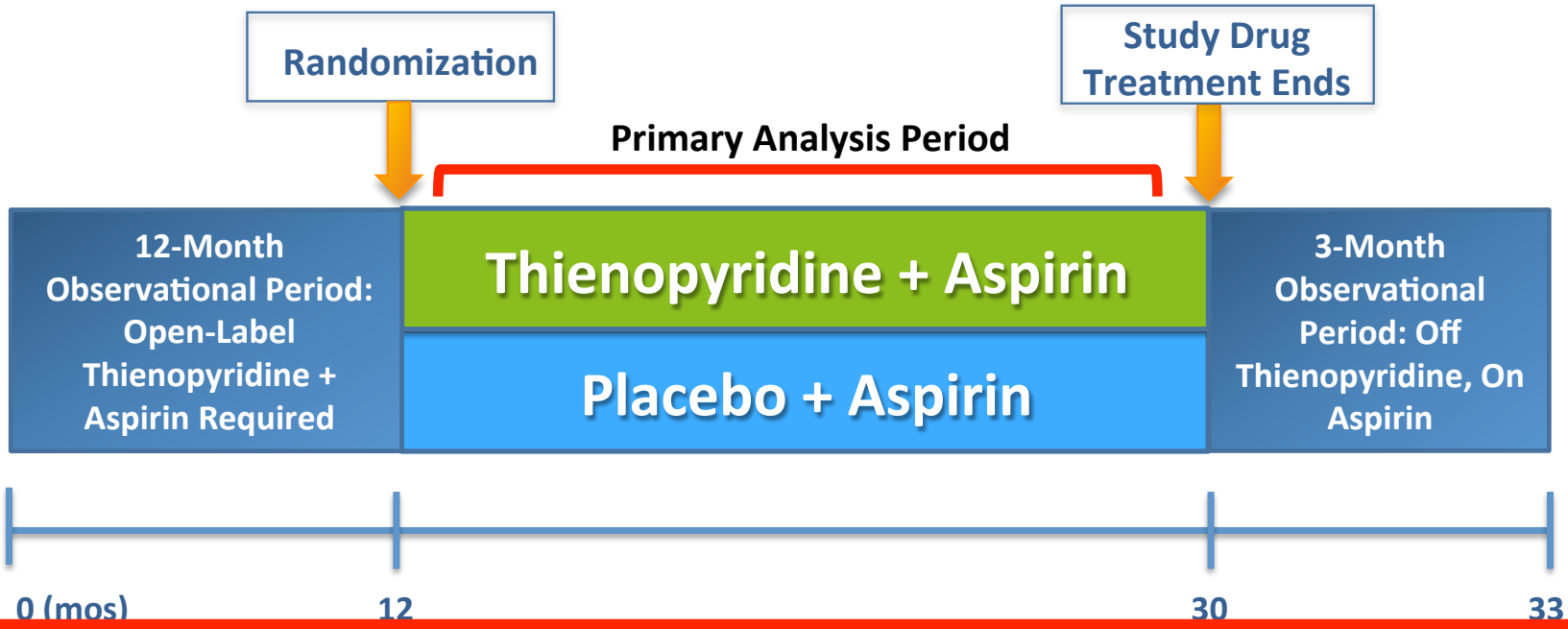
N Engl J Med 2014, N Engl J Med 2015

Dual Antiplatelet Therapy Beyond One Year After Drug-eluting Coronary Stent Procedures

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

on behalf of the Dual Antiplatelet Therapy (DAPT) Study Investigators

Design

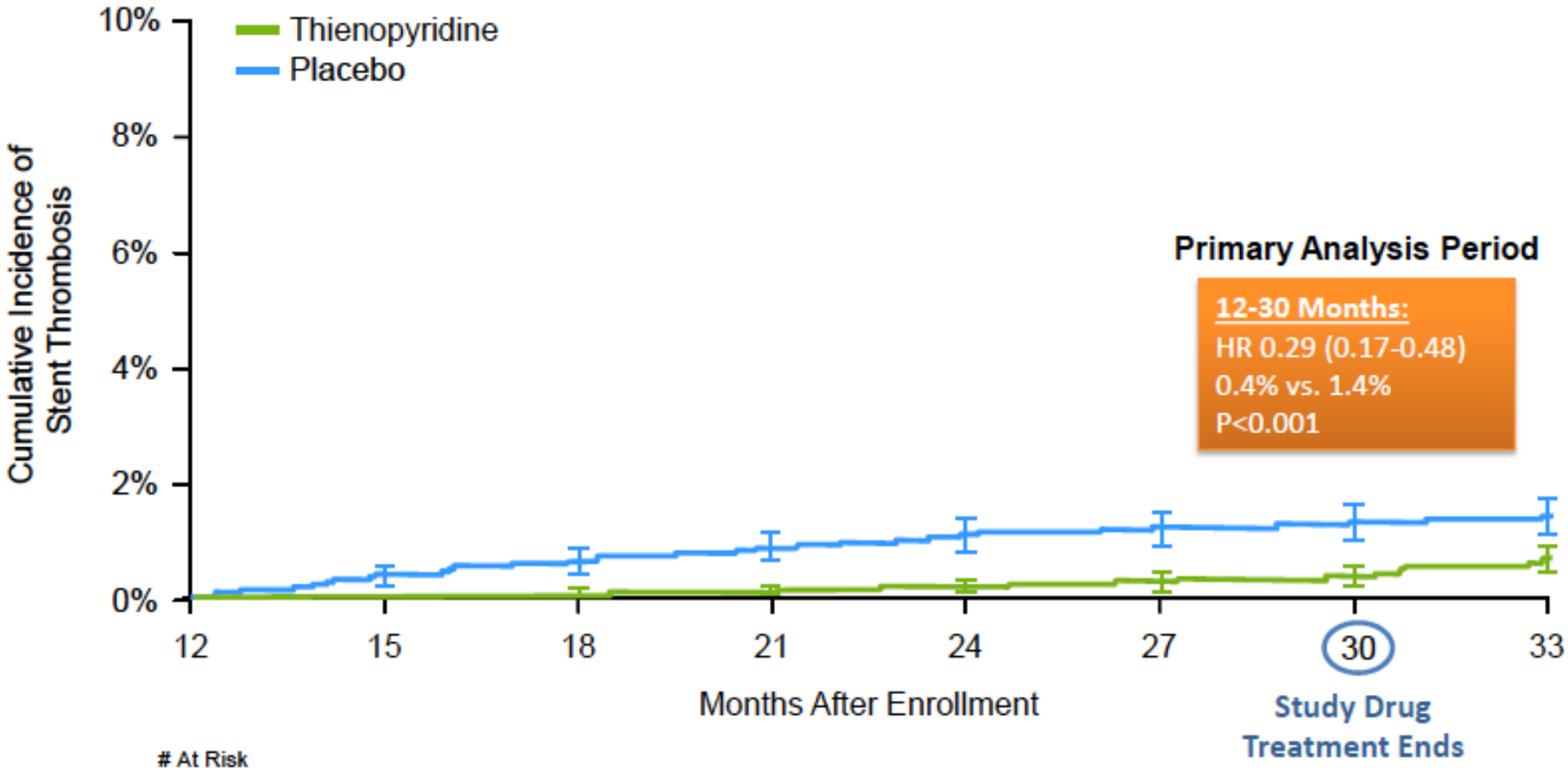


Inclusion: FDA-approved DES or BMS, candidates for thienopyridine

Excluded: Oral anticoagulant therapy; life expectancy < 3y

Randomized: Free from MI, stroke, repeat revascularization, moderate/severe bleeding, and adherent with therapy at 12 months

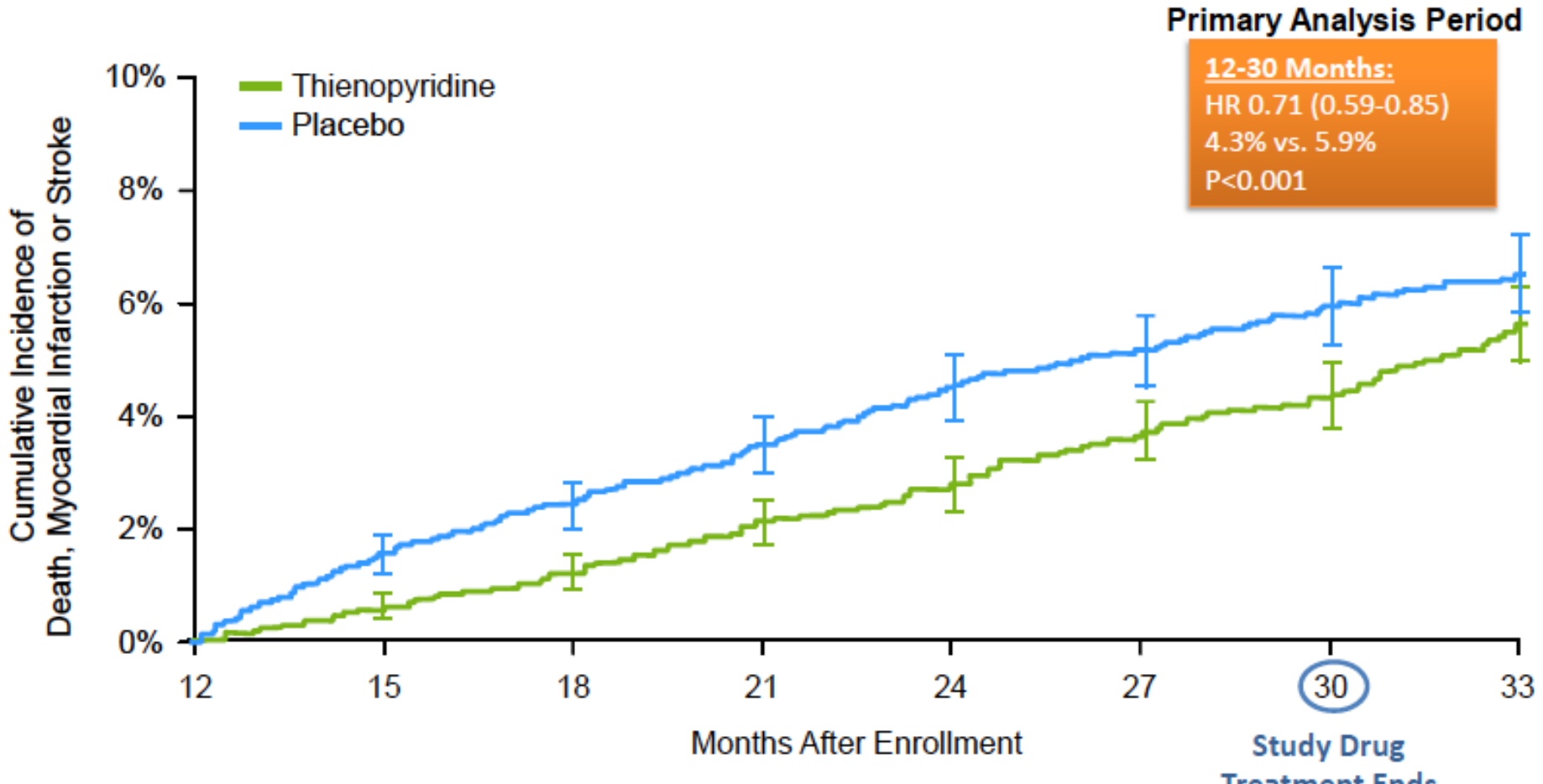
Co-Primary Effectiveness End Point
Stent Thrombosis



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

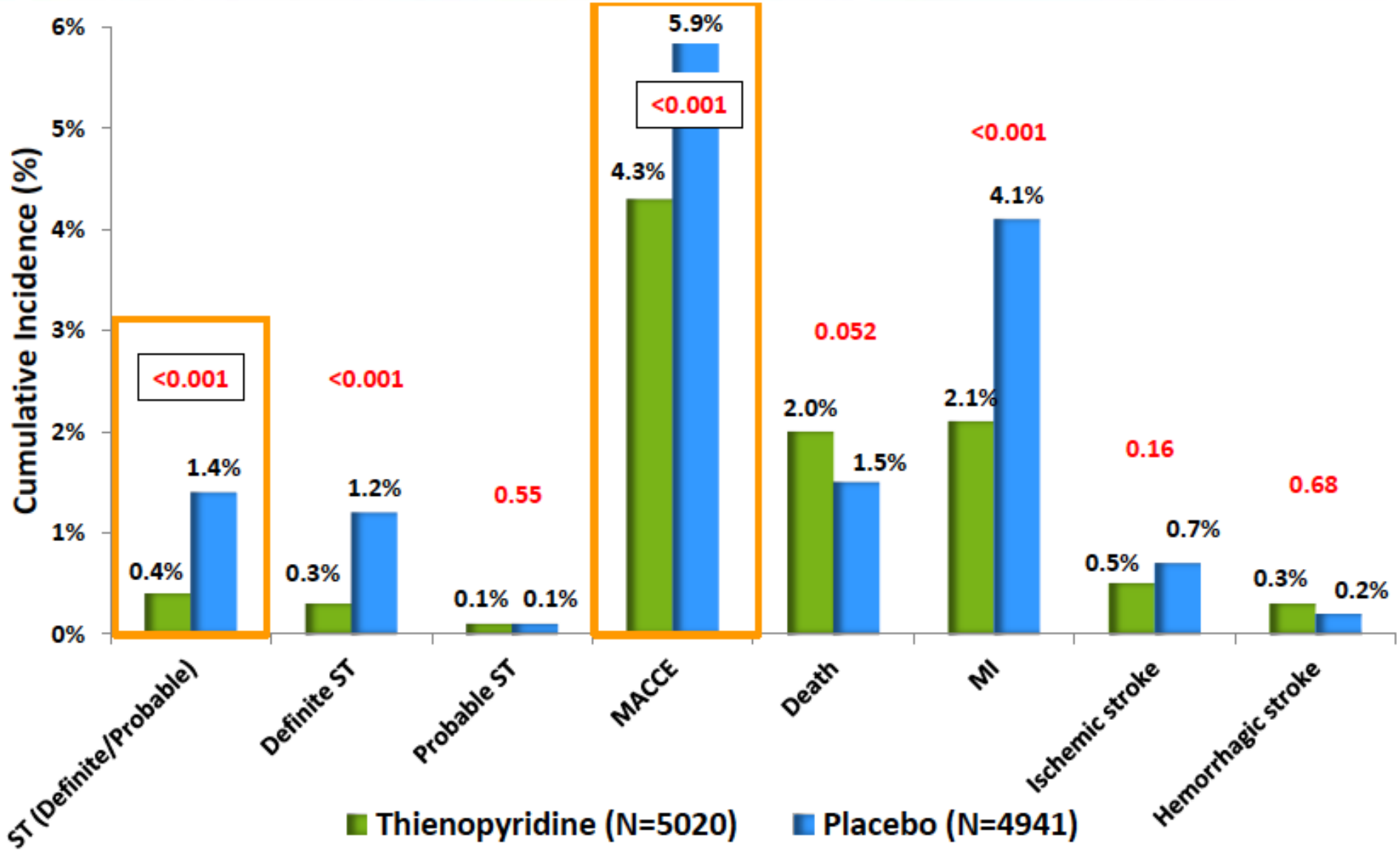
Co-Primary Effectiveness End Point MACCE

DAPT STUDY

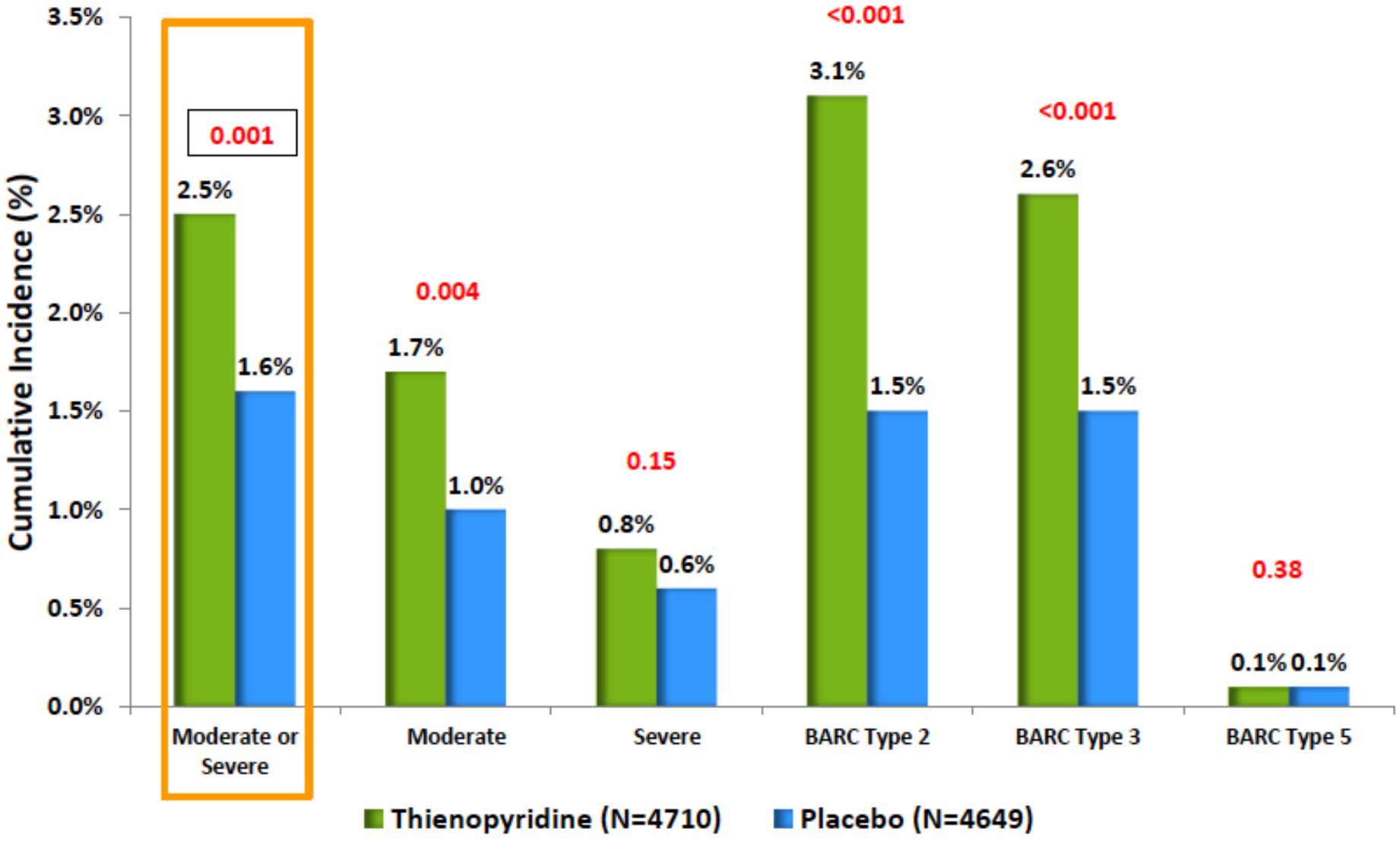


# At Risk								
Thienopyridine	5020	4917	4840	4778	4702	4611	4554	3029
Placebo	4941	4799	4715	4635	4542	4476	4412	2997

Co-Primary Effectiveness End Points & Components: 12-30 Months



Primary Safety End Point (Moderate or Severe Bleeding): 12-30 Months

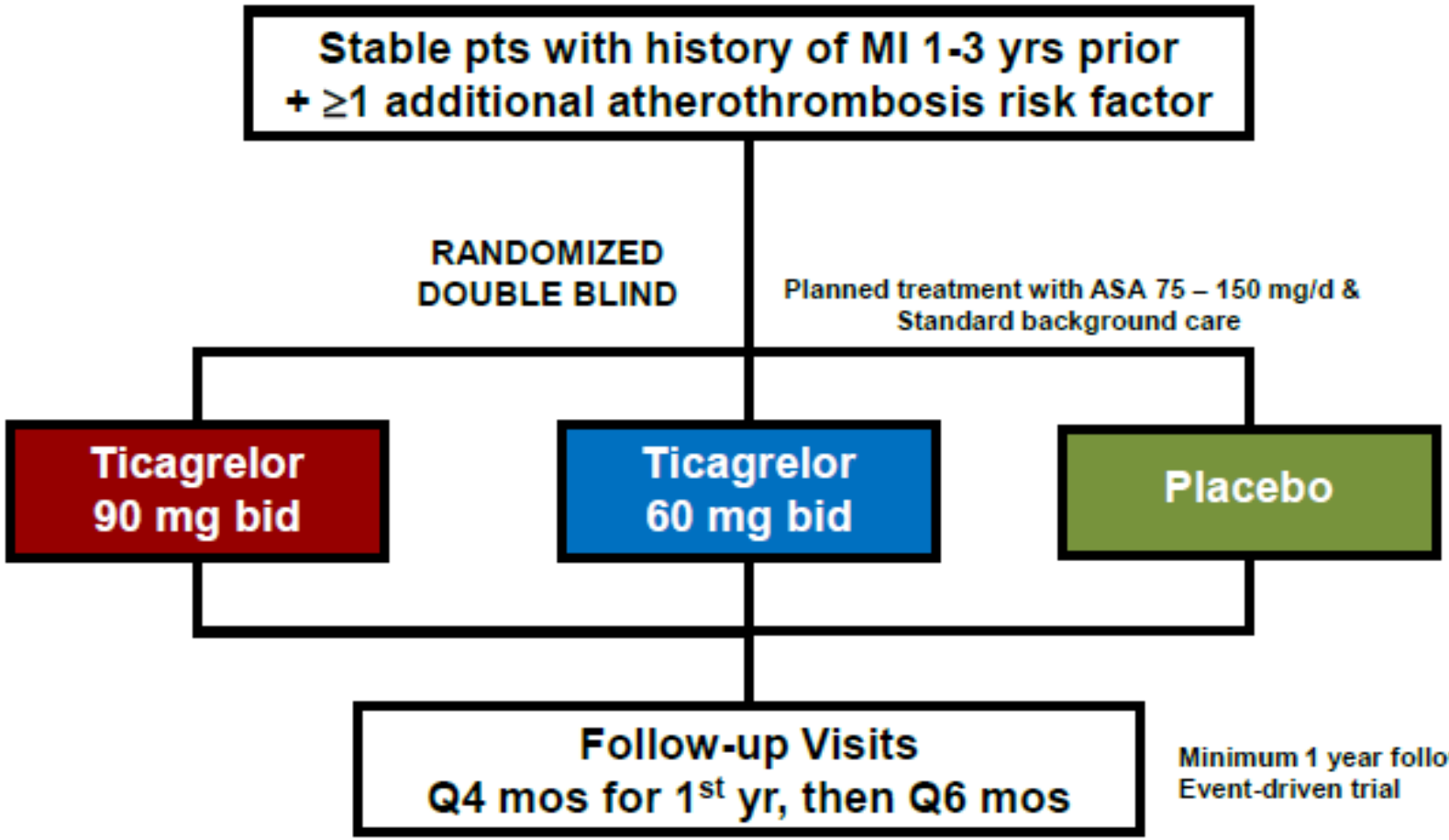


Prevention of Cardiovascular Events in Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin

Marc S. Sabatine, MD, MPH
on behalf of the PEGASUS-TIMI 54
Executive & Steering Committees and Investigators

NCT00526474

Trial Design



Bonaca MP et al. *Am Heart J* 2014;167:437-44

Key Inclusion & Exclusion Criteria

KEY INCLUSION

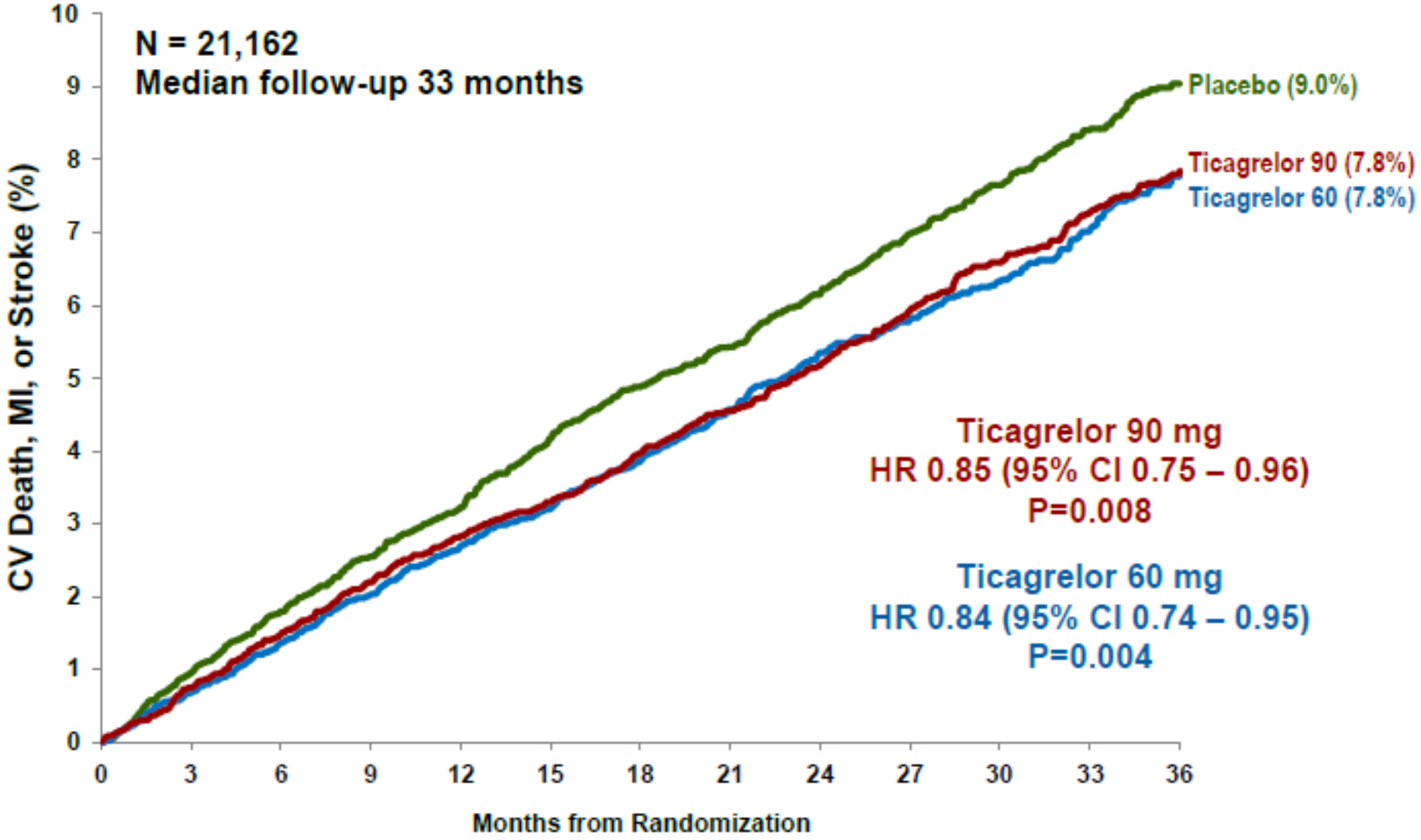
- Age ≥50 years
- At least 1 of the following:
  - Age ≥65 years
  - Diabetes requiring medication
  - 2nd prior MI (>1 year ago)
  - Multivessel CAD
  - CrCl <60 mL/min
- Tolerating ASA and able to be dosed at 75-150 mg/d

KEY EXCLUSION

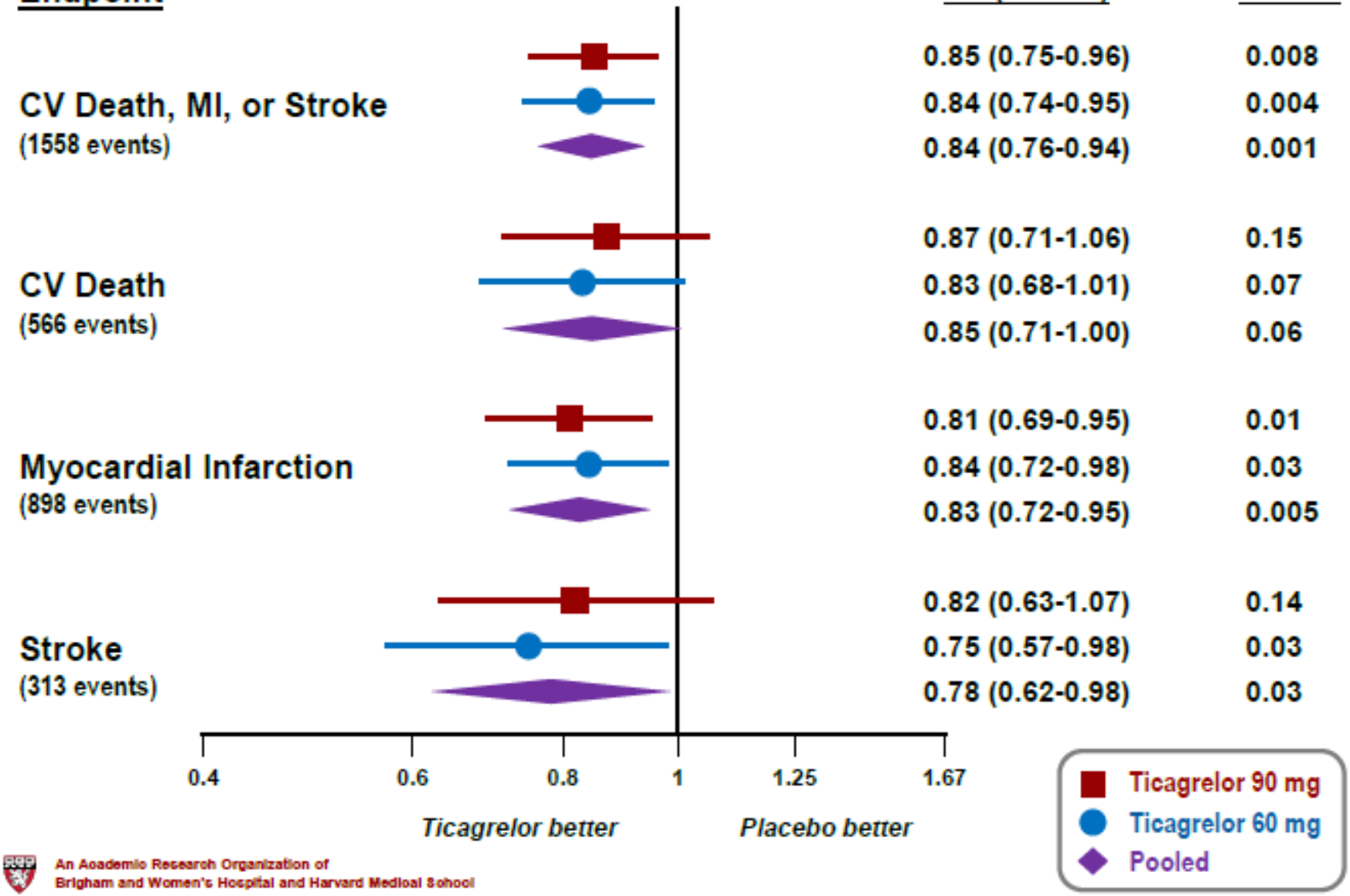
- Planned use of $P2Y_{12}$ antagonist, dipyridamole, cilostazol, or anticoag
- Bleeding disorder
- History of ischemic stroke, ICH, CNS tumor or vascular abnormality
- Recent GI bleed or major surgery
- At risk for bradycardia
- Dialysis or severe liver disease

Bonaca MP et al. *Am Heart J* 2014;167:437-44

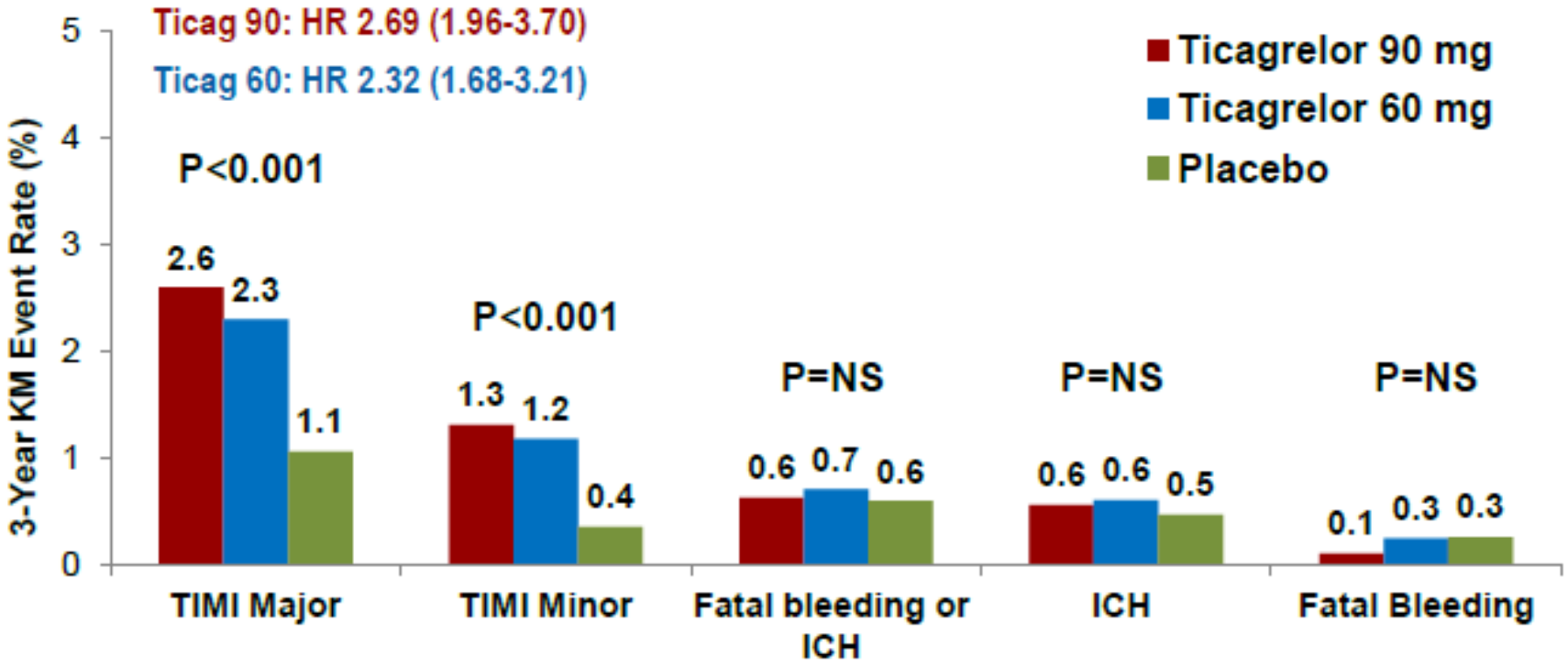
Primary Endpoint



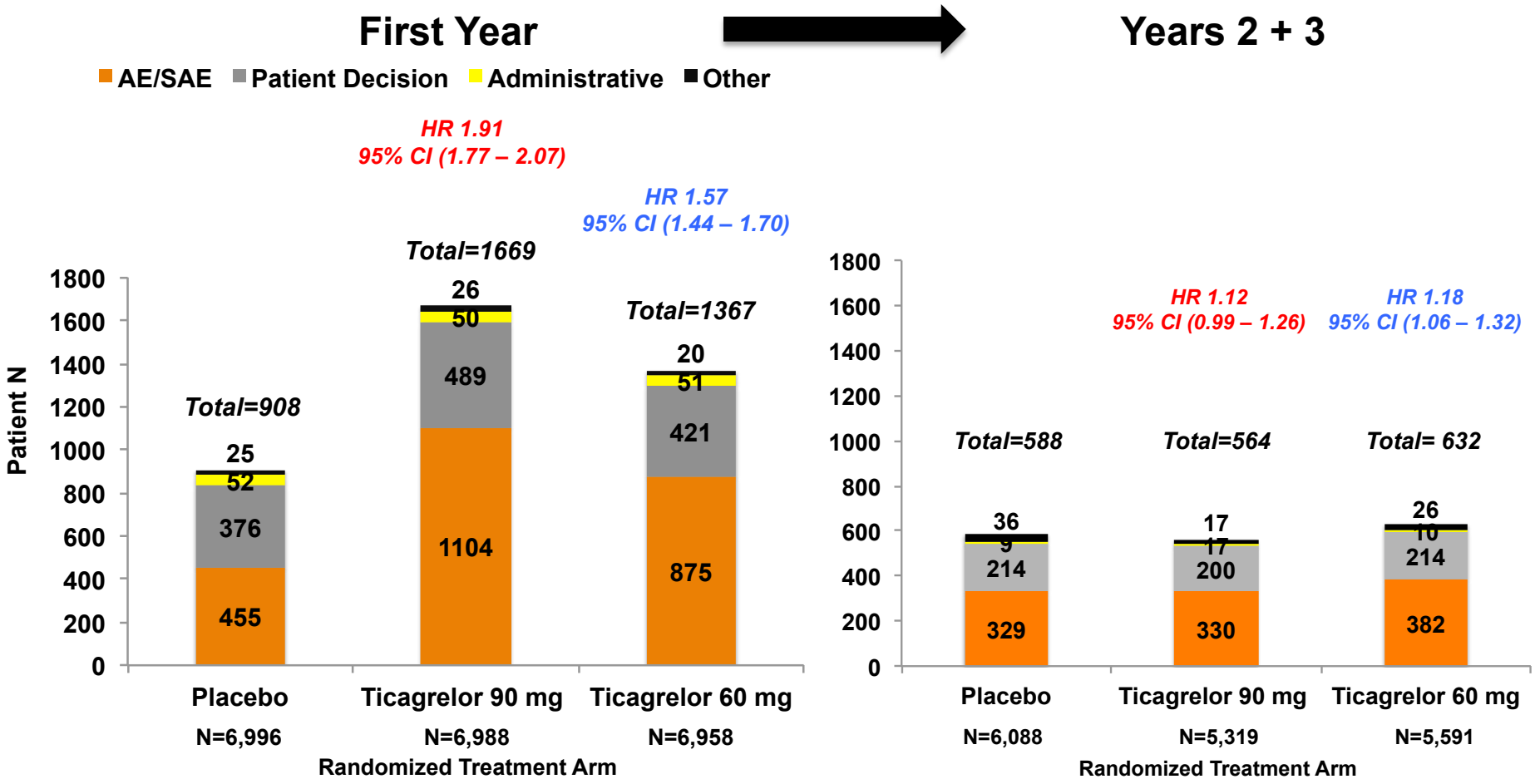
Components of Primary Endpoint



Bleeding


Ticag 90: HR 2.69 (1.96-3.70)
Ticag 60: HR 2.32 (1.68-3.21)
Ticagrelor 90 mg
Ticagrelor 60 mg
Placebo
3-Year KM Event Rate (%)
0
1
2
3
4
5
P<0.001
2.6
2.3
1.1
P<0.001
1.3
1.2
0.4
P=NS
0.6
0.7
0.6
P=NS
0.6
0.6
0.5
P=NS
0.1
0.3
0.3
TIMI Major
TIMI Minor
Fatal bleeding or ICH
ICH
Fatal Bleeding

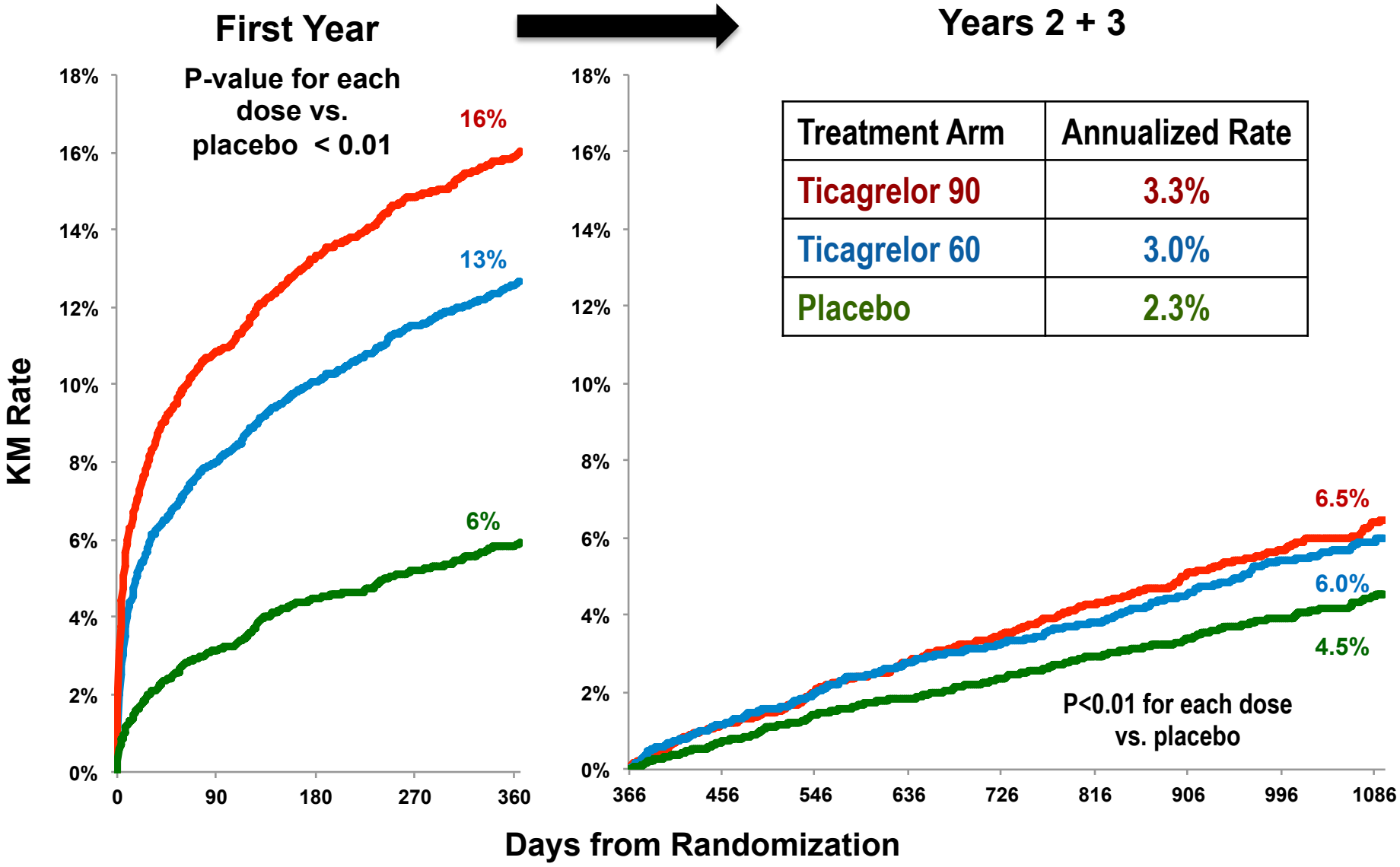
Drug discontinuation by Treatment Arm



Drug discontinuation for AE by Treatment

PEGASUS TIMI 54

Ticagarelor 90 mg twice daily | Ticagrelor 60 mg twice daily | Placebo

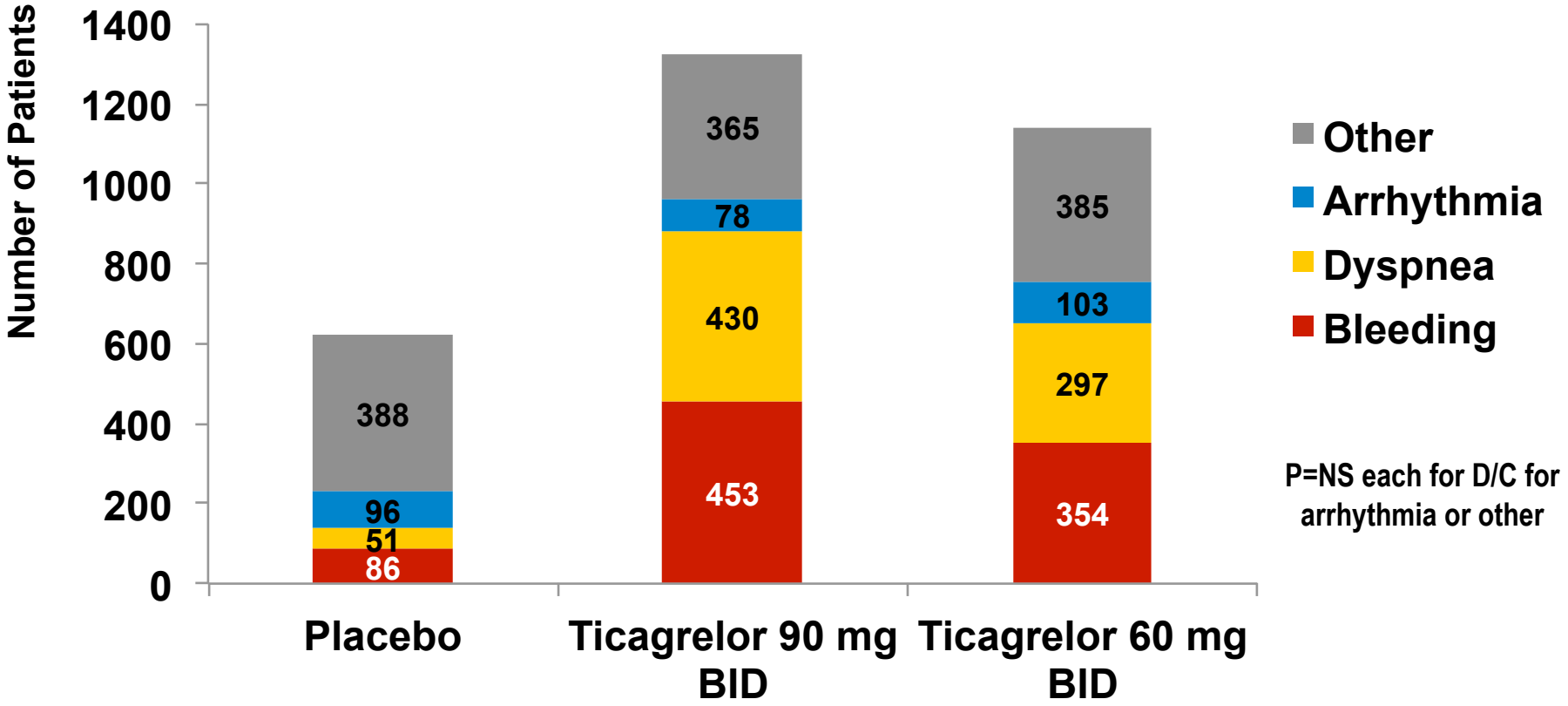


Treatment Arm	Annualized Rate
Ticagrelor 90	3.3%
Ticagrelor 60	3.0%
Placebo	2.3%

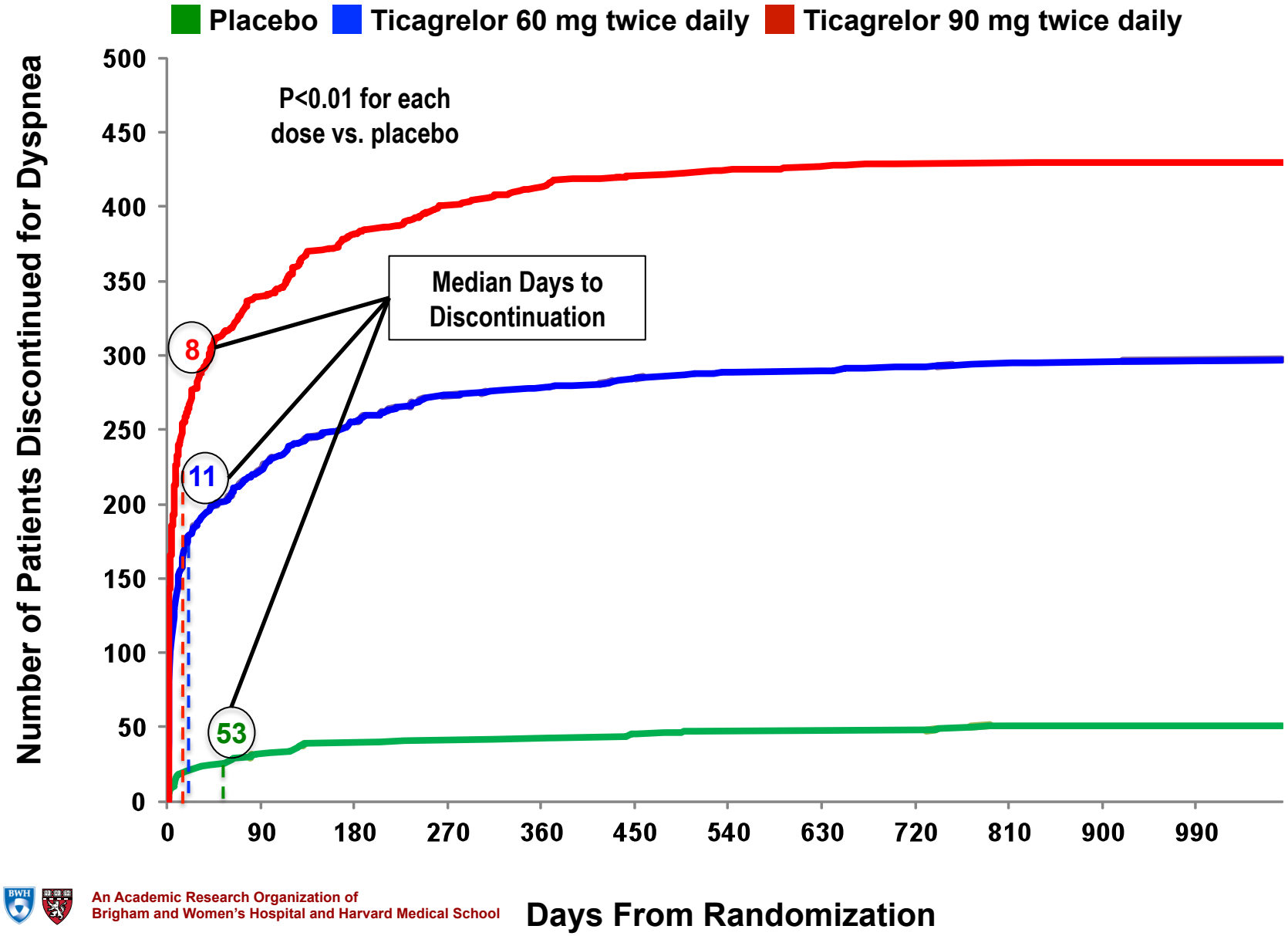
Adverse Events Leading to Discontinuation

3 Year KM Rate (%) – p-value for each dose vs. placebo <0.001

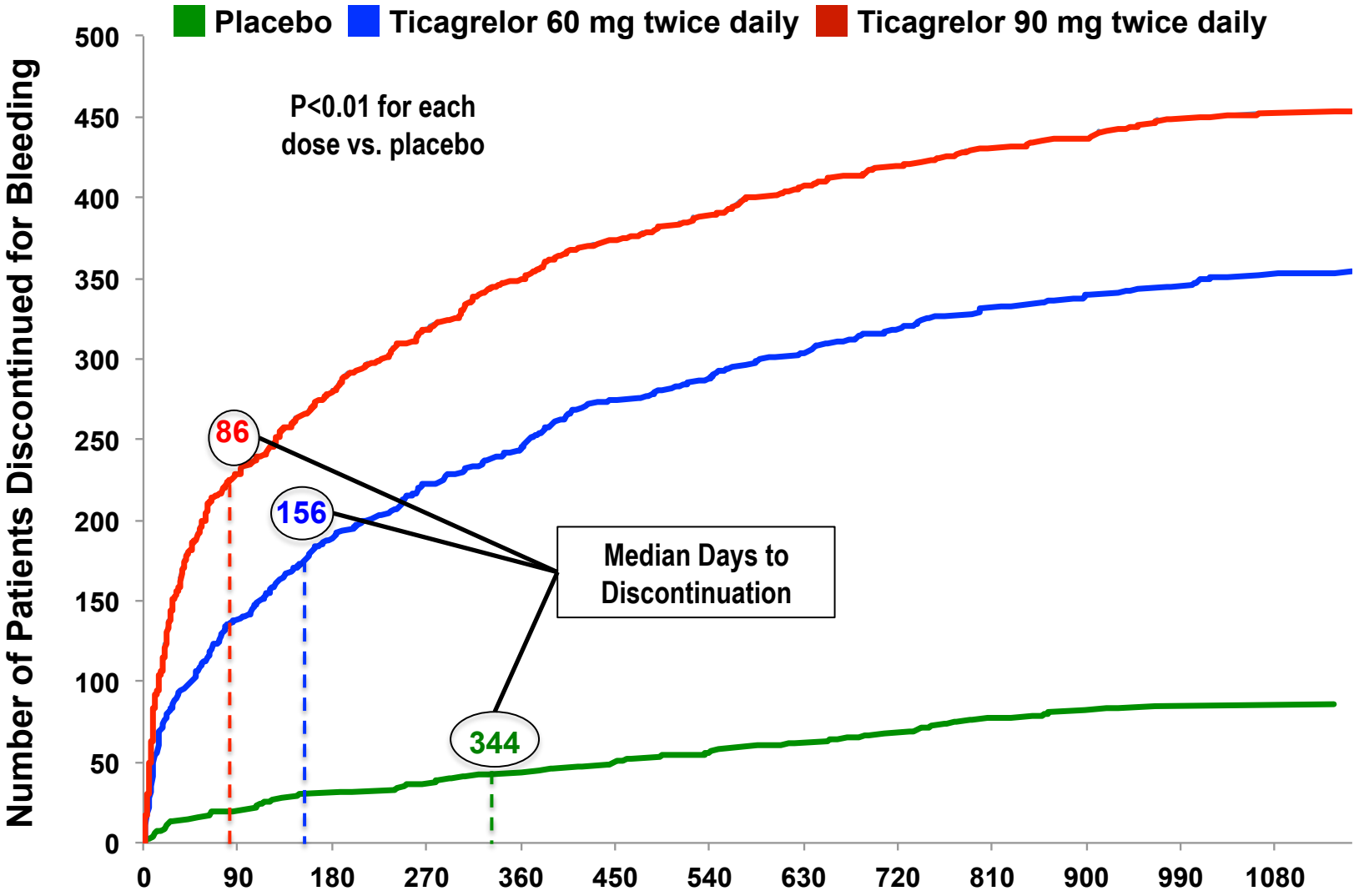
Treatment Arm	Any AE	Bleeding	Dyspnea
Ticagrelor 90	19.0%	7.8%	6.5%
Ticagrelor 60	16.4%	6.2%	4.6%
Placebo	8.9%	1.5%	0.8%



Discontinuation over time for Dyspnea by Randomization Group



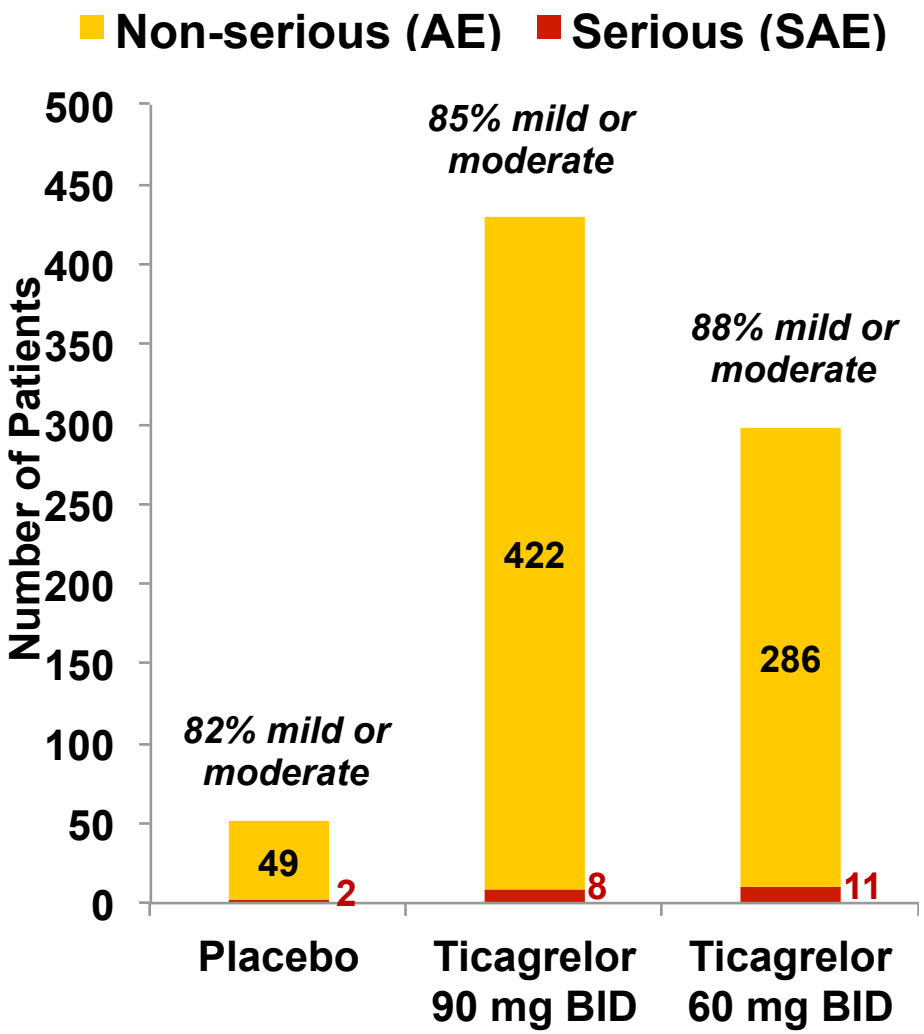
Discontinuation over time for Bleeding by Randomization Group



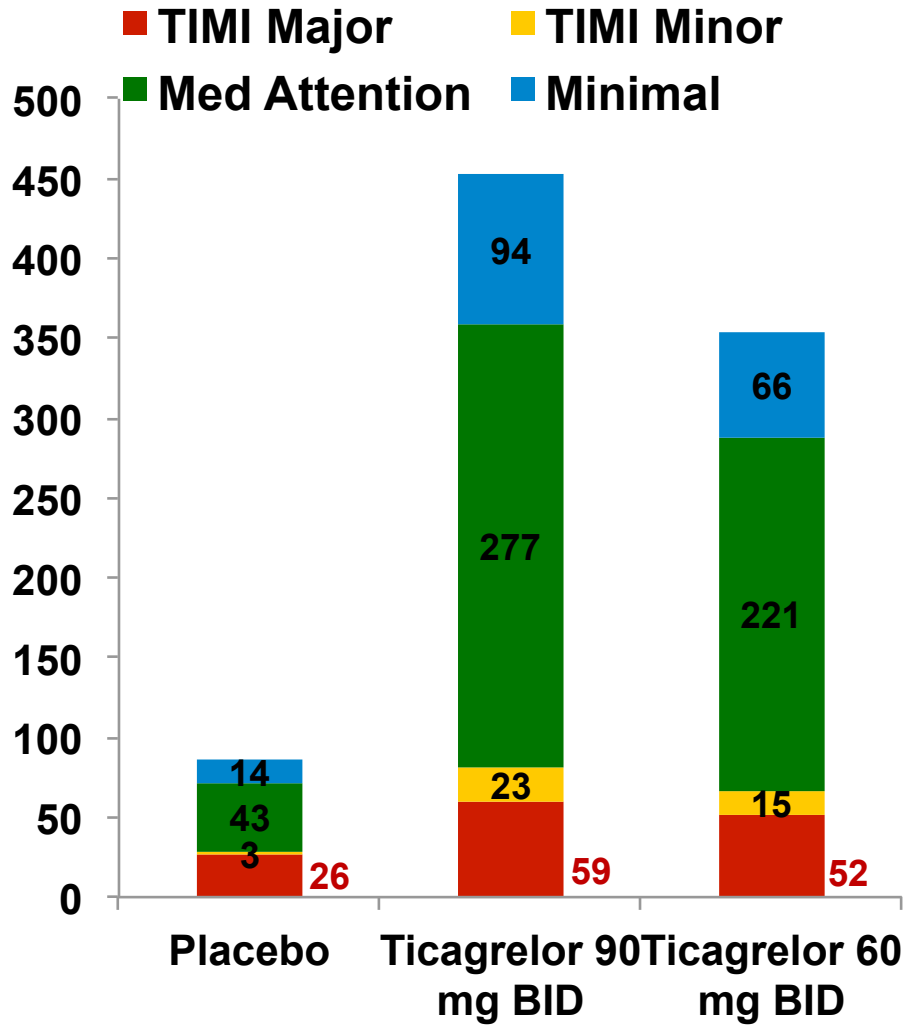
Dyspnea and Bleeding

PEGASUS TIMI 54

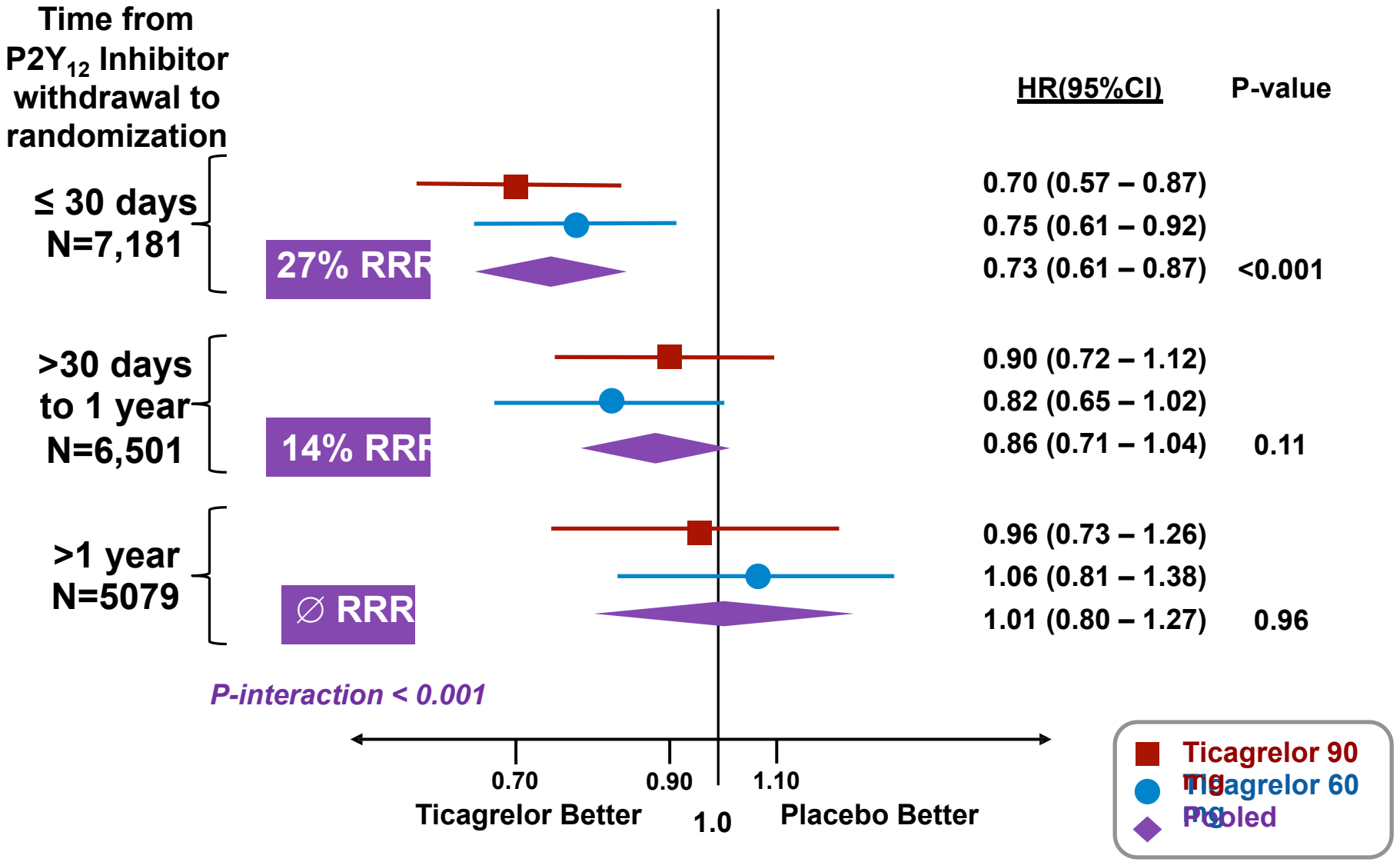
Dyspnea



Bleeding



Reduction in MACE with Ticagrelor by Time from $P2Y_{12}$ Inhibitor Withdrawal



European Heart Journal
doi:10.1093/eurheartj/ehv443

FASTTRACK
ESC Clinical Trial Update

Long-term dual antiplatelet therapy for secondary prevention of cardiovascular events in the subgroup of patients with previous myocardial infarction: a collaborative meta-analysis of randomized trials

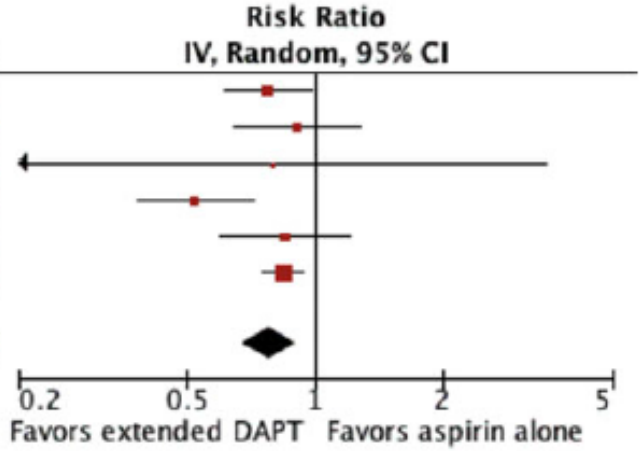
Jacob A. Udell[1,2*], Marc P. Bonaca[3], Jean-Philippe Collet[4], A. Michael Lincoff[5], Dean J. Kereiakes[6], Francesco Costa[7], Cheol Whan Lee[8], Laura Mauri[9], Marco Valgimigli[7,10], Seung-Jung Park[8], Gilles Montalescot[4], Marc S. Sabatine[3], Eugene Braunwald[3], and Deepak L. Bhatt[3*]

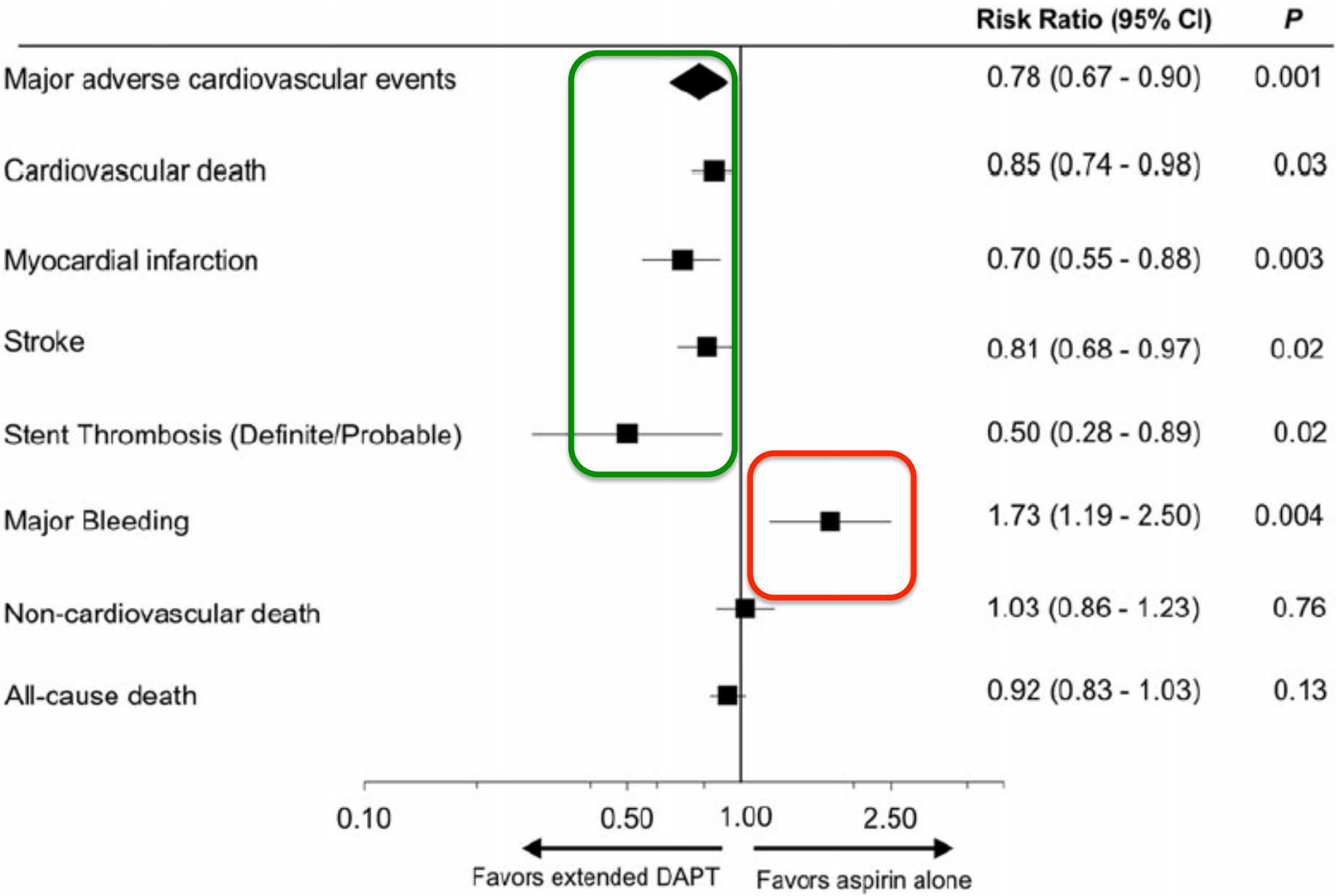
- 6 études randomisées prévention secondaire
  - ASA versus DAPT prolongée > 12 mois
  - Suivi > 12 mois
  - Présentation ou ATCD infarctus du myocarde

Study or Subgroup	Extended DAPT Events	Extended DAPT Total	Aspirin Alone Events	Aspirin Alone Total	Weight	Risk Ratio IV, Random, 95% CI
2006 CHARISMA MI cohort	125	1903	162	1943	21.4%	0.77 [0.61, 0.98]
2012 PRODIGY	63	732	69	733	13.3%	0.91 [0.65, 1.28]
2014 ARCTIC-Interruption	3	156	4	167	1.0%	0.79 [0.18, 3.51]
2014 DAPT	59	1805	108	1771	14.6%	0.52 [0.38, 0.72]
2014 DES-LATE	56	1512	66	1551	12.9%	0.85 [0.60, 1.21]
2015 PEGASUS-TIMI 54	980	14095	578	7067	36.8%	0.84 [0.76, 0.94]
Total (95% CI)		**20203**		**13232**	**100.0%**	**0.78 [0.67, 0.90]**
Total events	1286		987			

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 8.36$, df = 5 (P = 0.14); $I^2 = 40\%$

Test for overall effect: Z = 3.28 (P = 0.001)




Risk Ratio (95% CI)
P
Major adverse cardiovascular events
0.78 (0.67 - 0.90)
0.001
Cardiovascular death
0.85 (0.74 - 0.98)
0.03
Myocardial infarction
0.70 (0.55 - 0.88)
0.003
Stroke
0.81 (0.68 - 0.97)
0.02
Stent Thrombosis (Definite/Probable)
0.50 (0.28 - 0.89)
0.02
Major Bleeding
1.73 (1.19 - 2.50)
0.004
Non-cardiovascular death
1.03 (0.86 - 1.23)
0.76
All-cause death
0.92 (0.83 - 1.03)
0.13
0.10
0.50
1.00
2.50
Favors extended DAPT
Favors aspirin alone

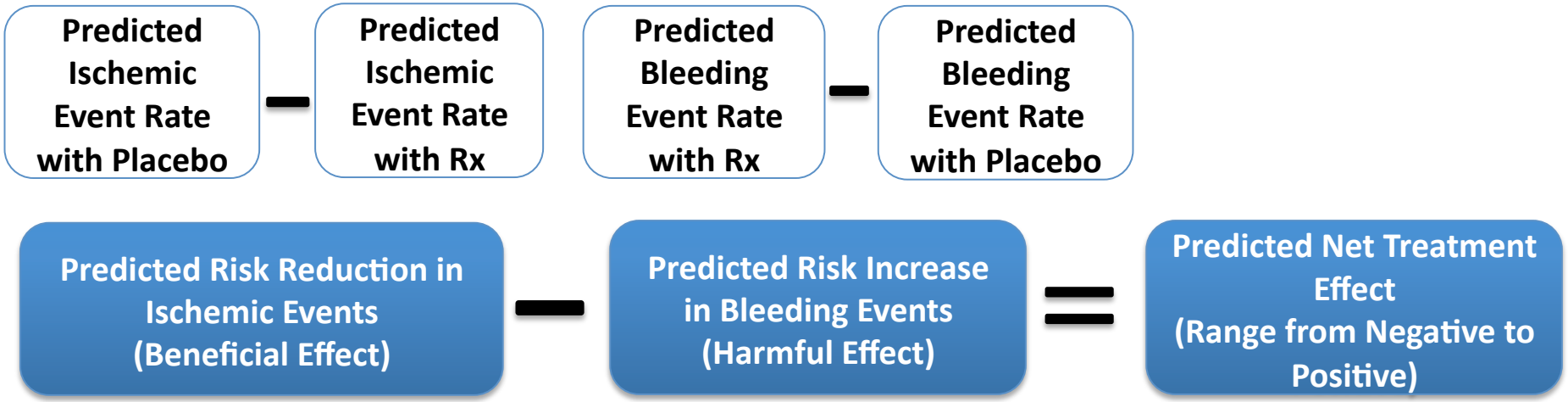
Individualizing Treatment Duration of Dual Antiplatelet Therapy after Percutaneous Coronary Intervention: An Analysis from the DAPT Study

Robert W. Yeh, Eric A. Secemsky, Dean J. Kereiakes, Sharon-Lise T. Normand, Anthony H. Gershlick, David J. Cohen, John A. Spertus, P. Gabriel Steg, Donald E. Cutlip, Michael J. Rinaldi, Edoardo Camenzind, William Wijns, Patricia K. Apruzzese, Yang Song, Joseph M. Massaro, and Laura Mauri, for the Dual Antiplatelet Therapy (DAPT) Study Investigators

Objective

- To develop a decision tool to identify whether an individual patient is more likely to derive benefit or harm from continuation of dual antiplatelet therapy beyond 1 year.
  - *Simultaneously* accounting for risks of ischemia AND bleeding with continued therapy.

Methods – Predicting Net Treatment Effect



- Predictors of net treatment effect with continued thienopyridine determined from linear regression and simplified to an integer point score ***(DAPT Score***)
- Actual outcomes presented by randomized treatment arm stratified by DAPT Score. Sensitivity analysis without paclitaxel-eluting stent-treated subjects.

Multivariable Prediction Models

DAPT STUDY

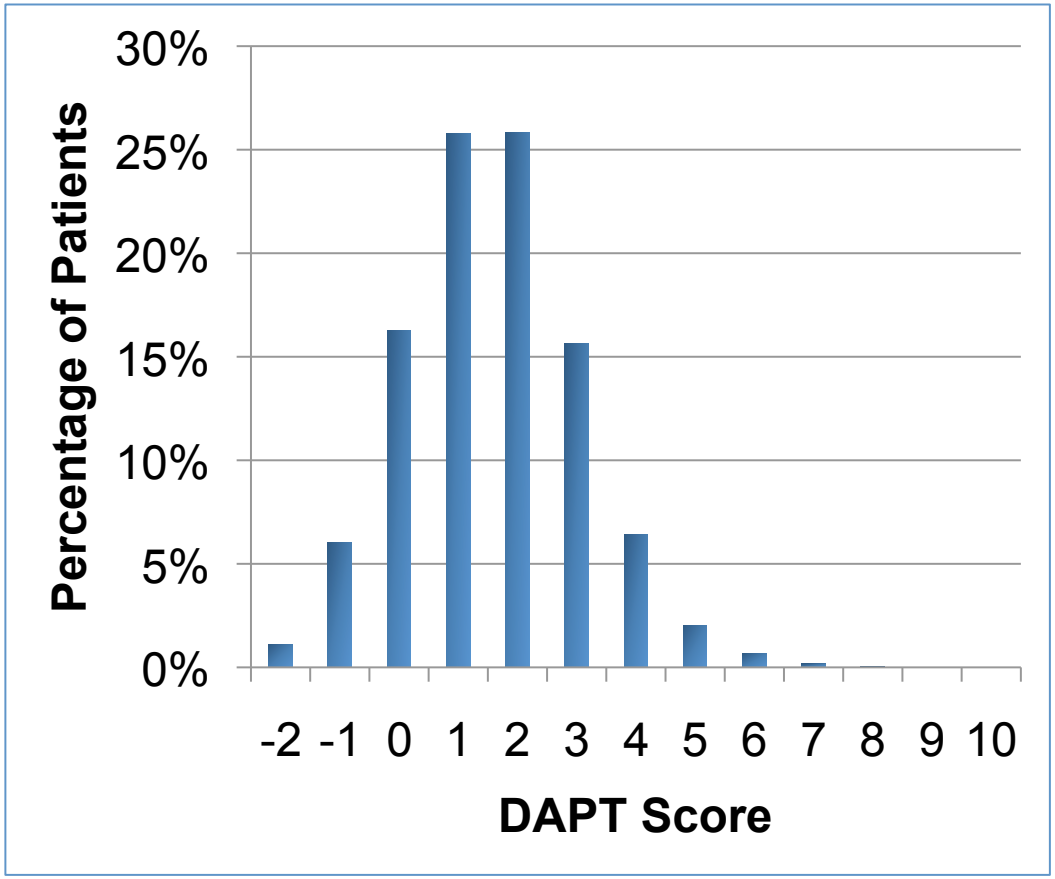
	Predictors of Myocardial Infarction or Stent Thrombosis		Predictors of Moderate/ Severe Bleeding	
Predictors of Events	**HR (95% CI)**	**P**	**HR (95% CI)**	**P**
Continued Thienopyridine vs. Placebo	0.52 (0.42 – 0.65)	<0.001	1.66 (1.26 - 2.19)	<0.001
MI at Presentation	1.65 (1.31 – 2.07)	<0.001	-	-
Prior PCI or Prior MI	1.79 (1.43 – 2.23)	<0.001	-	-
CHF or LVEF < 30%	1.88 (1.35 – 2.62)	<0.001	-	-
Vein Graft PCI	1.75 (1.13 – 2.73)	0.01	-	-
Stent Diameter < 3 mm	1.61 (1.30 – 1.99)	<0.001	-	-
Paclitaxel-Eluting Stent	1.57 (1.26 – 1.97)	<0.001	-	-
Cigarette Smoker	1.40 (1.11 – 1.76)	0.01	-	-
Diabetes	1.38 (1.10 – 1.72)	0.01	-	-
Peripheral Arterial Disease	1.49 (1.05 – 2.13)	0.03	2.16 (1.46, 3.20)	<0.001
Hypertension	1.37 (1.03 – 1.82)	0.03	1.45 (1.00, 2.11)	0.05
Renal Insufficiency	1.55 (1.03 – 2.32)	0.04	1.66 (1.04, 2.66)	0.03
Age (per 10 years)	-	-	1.54 (1.34, 1.78)	<0.001

*The ischemia model C-statistic: 0.70 in DAPT Study; 0.64 in PROTECT
**The bleeding model C-statistic: 0.68 in DAPT Study; 0.64 in PROTECT

The DAPT Score

Variable	Points
Patient Characteristic	
Age	
≥ 75	-2
65 - <75	-1
< 65	0
Diabetes Mellitus	1
Current Cigarette Smoker	1
Prior PCI or Prior MI	1
CHF or LVEF < 30%	2
Index Procedure Characteristic	
MI at Presentation	1
Vein Graft PCI	2
Stent Diameter < 3mm	1

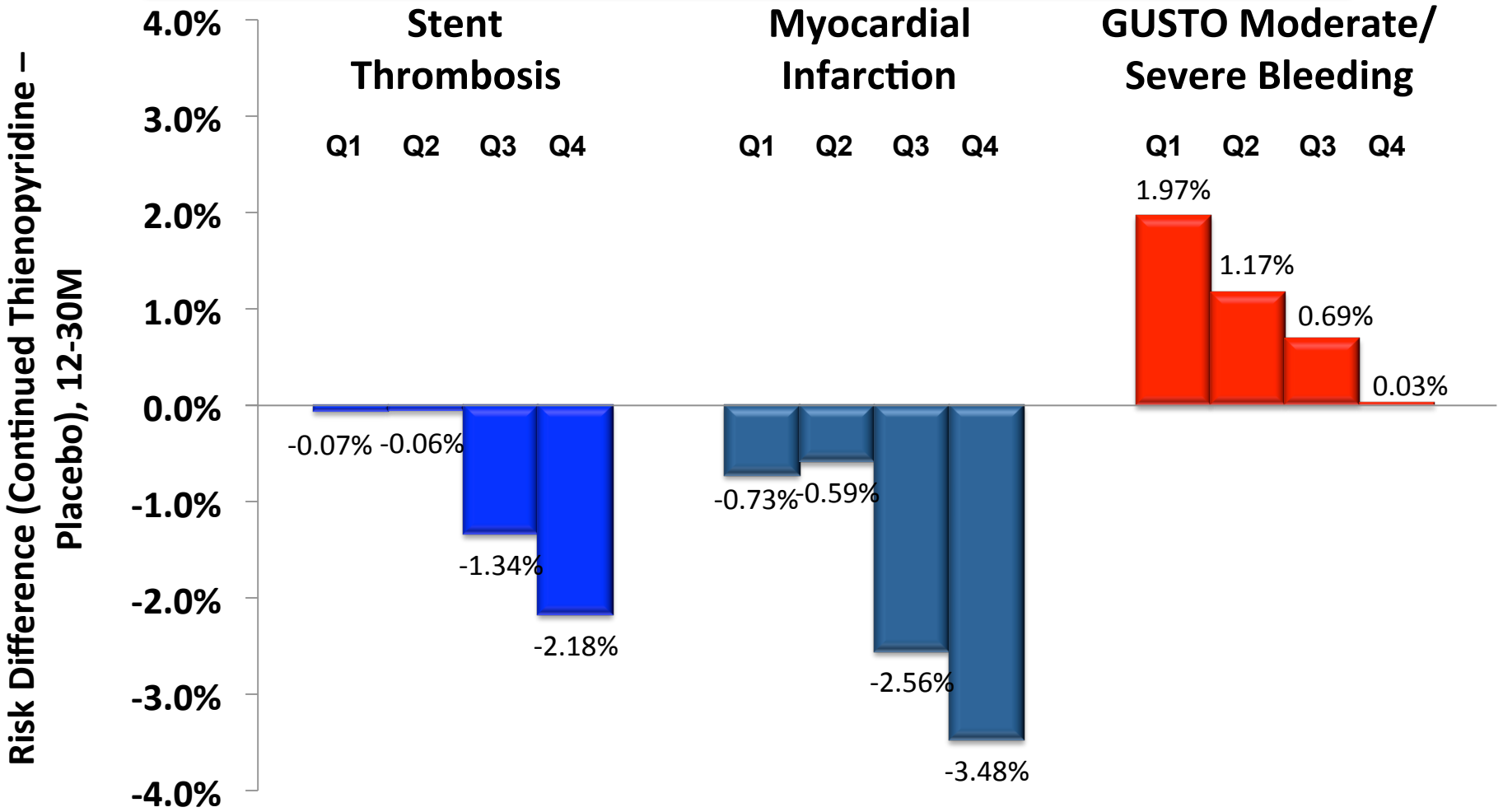
Distribution of DAPT Scores among all randomized subjects in the DAPT Study



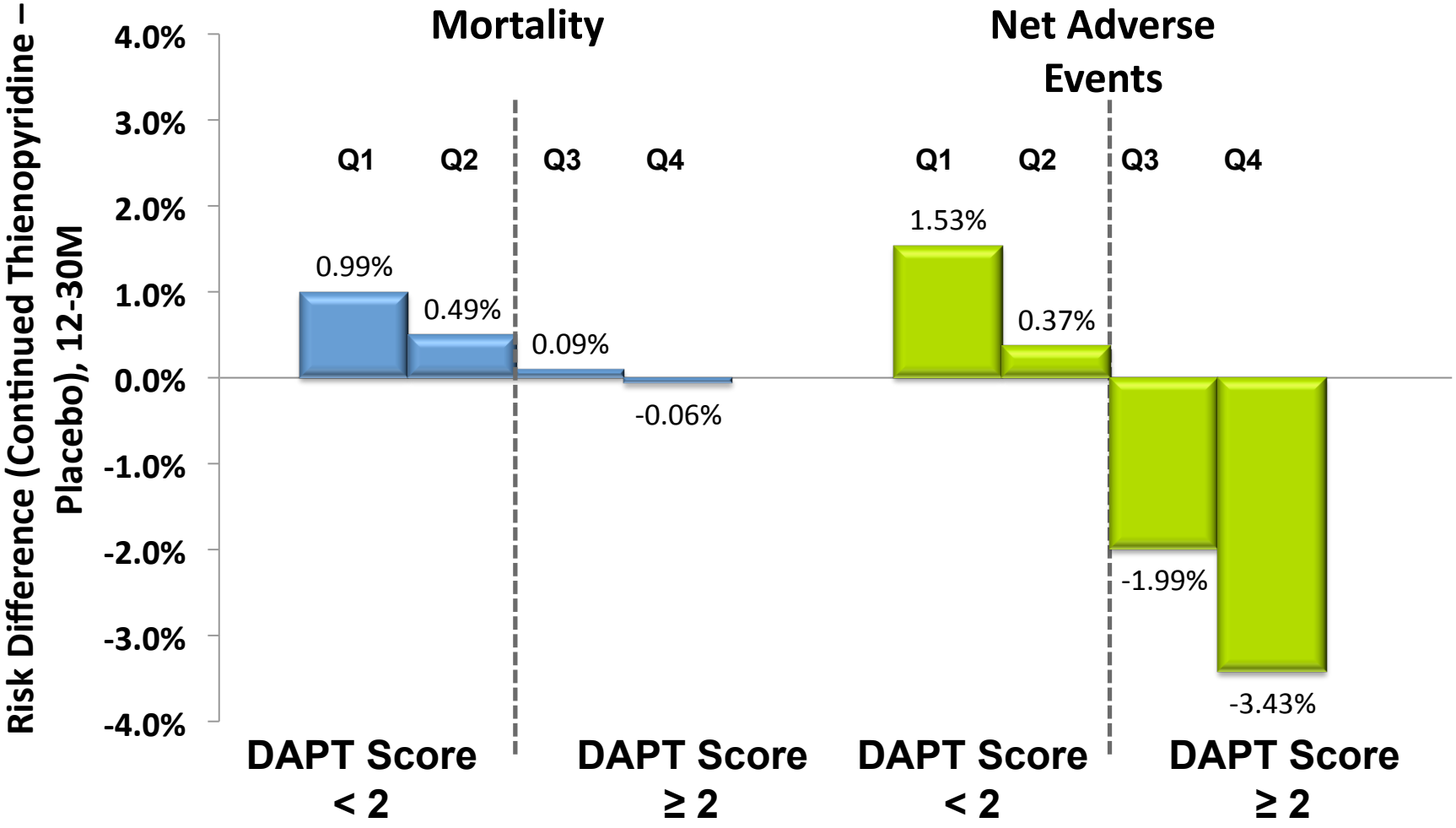
Continued Thienopyridine vs. Placebo Treatment Effect by DAPT Score Quartile (N = 11,648)

DAPT STUDY

Q1 = DAPT Score -2 to 0
Q2 = DAPT Score 1
Q3 = DAPT Score 2
Q4 = DAPT Score > 2



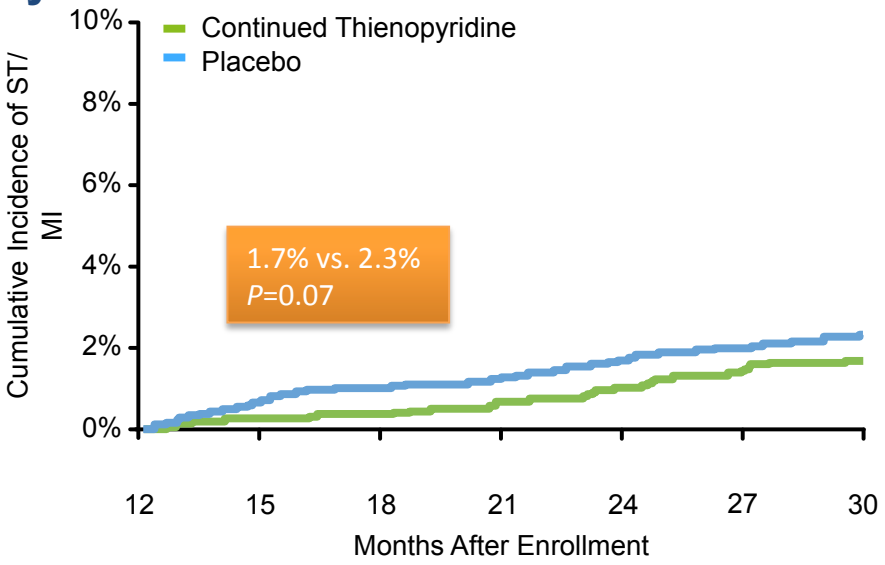
Continued Thienopyridine vs. Placebo Treatment Effect by DAPT Score Quartile (N = 11,648)



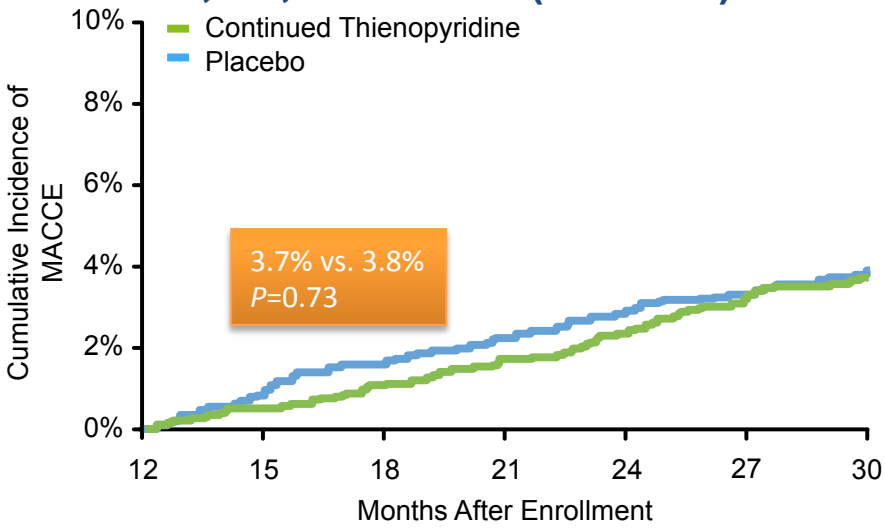
Continued Thienopyridine vs. Placebo
DAPT Score <2 (Low); N=5731

DAPT STUDY

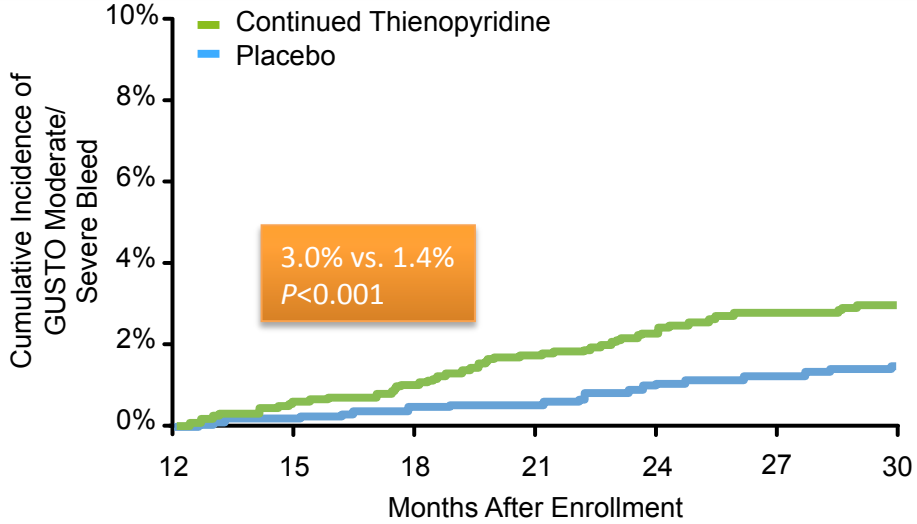
Myocardial Infarction or Stent Thrombosis



Death, MI, or Stroke (MACCE)



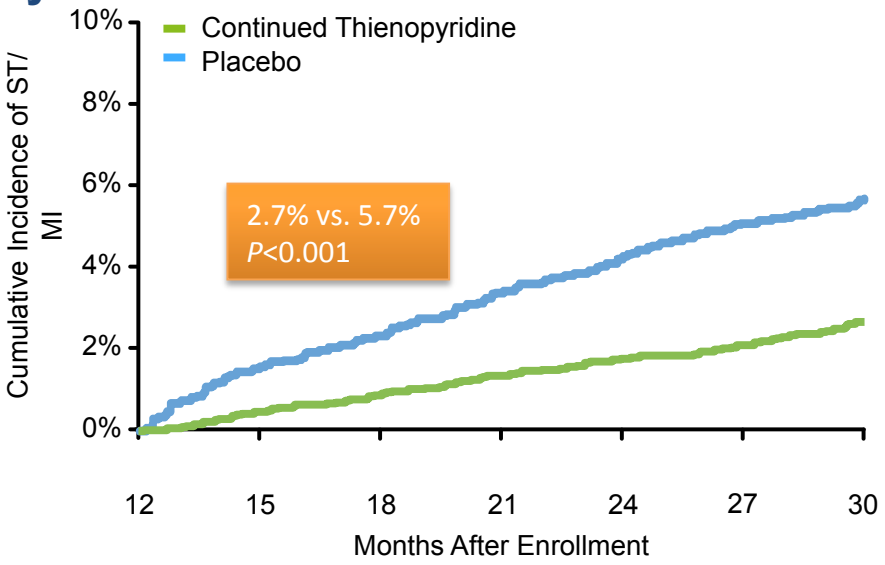
GUSTO Moderate/ Severe Bleeding



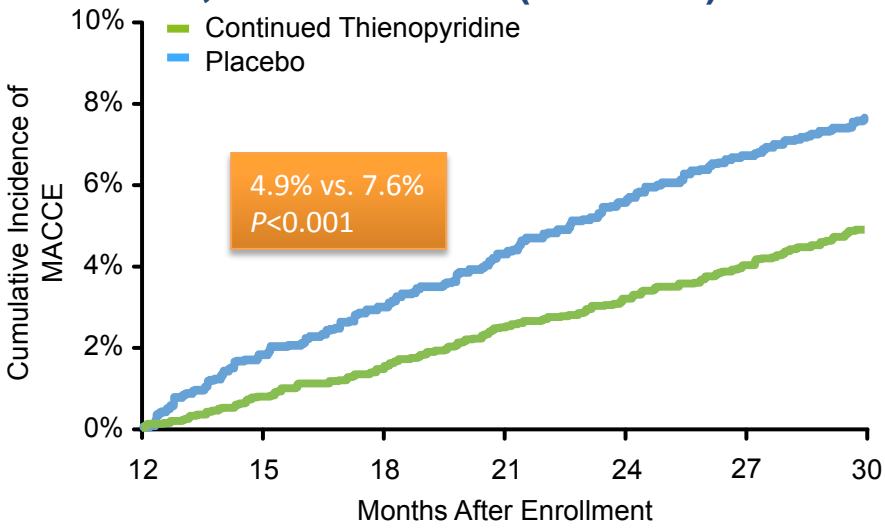
Continued Thienopyridine vs. Placebo
DAPT Score ≥ 2 (High); N=5917

DAPT STUDY

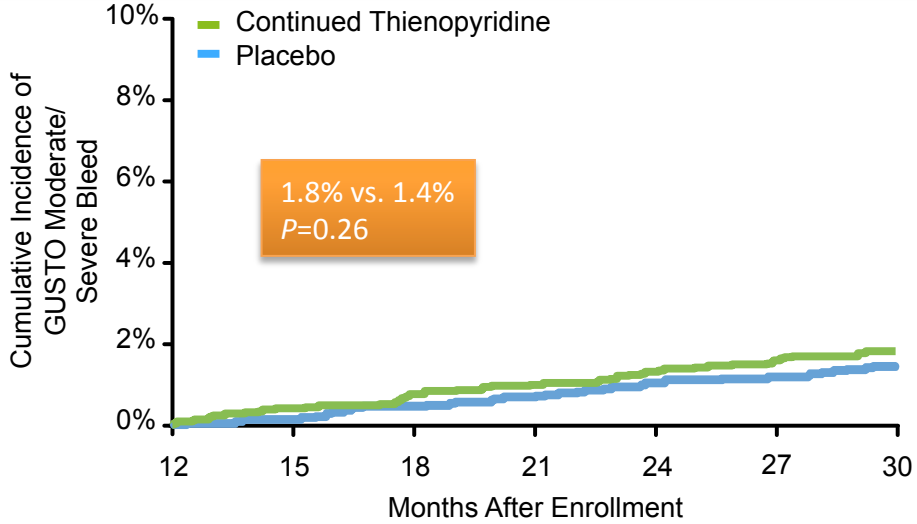
Myocardial Infarction or Stent Thrombosis



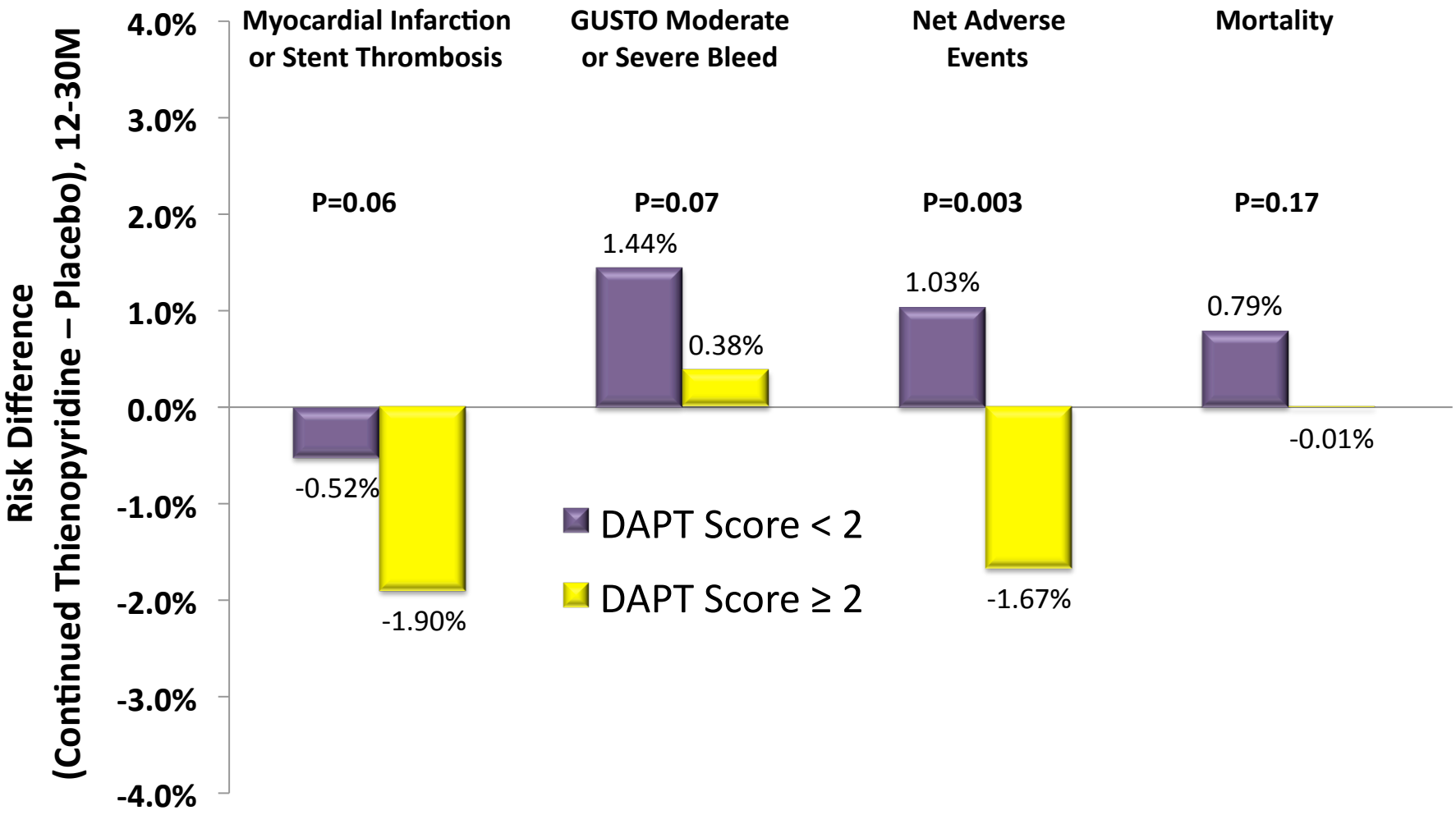
Death, MI or Stroke (MACCE)



GUSTO Moderate/ Severe Bleeding



Continued Thienopyridine vs. Placebo, by DAPT Score, Excluding PES



P values are for comparison of risk differences across DAPT Score category (interaction).

Conclusions

Among patients who have not had a major ischemic or bleeding event within the first year after PCI:

The DAPT Score identified patients for whom ischemic benefits outweighed bleeding risks, and patients for whom bleeding risks outweighed ischemic benefits.

Low DAPT Score (< 2)
NNT to prevent ischemia = 153
NNH to cause bleeding = 64

High DAPT Score ≥ 2
NNT to prevent ischemia = 34
NNH to cause bleeding = 272

DAPT Score may help clinicians decide *who should, and who should not* be treated with extended DAPT

- **Syndrome coronarien aigu**
  - Recommandations CCS
    - 12 mois

      Peu importe tx médical, PCI ou PAC (clopido ou ticagrelor)

- Après mise en place de ***stent* médicamenté**
  - Clopidogrel (MCAS stable)
    - Durée minimale: 3-6 mois
    - Durée idéale: 12 mois
  - Considérer DAPT Score

- **Prévention secondaire à long terme** après infarctus du myocarde
  - <u>Pts tolérant 12 mois DAPT</u>
  - Clopidogrel ou ticagrelor 60
    - Évaluer risque versus bénéfice
  - Considérer DAPT Score