

Why DAPT Trial Not Followed?: Moving Forward Less Duration with Smart DES, De-Escalating Strategy, and P2Y12 Inhibitor Monotherapy



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Presenter Disclosure Information

Name: Dominick J Angiolillo

Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization listed below.

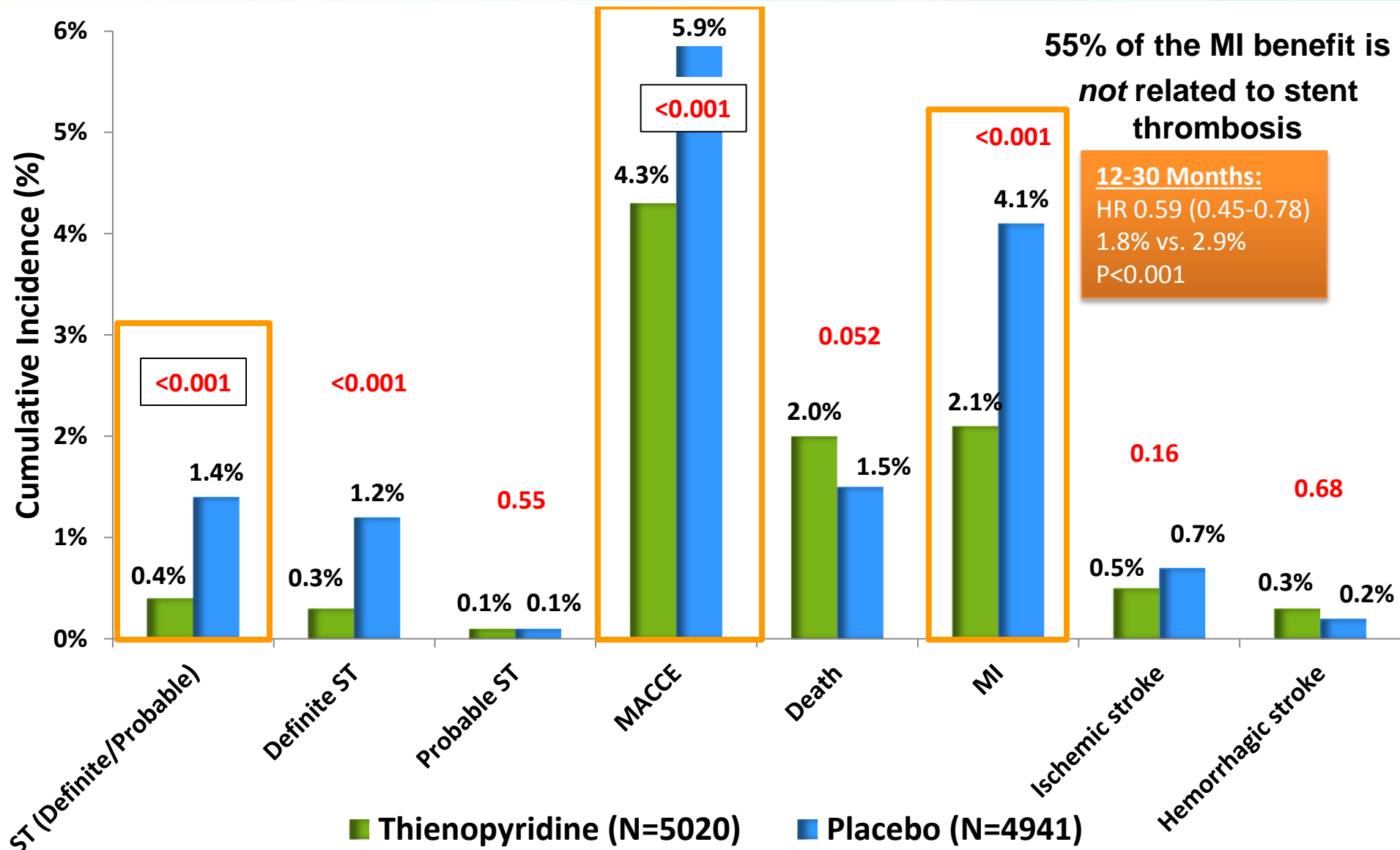
Received payment as an individual for:

- a) Consulting fee or honorarium from Amgen, Bayer, Chiesi, Sanofi, Eli Lilly, Daiichi-Sankyo, The Medicines Company, AstraZeneca, Merck, Abbott Vascular, Pfizer, and PLx Pharma;
- b) Honorarium for participation in review activities (DSMB member) from CeloNova, Johnson & Johnson, St. Jude, and Sunovion.
- c) Honorarium from the American Board of Internal Medicine (Interventional Cardiology Subspecialty Exam Writing Committee Member)

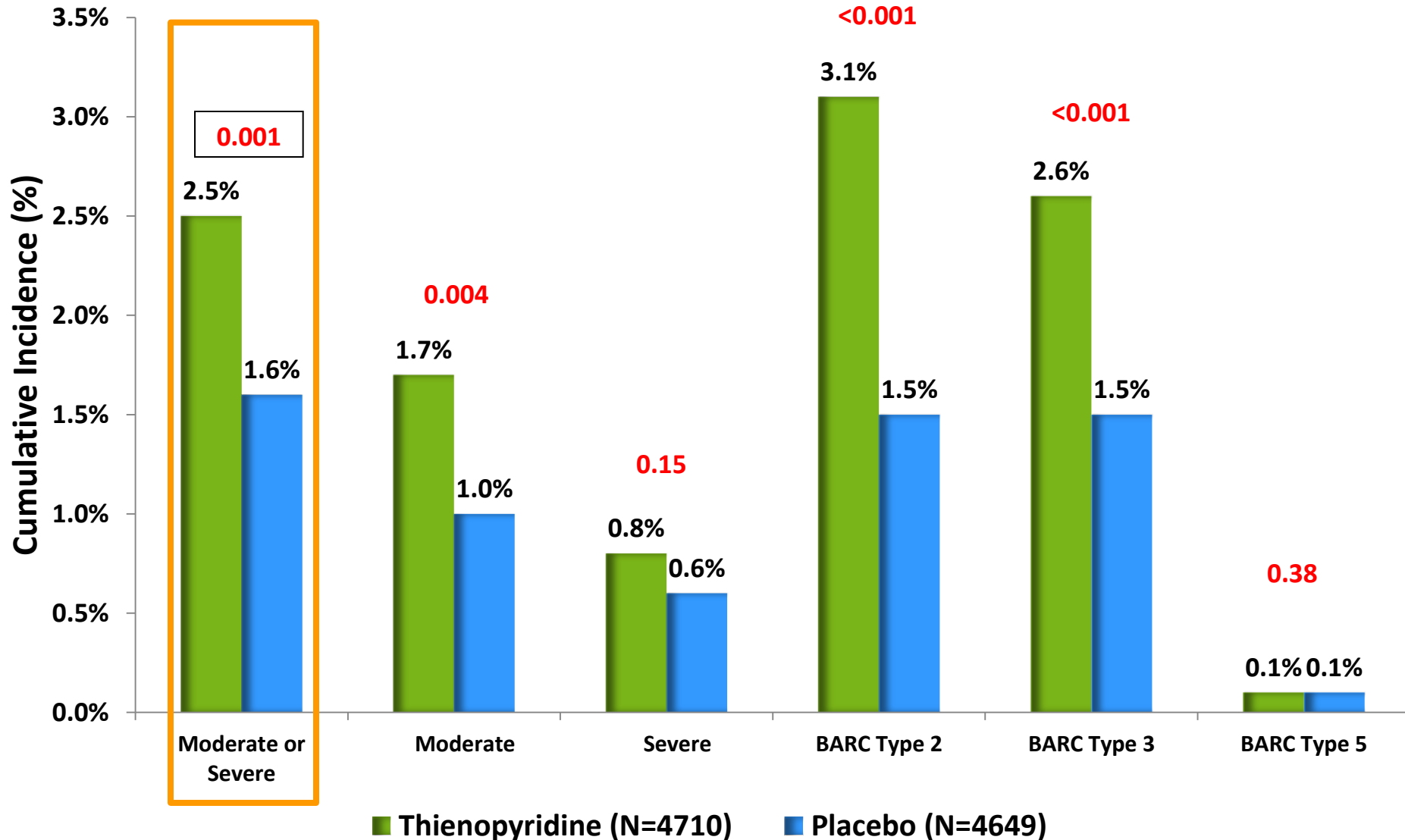
Institutional payments for:

- a) Grant support industry: from Amgen, Glaxo-Smith-Kline, Eli Lilly, Daiichi-Sankyo, The Medicines Company, AstraZeneca, Janssen Pharmaceuticals, Inc., Osprey Medical, Inc., Novartis, CSL Behring, and Gilead.
- b) Grant in gift: Spartan; Scott R. MacKenzie Foundation
- c) Federal agency: NIH

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

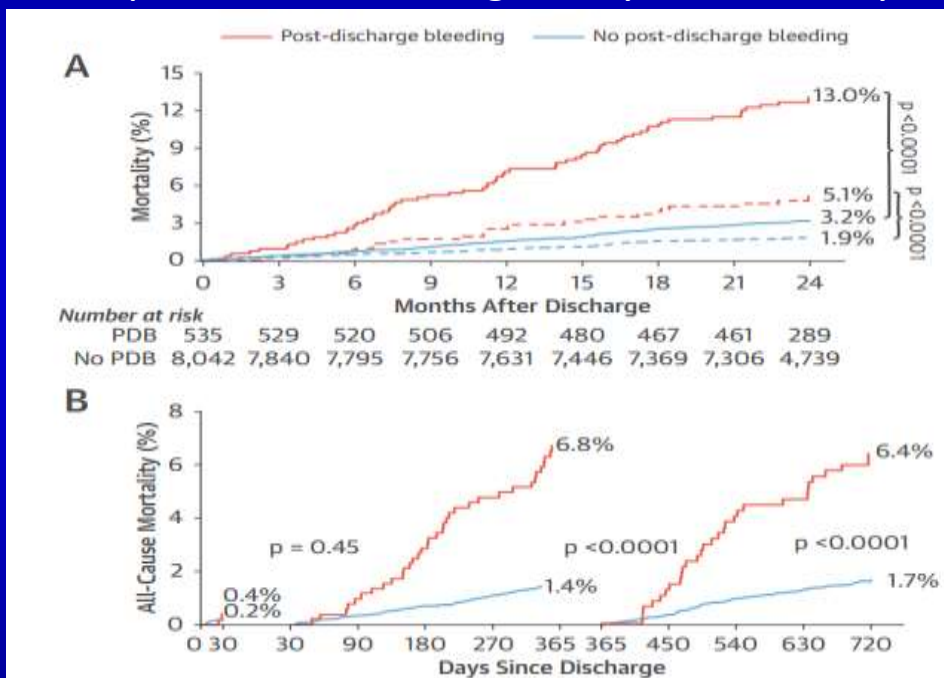


Primary Safety End Point (Moderate or Severe Bleeding): 12-30 Months



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

Bleeding reduction strategies (to overcome prolonged DAPT)

- 1. Smart DES requiring shorter DAPT duration**
- 2. De-escalating P2Y12 inhibition**
- 3. P2Y12 inhibitor monotherapy (stop aspirin)**

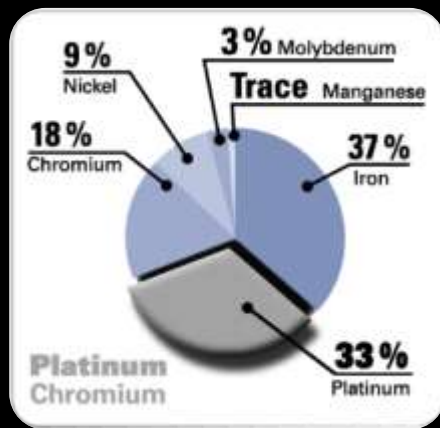
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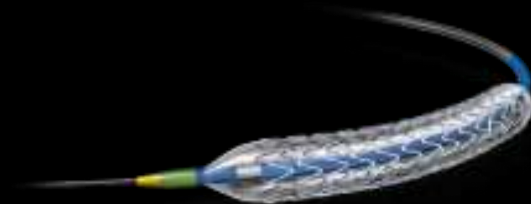
Elements of DES Design

DES design affects procedural success and clinical outcomes

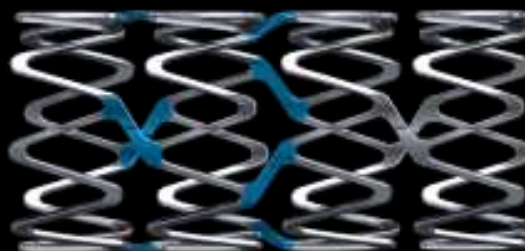
Metal Alloy



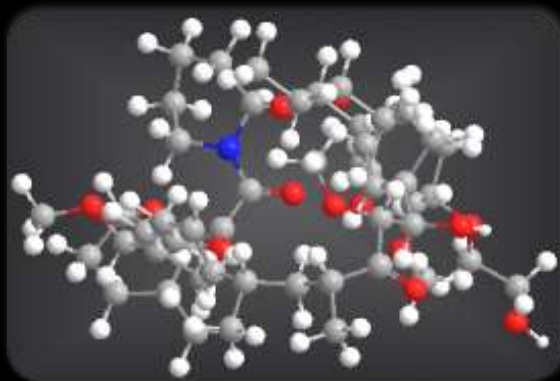
Stent Delivery System



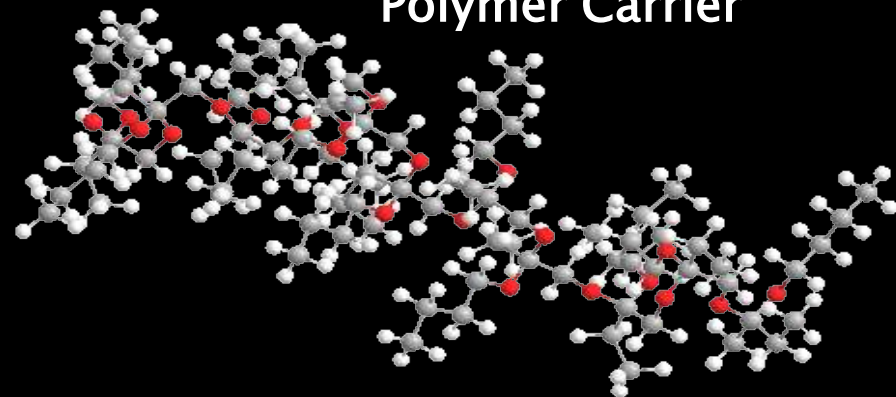
Stent Architecture



Drug

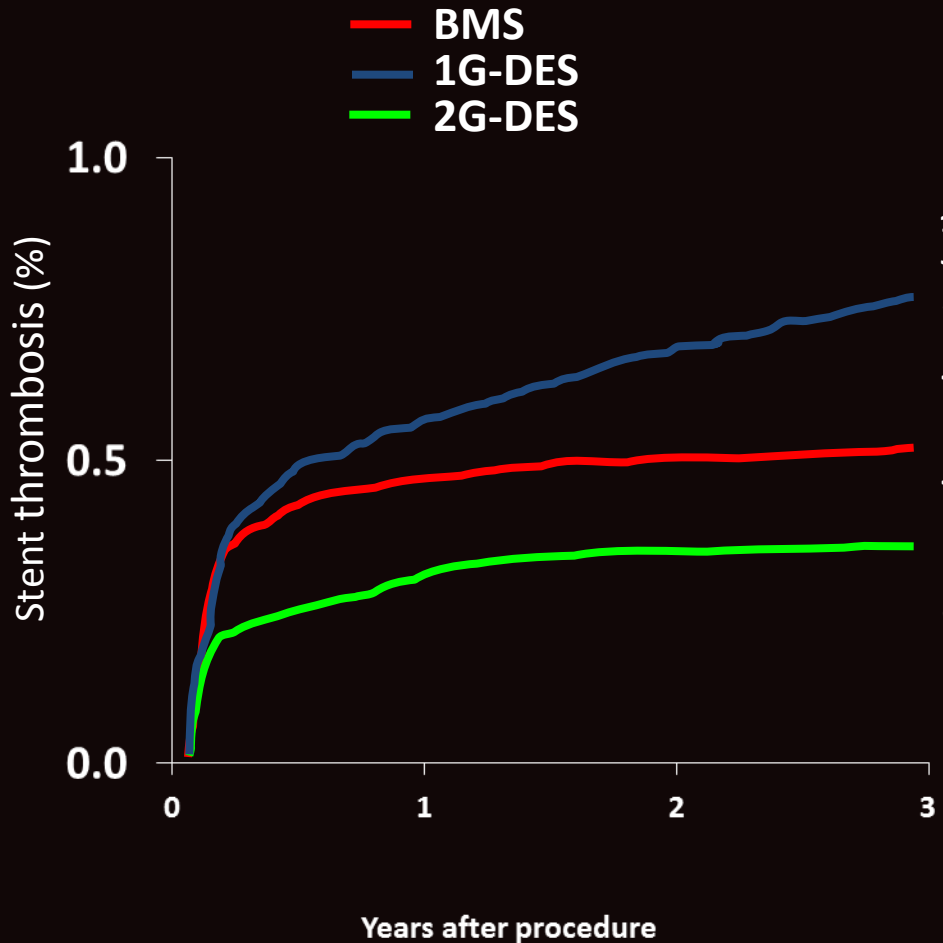


Polymer Carrier

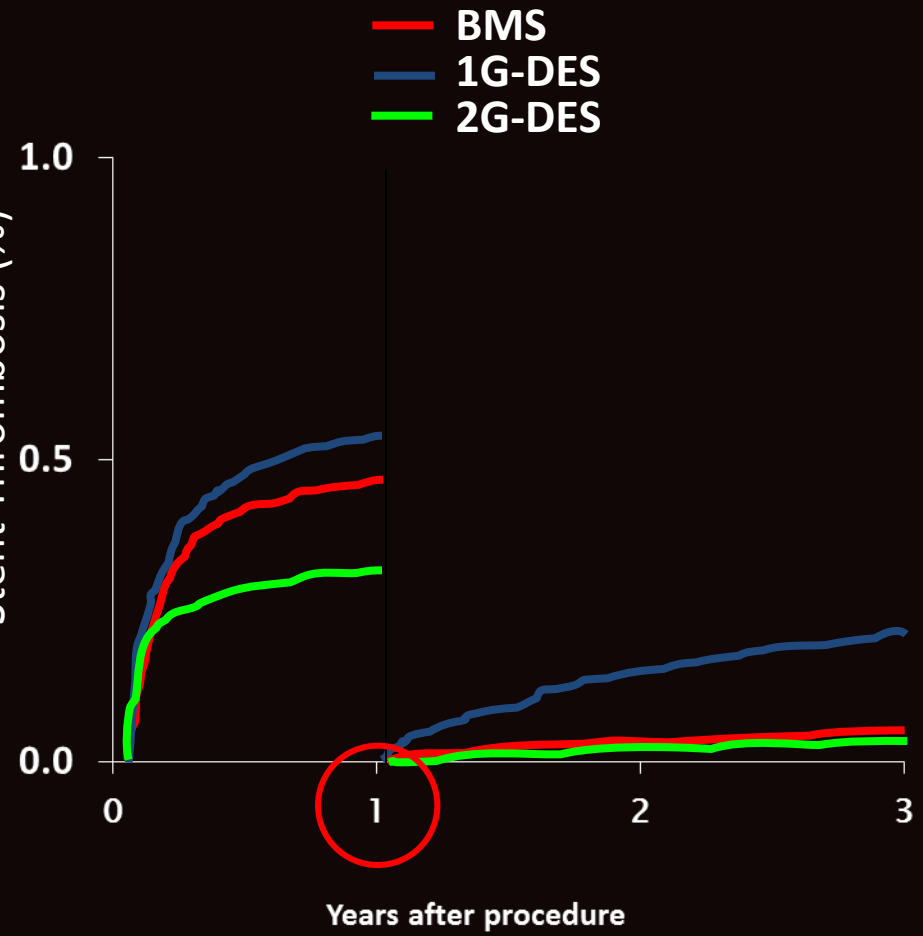


Definite Stent Thrombosis Through 3 Years In 18,334 Patients (28,739 Lesions) By Stent Type

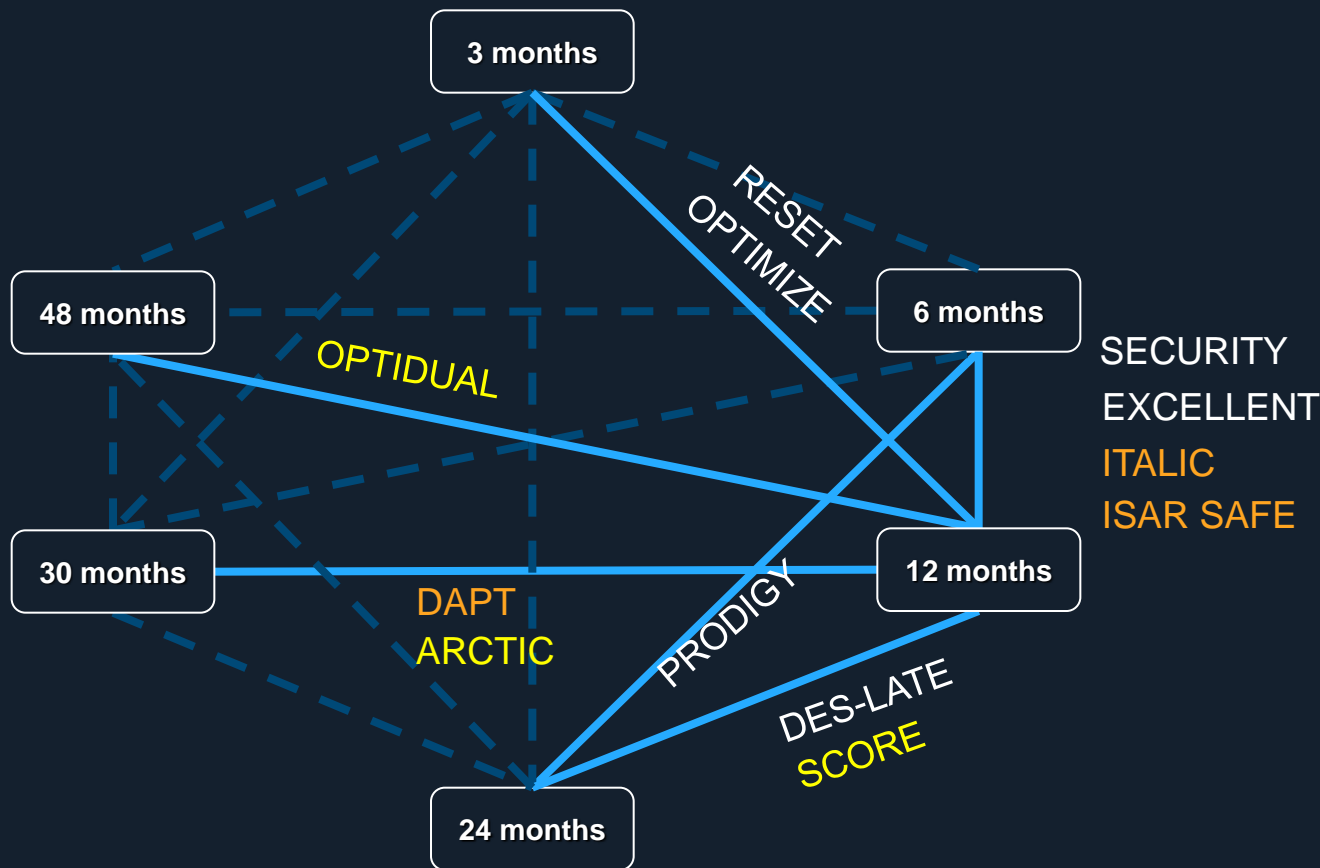
3-Year Incidence of Stent Thrombosis



1-Year Landmark Analysis



Trials of DAPT duration support short length after elective PCI, particularly if 2nd gen DES are used



Bleeding reduction strategies (to overcome prolonged DAPT)

1. Smart DES requiring shorter DAPT duration
2. De-escalating P2Y12 inhibition
3. P2Y12 inhibitor monotherapy (stop aspirin)

International Expert Consensus on Switching Platelet P2Y₁₂ Receptor–Inhibiting Therapies

Dominick J. Angiolillo, Fabiana Rollini, Robert F. Storey, Deepak L. Bhatt, Stefan James, David J. Schneider, Dirk Sibbing, Derek YF So, Dietmar Trenk, Dimitrios Alexopoulos, Paul A. Gurbel, Willibald Hochholzer, Leonardo De Luca, Laurent Bonello, Daniel Aradi, Thomas Cuisset, Udaya S. Tantry, Tracy Y. Wang, Marco Valgimigli, Ron Waksman, Roxana Mehran, Gilles Montalescot, Francesco Franchi, Matthew J. Price

Bleeding reduction strategies: De-escalation

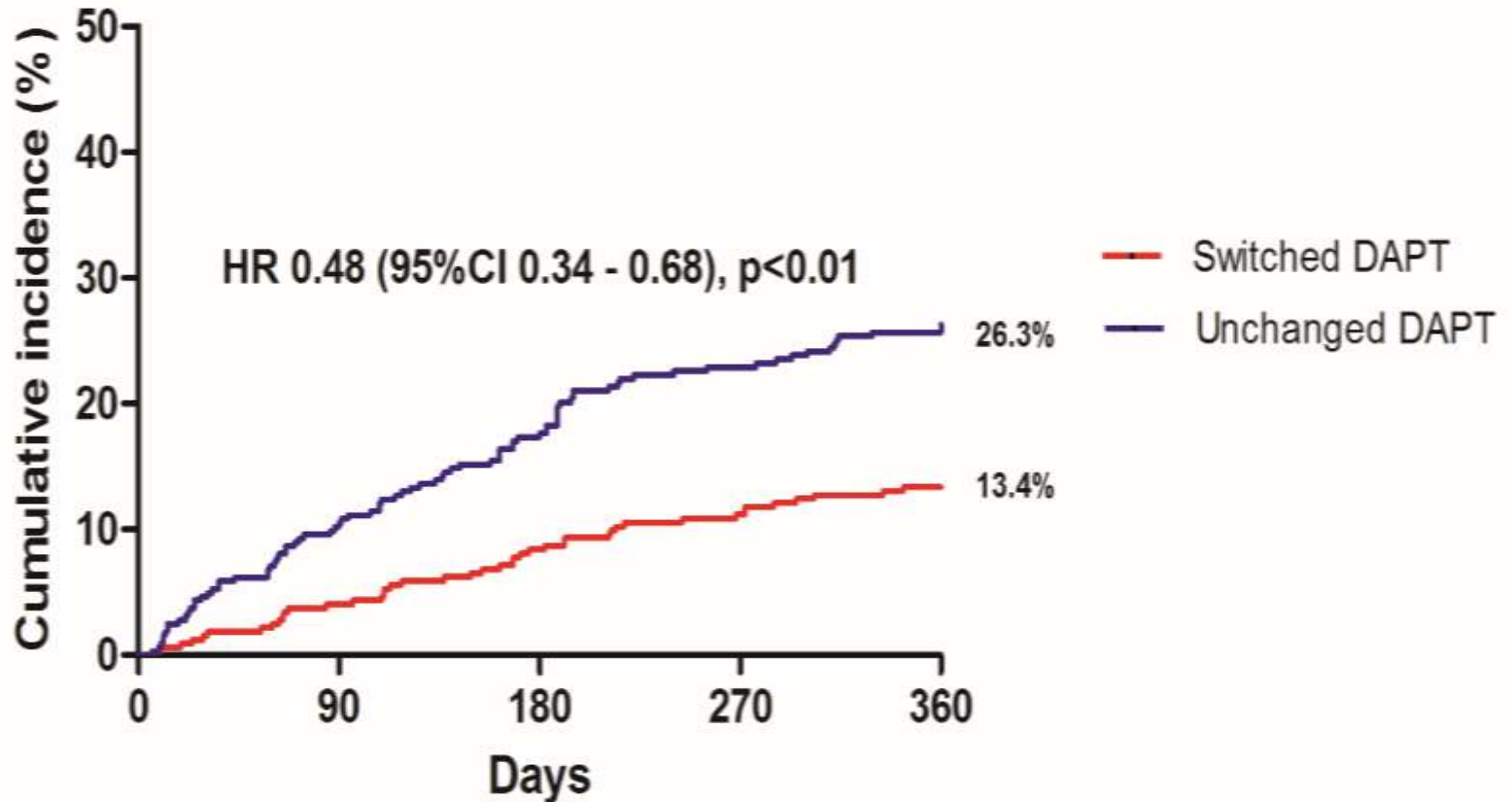
De-escalation (switching from prasugrel or ticagrelor to clopidogrel) as a strategy to reduce long-term bleeding events without a trade-off in ischemic protection





Primary Endpoint

Death, Urgent revasc., Stroke, BARC ≥ 2



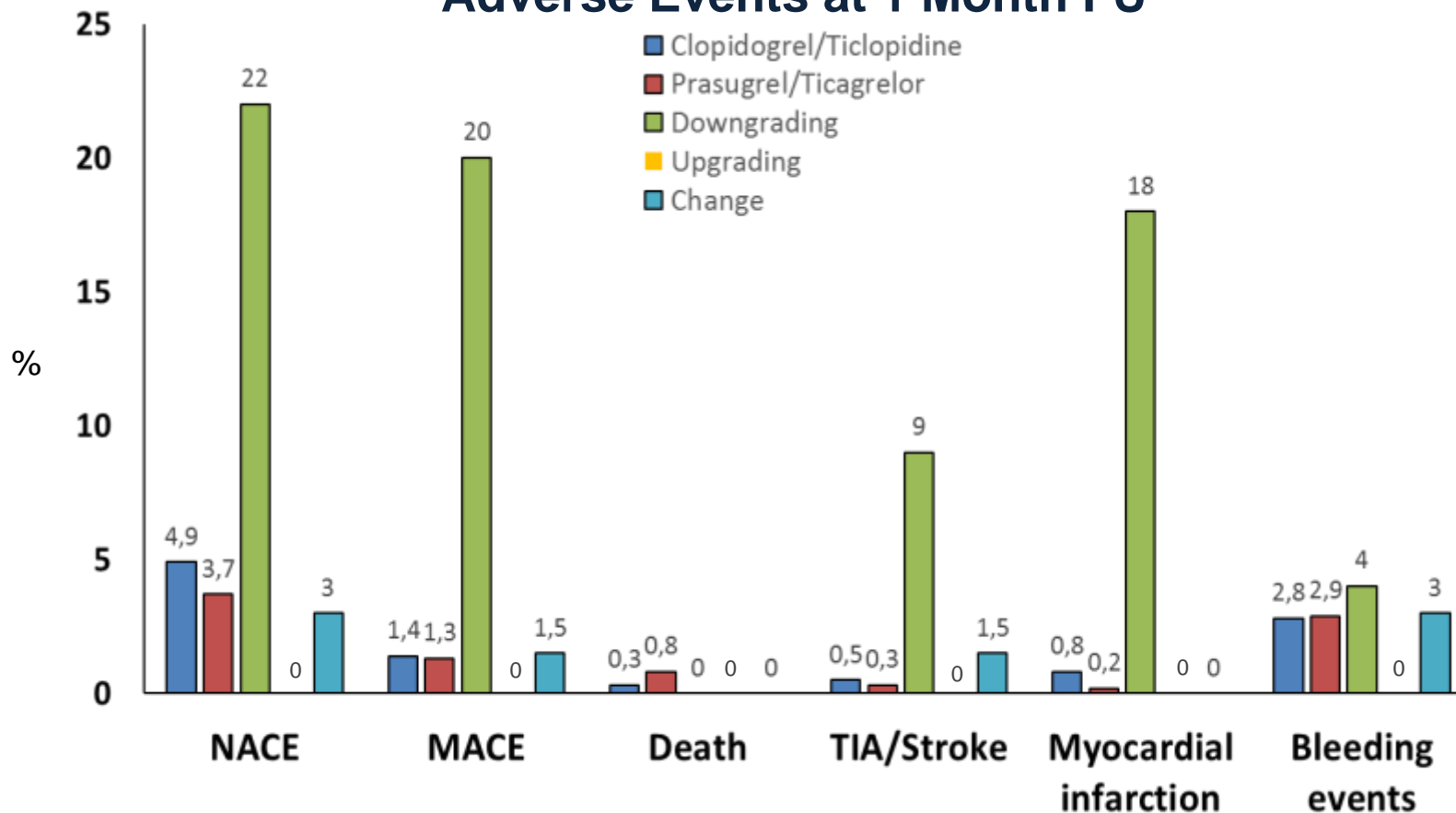
Better Prognosis with switched DAPT



SCOPE (Switching from Clopidogrel to New Oral Antiplatelet Agents during Percutaneous Coronary Intervention)



Adverse Events at 1 Month FU



1363 ACS patients undergoing PCI enrolled during a 3-month period at 40 Italian medium-to-high volume centers

Should we routinely de-escalate P2Y12 Receptor Inhibitors?

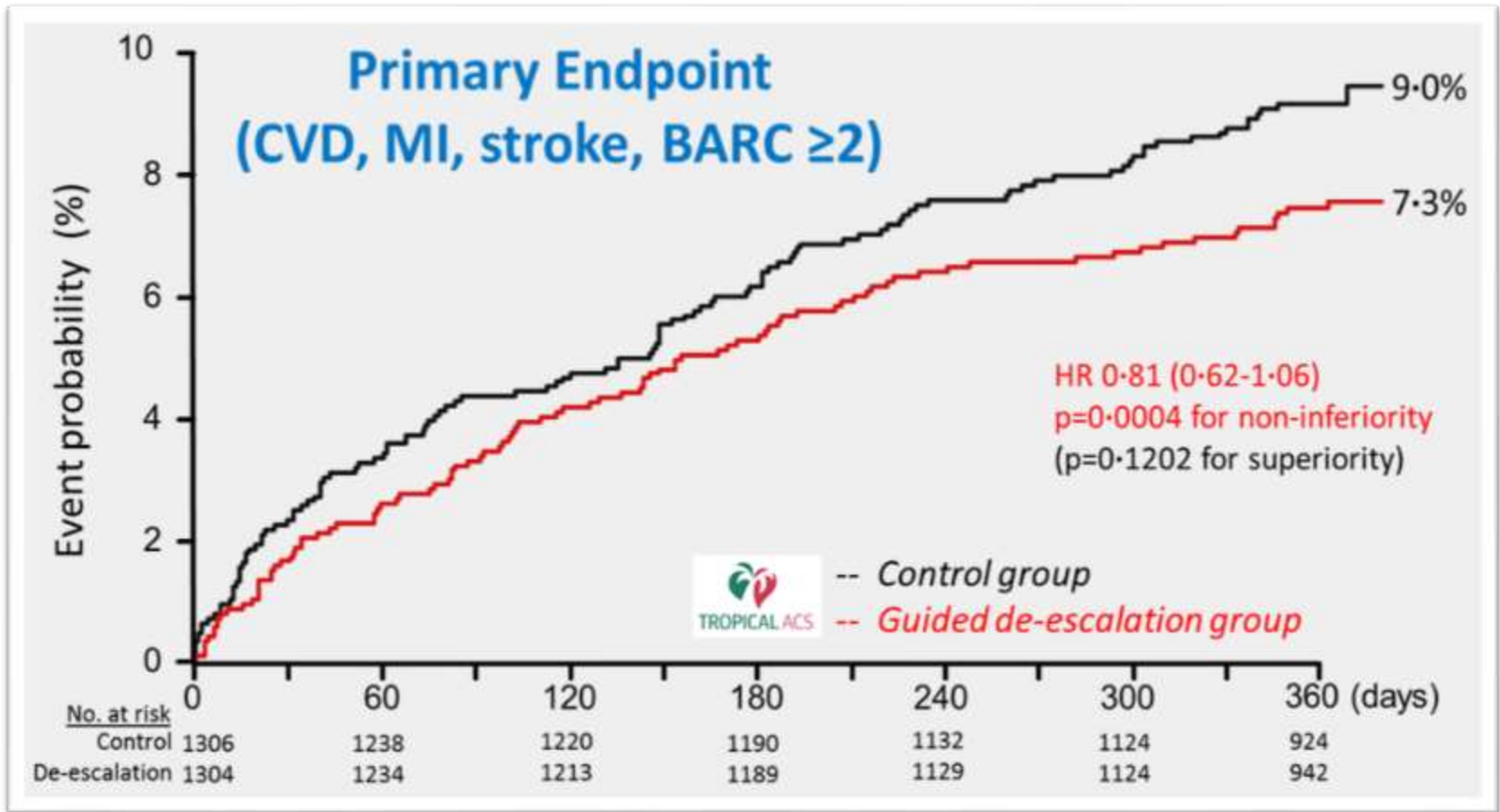
Probably not

➤ Identify patients who can benefit from de-escalation

- History of major bleeding
- Patients with high bleeding risk (need for OAC, prior stroke, elderly)
- Patients with low ischemic risk
- Platelet function/genetic testing?
- Need more investigations (currently ongoing)



Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention (TROPICAL-ACS)



Sibbing D, et al. Lancet. 2017
Angiolillo DJ. Lancet. 2017

Limitations of PFT-guided de-escalation

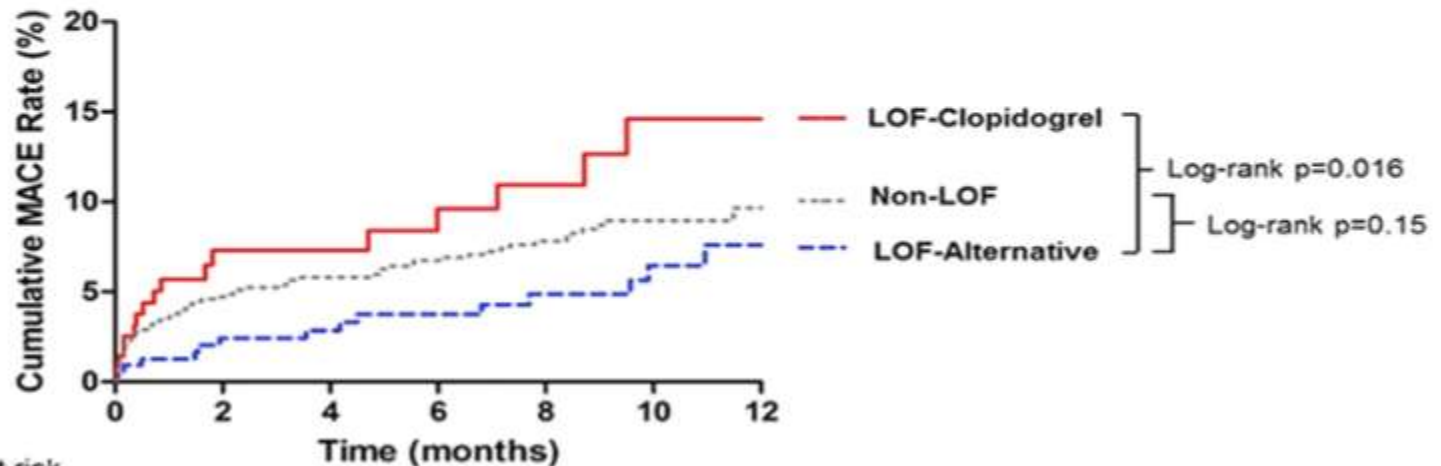
- **Availability of PFT**
- **Back and forth management of antiplatelet therapy**
- **Variability in PFT results**

Genetic testing-guided de-escalation

Clinical Implementation of *CYP2C19* Genotype-Guided Antiplatelet Therapy after PCI at 7 U.S. Institutions



Kaplan-Meier Survival Estimates of MACE in Relation to *CYP2C19* Genotype and Antiplatelet Therapy

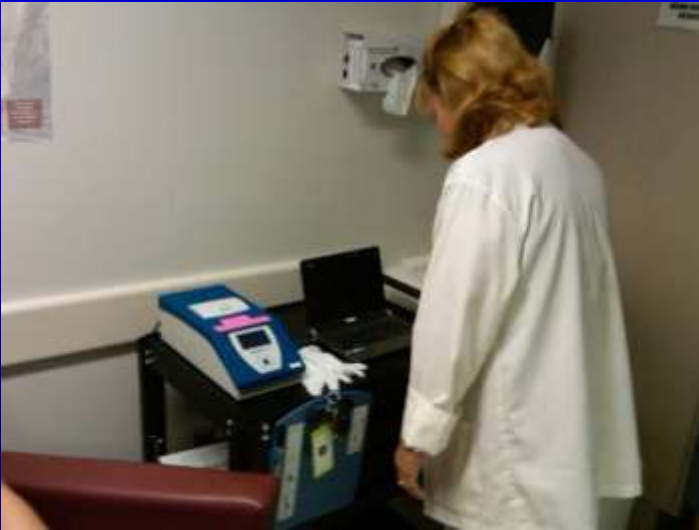
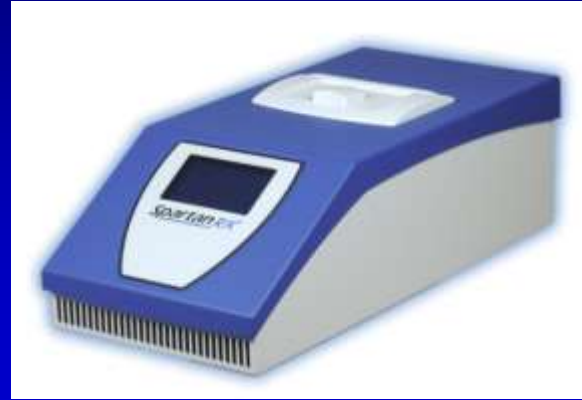


	No. at risk						
	0	2	4	6	8	10	12
LOF-Clopidogrel	226	112	89	76	63	39	3
Non-LOF	1243	759	636	577	451	293	28
LOF-Alternative	346	245	221	195	161	112	9

Genetic testing-guided de-escalation:

- **TAILOR-PCI**
- **POPGenetics**
- **TARGET-PCI**
- **ADAPT**
- **PHARMCLO**

The RAPID Program: Spartan RX CYP2C19



- Buccal Swab performed by nurses (no prior training in genetics) – ½ hour course on machine
- 1 step insertion into machine
- 60 minutes to identify:
 - CYP2C19*2 carrier status
 - Heterozygous vs. Homozygous

Bleeding reduction strategies (to overcome prolonged DAPT)

1. Smart DES requiring shorter DAPT duration
2. De-escalating P2Y12 inhibition
3. P2Y12 inhibitor monotherapy (stop aspirin)

With advances in antiplatelet therapy we keep adding treatments to aspirin



OR



OR



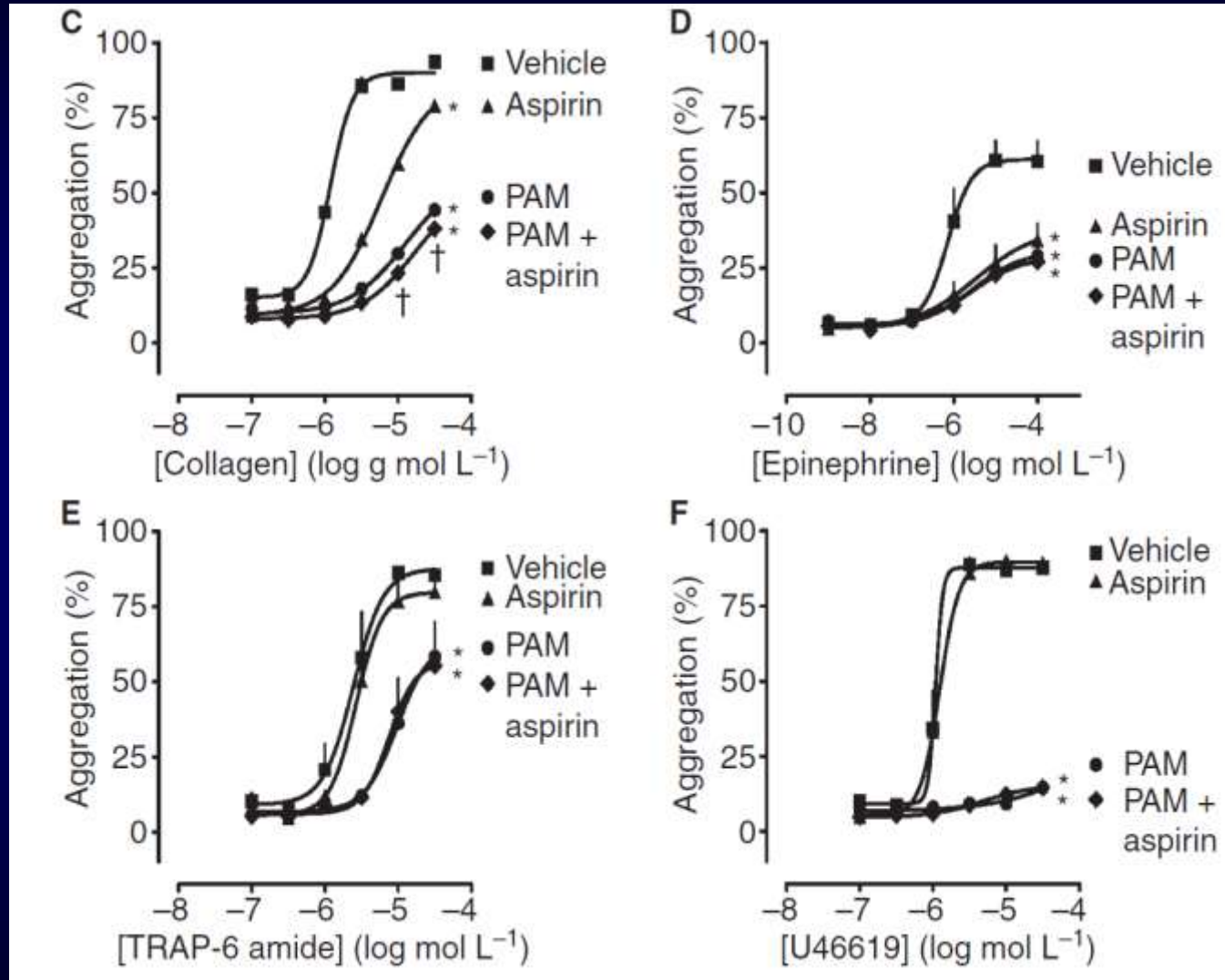
OR



AND



In the presence of strong P2Y12 receptor blockade, aspirin provides little additional platelet inhibition: *in vitro* findings

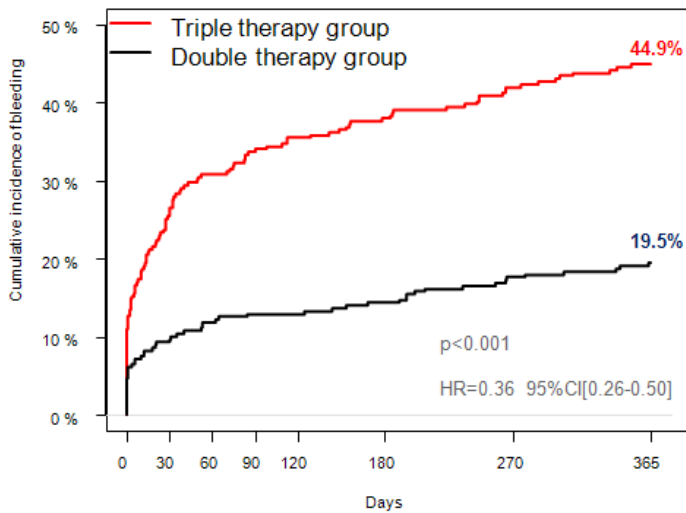


Armstrong PCJ et al. *J Thromb Haemost* 2011; 9: 552–61

The WOEST Trial: First randomised trial comparing two regimens with and without aspirin in patients on oral anticoagulant therapy undergoing coronary stenting

WOEST

Primary Endpoint: Total number of TIMI bleeding events

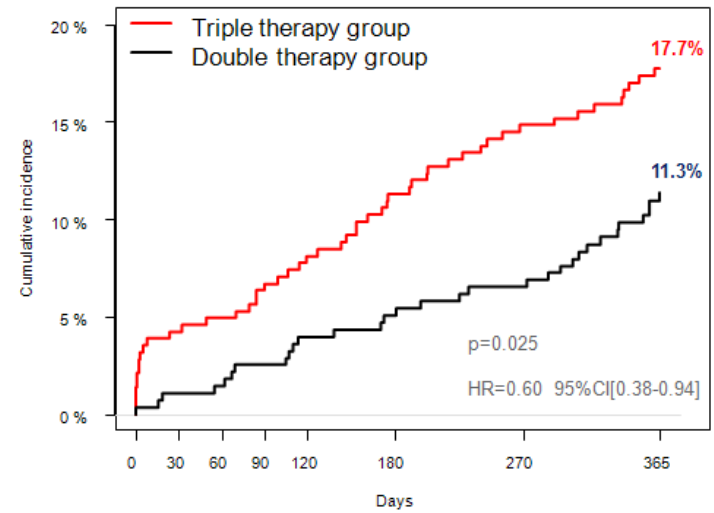


n at risk: 284 210 194 186 181 173 159 140
279 253 244 241 241 236 226 208

ST ANTONIUS

WOEST

Secondary Endpoint (Death, MI, TVR, Stroke, ST)



n at risk: 284 272 270 266 261 252 242 223
279 276 273 270 266 263 258 234

ST ANTONIUS

*Paradigm Shift in Interventional Pharmacology:
Is it time to drop aspirin?*

Dewilde WJ et al. Lancet. 2013;381(9872):1107-15

Paradigm Shift: Is it time to drop aspirin?

**There are >10 Ongoing Cardiovascular Trials With
or Without Aspirin in >100,000 patients**

- ACS (GEMINI-ACS)
- PCI (TWILIGHT, GLOBAL LEADERS) (Ticagrelor mono-rx)
- AF (PIONEER, RE-DUAL, AUGUSTUS, ENTRUST)
- Secondary Prevention (COMPASS)
- PAD (VOYAGER)