UNIVERSITY OF UTAH
HEALTH CARE

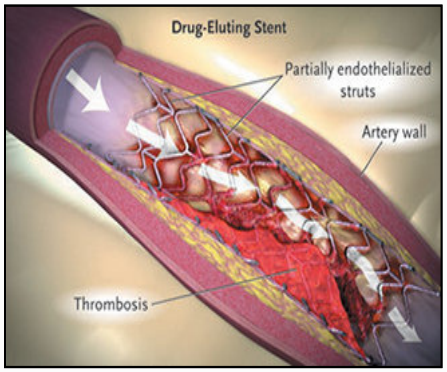
Update on DAPT

Frederick Welt, MD

Disclosures

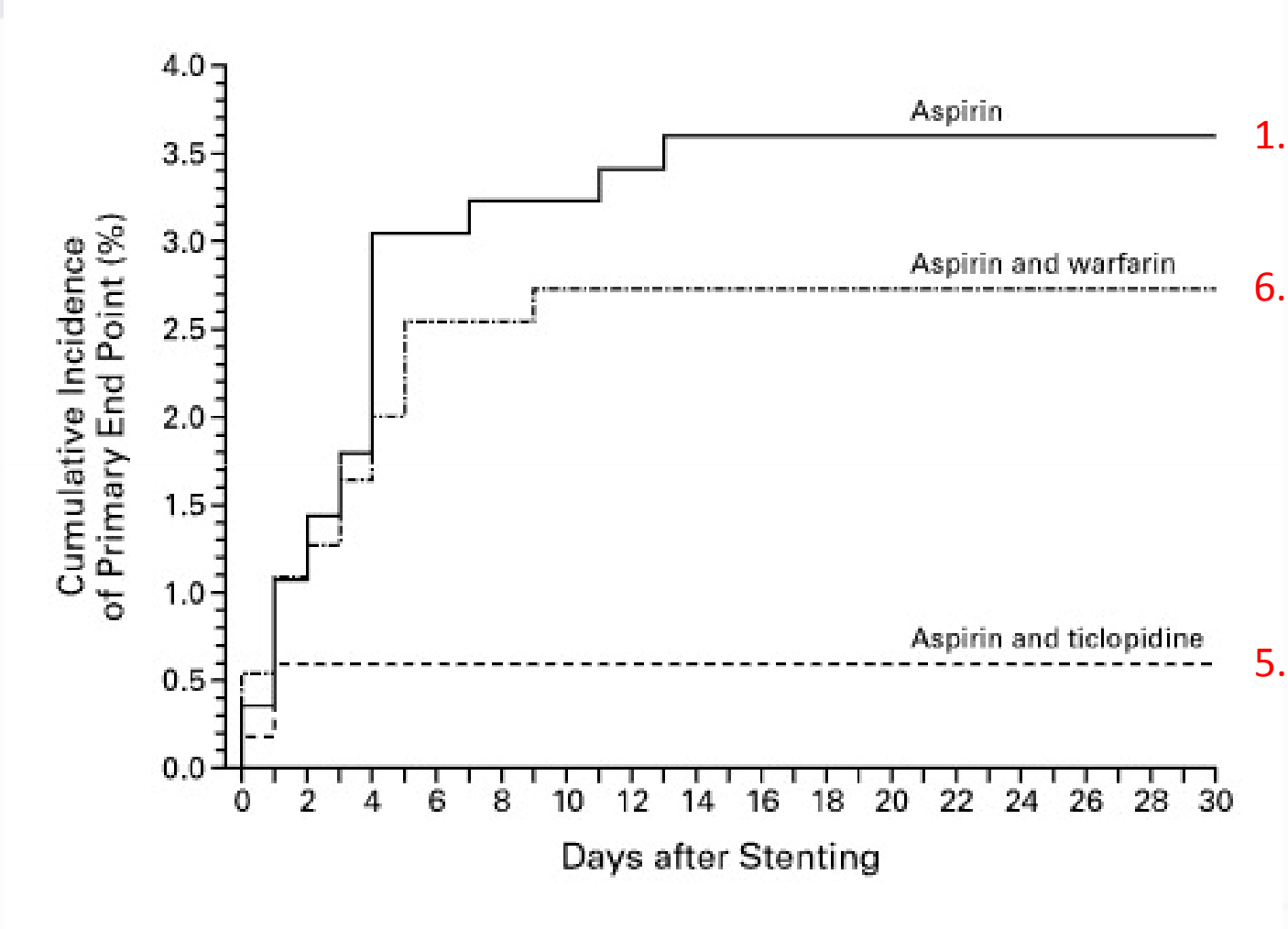
- **Medtronic Advisory Board**
- **Siemens Research Grant**

Stent Thrombosis Initial Experience



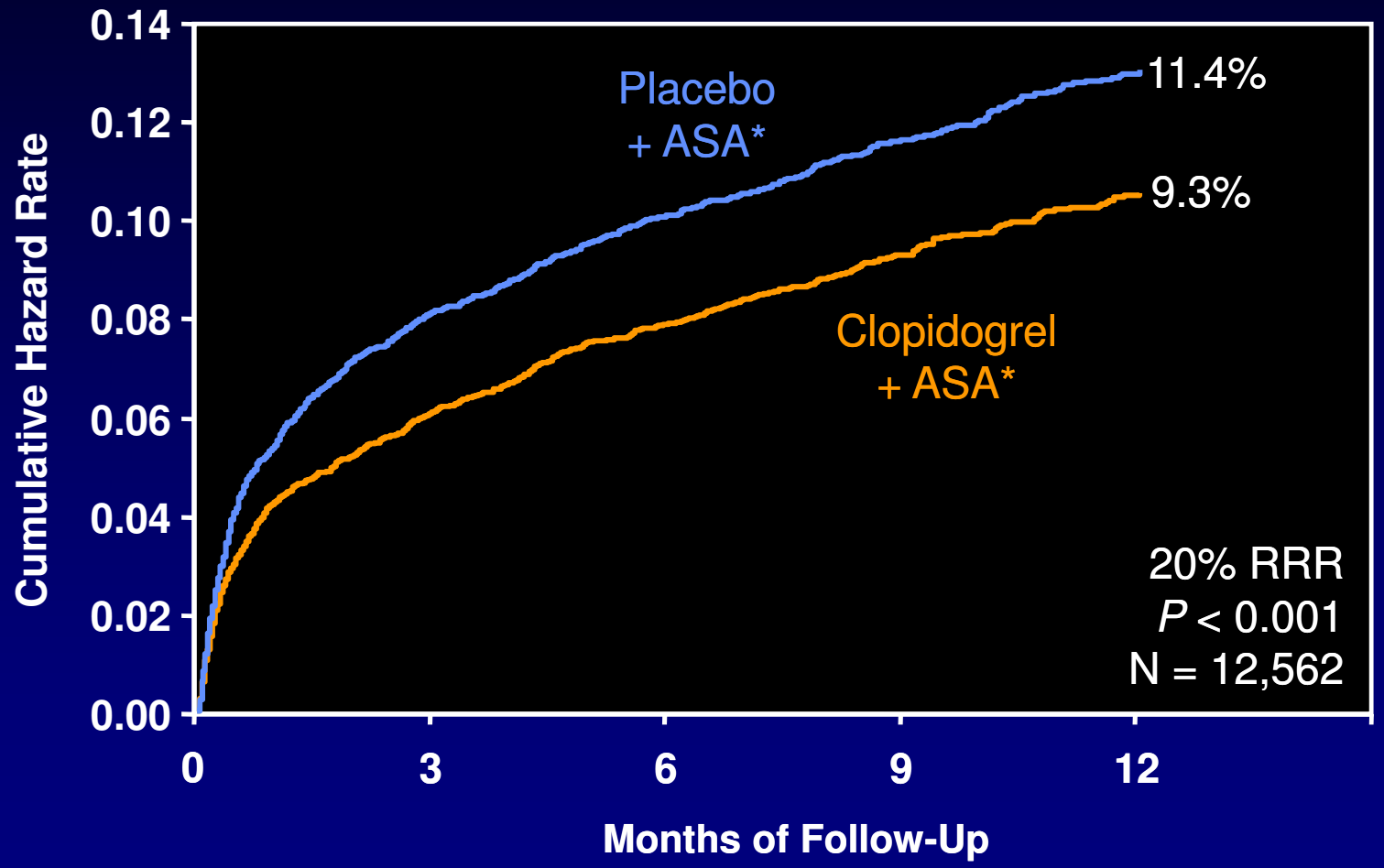
- ~20%
- ~3.5% with:
  - IV low molecular weight Dextran
  - ASA
  - IV Heparin
  - Dipyrimadole
- Registry Data- High Pressure Dilatation

STARS Trial
Cumulative Incidence of the Primary End Point in the Three Treatment Groups.



Leon MB et al. N Engl J Med 1998;339:1665-1671.

Primary End Point: MI/Stroke/CV Death



* In combination with standard therapy

The CURE Trial Investigators. *N Engl J Med.* 2001;345:494-502.

Millions face risk from drug-coated stents

"Millions of Americans could be walking around with tiny time bombs in their hearts"

"Potentially lethal heart devices a frightening problem for patients, doctors"

"The FDA panel might recommend they not be used at all"

By Robert Bazell
Chief science correspondent
NBC News
Nov 2006 – March 2007

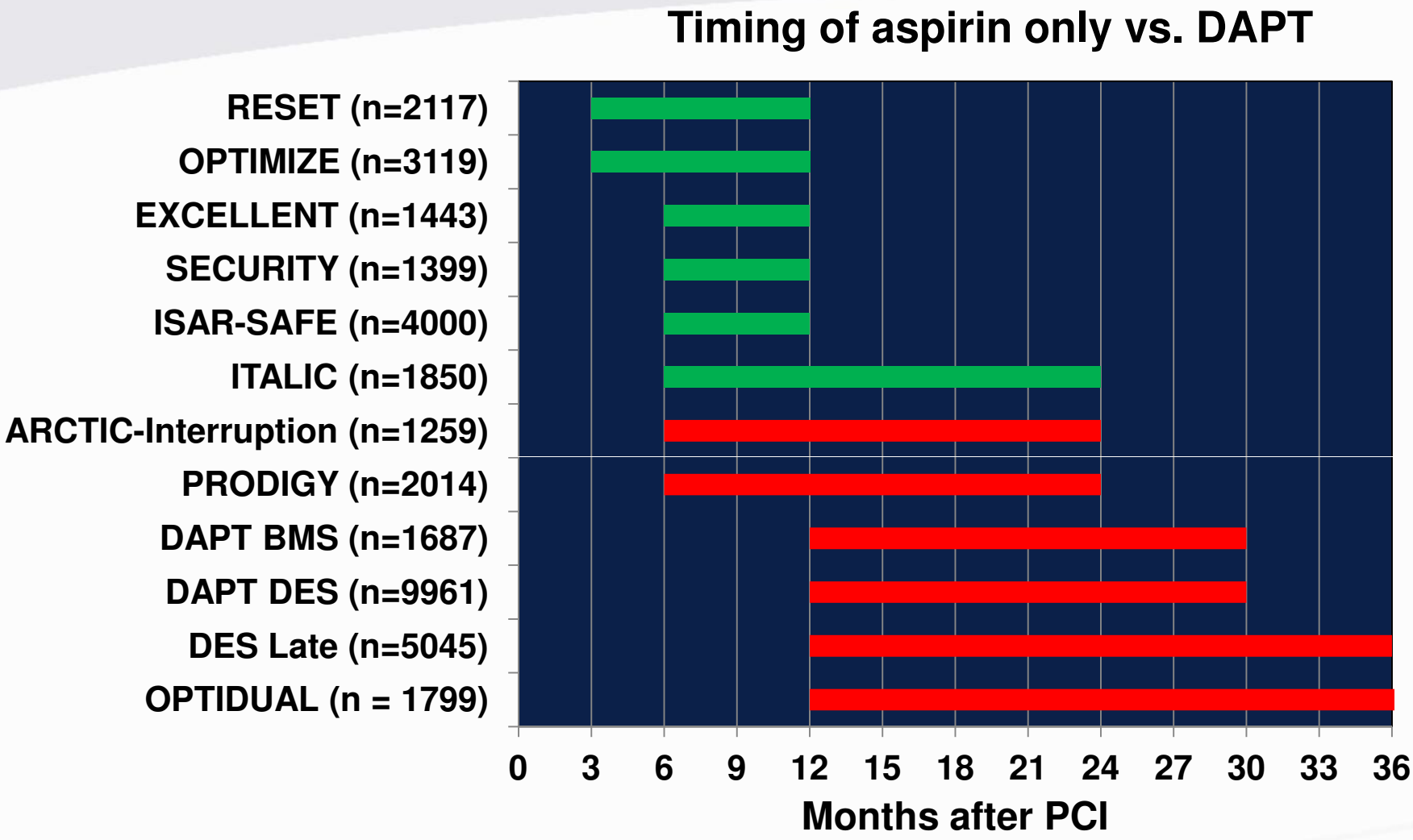
Questions

- **What's the shortest duration of DAPT I can get away with?**
- **If I don't need to stop DAPT for any particular reason, how long should I continue?**
- **Is there a mortality issue with DAPT?**
- **Why do newer generation DES confer less risk of stent thrombosis and how does this inform stent development?**
  - **Do we ever need to use a BMS?**
  - **Are we poised for another public relations disaster with biodegradable stents?**

Questions

- **What's the shortest duration of DAPT I can get away with?**
- **If I don't need to stop DAPT for any particular reason, how long should I continue?**
- **Is there a mortality issue with DAPT?**
- **Why do newer generation DES confer less risk of stent thrombosis and how does this inform stent development?**
  - **Do we ever need to use a BMS?**
  - **Are we poised for another public relations disaster with biodegradable stents?**

Trials of DAPT Duration after Stenting: a review of the evidence



More than 30,000 randomized patients!

UNIVERSITY OF UTAH HEALTH CARE

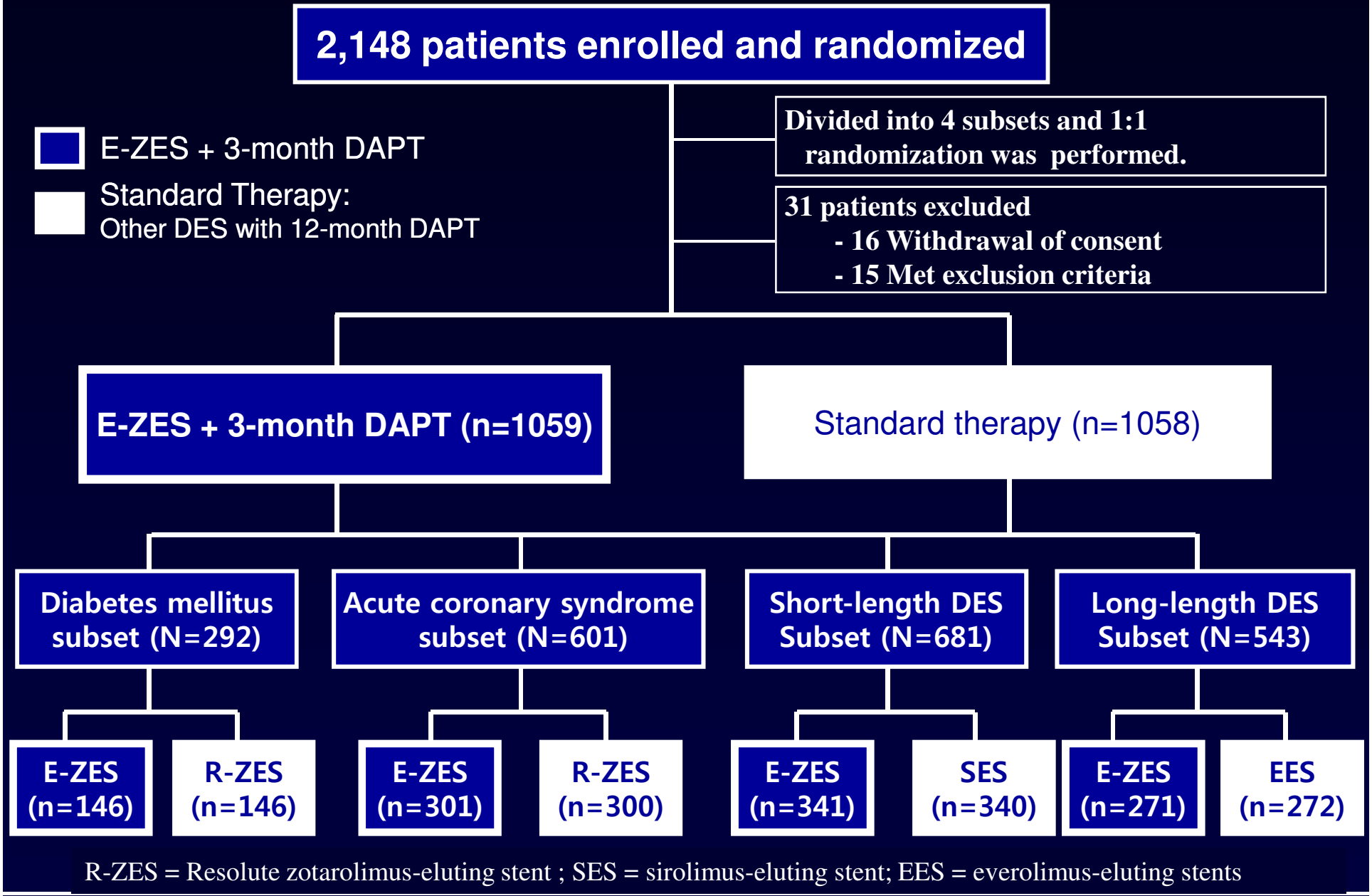
A New Strategy for Discontinuation of Dual Antiplatelet Therapy: Real Safety and Efficacy of 3-Month Dual Antiplatelet Therapy Following Zotarolimus-Eluting Stent Implantation: RESET Trial

Myeong-Ki Hong, MD. Ph D,
on behalf of RESET investigators

Professor, Division of Cardiology,
Severance Cardiovascular Hospital
Yonsei University College of Medicine, Seoul, Korea

RESET ClinicalTrials.gov identifier: NCT01145079

Study at a glance & Final Enrollment



R-ZES = Resolute zotarolimus-eluting stent ; SES = sirolimus-eluting stent; EES = everolimus-eluting stents

Inclusion criteria

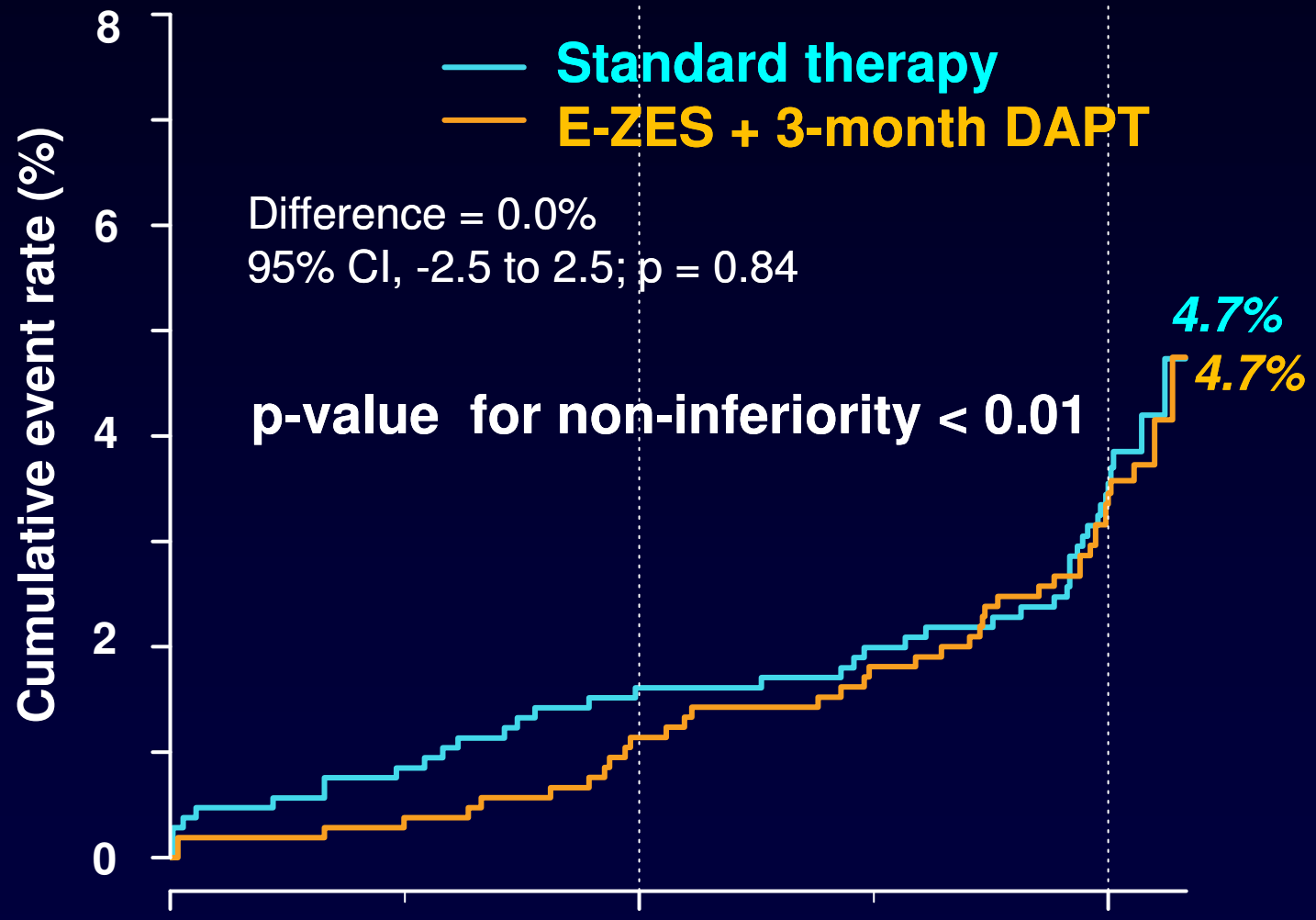
- Patients with stable angina, unstable angina, or acute MI
- Diameter stenosis ≥ 50% and reference vessel diameter of 2.5 to 4.0 mm by visual estimation
- Elective PCI, eligible for participation

Exclusion criteria

- Prior history of cerebral vascular accidents, peripheral artery diseases, thromboembolic disease or stent thrombosis
- Left ventricular ejection fraction < 40%
- Lesions with in-stent restenotic lesion, chronic total occlusion, or significant left main disease requiring intervention
- Cardiogenic shock
- Acute ST-elevation MI within 48 hours after onset of symptoms
- Contraindication to antiplatelet agents
- Severe hepatic (≥3 times normal values) or renal dysfunction (serum creatinine >2.0 mg/dl)

Primary endpoint, by Kaplan-Meier method

* Primary end-point; A composite of death from CV cause, MI, stent thrombosis, TVR or bleeding at 1 year

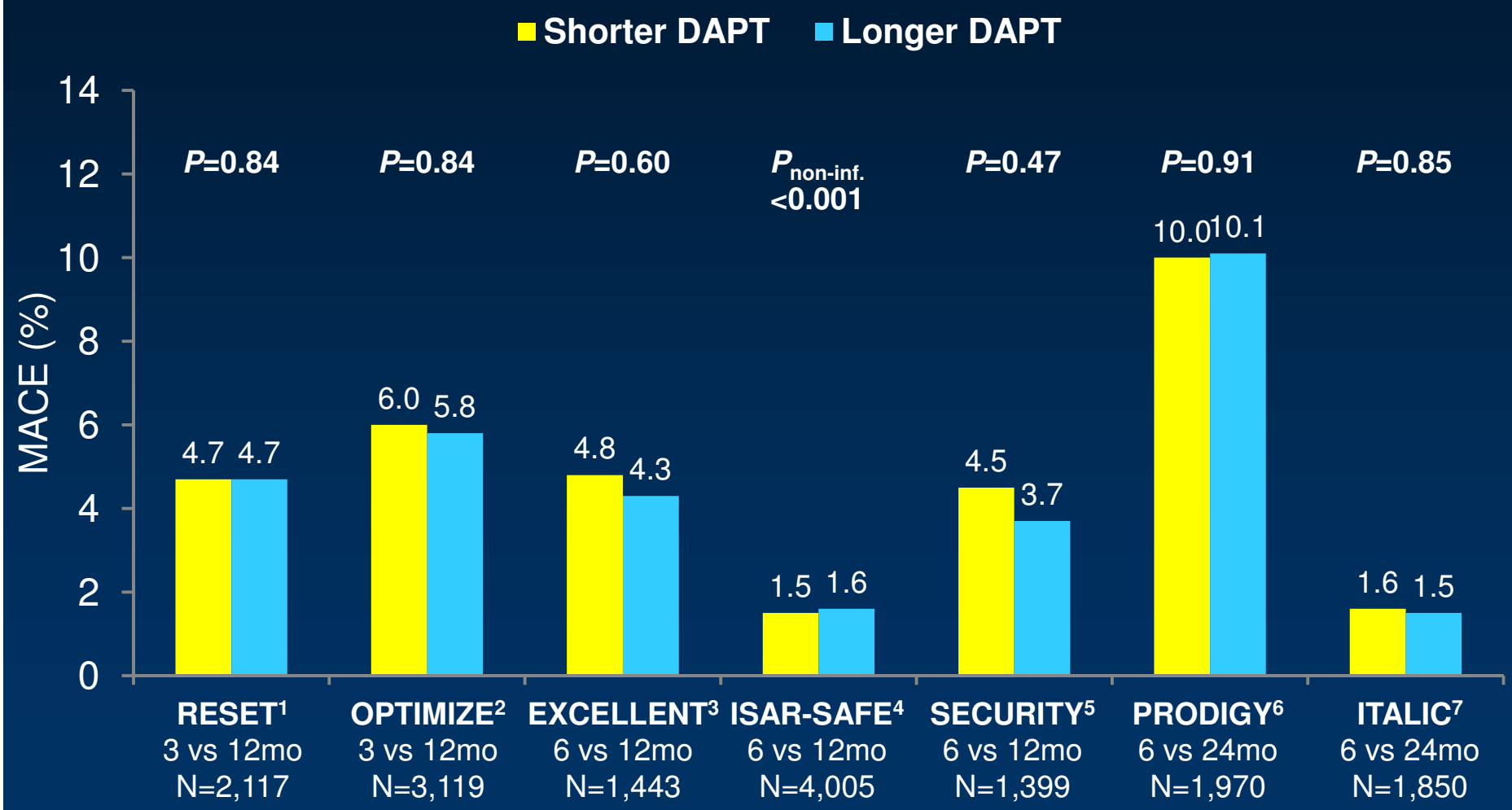


No. at Risk	0	6	12 Months
E-ZES +3-month DAPT	1059	1037	945
Standard therapy	1058	1032	920

RESET

Short term DAPT: Randomized Trials

No Difference Observed in Primary Endpoints



[1] Kim BK, et al. *J Am Coll Cardiol* .2012;60:1340–8. [2] Feres F, et al. *JAMA*. 2013;310:2510–22. [3] Gwon HC, et al. *Circulation*. 2012;125:505–13.
[4] Schulz-Schupke S, et al. *Eur Heart J* .2015;36(20):1252-63. [5] Colombo A, et al. *J Am Coll Cardiol* .2014;64:2086–97.
[6] Valgimigli M,, et al. *Circulation*. 2012;125: 2015–26. [7] Gilard M, et al. *J Am Coll Cardiol*. 2015;65:777–86.

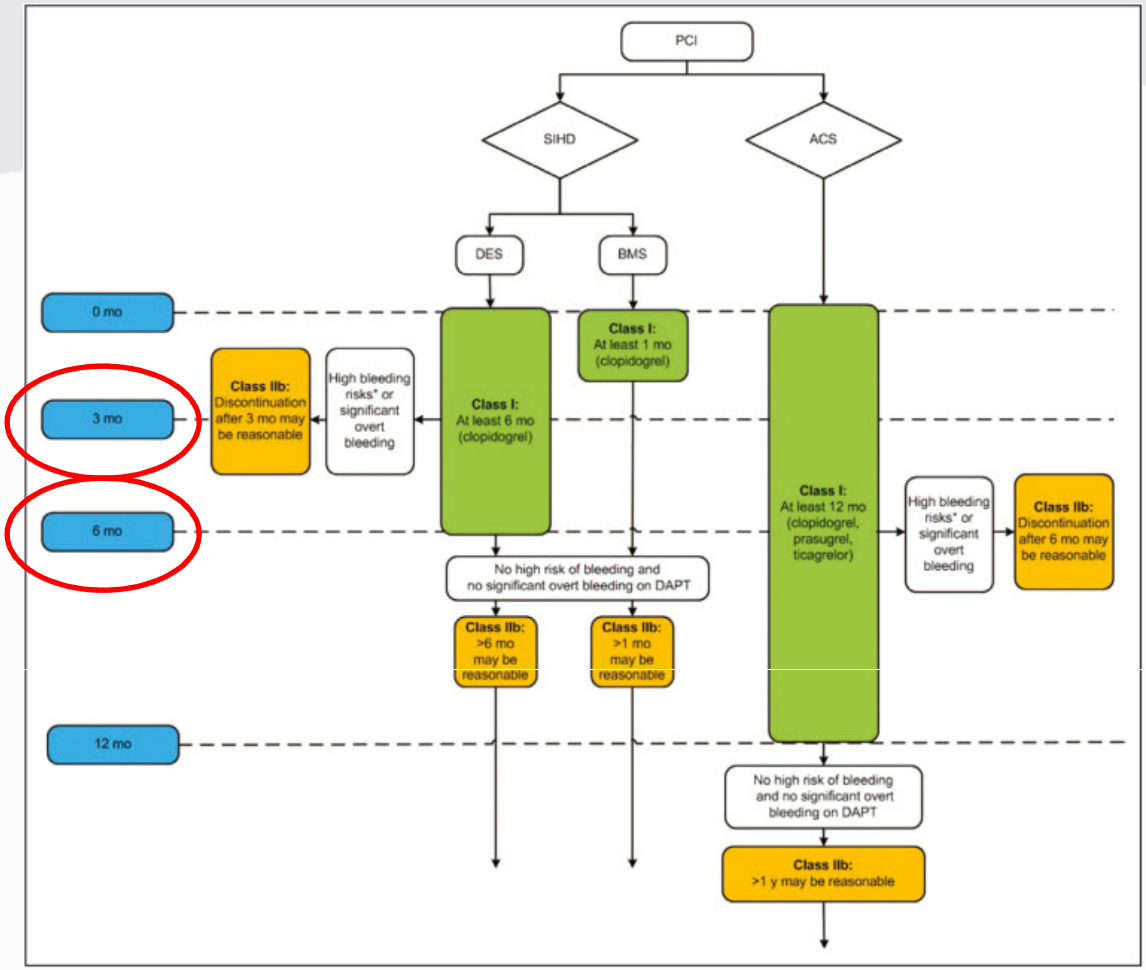


Figure 2. Treatment algorithm for duration of P2Y12 inhibitor therapy in patients treated with PCI. Colors correspond to Class of Recommendation in Table 1. Arrows at the bottom of the figure denote that the optimal duration of prolonged DAPT is not establish...

2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease : A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

The Journal of Thoracic and Cardiovascular Surgery, Volume 152, Issue 5, 2016, 1243–1275

http://dx.doi.org/10.1016/j.jtcvs.2016.07.044

Questions

- What's the shortest duration of DAPT I can get away with?
- If I don't need to stop DAPT for any particular reason, how long should I continue?
- Is there a mortality issue with DAPT?
- Why do newer generation DES confer less risk of stent thrombosis and how does this inform stent development?
  - Do we ever need to use a BMS?
  - Are we poised for another public relations disaster with biodegradable stents?

DAPT STUDY

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*

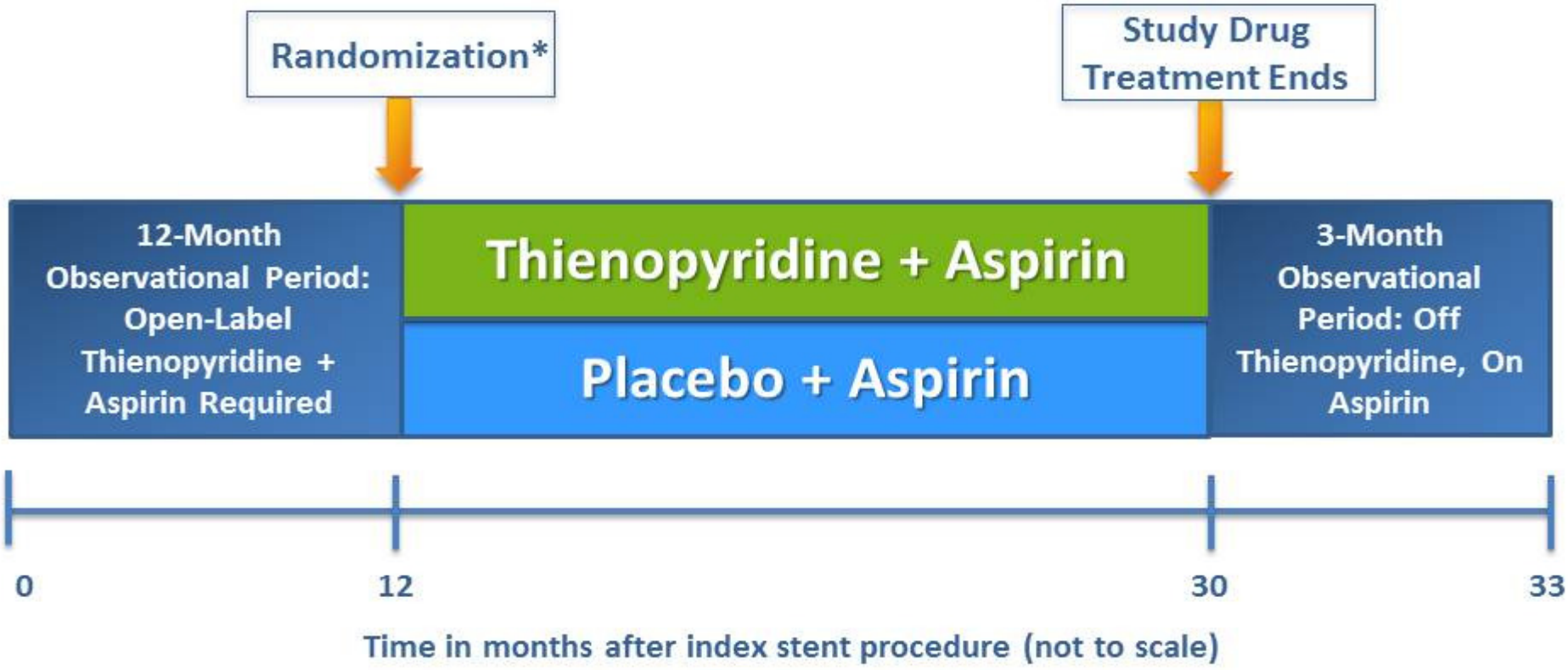
Is there a benefit in extending DAPT beyond one year?

Mauri et al. NEJM 2014
DOI: 10.1056/NEJMoa1409312

UNIVERSITY OF UTAH HEALTH CARE

Design

DAPT STUDY



Enrolled: Subjects treated with FDA-approved DES or BMS. Subjects on oral anticoagulant therapy or with life expectancy < 3 years excluded.

Randomized: Free from MI, stroke, repeat revascularization, and moderate or severe bleeding, and adherent with thienopyridine (80% to 120% of doses taken and no interruption > 14 days).

Mauri, Kereiakes et al AHJ 2010; 160(6): 1035-1041

ClinicalTrials.gov number NCT00977938

Primary End Points

DAPT STUDY

Two powered co-primary effectiveness end points

- **Definite or probable stent thrombosis**
  (Academic Research Consortium definition)
- **Major adverse cardiovascular or cerebrovascular events**
  (MACCE, death, MI or stroke)

Powered primary safety end point

- **Moderate or severe bleeding**
  (Global Utilization of Streptokinase and TPA for Occluded Arteries classification [GUSTO])

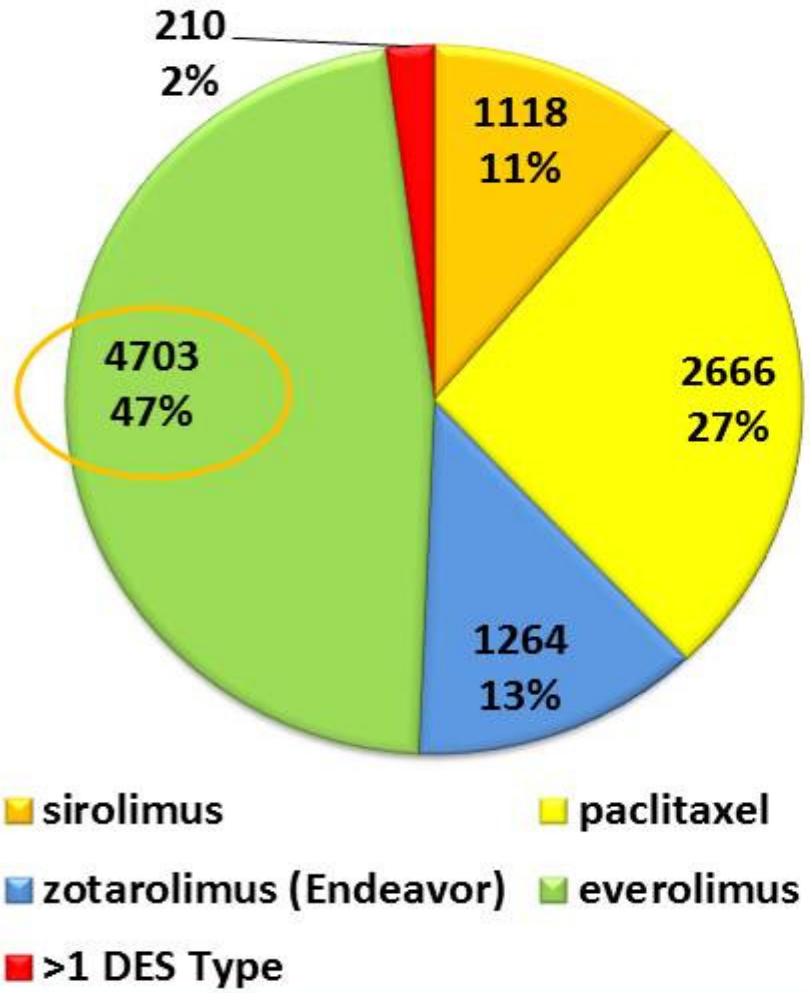
Primary analysis period = drug treatment period of 12-30 m

Primary analysis cohort: randomized DES-treated subjects

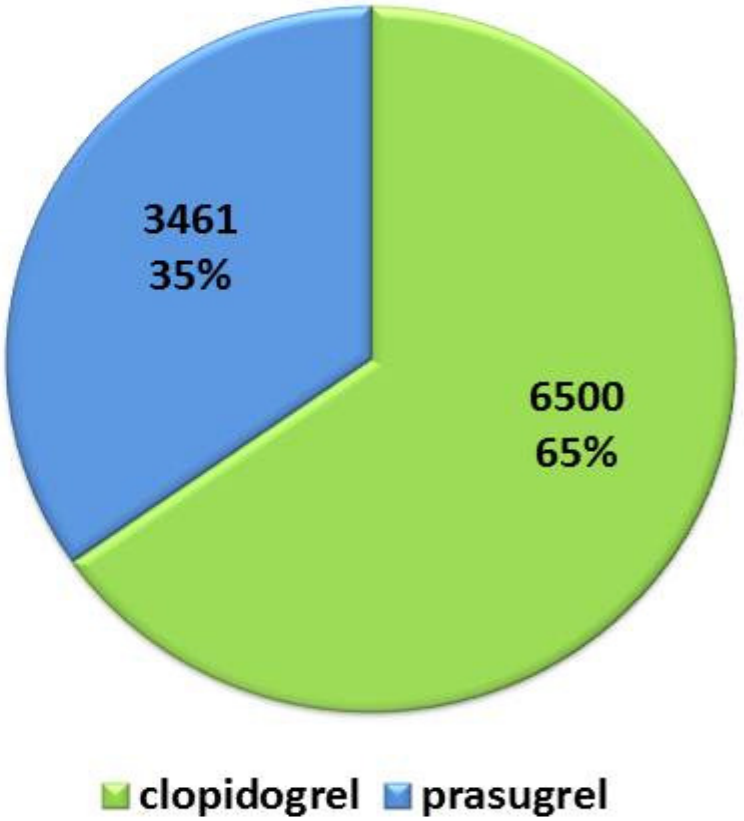
Stent & Drug Types

DAPT STUDY

Drug Eluting Stent Type



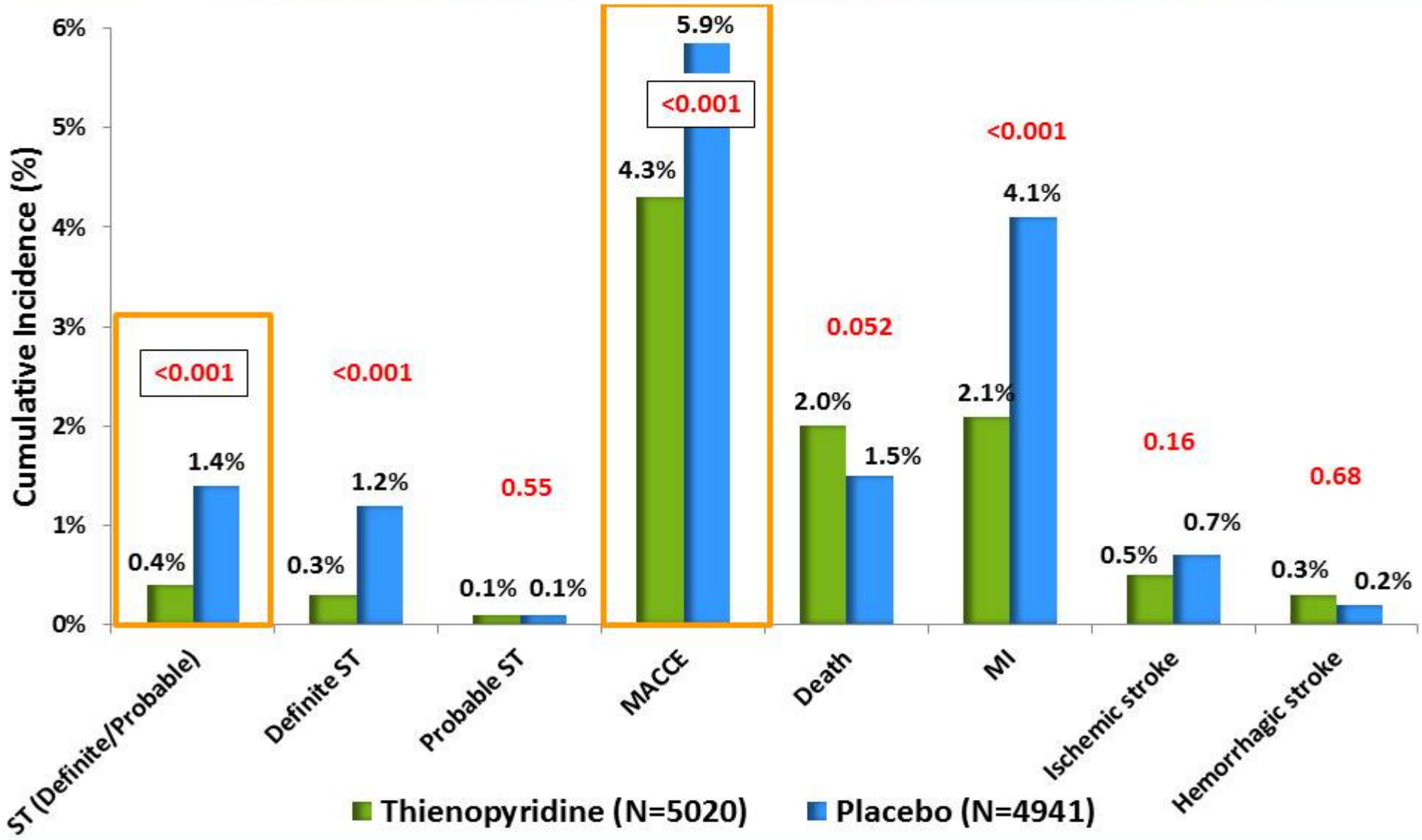
Thienopyridine Type



Mauri L, et al. *N Engl J Med.* 2014;371:2155–66.

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

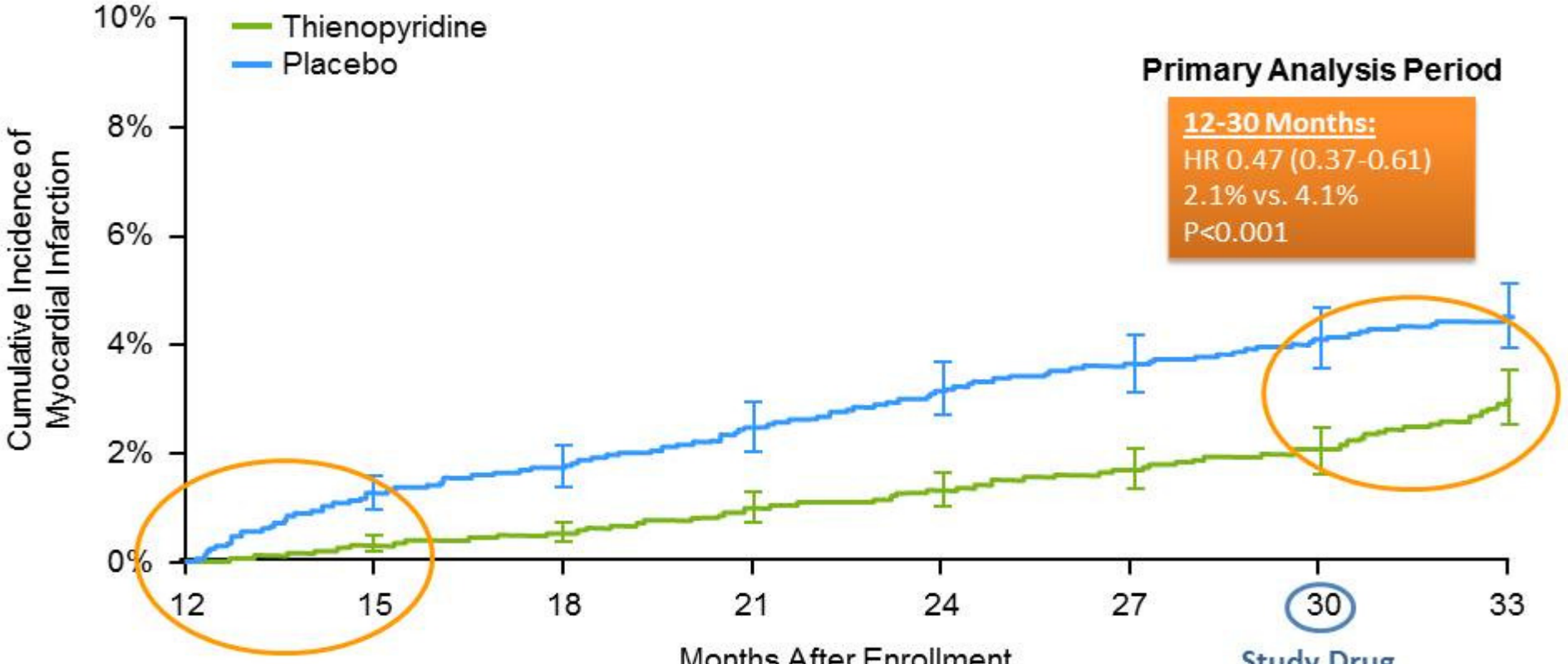
DAPT STUDY



Mauri L, et al. *N Engl J Med.* 2014;371:2155–66.

Myocardial Infarction

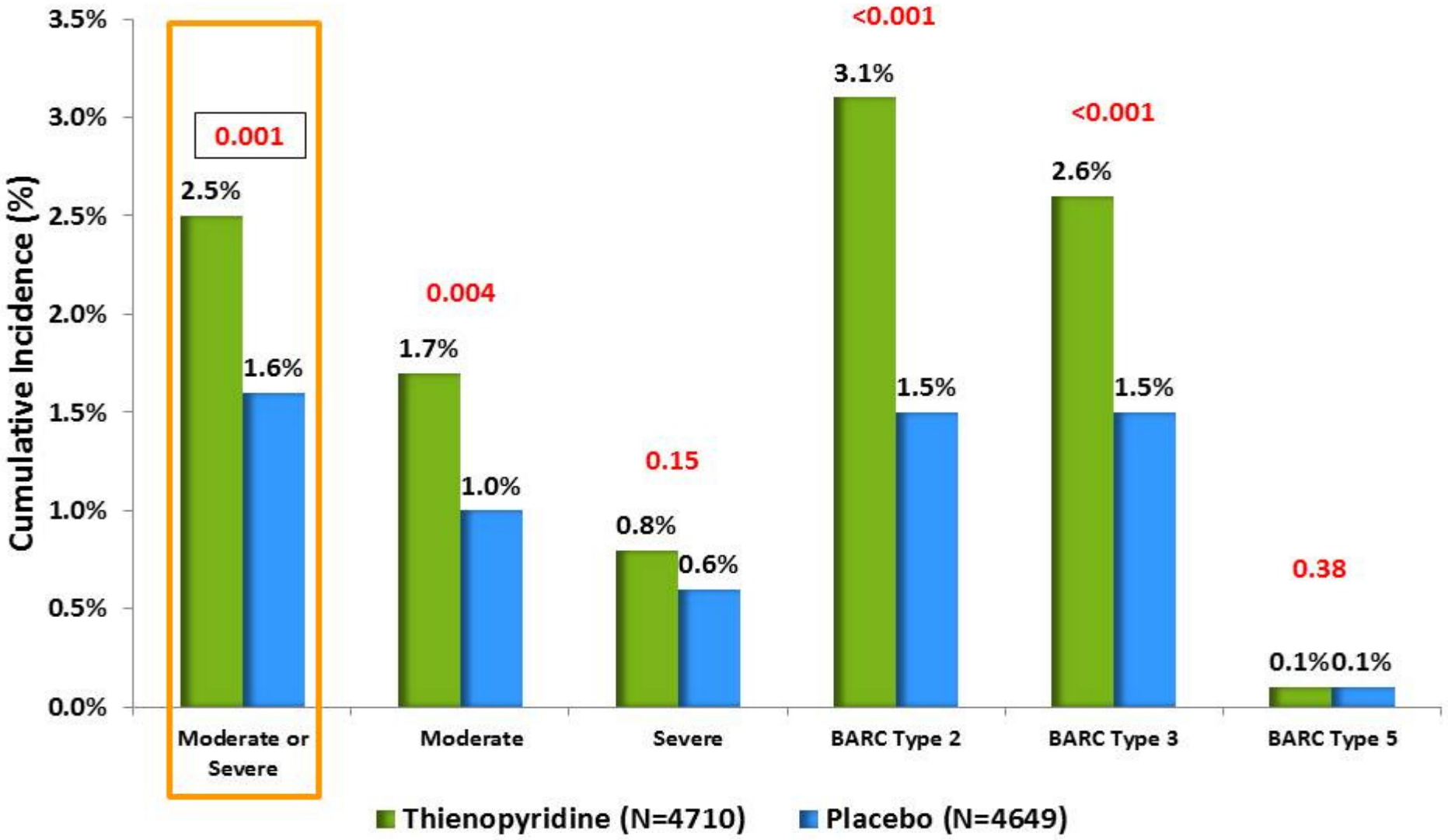
DAPT STUDY



# At Risk							
Thienopyridine 5020	4920	4849	4789	4717	4634	4580	3051
Placebo 4941	4804	4727	4653	4565	4501	4440	3012

Mauri L, et al. *N Engl J Med.* 2014;371:2155–66.

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



Mauri L, et al. *N Engl J Med.* 2014;371:2155–66.

Consistency of Treatment Effect Stent Thrombosis (12-30 Months)

DAPT STUDY

Factor	N	HR and 95% CI	Interaction P
< 75 Years	N=8929	0.29 (0.17,0.49)	0.84
>= 75 Years	N=1032	0.23 (0.03,2.06)	
Male	N=7435	0.21 (0.11,0.39)	0.04
Female	N=2526	0.73 (0.28,1.91)	
No diabetes	N=6924	0.20 (0.10,0.40)	0.08
Diabetes	N=3037	0.53 (0.23,1.20)	
No Risk Factors for ST	N=5162	0.27 (0.12,0.63)	0.89
Risk Factors for ST	N=4799	0.29 (0.15,0.56)	
Clopidogrel	N=6500	0.33 (0.16,0.71)	0.54
Prasugrel	N=3461	0.24 (0.12,0.50)	
Sirolimus	N=1118	NA*	
Zotarolimus	N=1264	0.39 (0.08,2.00)	0.76
Paclitaxel	N=2666	0.25 (0.13,0.51)	
Everolimus	N=4703	0.38 (0.15,0.97)	

Continued thienopyridine better

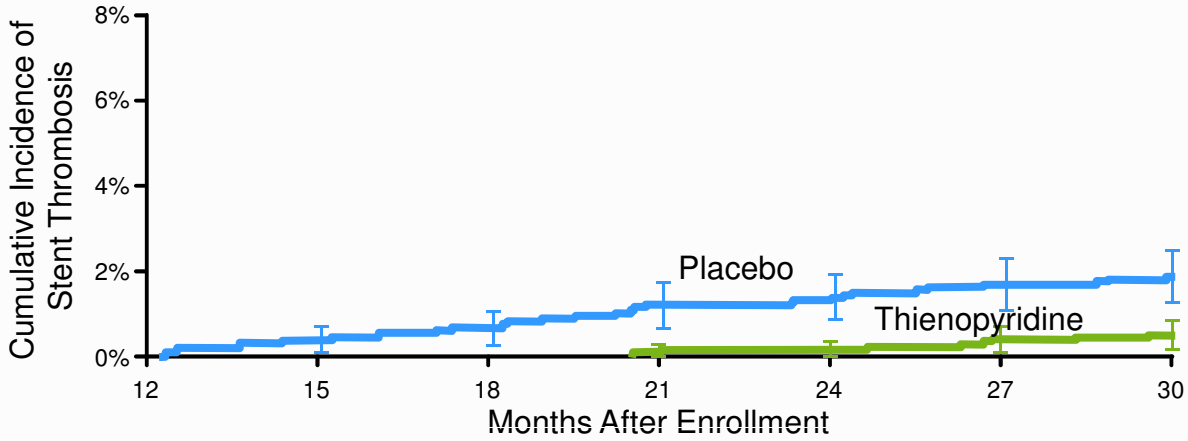
Placebo better

*zero events in thienopyridine arm

Continued Thienopyridine vs. Placebo in Patients With and Without ACS: Stent Thrombosis

A. ACS Patients

All DES and BMS randomized patients

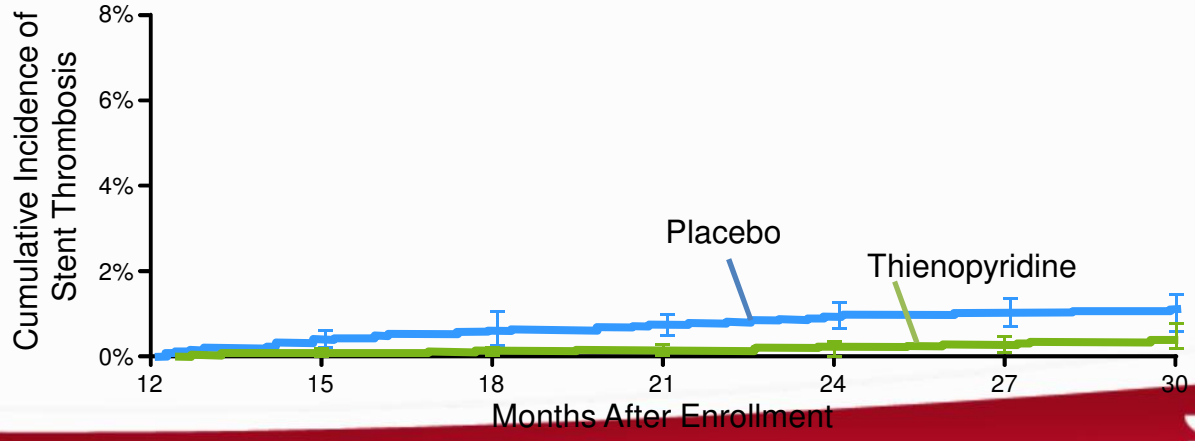


Thienopyridine	1802	1790	1769	1750	1729	1705	1680
Placebo	1766	1748	1719	1693	1659	1629	1602

1.9%
0.5%

HR 0.27 (0.13-0.57)
p<0.001

B. Non-ACS Patients



Thienopyridine	4050	4015	3959	3918	3881	3822	3771
Placebo	4008	3979	3918	3873	3833	3785	3747

1.1%
0.4%

HR 0.33 (0.18-0.60)
p<0.001

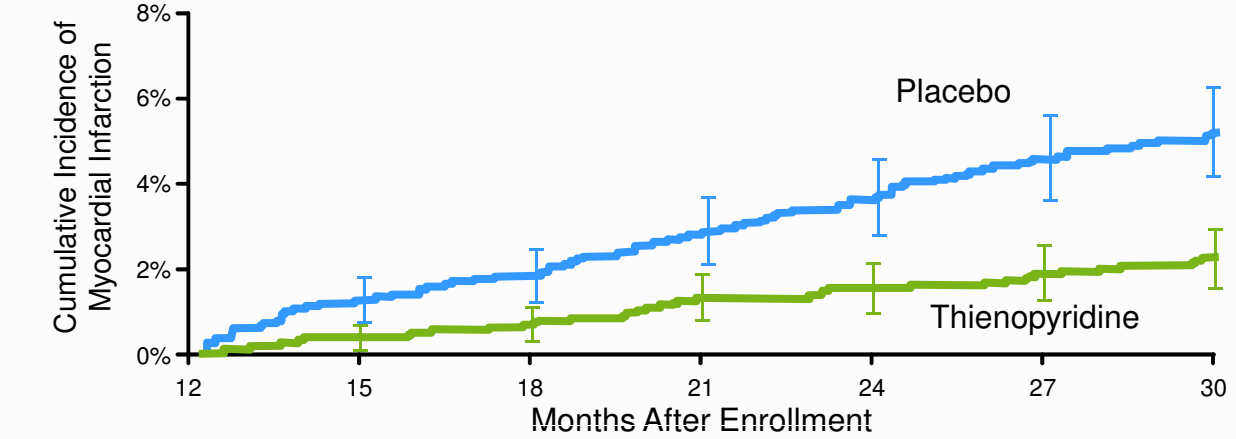
Interaction
P = 0.69

UNIVERSITY OF UTAH HEALTH CARE

Continued Thienopyridine vs. Placebo in Patients With and Without ACS: Myocardial Infarction

A. ACS Patients

All DES and BMS randomized patients

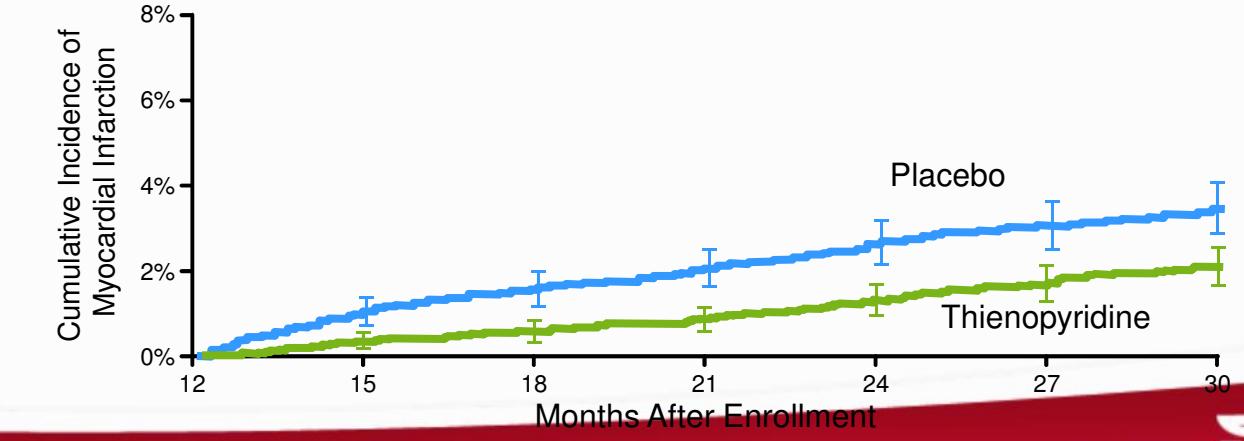


Thienopyridine	1802	1790	1762	1738	1709	1683	1656
Placebo	1766	1748	1704	1675	1633	1594	1558

HR 0.42 (0.29-0.62)
p<0.001

Interaction
P = 0.15

B. Non-ACS Patients

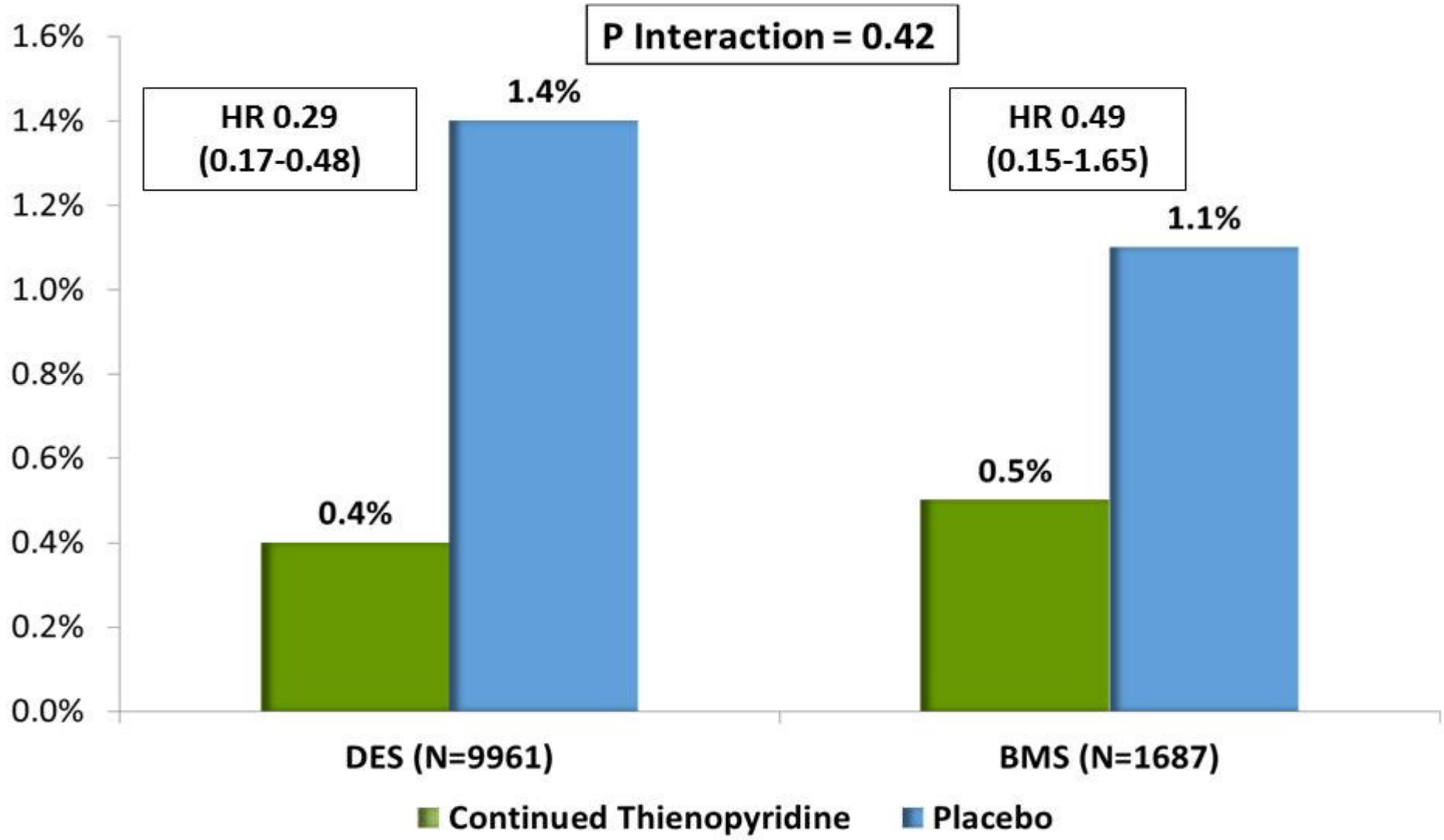


Thienopyridine	4050	4016	3974	3914	3876	3818	3746
Placebo	4008	3979	3893	3839	3786	3724	3677

HR 0.60 (0.45-0.79)
p<0.001

UNIVERSITY OF UTAH HEALTH CARE

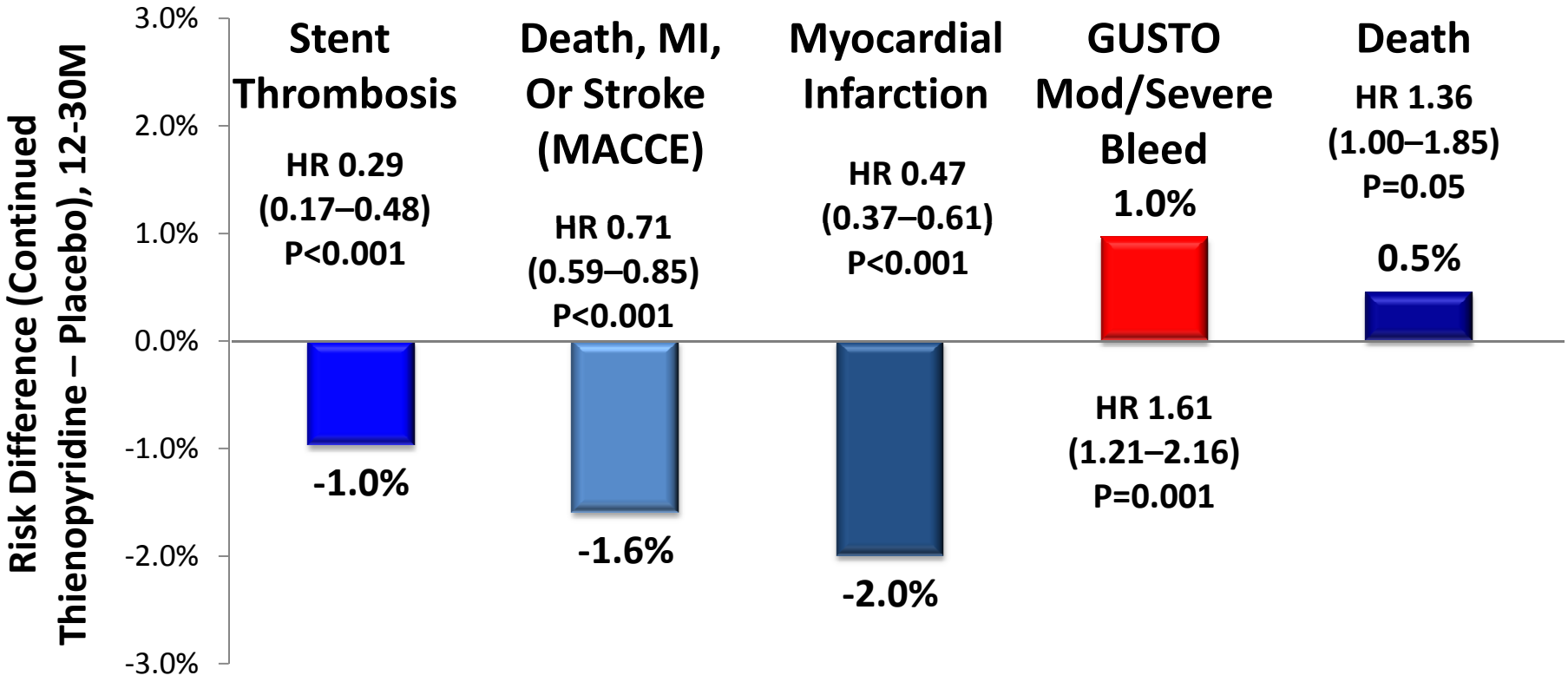
Treatment Duration by Stent Type Interaction on Stent Thrombosis



Kereiakes et al. *JAMA*. 2015;313(11):1113-21.

Background

- In the DAPT Study, continuation of dual antiplatelet therapy beyond 12 months reduced ischemic complications after coronary stenting compared with aspirin alone, yet increased moderate or severe bleeding.



Mauri, Kereiakes, Yeh et al. NEJM. 2014 Dec 4:371:2155-66.

Baseline Characteristics; All Randomized Patients With vs. Without Ischemic or Bleeding Events

	MI and/or Definite/Probable Stent Thrombosis Events			GUSTO Severe/Moderate Events		
Measure*	MI or ST N=348 Patients	No MI or ST N=11300 Patients	P	Bleeding N=215 Patients	No Bleeding N=11433 Patients	P
Age (years)	61.7	61.3	0.47	66.4	61.2	<.001
Female	26.4%	25.1%	0.57	29.3%	25.0%	0.15
BMI (Kg/m^2)	30.1	30.4	0.28	29.5	30.4	0.01
Diabetes mellitus	39.9%	28.9%	<.001	31.3%	29.2%	0.50
Hypertension	81.0%	73.1%	<.001	84.2%	73.2%	<.001
Cigarette smoker	33.0%	27.2%	0.02	18.2%	27.6%	0.002
Stroke/TIA	5.8%	3.4%	0.02	7.6%	3.4%	0.003
Congestive heart failure	10.4%	4.3%	<.001	8.0%	4.5%	0.02
LVEF < 30%	4.6%	1.9%	0.002	3.1%	1.9%	0.28
Prior PCI	42.4%	28.6%	<.001	37.7%	28.9%	0.01
Prior CABG	17.5%	10.5%	<.001	14.4%	10.7%	0.09
Prior myocardial infarction	32.7%	21.1%	<.001	22.2%	21.4%	0.80
Indication for index procedure						
STEMI	14.4%	14.4%	1.00	10.2%	14.5%	0.08
NSTEMI	22.1%	16.1%	0.004	12.1%	16.4%	0.11
Renal insufficiency/failure	7.9%	3.9%	0.001	9.4%	3.9%	<.001
Peripheral arterial disease	10.9%	5.5%	<.001	14.3%	5.5%	<.001

Baseline Characteristics; All Randomized Patients With vs. Without Ischemic or Bleeding Events

	MI and/or Definite/Probable Stent Thrombosis Events			GUSTO Severe/Moderate Events		
Measure*	Event N=348 Patients	No Event N=11300 Patients	P Value	Event N=215 Patients	No Event N=11433 Patients	P Value
Continued thienopyridine (Vs. Placebo)	35.3%	50.8%	< 0.001	62.8%	50.1%	< 0.001
Stent Type			0.64			0.12
Drug-Eluting	86.5%	85.5%		89.3%	85.4%	
Bare Metal	13.5%	14.5%		10.7%	14.6%	
No. treated vessels	1.1±0.3	1.1±0.3	0.84	1.1±0.3	1.1±0.3	0.87
No. stents	1.5±0.8	1.4±0.7	0.11	1.4±0.7	1.4±0.7	0.58
>2 vessels stented	0.0%	0.43%	0.41	0.0%	0.4%	1.00
Total stent length (mm)	28.1±16.8	27.0±16.43	0.21	26.1±15.0	27.1±16.5	0.39
Vein bypass graft stented	6.3%	2.7%	<.001	3.7%	2.8%	0.40
Thrombus-containing lesion	15.3%	14.2%	0.57	9.6%	14.3%	0.06
Minimum stent diameter <3mm	55.5%	42.9%	<0.001	44.2%	43.3%	0.78

DAPT Score Calculator

Patient Characteristics

Age: Less than 65

Diabetes Mellitus

Cigarette Smoking Within Last Two Years

Prior Myocardial Infarction or Percutaneous Coronary Intervention

History of Congestive Heart Failure or Left Ventricular Ejection Fraction < 30%

Index Procedure Characteristics

Myocardial Infarction at Presentation

Stenting of Vein of Graft

Stent Diameter < 3mm

Calculate | Clear All

The DAPT Score was developed to predict combined ischemic and bleeding risk for patients being considered for continued thienopyridine therapy in addition to aspirin beyond 1 year after coronary stent treatment. The Score was developed from the DAPT Study randomized trial data, in which patients were randomized to continued thienopyridine therapy (clopidogrel or prasugrel) vs. placebo. Patients were randomized only if they had not sustained a heart attack, stent thrombosis, stroke, repeat revascularization, or bleed, and had been adherent with medications during the first year. Patients receiving oral anticoagulation or with limited life expectancy were excluded.* Outcomes are shown according to DAPT Score limited to patients not receiving a paclitaxel-eluting stent, since such stents are no longer commonly used in clinical practice.

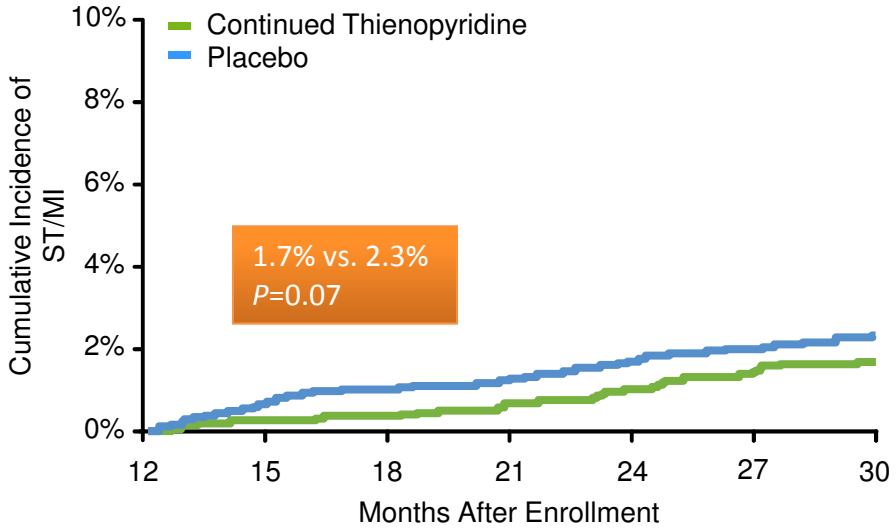
Mauri et al., NEJM 2014.

Yeh et al., JAMA 2016.

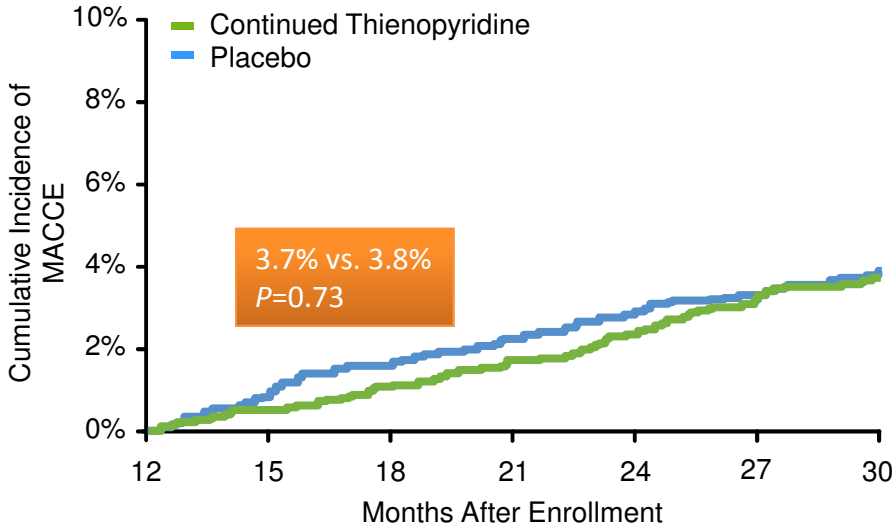
Continued Thienopyridine vs. Placebo
DAPT Score <2 (Low); N=5731

DAPT STUDY

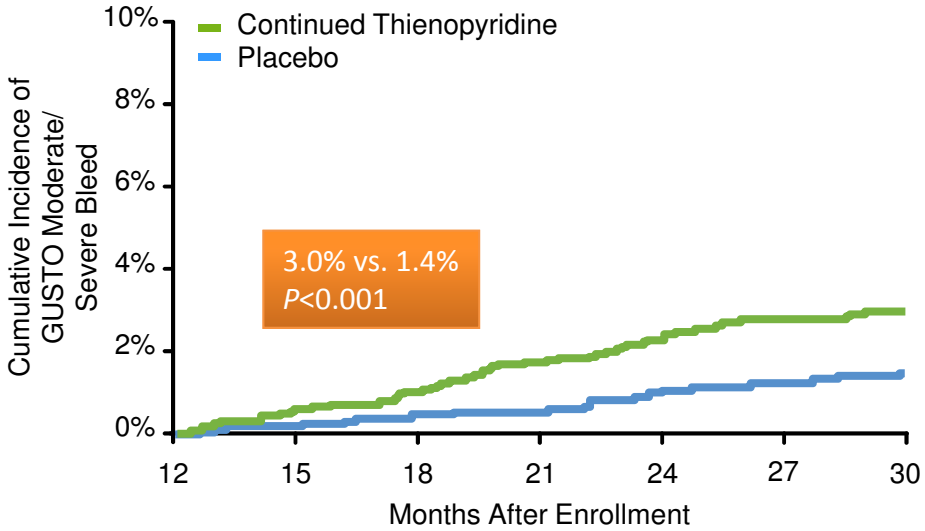
Stent Thrombosis or MI



MACCE



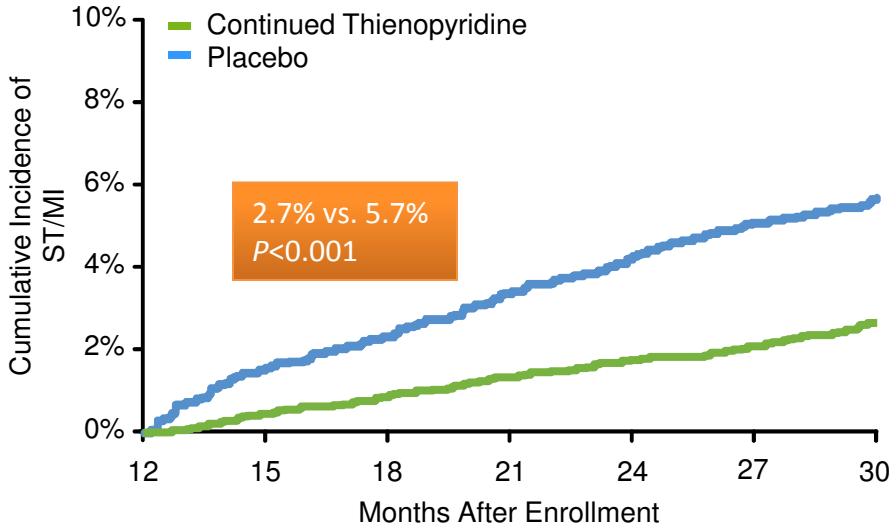
GUSTO Moderate/ Severe Bleeding



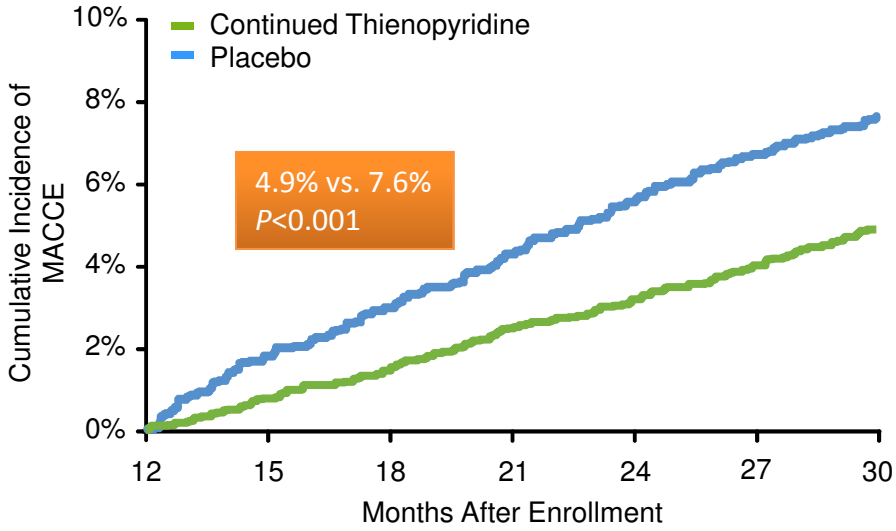
Continued Thienopyridine vs. Placebo
DAPT Score ≥ 2 (High); N=5917

DAPT STUDY

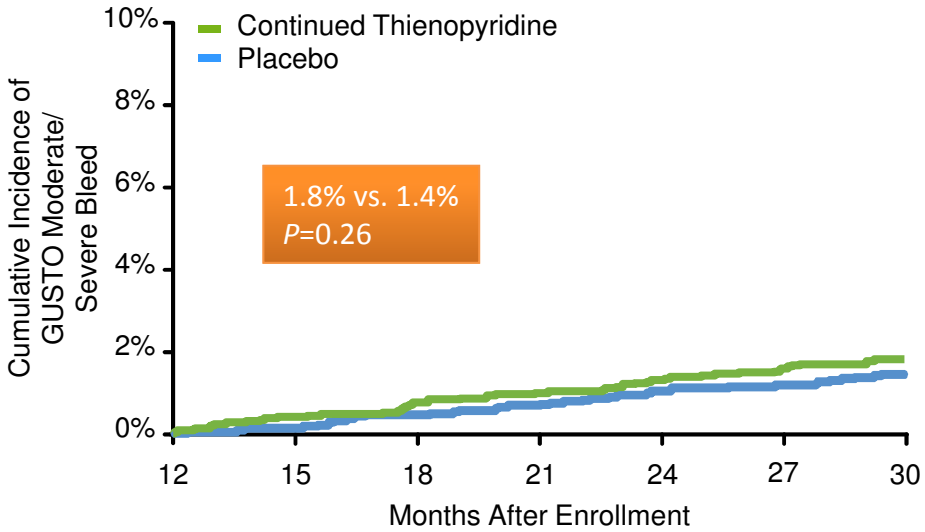
Stent Thrombosis or MI



MACCE



GUSTO Moderate/ Severe Bleeding



Conclusions

- The DAPT Score accurately identifies patients with the greatest anticipated benefit vs. harm from continuing dual antiplatelet therapy beyond 12 months among randomized patients in the DAPT Study

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

Trade-Off Between Stent Thrombosis and Bleeding Over Time

Incidence rates and standardized incidence risk difference for Stent Thrombosis and Clinically Significant Bleeding per 100 person/year between S-DAPT and L-DAPT

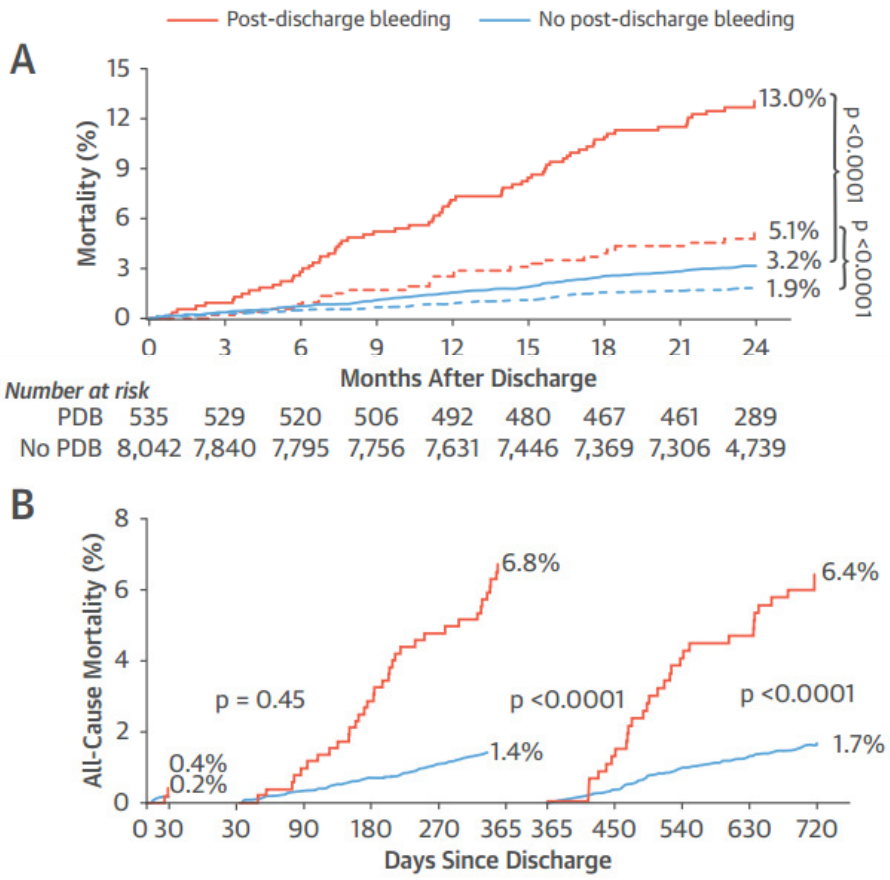
	Stent Thrombosis						Clinically Significant Bleeding					
	S-DAPT		L-DAPT				S-DAPT		L-DAPT			
Study (Ref. #)	No. of Events	IR*	No. of Events	IR*	IRD*	95% CI*	No. of Events	IR*	No. of Events	IR*	IRD*	95% CI*
ARCTIC-Interruption (21)	3	0.33	0	0	0.33	-0.04 to 0.72	1	0.11	7	0.78	-0.67	-1.29 to -0.04
DAPT (7)	69	0.80	31	0.35	0.44	0.22 to 0.67	84	0.98	124	1.42	-0.44	-0.77 to -0.12
DES-LATE (22)	25	0.29	13	0.15	0.13	0.00 to 0.27	63	0.73	99	1.14	-0.41	-0.70 to -0.13
EXCELLENT (19)	6	0.83	1	0.14	0.69	-0.02 to 1.41	2	0.28	4	0.56	-0.27	-0.94 to 0.38
ISAR-SAFE (16)	5	0.50	4	0.40	0.10	-0.48 to 0.69	6	0.60	13	1.30	-0.70	-1.56 to 0.16
ITALIC (17)	3	0.66	0	0	0.66	-0.08 to 1.40	5	1.10	7	1.54	-0.44	-1.94 to 1.05
OPTIMIZE (15)	13	0.84	12	0.77	0.06	-0.56 to 0.69	10	0.64	14	0.90	-0.26	-0.88 to 0.35
PRODIGY (23)	15	0.80	13	0.69	0.11	-0.44 to 0.66	15	0.80	27	1.44	-0.64	-1.32 to 0.03
RESET (14)	2	0.19	3	0.28	-0.09	-0.50 to 0.31	5	0.47	10	0.95	-0.48	-1.20 to 0.24
SECURITY (18)	2	0.29	3	0.42	-0.12	-0.75 to 0.49	4	0.59	8	1.12	-0.53	-1.50 to 0.43
Combined	–	–	–	–	0.21	0.11 to 0.31	–	–	–	–	-0.45	-0.62 to -0.28

For every ST event averted with L-DAPT, approximately 2.1 extra CSB events are estimated to occur (- 0.45 ST / 0.21 CSB per 100 person / year).

Giustino et al., J Am Coll Cardiol. 2015 Apr 7;65(13):1298-310

Incidence, Predictors, and Impact of Post-Discharge (PD) Bleeding After Percutaneous Coronary Intervention: Analysis on 8,582 patients from the ADAPT-DES Study

Impact of PD bleeding on 2-year Mortality



PD bleeding Vs. PD MI

Variable*	Adjusted HR (95% CI)	p Value
PDB†	5.03 (3.29-7.66)	<0.0001
With transfusion	4.71 (2.76-8.03)	<0.0001
Without transfusion	5.27 (3.32-8.35)	<0.0001
Post-discharge MI†	1.92 (1.18-3.12)	0.009

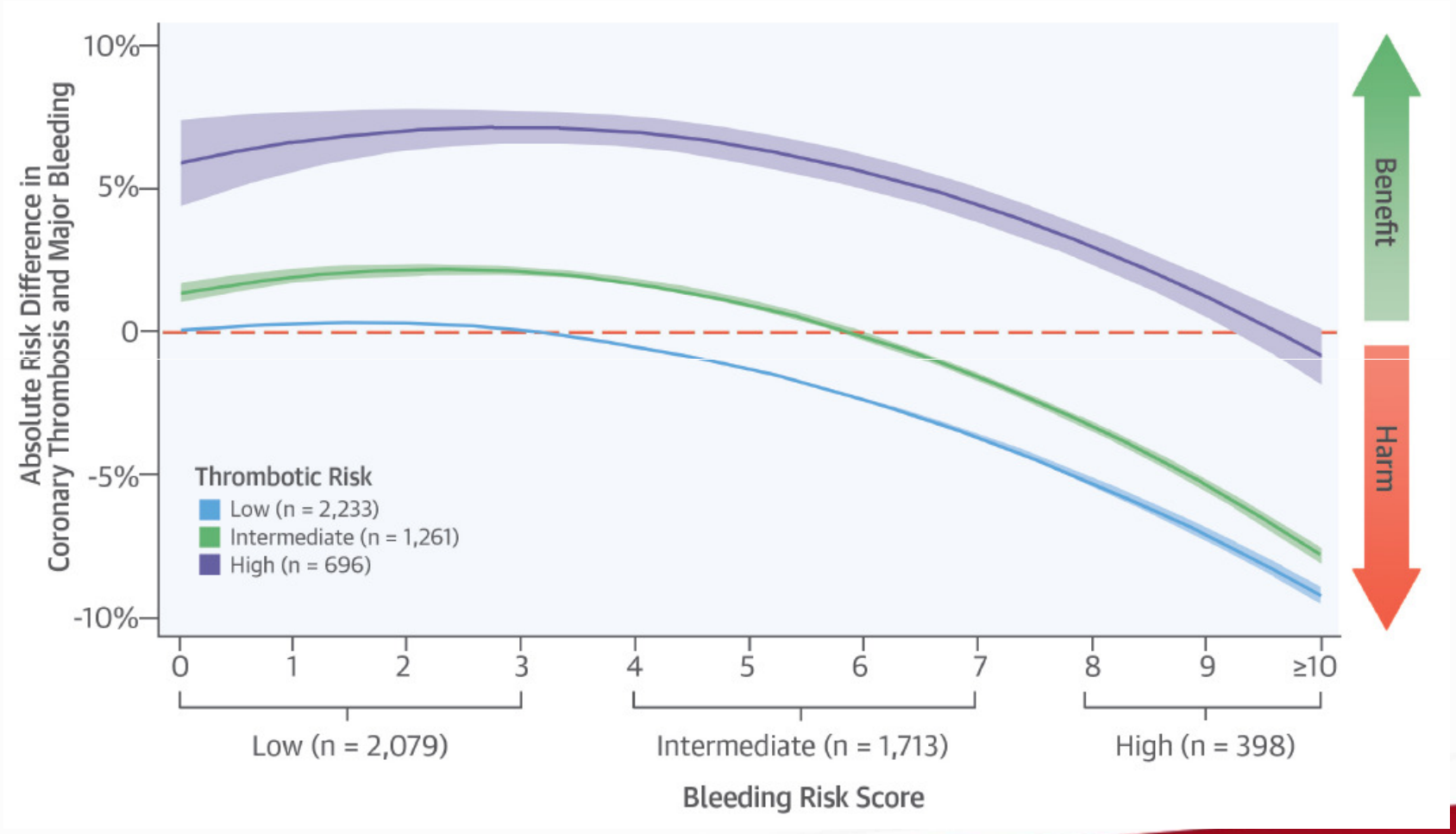
Predictors of PD bleeding

Variable*	HR (95% CI)	p Value
Age (per yr increase)	1.02 (1.01-1.03)	<0.0001
Warfarin, at discharge	2.31 (1.78-2.99)	<0.0001
Peripheral artery disease	1.57 (1.25-1.98)	0.0001
Calcified lesion	1.25 (1.05-1.50)	0.01
Bifurcation lesion	1.32 (1.06-1.64)	0.01
Platelet reactivity units (per 10-unit decrease)	1.01 (1.01-1.02)	0.002
Baseline hemoglobin (per g/dl decrease)	1.28 (1.22-1.37)	<0.0001

Genereux et al., J Am Coll Cardiol. 2015 Sep 1;66(9):1036-45

UNIVERSITY OF UTAH HEALTH CARE

Risk/Benefit Trade-off with Prolonged DAPT as a Function of Thrombotic and Bleeding Risk



Baber et al., J Am Coll Cardiol. 2016 May 17;67(19):2224-34

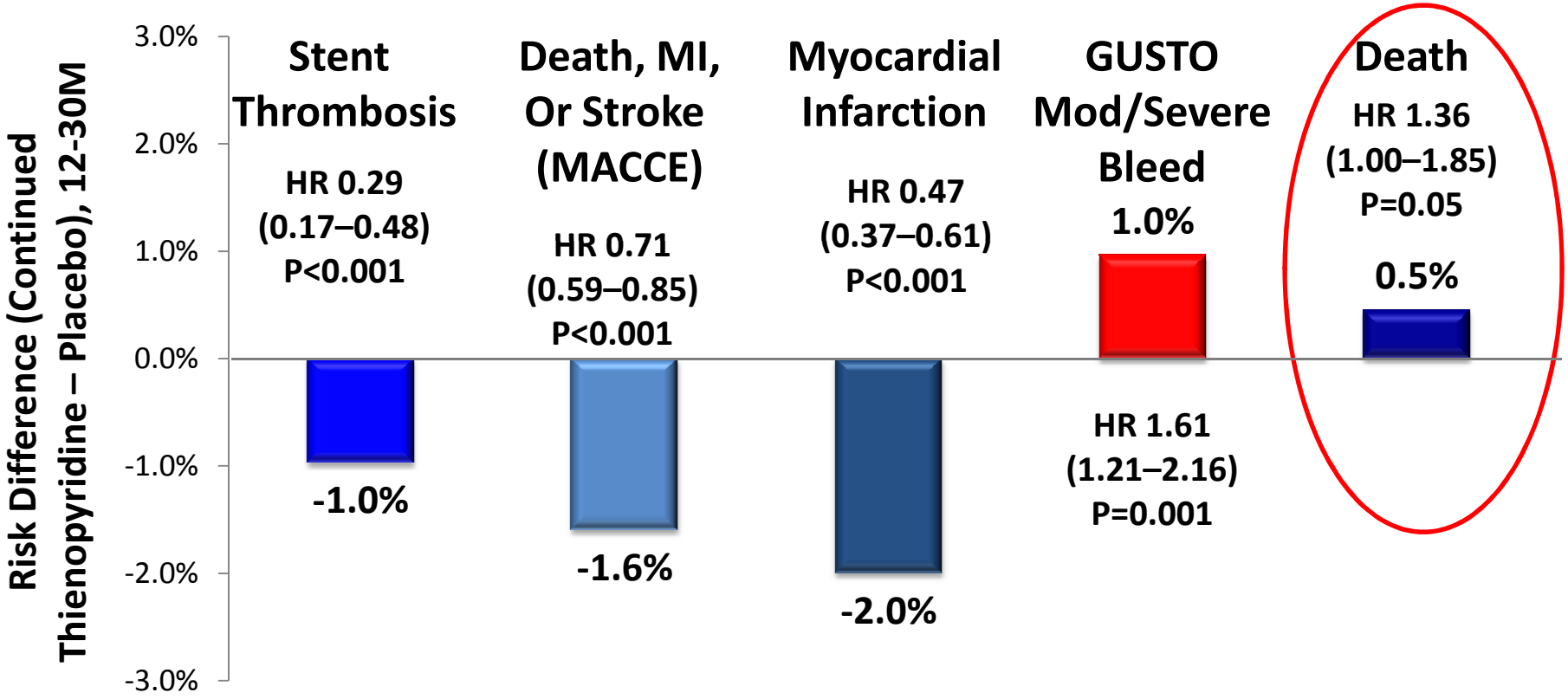
UNIVERSITY OF UTAH HEALTH CARE

Questions

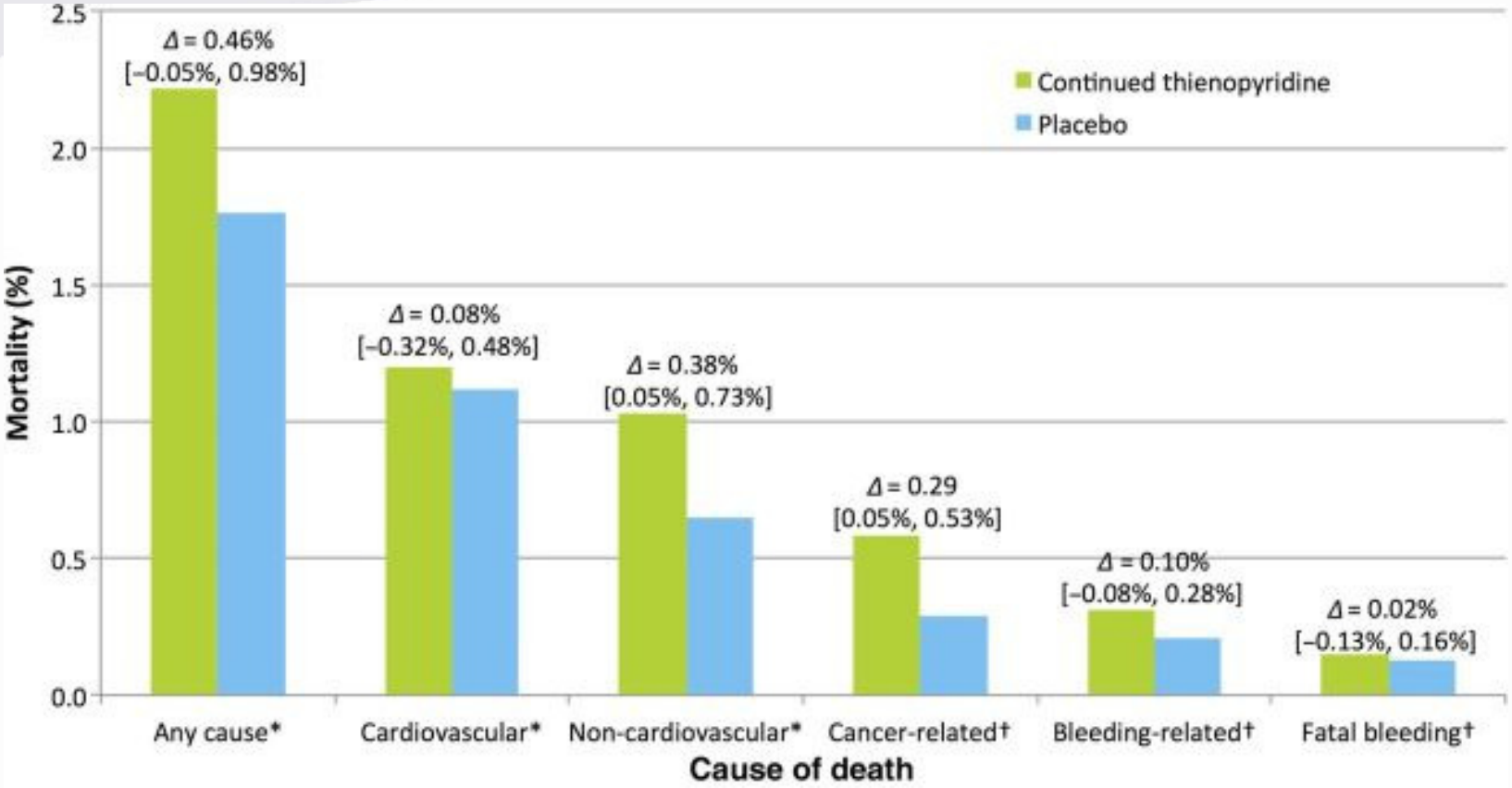
- **What's the shortest duration of DAPT I can get away with?**
- **If I don't need to stop DAPT for any particular reason, how long should I continue?**
- **Is there a mortality issue with DAPT?**
- **Why do newer generation DES confer less risk of stent thrombosis and how does this inform stent development?**
  - **Do we ever need to use a BMS?**
  - **Are we poised for another public relations disaster with biodegradable stents?**

Background

- In the DAPT Study, continuation of dual antiplatelet therapy beyond 12 months reduced ischemic complications after coronary stenting compared with aspirin alone, yet increased moderate or severe bleeding.

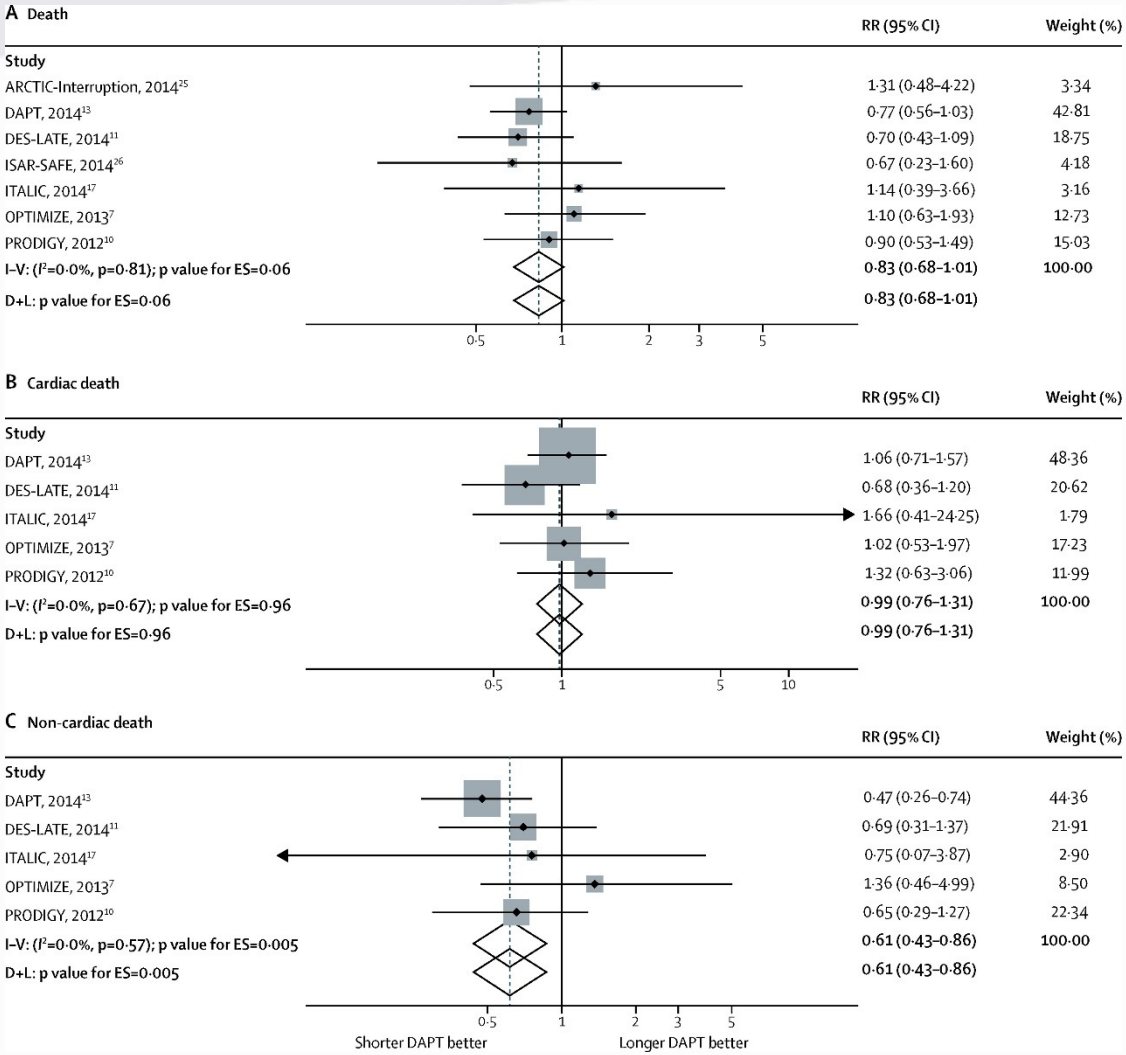


Mauri, Kereiakes, Yeh et al. NEJM. 2014 Dec 4:371:2155-66.



Eur Heart J. 2016 Jan 21; 37(4): 378–385.

Figure 3



The Lancet 2015 385, 2371-2382DOI: (10.1016/S0140-6736(15)60263-X)

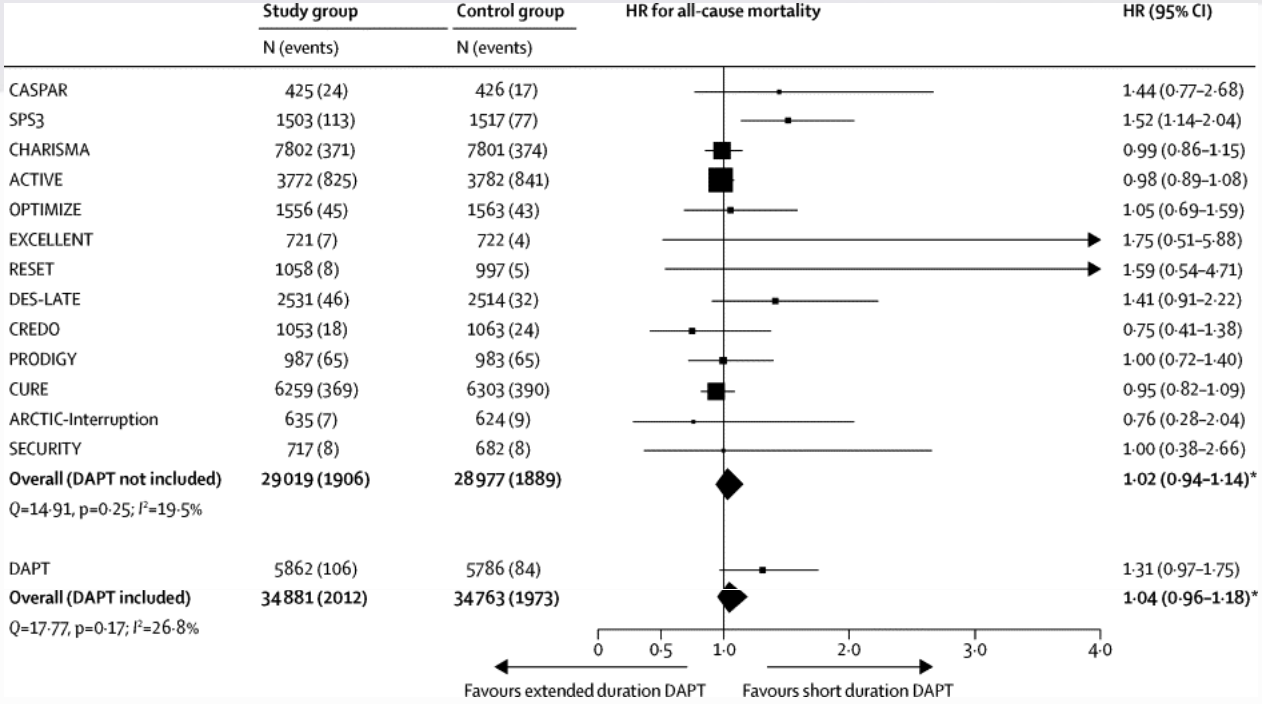


Figure 2. Bayesian meta-analysis of all-cause mortality associated with extended duration DAPT versus short duration or no DAPTResults are presented before and after inclusion of the DAPT Study.3 DAPT=dual antiplatelet therapy. HR=hazard ratio. *Overall summar...

Sammy Elmariah, Laura Mauri, Gheorghe Doros, Benjamin Z Galper, Kelly E O'Neill, Philippe Gabriel Steg, Dean J Kereiakes, Robert W Yeh

Extended duration dual antiplatelet therapy and mortality: a systematic review and meta-analysis

null, Volume 385, Issue 9970, 2015, 792–798

http://dx.doi.org/10.1016/S0140-6736(14)62052-3

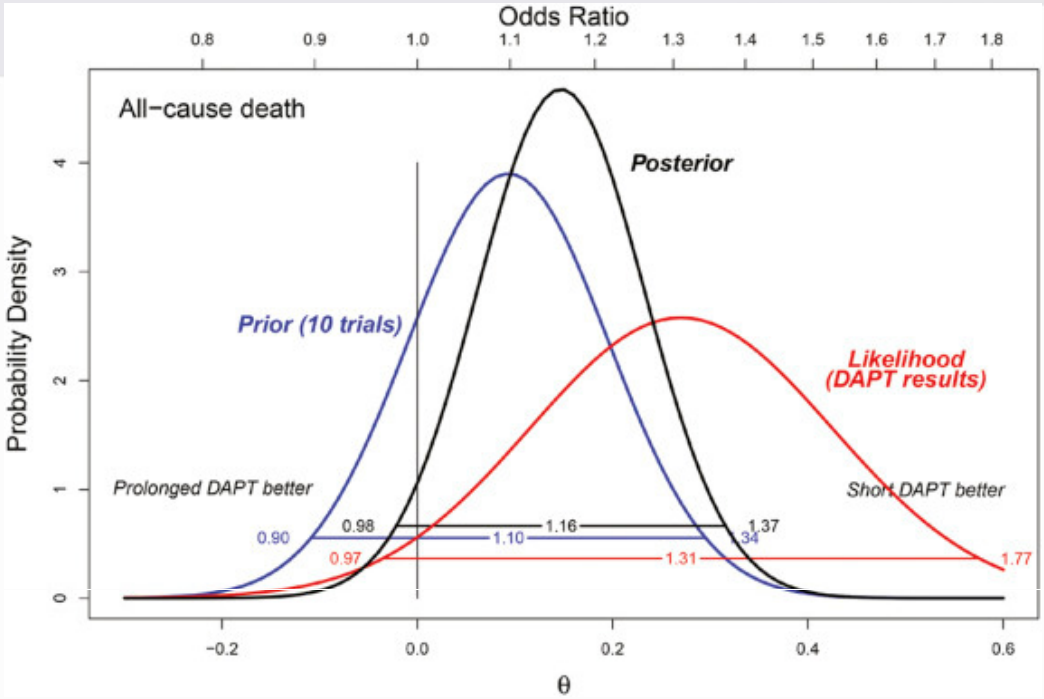


Figure 4. Mortality RateA triplot illustrates the way that the Bayesian approach combines information from various sources. The prior (blue) shows the distribution of OR describing the mortality rate differences between prolonged and short-course DAPT seen in ...

John A. Bittl, Usman Baber, Steven M. Bradley, Duminda N. Wijeysundera

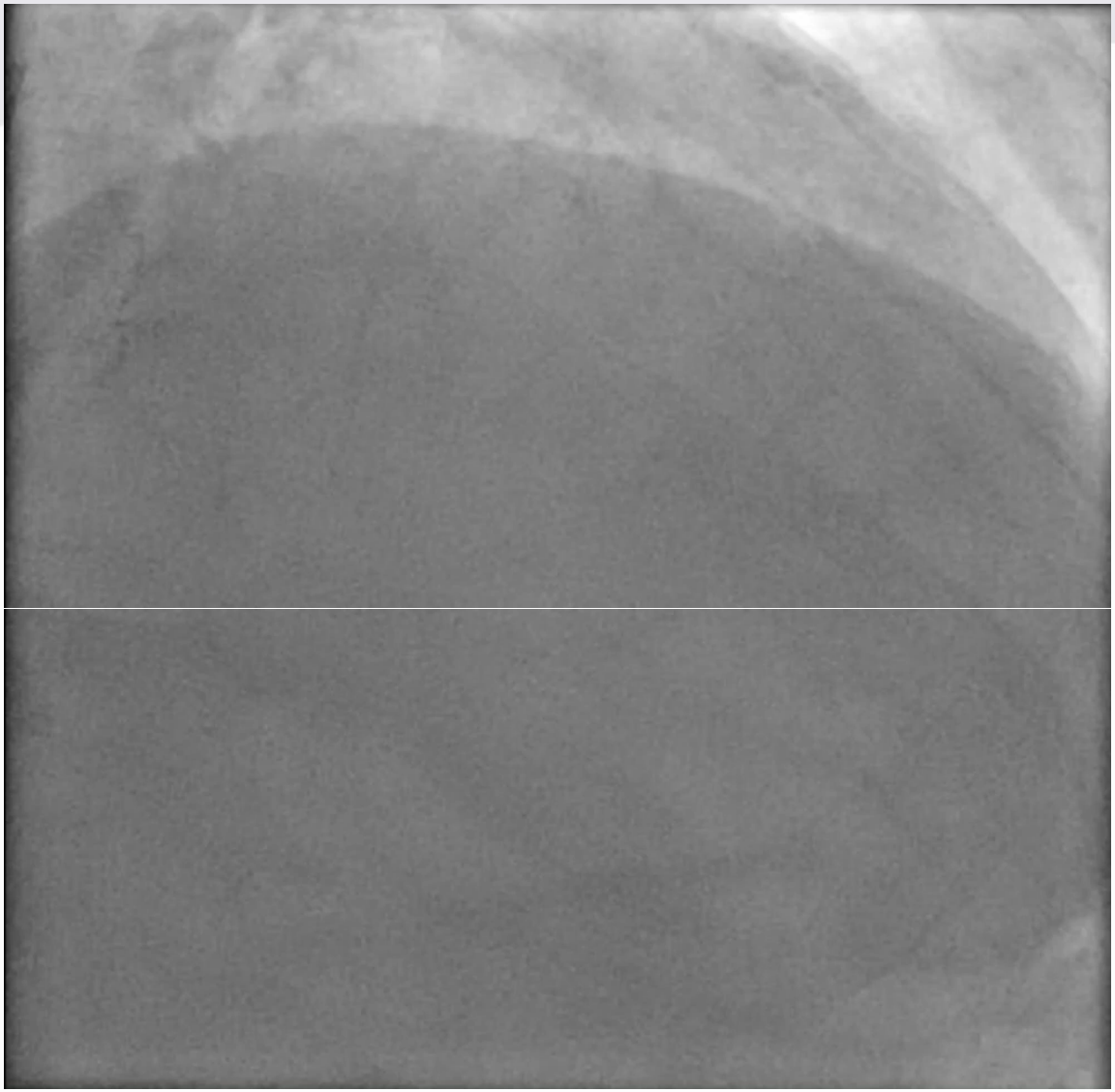
Duration of Dual Antiplatelet Therapy: A Systematic Review for the 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease : A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Journal of the American College of Cardiology, Volume 68, Issue 10, 2016, 1116–1139

http://dx.doi.org/10.1016/j.jacc.2016.03.512

Questions

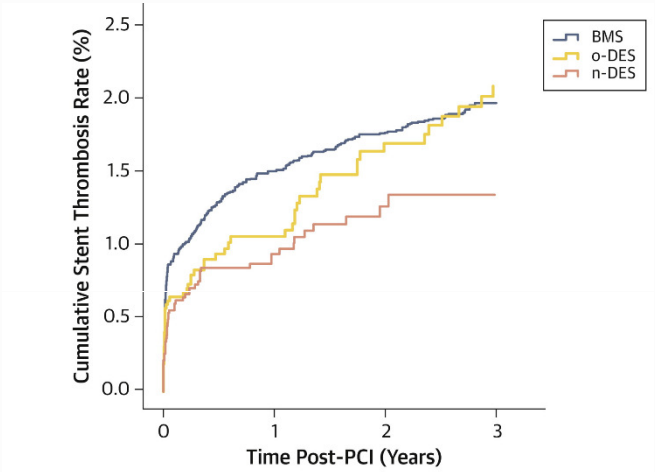
- What's the shortest duration of DAPT I can get away with?
- If I don't need to stop DAPT for any particular reason, how long should I continue?
- Is there a mortality issue with DAPT?
- Why do newer generation DES confer less risk of stent thrombosis and how does this inform stent development?
  - Do we ever need to use a BMS?
  - Are we poised for another public relations disaster with biodegradable stents?



JACC Journals

From: **Stent Thrombosis in New-Generation Drug-Eluting Stents in Patients With STEMI Undergoing Primary PCI: A Report From SCAAR**

J Am Coll Cardiol. 2014;64(1):16-24. doi:10.1016/j.jacc.2014.04.022

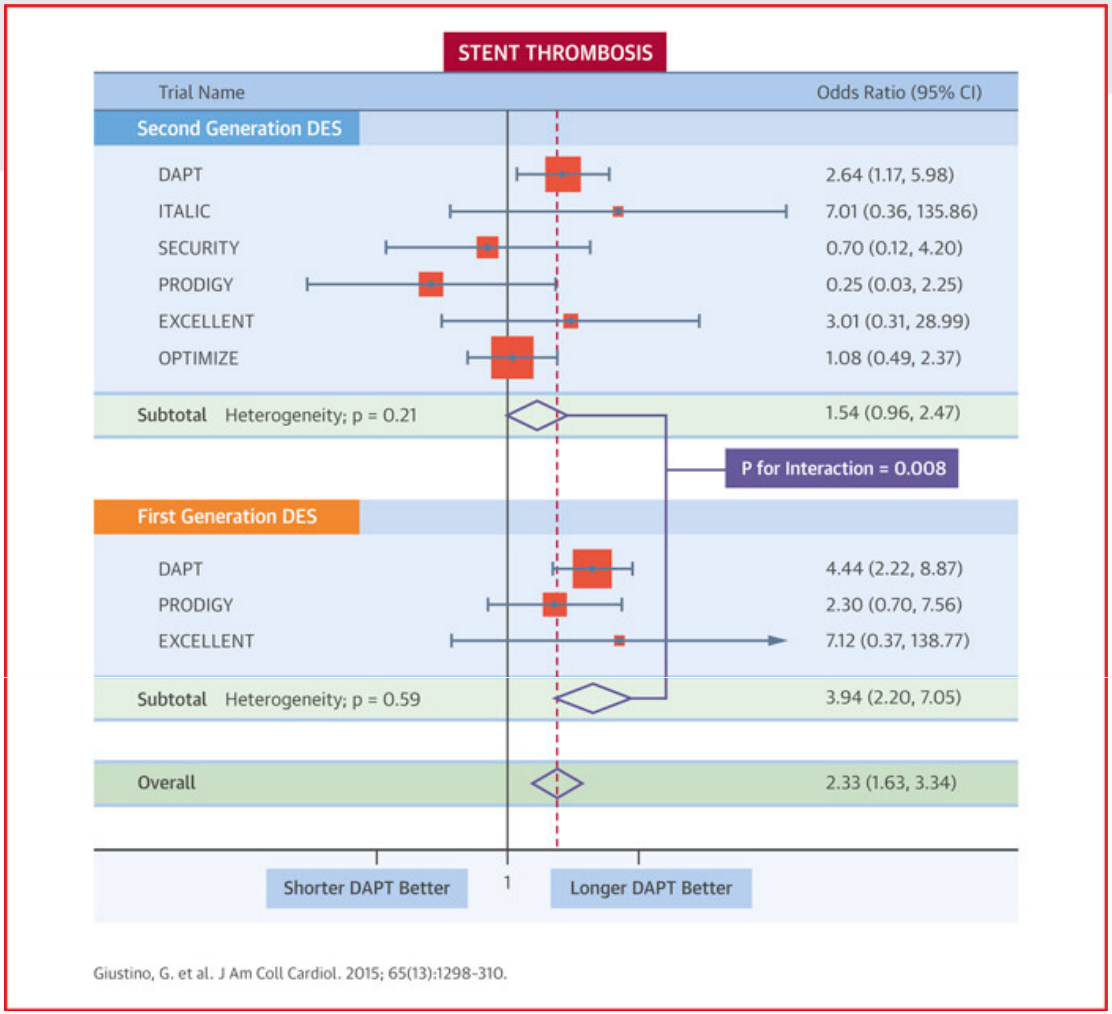


N patients at risk. (event rate %)	0 months	30 days	1 year	2 years	3 years
BMS	25065	24851 (0.9%)	21962 (1.5%)	19336 (1.8%)	15882 (2.0%)
o-DES	4271	4137 (0.6%)	3869 (1.1%)	2154 (1.7%)	1661 (2.1%)
n-DES	4811	4649 (0.5%)	4497 (0.9%)	2751 (1.2%)	1235 (1.3%)

Figure Legend:

Cumulative Rates of Definite Stent Thrombosis Up to 3 Years in the n-DES, o-DES, and BMS Groups

The curves showing the cumulative rates of stent thrombosis in the n-DES and o-DES groups start to diverge before 6 months post-percutaneous coronary intervention (PCI) with a further step-up in the o-DES group after 1 year. The rates of stent thrombosis in the BMS group increased constantly up to 3 years. Abbreviations as in Figure 1.



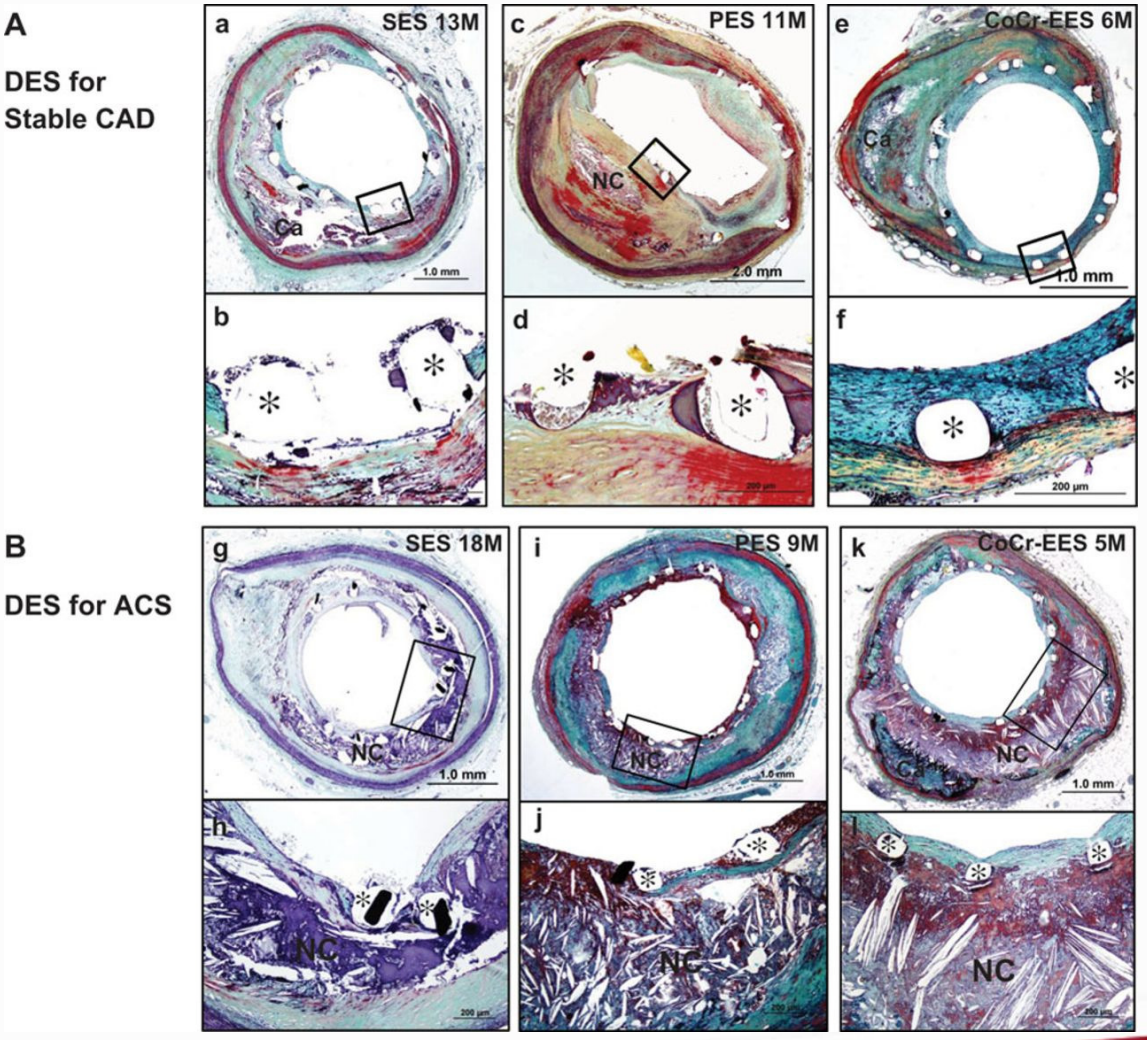
Central Illustration. Stent Thrombosis With First- and Second-Generation Drug-Eluting StentsA statistically significant interaction was observed between drug-eluting stent (DES) generation and dual antiplatelet therapy (DAPT) duration on risk of stent thrombos...

Gennaro Giustino, Usman Baber, Samantha Sartori, Roxana Mehran, Ioannis Mastoris, Annapoorna S. Kini, Samin K. Sharma, Stuart J. Pocock, George D. Dangas

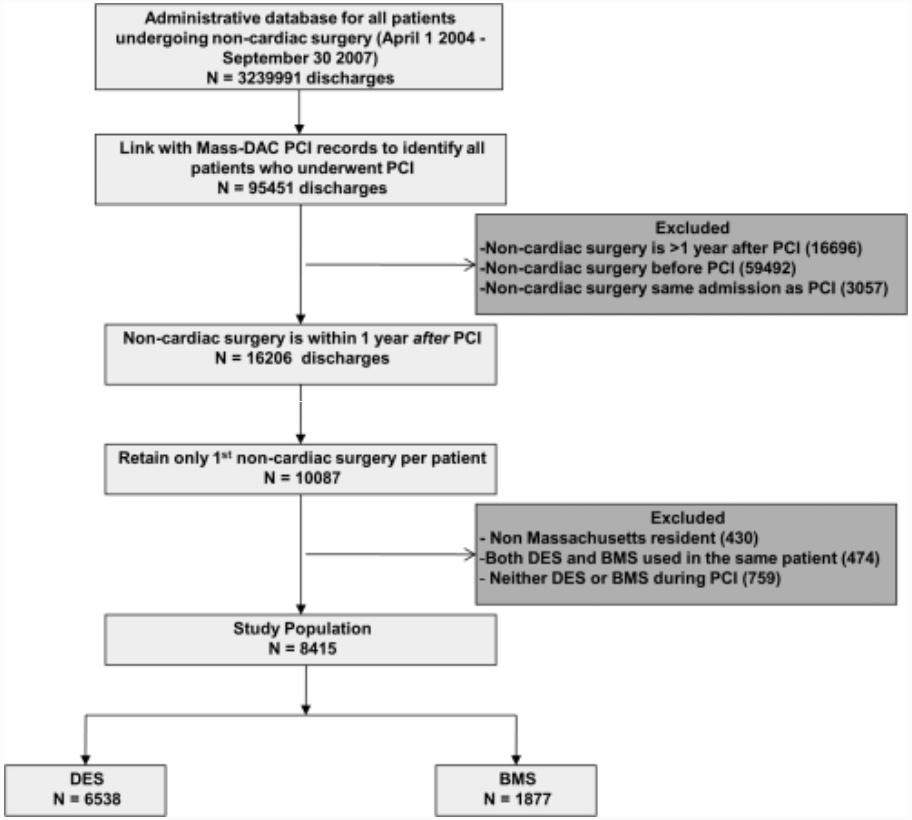
Journal of the American College of Cardiology, Volume 65, Issue 13, 2015, 1298–1310

http://dx.doi.org/10.1016/j.jacc.2015.01.039

Representative images of sirolimus-eluting stent (SES), paclitaxel-eluting stent (PES), and cobalt-chromium everolimus-eluting stent (CoCr-EES) implanted for stable coronary artery disease (CAD; A: a to f) and for acute coronary syndromes (ACS; B: g to l). a and b, Histological sections from a 53-year-old-man with SES implanted in the proximal left anterior descending coronary artery for 13 months.



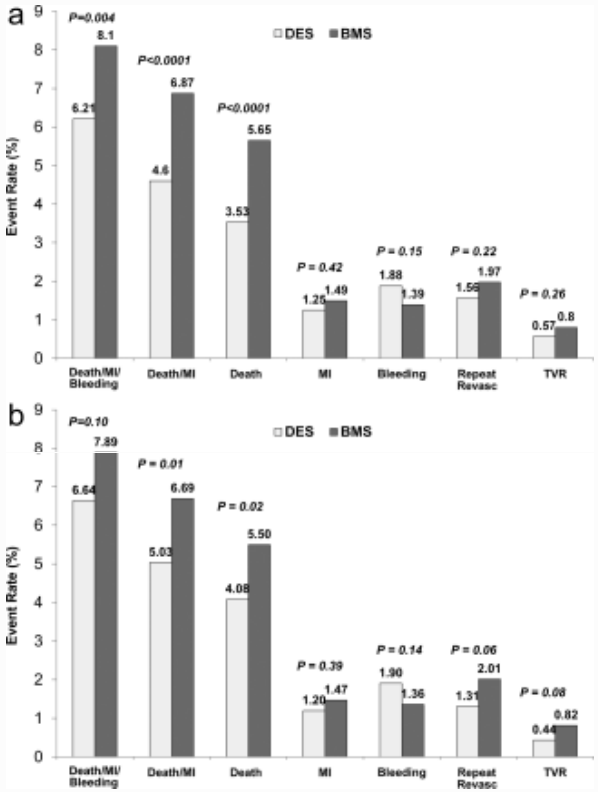
Drug-eluting stents versus bare metal stents prior to noncardiac surgery



Catheterization and Cardiovascular Interventions
Volume 85, Issue 4, pages 533-541, 20 AUG 2014 DOI: 10.1002/ccd.25617
http://onlinelibrary.wiley.com/doi/10.1002/ccd.25617/full#ccd25617-fig-0001

UNIVERSITY OF UTAH HEALTH CARE

Drug-eluting stents versus bare metal stents prior to noncardiac surgery



Thirty-day outcomes for DES vs. BMS (a) before propensity score matching and (b) after propensity score matching.

Catheterization and Cardiovascular Interventions
Volume 85, Issue 4, pages 533-541, 20 AUG 2014 DOI: 10.1002/ccd.25617
http://onlinelibrary.wiley.com/doi/10.1002/ccd.25617/full#ccd25617-fig-0003

UNIVERSITY OF UTAH HEALTH CARE

Millions face risk from drug-coated stents

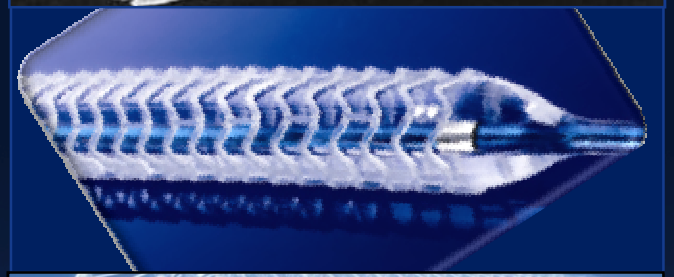
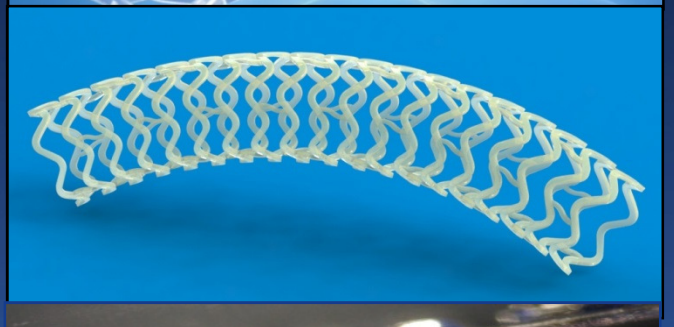
"Millions of Americans could be walking around with tiny time bombs in their hearts"

"Potentially lethal heart devices a frightening problem for patients, doctors"

"The FDA panel might recommend they not be used at all"

By Robert Bazell
Chief science correspondent
NBC News
Nov 2006 – March 2007

Bioresorbable Vascular Scaffolds (BRS)

Igaki-Tamai		*PLLA*
Abbott Absorb		*PLLA (eluting everolimus)*
Elixir DESolve		*PLLA (eluting novolimus)*
Reva Fantom		*Iodinated tyrosine-derivative (eluting sirolimus)*
Biotronik Dreams		*Magnesium (eluting sirolimus)*

Mount Sinai Heart

	Absorb group	Xience group	Relative risk (95% CI)	Difference (95% CI)	p value
(Continued from previous page)					
Thrombosis endpoints					
Definite scaffold or stent thrombosis	8/320 (3%)	0/159	NA	2·50% (–0·16 to 4·85)	0·06
Acute (0–1 day)	1/335 (<1%)	0/166	NA	0·30% (–1·98 to 1·67)	1·0
Sub-acute (2–30 days)	1/334 (<1%)	0/166	NA	0·30% (–1·98 to 1·68)	1·0
Late (31–365 days)	0/329	0/164	NA	0·00% (–2·29 to 1·15)	1·0
Very late (>365 days)	6/329 (2%)	0/164	NA	1·82% (–0·67 to 3·92)	0·19
Definite or probable scaffold or stent thrombosis	9/320 (3%)	0/159	NA	2·81% (0·11 to 5·26)	0·0331
Acute (0–1 day)	1/335 (<1%)	0/166	NA	0·30% (–1·98 to 1·67)	1·0
Sub-acute (2–30 days)	1/334 (<1%)	0/166	NA	0·30% (–1·98 to 1·68)	1·0
Late (31–365 days)	1/329 (<1%)	0/164	NA	0·30% (–2·00 to 1·70)	1·0
Very late (>365 days)	6/329 (2%)	0/164	NA	1·82% (–0·67 to 3·92)	0·19
Patients on dual antiplatelet therapy at day 1095	102/334 (31%)	49/166 (30%)	NA	1·02% (–7·69 to 9·24)	0·81
Duration of dual antiplatelet therapy within 1095 days (days)	565·5 (324·2), n=334	561·0 (319·1), n=166	NA	4·5 (–55·5 to 64·4)	0·88

Data are n/N (%), unless stated otherwise. Denominators exclude patients who were lost to follow-up or who withdrew consent, except for those who died or experienced the corresponding endpoint before their withdrawal of consent. NA=not available. *Numbers are hierarchical counts in the composite endpoints.

Table 4: **Secondary clinical outcomes at 3 year follow-up**

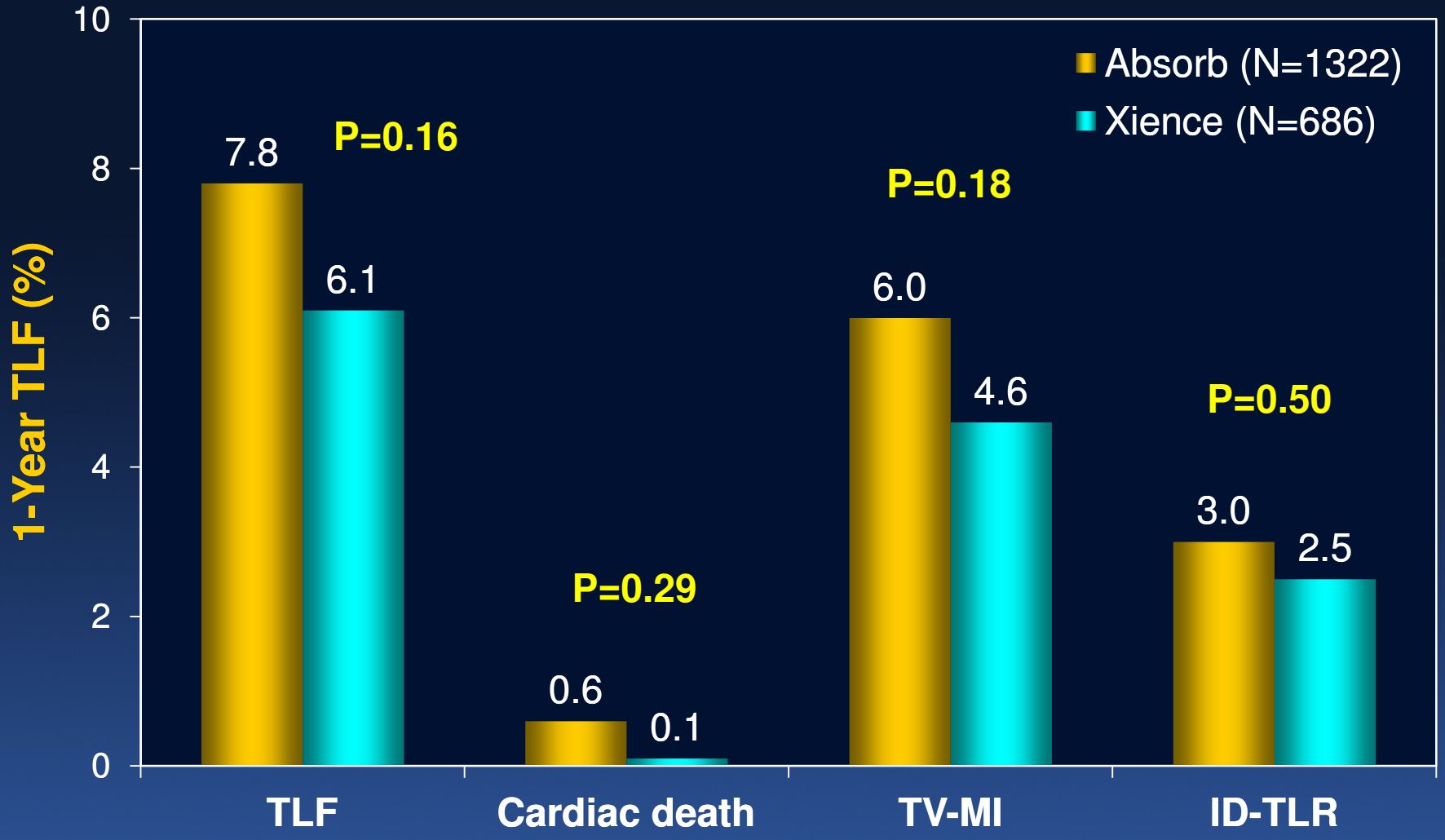
Patrick W Serruys, Bernard Chevalier, Yohei Sotomi, Angel Cequier, Didier Carrié, Jan J Piek, Ad J Van Boven, Marcello Dominici, Dariusz Dudek, Dougal McClean, Steffen Helqvist, Michael Haude, Sebastian Reith, Manuel de Sousa Almeida, Gianluca Campo, Andrés Iñiguez, Manel Sabaté, Stephan Windecker, Yoshinobu Onuma

Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent for the treatment of coronary artery stenosis (ABSORB II): a 3 year, randomised, controlled, single-blind, multicentre clinical trial

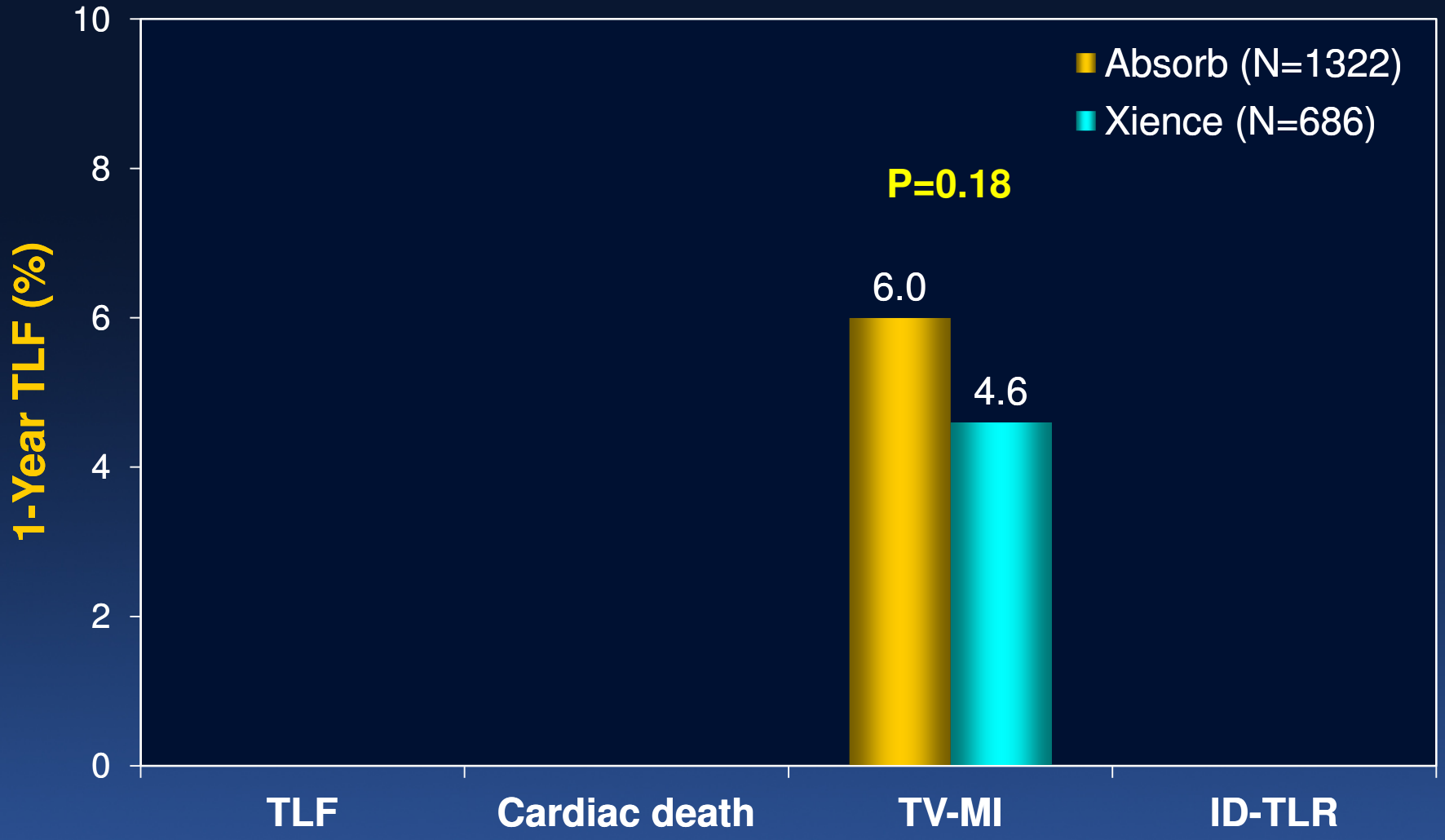
null, Volume 388, Issue 10059, 2016, 2479–2491

http://dx.doi.org/10.1016/S0140-6736(16)32050-5

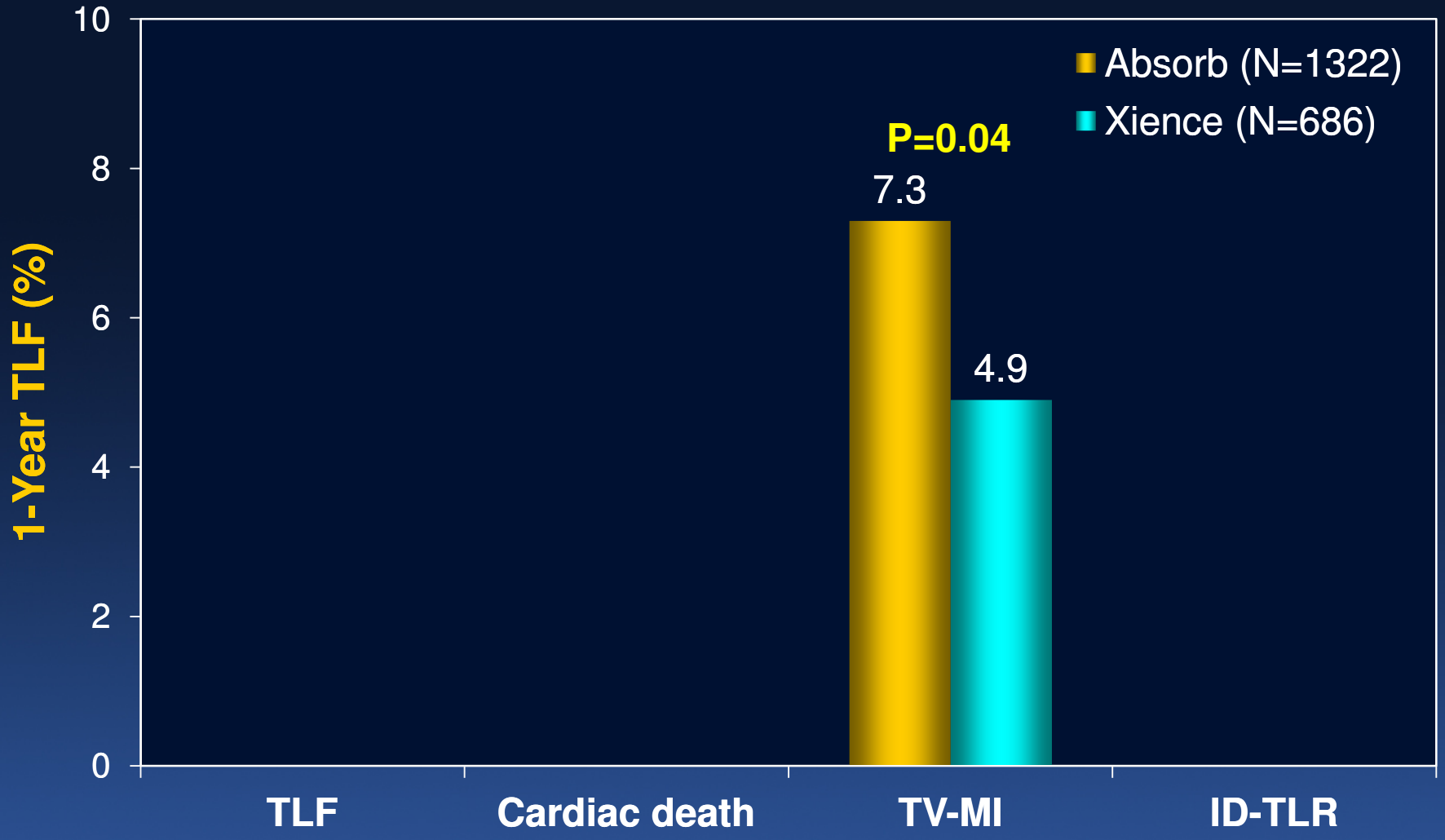
1-Year TLF Components

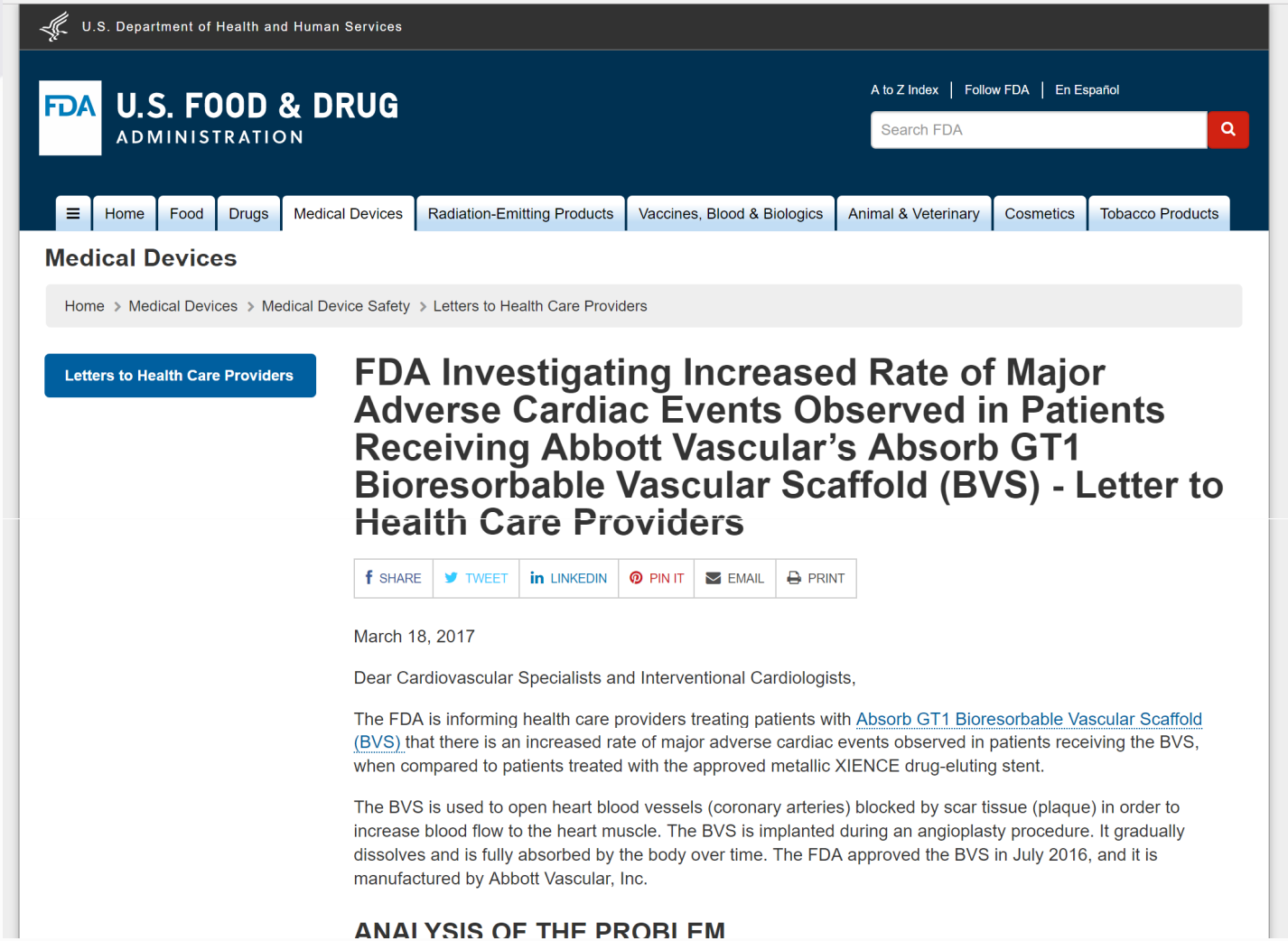


1-Year TLF Components



2-Year TLF Components





U.S. Department of Health and Human Services

FDA U.S. FOOD & DRUG ADMINISTRATION

A to Z Index | Follow FDA | En Español

Search FDA

Home | Food | Drugs | Medical Devices | Radiation-Emitting Products | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Tobacco Products

Medical Devices

Home > Medical Devices > Medical Device Safety > Letters to Health Care Providers

Letters to Health Care Providers

FDA Investigating Increased Rate of Major Adverse Cardiac Events Observed in Patients Receiving Abbott Vascular's Absorb GT1 Bioresorbable Vascular Scaffold (BVS) - Letter to Health Care Providers

SHARE TWEET LINKEDIN PIN IT EMAIL PRINT

March 18, 2017

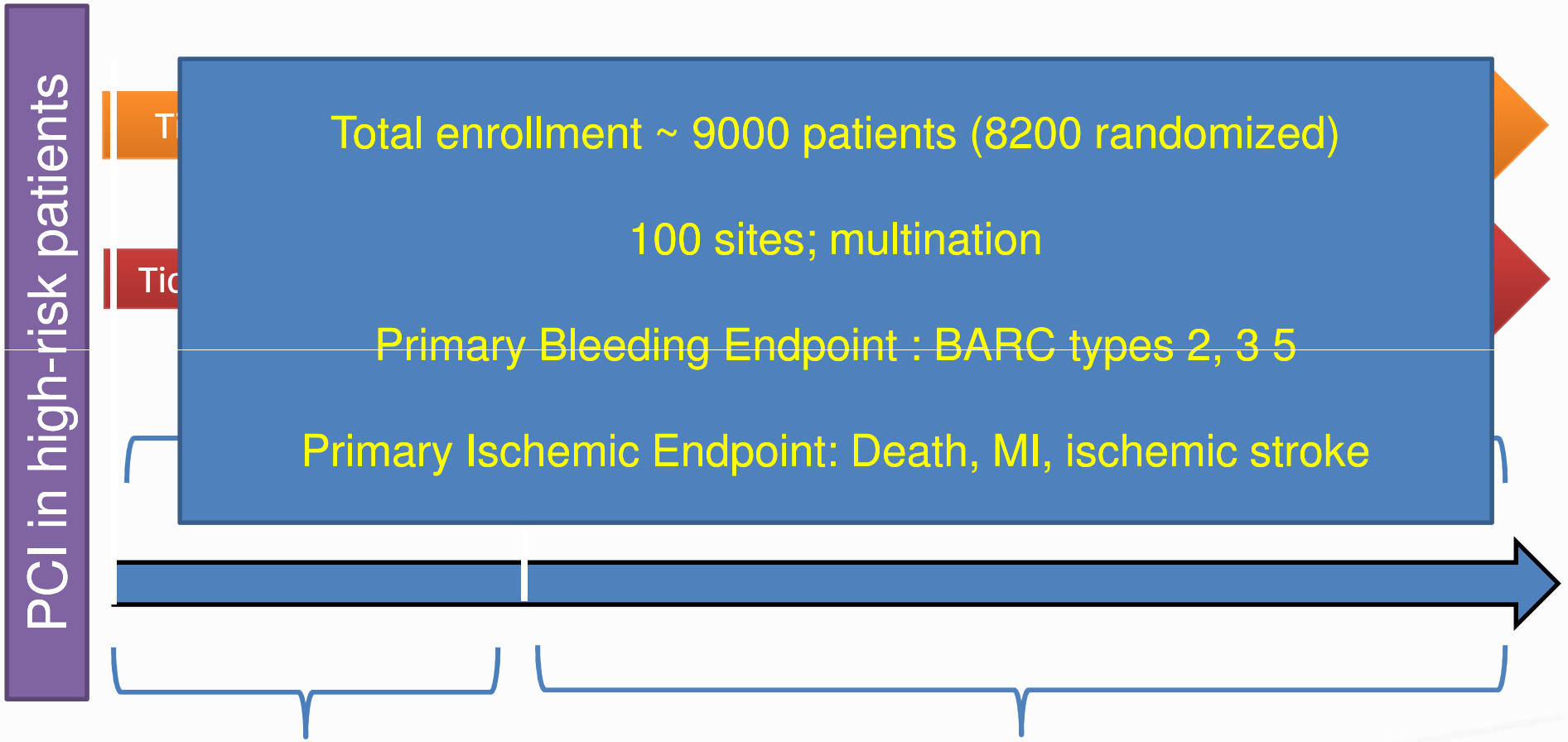
Dear Cardiovascular Specialists and Interventional Cardiologists,

The FDA is informing health care providers treating patients with Absorb GT1 Bioresorbable Vascular Scaffold (BVS) that there is an increased rate of major adverse cardiac events observed in patients receiving the BVS, when compared to patients treated with the approved metallic XIENCE drug-eluting stent.

The BVS is used to open heart blood vessels (coronary arteries) blocked by scar tissue (plaque) in order to increase blood flow to the heart muscle. The BVS is implanted during an angioplasty procedure. It gradually dissolves and is fully absorbed by the body over time. The FDA approved the BVS in July 2016, and it is manufactured by Abbott Vascular, Inc.

ANALYSIS OF THE PROBLEM

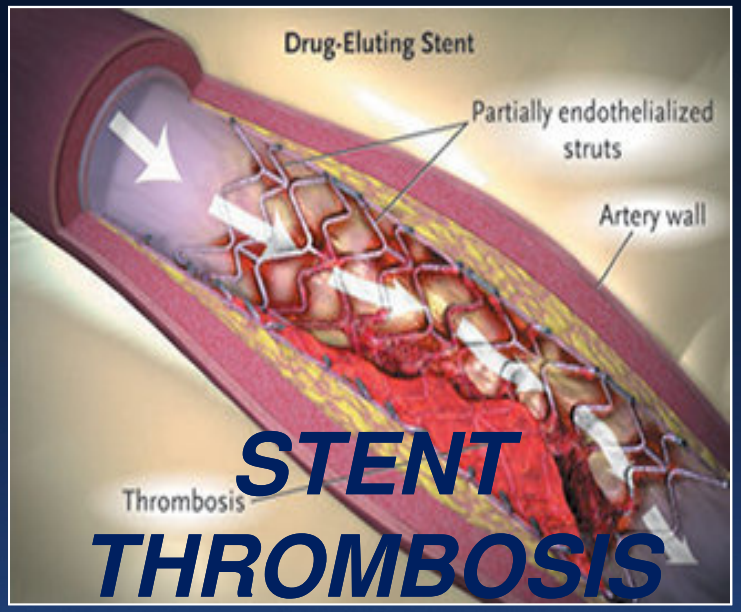
Dual Antiplatelet Therapy After PCI: The TWILIGHT Study



UNIVERSITY OF UTAH HEALTH CARE

The clinical challenge in patients with atrial fibrillation undergoing PCI

5-10% of patients undergoing PCI have atrial fibrillation



OAC > DAPT for Stroke prevention

DAPT > OAC for Stent Thrombosis prevention

TRIPLE THERAPY

BLEEDING

Connolly et al. Lancet. 2006; 367:1903-12.

Mount Sinai Heart

Conclusions

- After DES, prolonged DAPT is associated with less stent thrombosis at a cost of higher bleeding.
- Newer generation DES appear to have improved in regards to likelihood of stent thrombosis.
- With newer generation DES, DAPT discontinuation in as few as 3 months may be safe.
- However, no matter the timepoint, discontinuation of DAPT is a balance between bleeding and thrombosis risk and should therefore be individualized.
- Evolving technology may alter the balance of risks.