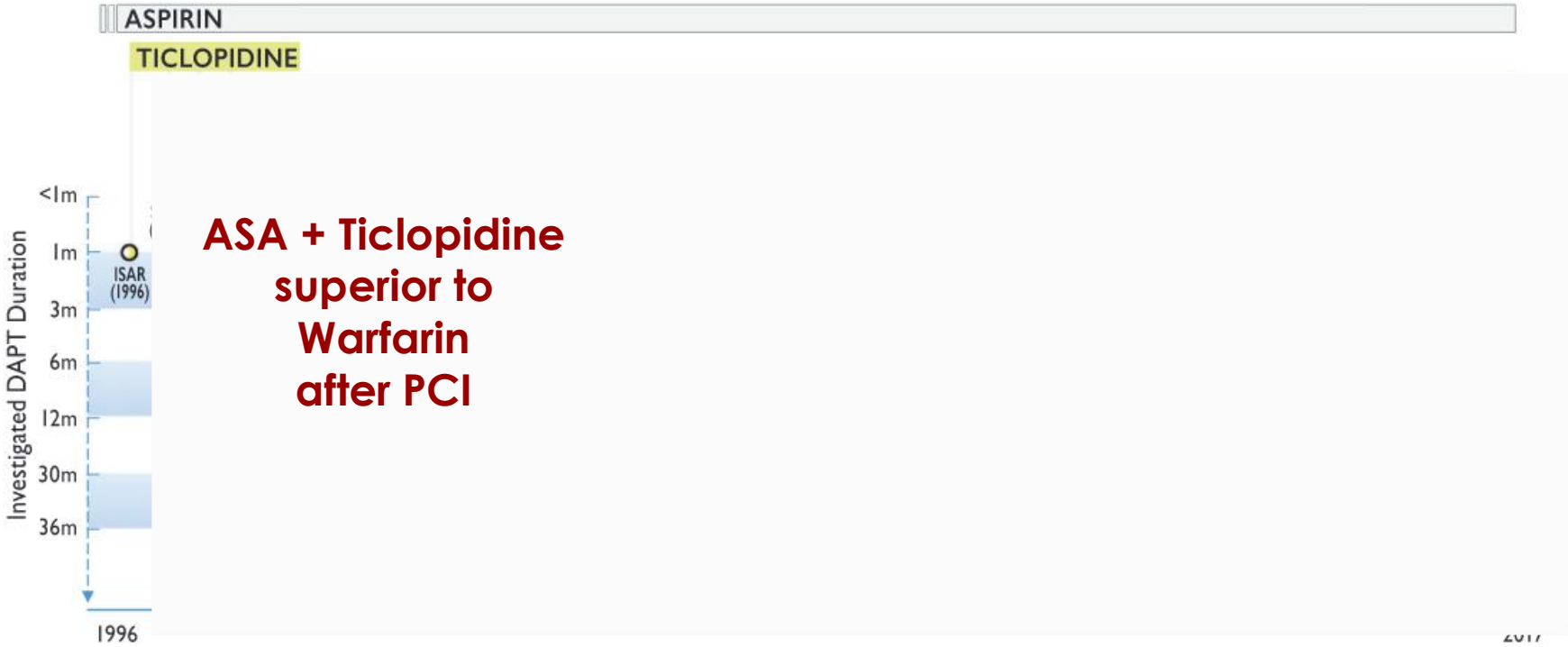
Antiaggregazione post SCA: short e long DAPT

Dr Francesco Colombo, Ospedale San Giovanni Bosco - Torino

A neverending story...

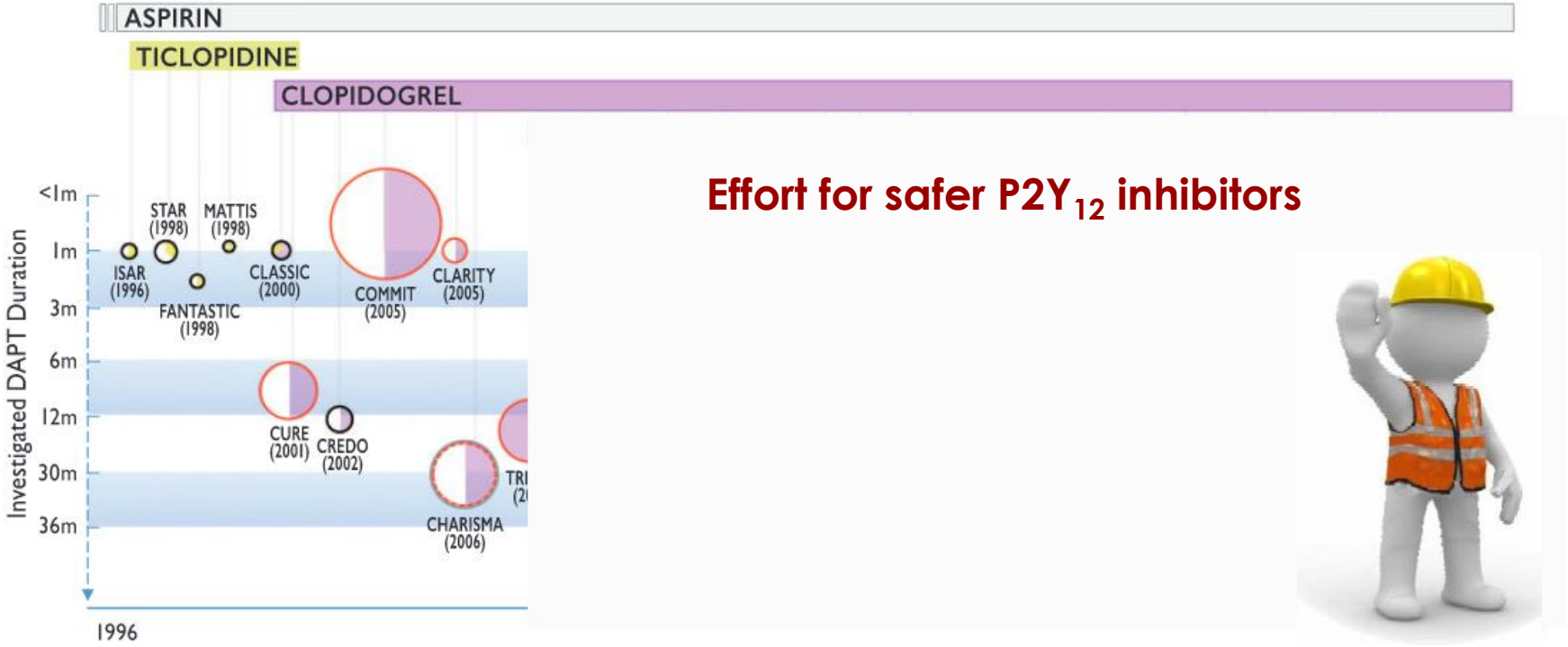
23 years story, 35 RCTs, > 225000 patients enrolled



ASA + Ticlopidine superior to Warfarin after PCI

A neverending story...

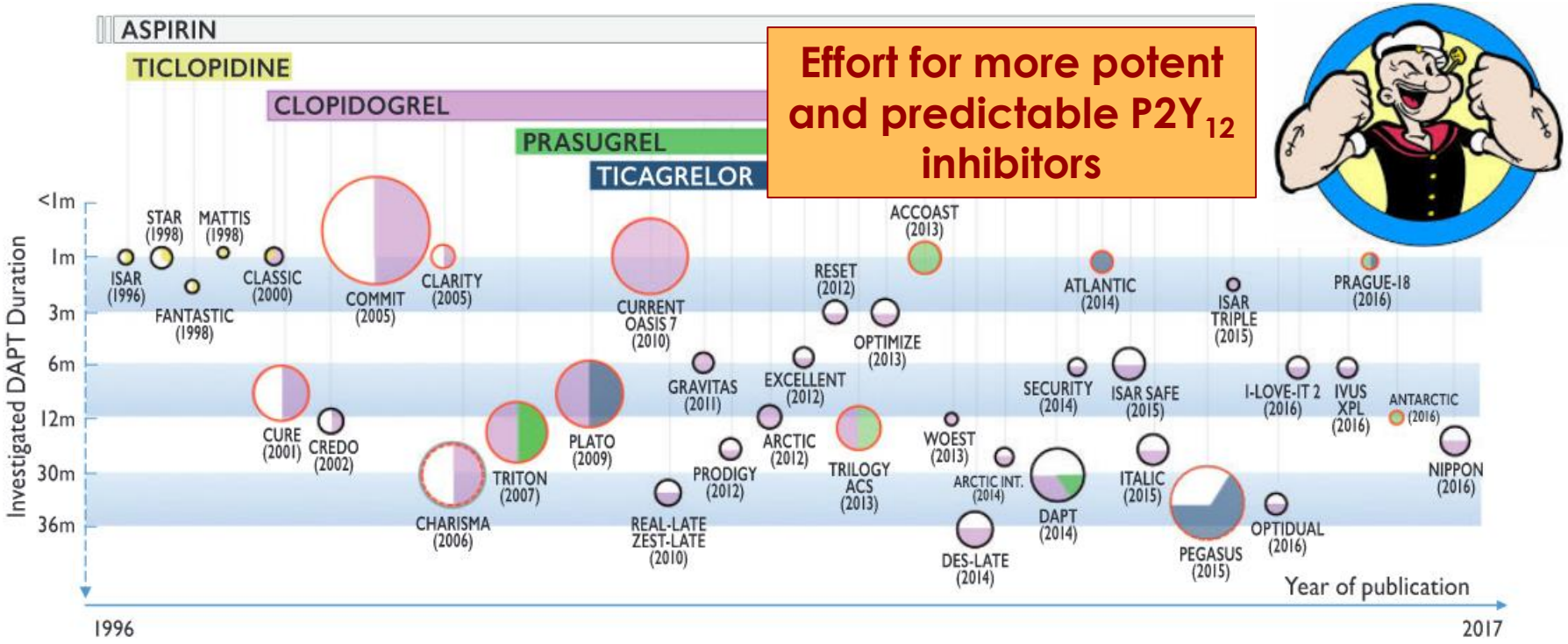
23 years story, 35 RCTs, > 225000 patients enrolled

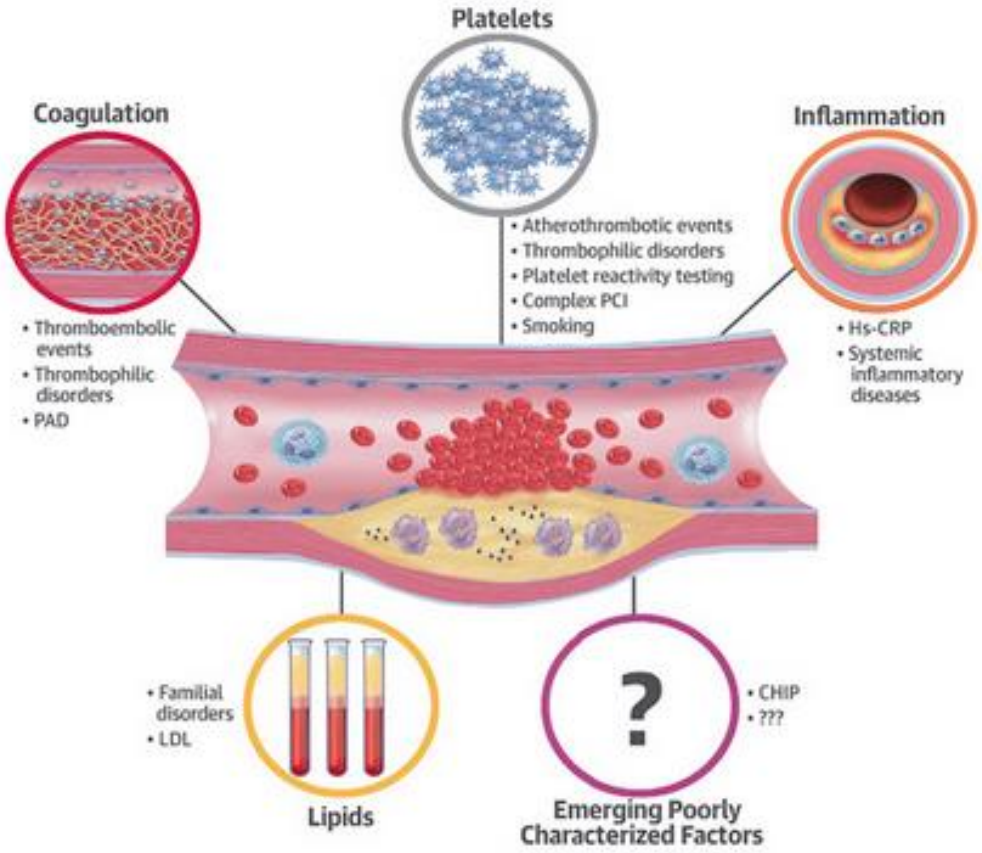


Effort for safer $P2Y_{12}$ inhibitors

A neverending story...

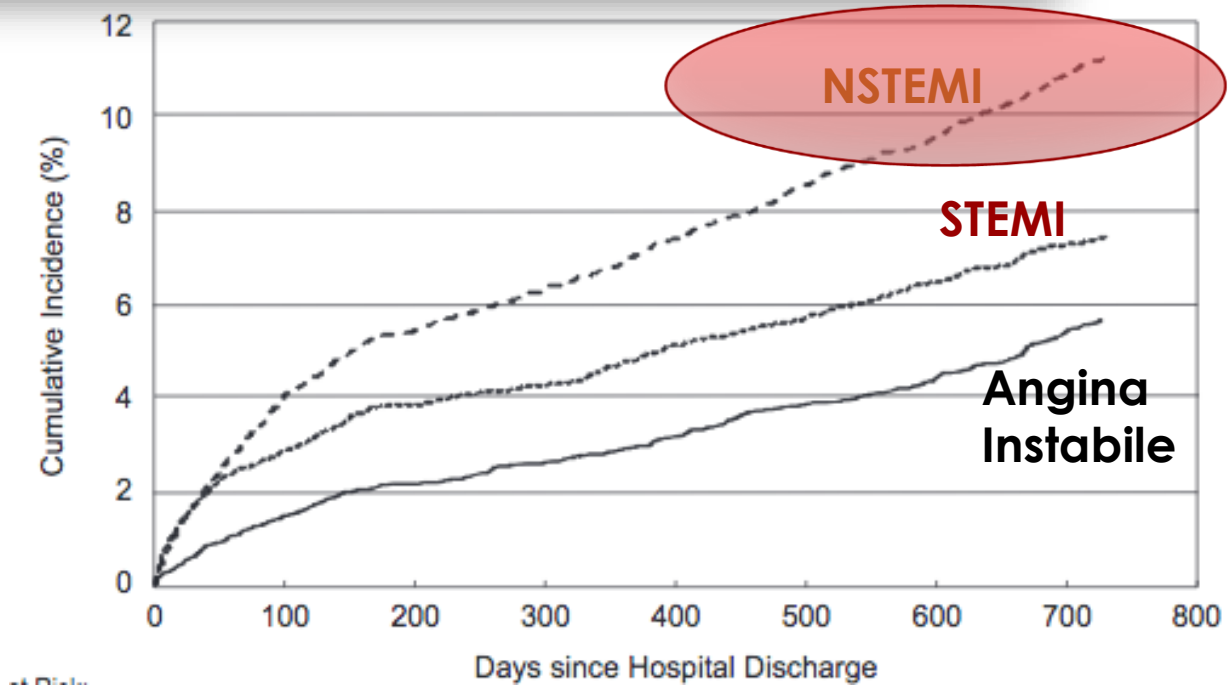
23 years story, 35 RCTs, > 225000 patients enrolled





Gallone G et al. J Am Coll Cardiol 2018;72:2886-2903

Late Consequences of Acute Coronary Syndromes: Global Registry of Acute Coronary Events (GRACE) Follow-up

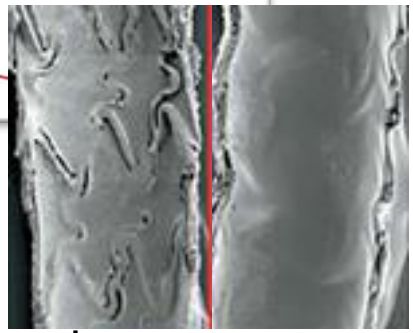


Alnasser SMA et al. Am J Med 2015; 128:766-775

Stent Thrombosis Late After Implantation of First-Generation Drug-Eluting Stents

A Cause for Concern

Edoardo Camenzind, MD; P. Gabriel Steg, MD; William Wijns, MD

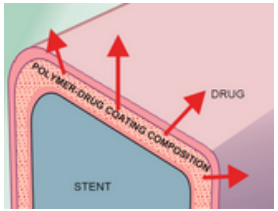


1st gen DES

BMS

delayed endothelialization secondary to antiproliferative drug

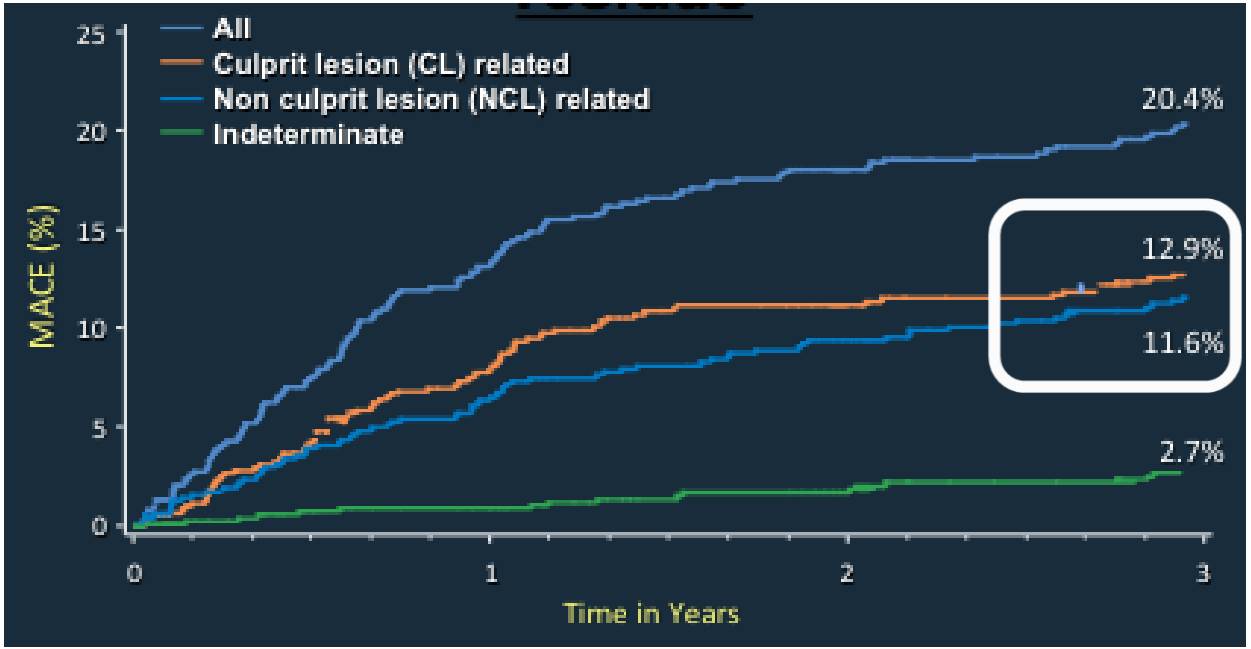
hypersensitivity reaction to the polymer coating



Camezind E et al. Circulation 2007 2015;(11):1440-55

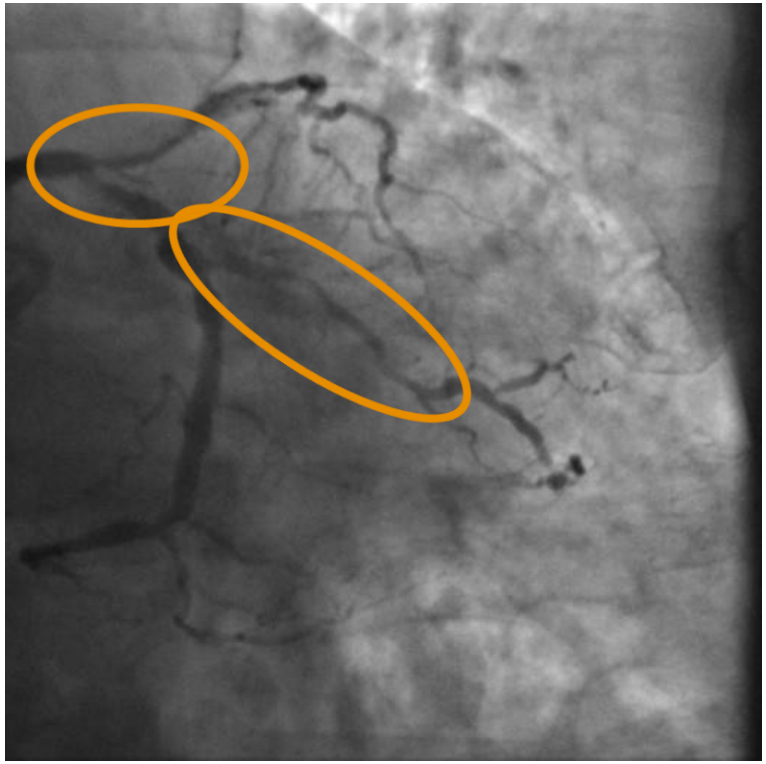
A progressive disease, not only stent thrombosis...

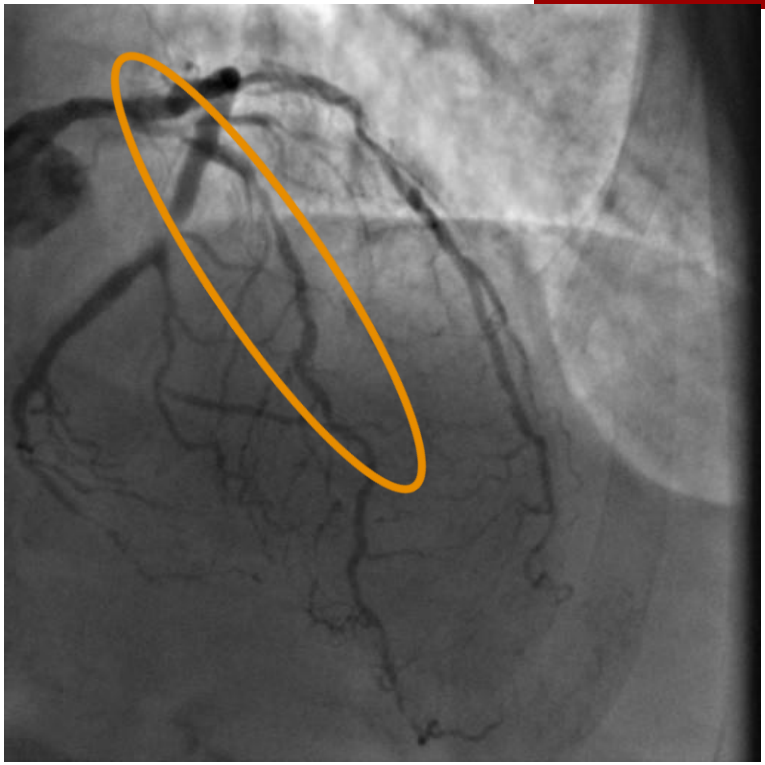
PROSPECT Study (697 ACS patients treated with PCI)



Stone GW et al. N Engl J Med 2011; 364:226-235

Increasingly complex CAD patterns

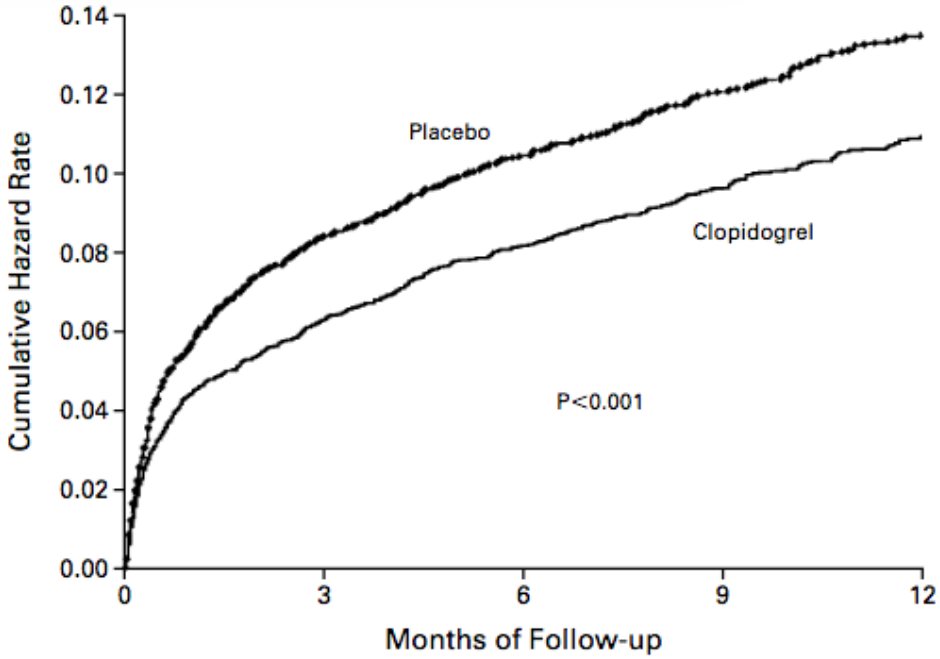




The New England Journal of Medicine

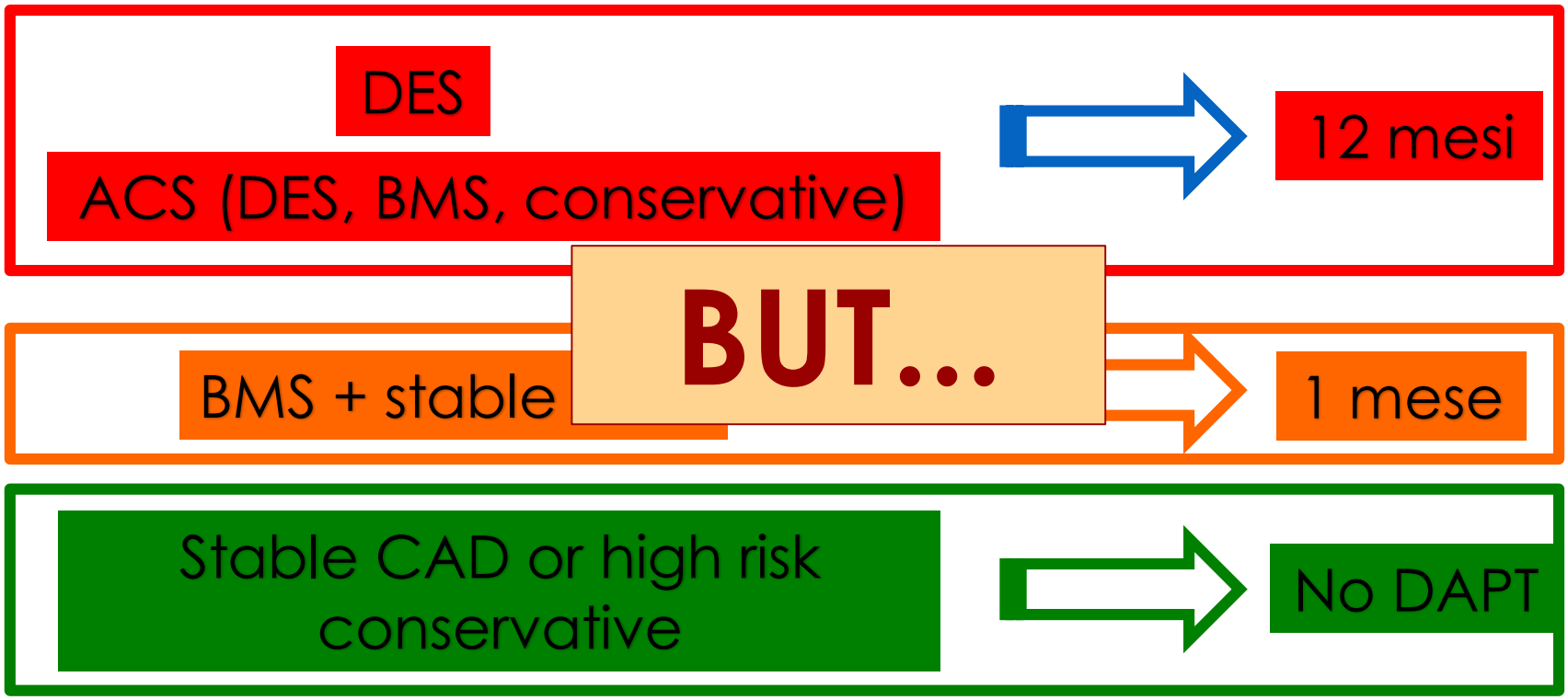
EFFECTS OF CLOPIDOGREL IN ADDITION TO ASPIRIN IN PATIENTS WITH ACUTE CORONARY SYNDROMES WITHOUT ST-SEGMENT ELEVATION

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



Yusuf S et al. N Engl J Med 2001; 345:494-502

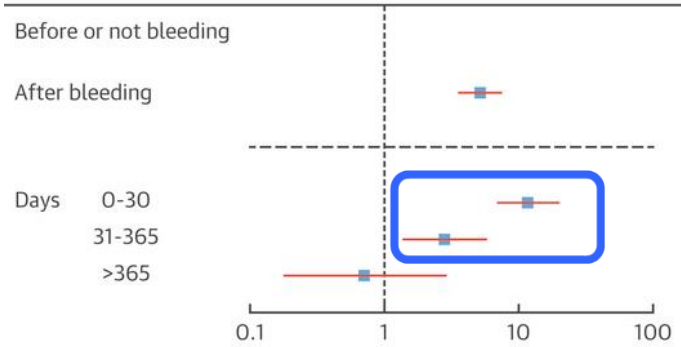
The "classical" paradigm



Thrombotic risk

Haemorragic risk

Bleeding risk



		Hazard ratio (95% CI)	p value	Number death	Number months	Incidence rate (100 pts-months)
Before or not bleeding				231	201131	0.12
After bleeding		5.15 (3.58-7.42)	< 0.0001	36	2252	1.59
Days	0-30	11.66 (6.91-19.71)	< 0.0001	25	160	15.62
	31-365	2.80 (1.37-5.71)	0.005	9	1457	0.62
	>365	0.71 (0.18-2.87)	0.63	2	635	0.31
Before or not MI						
After MI						
Days	0-30	26.45 (16.15-43.32)	< 0.0001	32	190	16.84
	31-365	3.25 (1.55-6.81)	0.002	8	1767	0.45
	>365	1.53 (0.63-3.72)	0.35	5	887	0.56

Hazard Ratio

Bleedings <30 days and 30 days-1 year INDIPENDENT PREDICTORS OF MORTALITY

Palmerini T et al. J Am Coll Cardiol 2017;69:2011–22c

A new paradigm...

Thrombotic risk

Haemorragic risk

Focus on DAPT duration

Reducing or prolonging DAPT duration?

Shortened DAPT

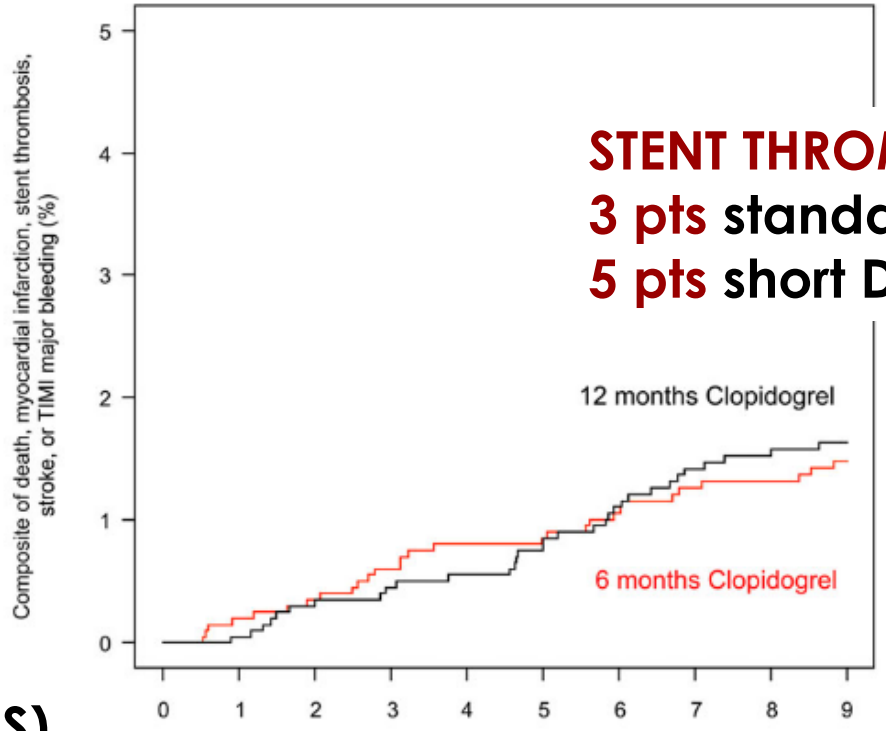
ISAR-SAFE Trial: 6 vs 12 months DAPT after DES

Non inferiority trial

Clopidogrel vs Placebo

4005 pts (stopped prematurely for low events rate)

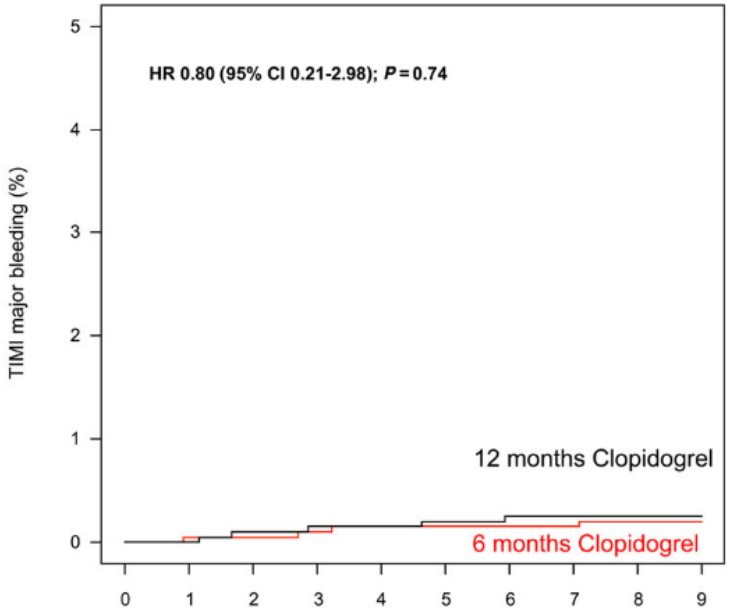
50% ACS
100% DES implantation
(90% new generation DES)

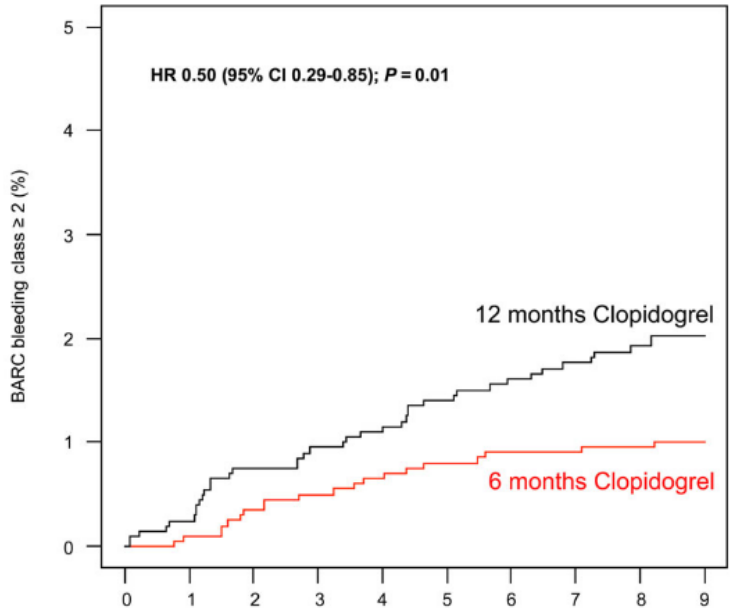


STENT THROMBOSIS
3 pts standard DAPT
5 pts short DAPT

Schulz-Schüpke S et al. Eur Heart J 2015;36(20):1252-63

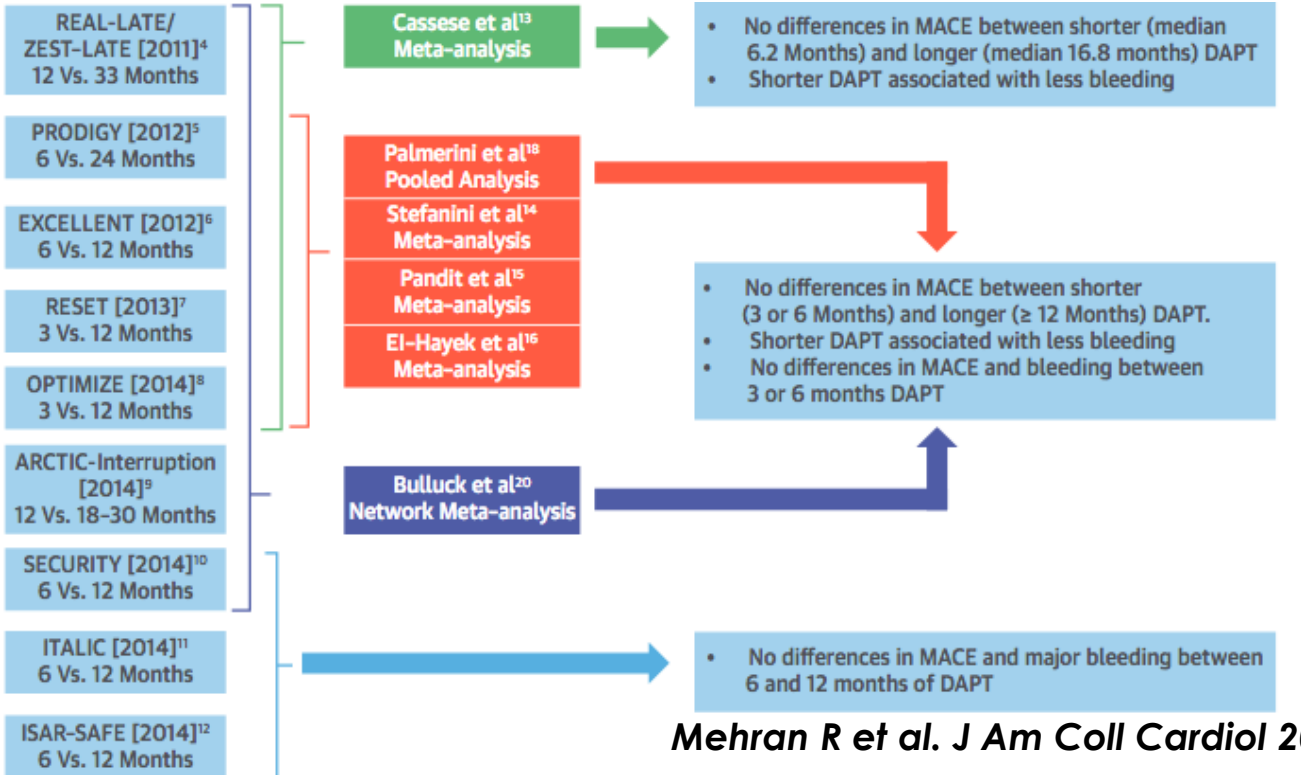
ISAR-SAFE Trial: 6 vs 12 months DAPT after DES





Schulz-Schüpke S et al. Eur Heart J 2015;36(20):1252-63

Metanalysis of short DAPT trials (3-6 vs 12 months)



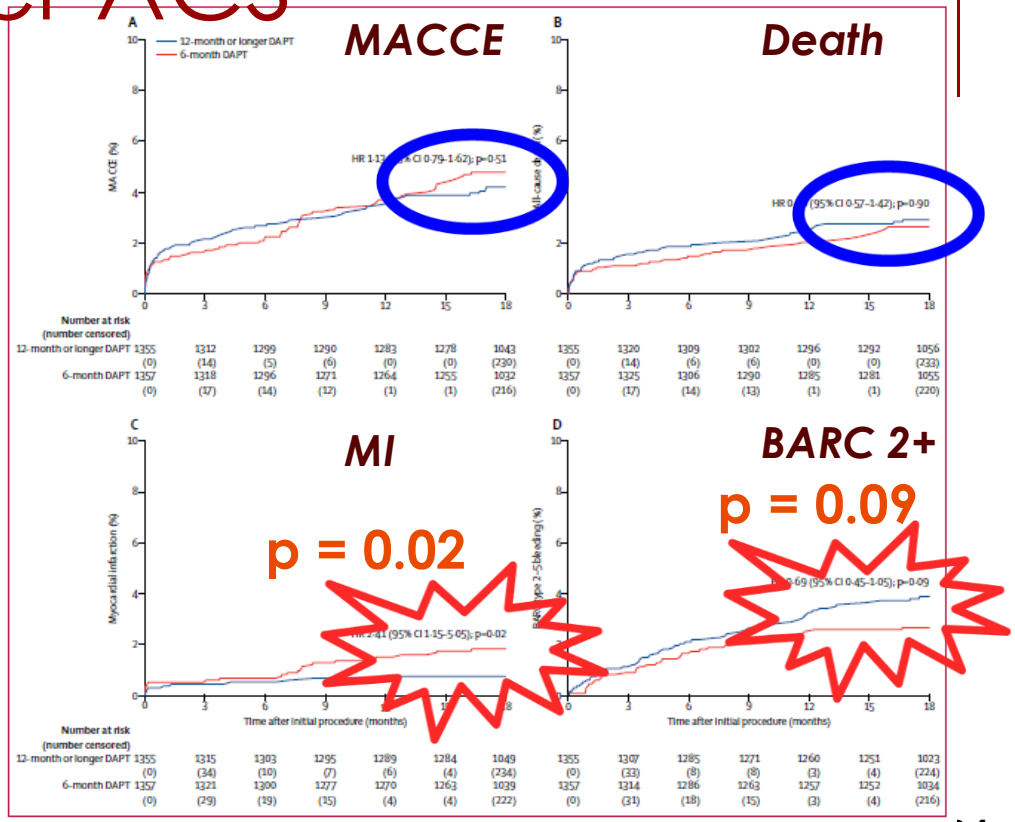
Mehran R et al. J Am Coll Cardiol 2015;65:1103-06

SMART-DATE Trial: 6 vs 12 months DAPT after ACS

Non inferiority trial

80% Clopidogrel

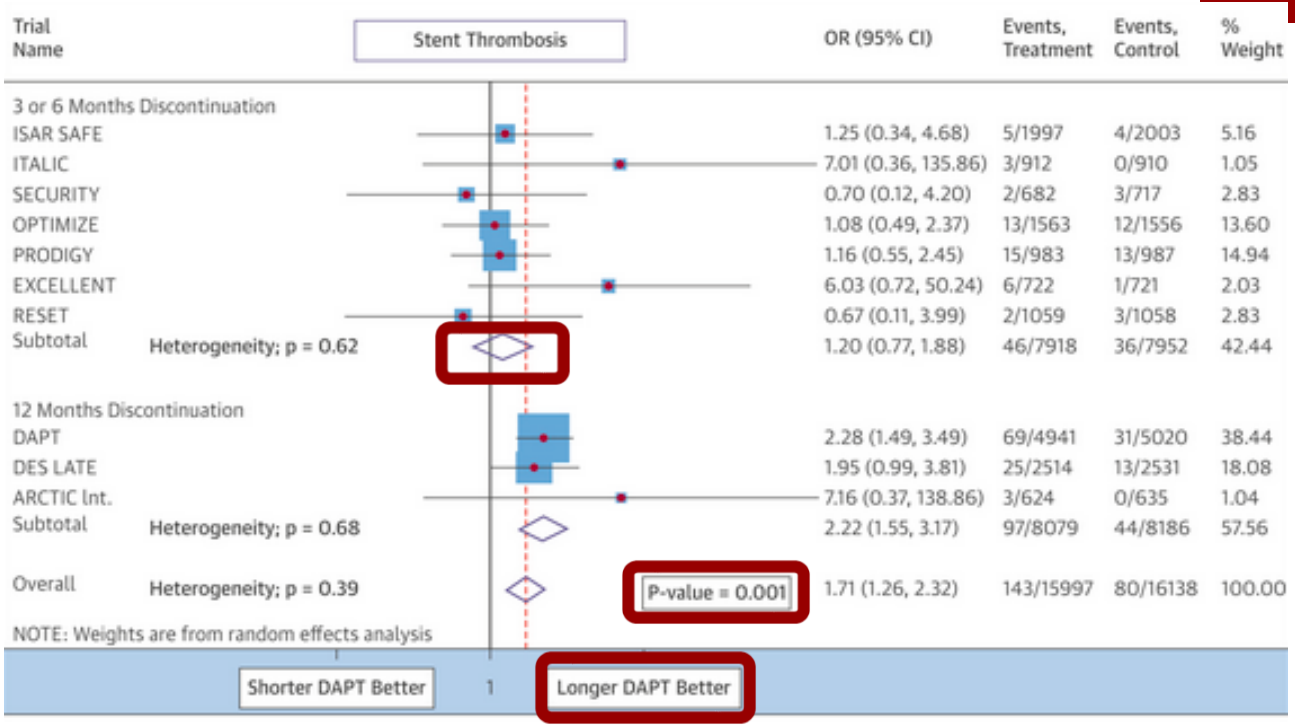
2712 pts



Hanh JY et al. Lancet 2018;391(10127):1274-1284

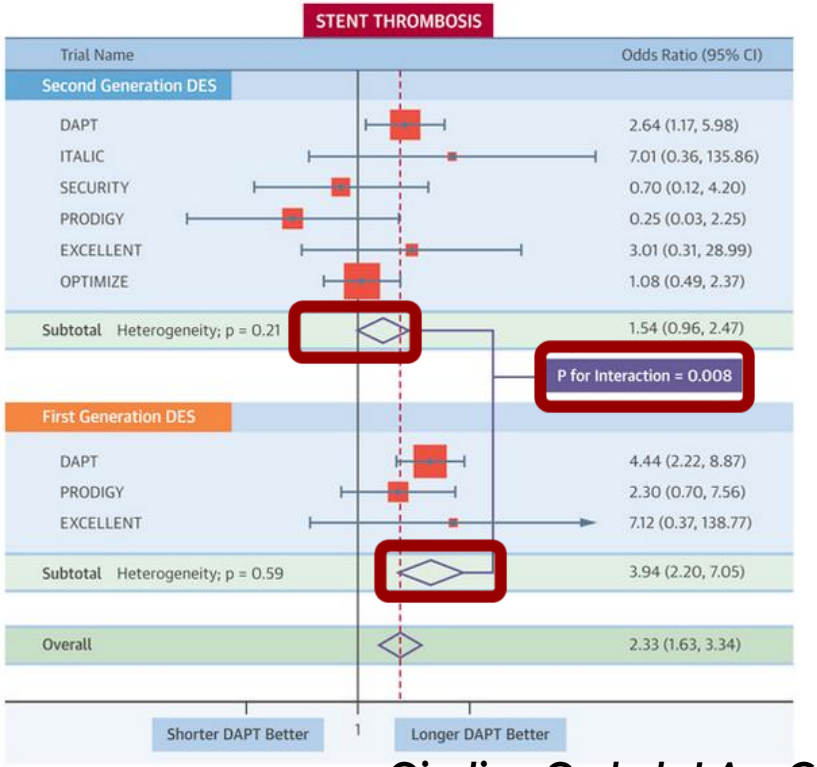
Shortened DAPT… but stent thrombosis?

32.135 patients, 3-6 months vs 12 months DAPT



Giustino G et al. J Am Coll Cardiol 2015;65(13):1298-1310

32.135 patients, 3-6 months vs 12 months DAPT



Giustino G et al. J Am Coll Cardiol 2015;65(13):1298-1310

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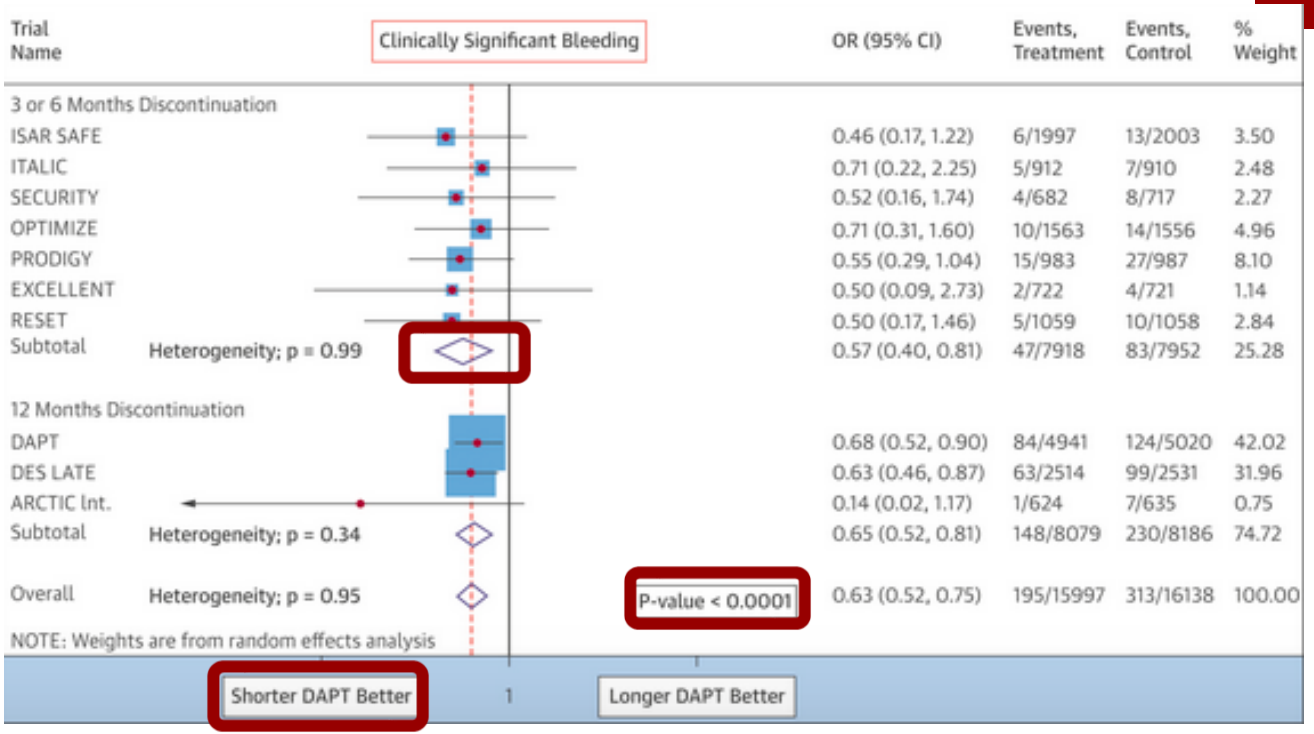
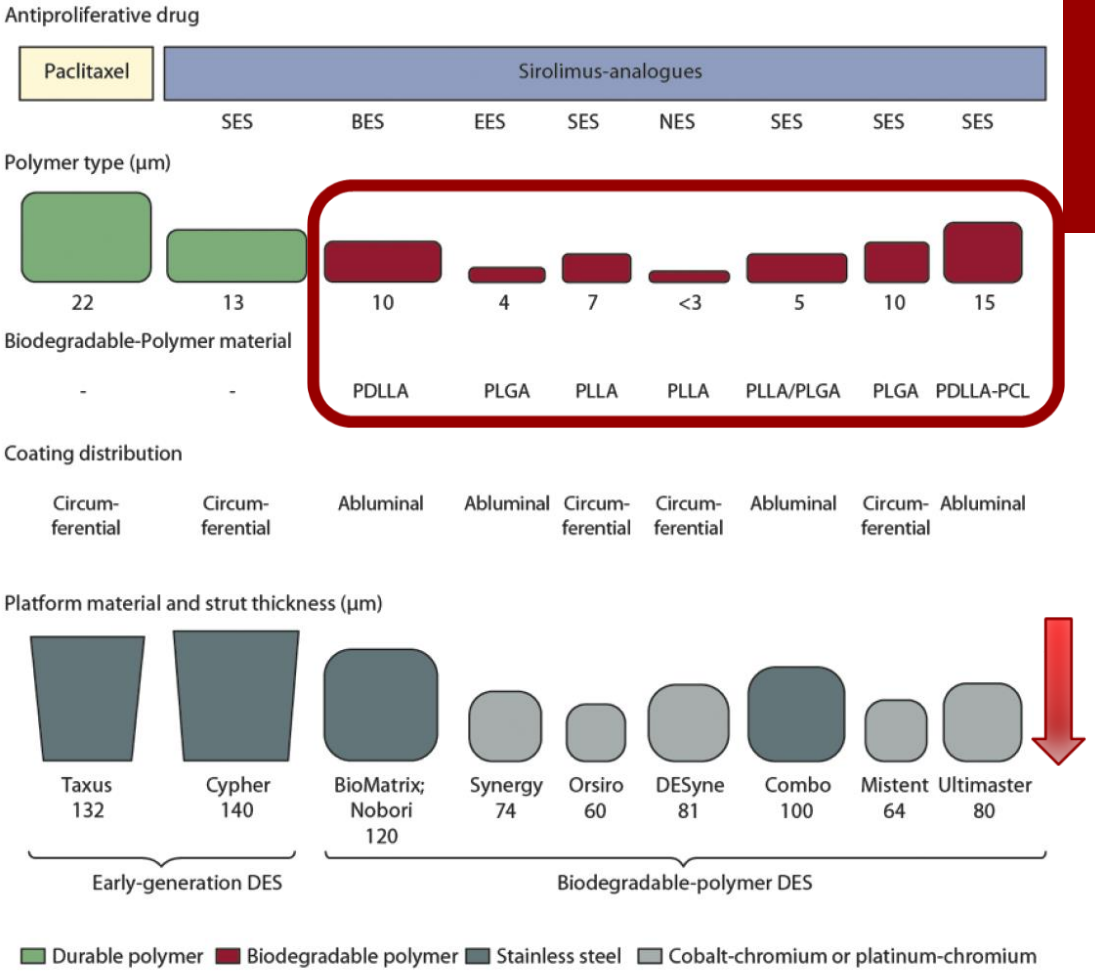
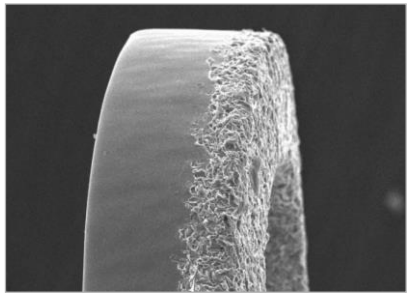


Giustino G et al. J Am Coll Cardiol 2015;65(13):1298-1310

Newer stents



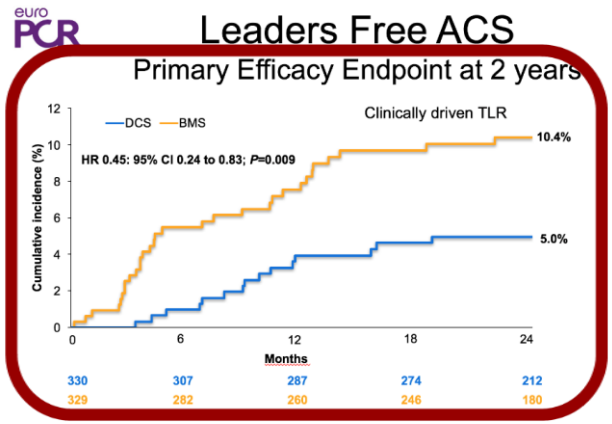
LEADERS FREE

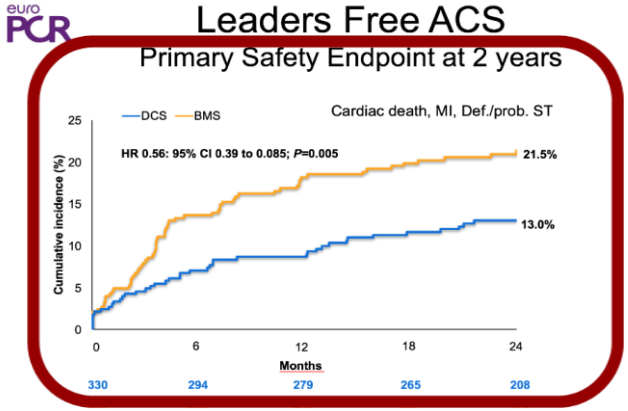


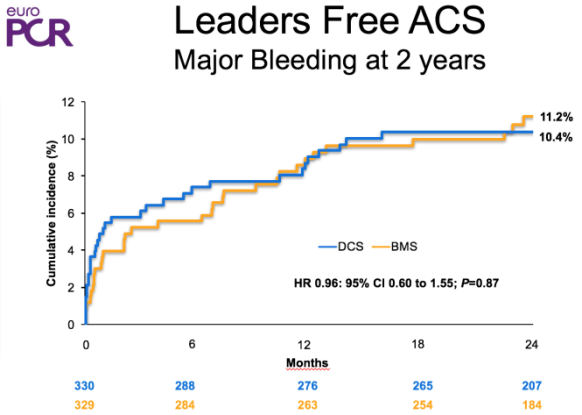
BIOFREEDOM 1 month DAPT SUPERIOR SAFETY & EFFICACY POLYMER FREE DRUG-COATED CORONARY STENT

662 ACS patients enrolled in LEADERS FREE

554 (84%) NSTEMI & 105 (16%) STEMI



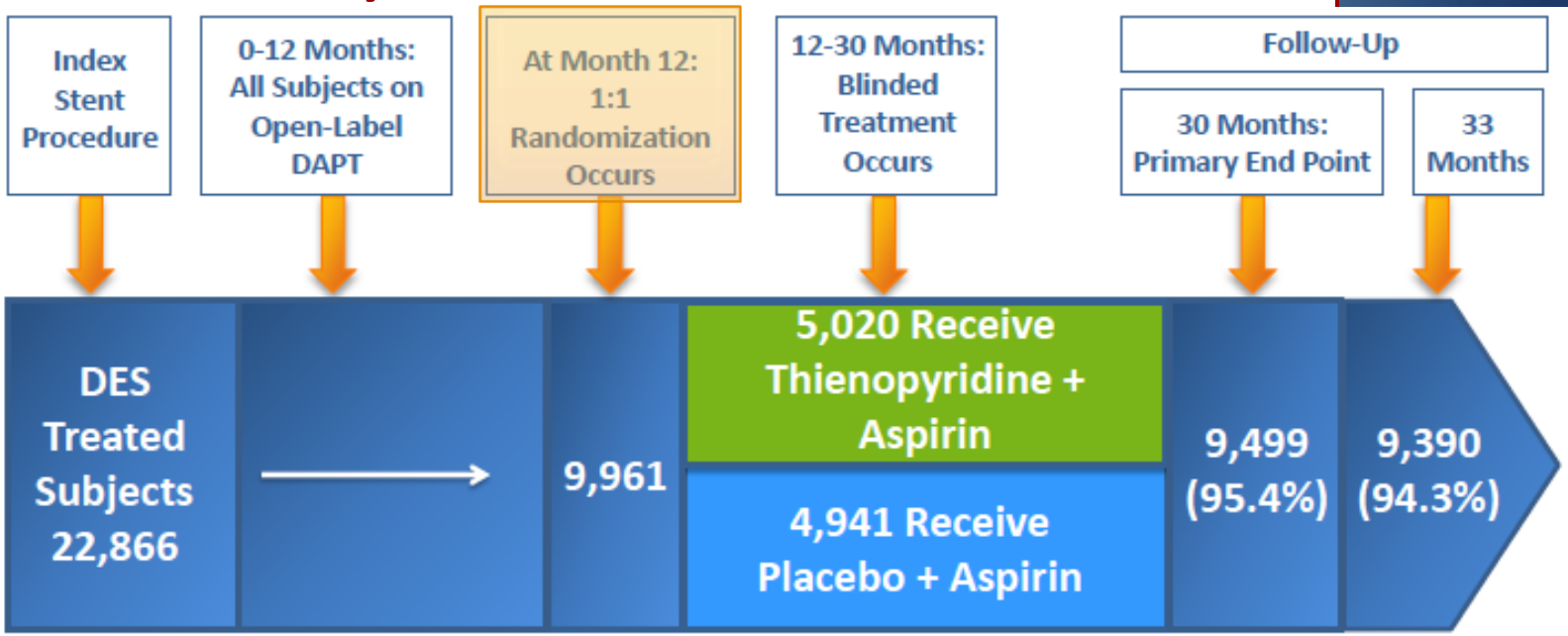




Naber CK et al. Eur Heart J 2017;38(13):961-969

Prolonged DAPT

DAPT beyond 12 months: DAPT Study

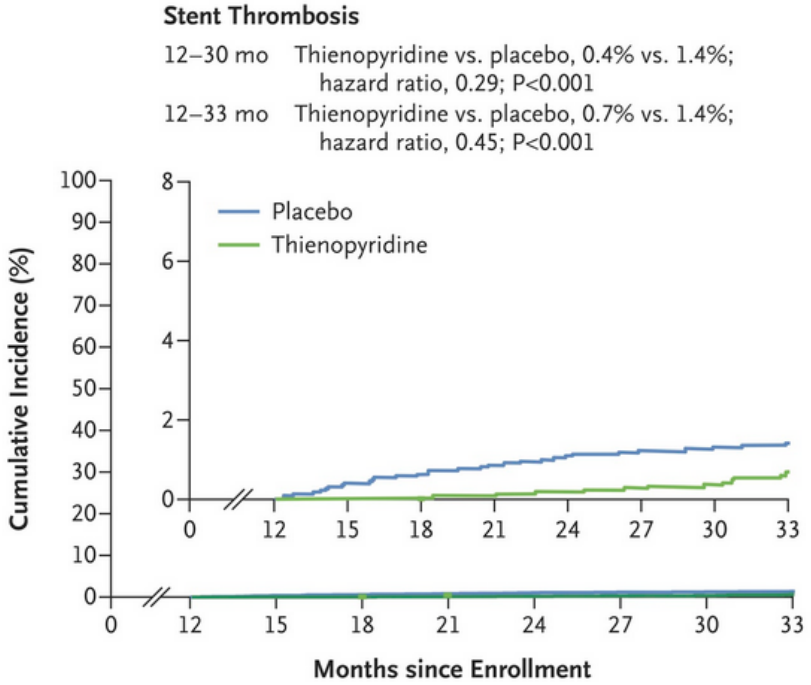


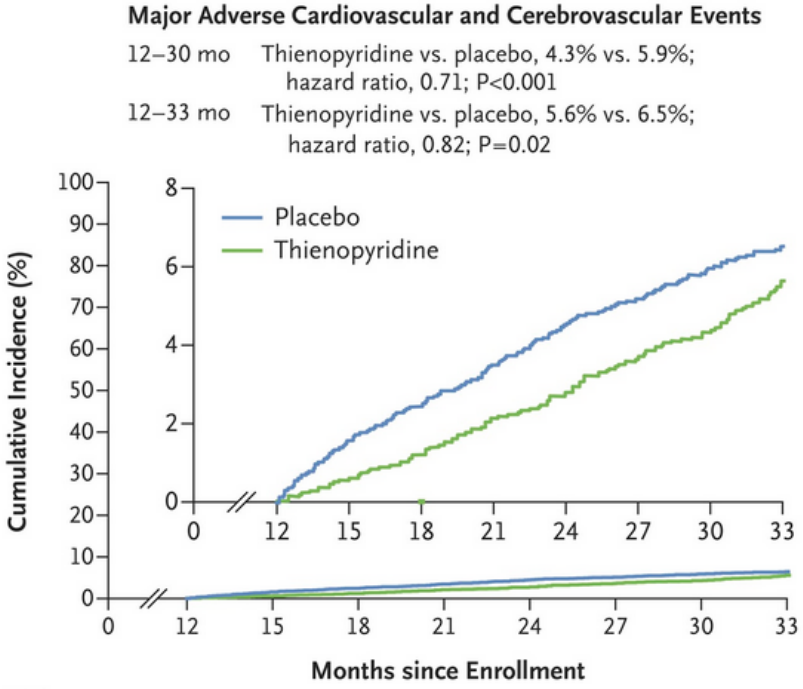
62% patients had an ACS

Thienopyridine: Clopidogrel (35%) or Prasugrel (65%)

Mauri L et al. N Engl J Med 2014; 371:2155-2166

DAPT beyond 12 months: DAPT Study





Mauri L et al. N Engl J Med 2014; 371:2155-2166

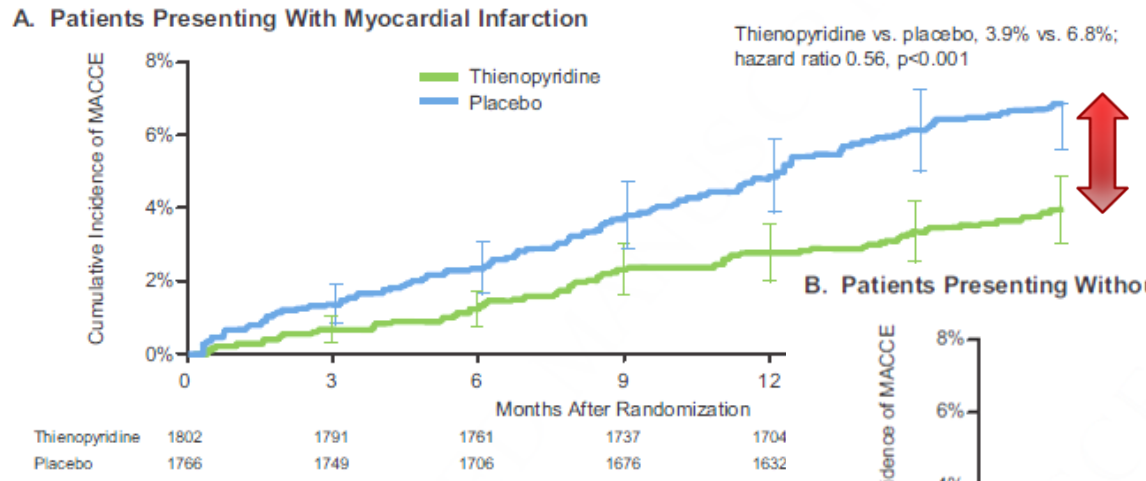
DAPT beyond 12 months: DAPT Study

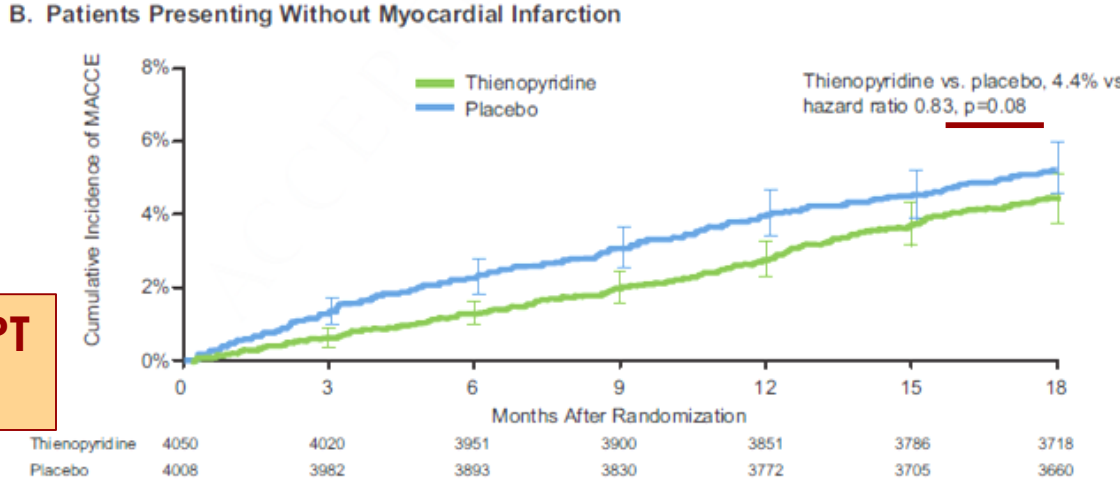
Table 3. Bleeding End Point during Month 12 to Month 30.*

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

Mauri L et al. N Engl J Med 2014; 371:2155-2166

DAPT beyond 12 months: DAPT Study

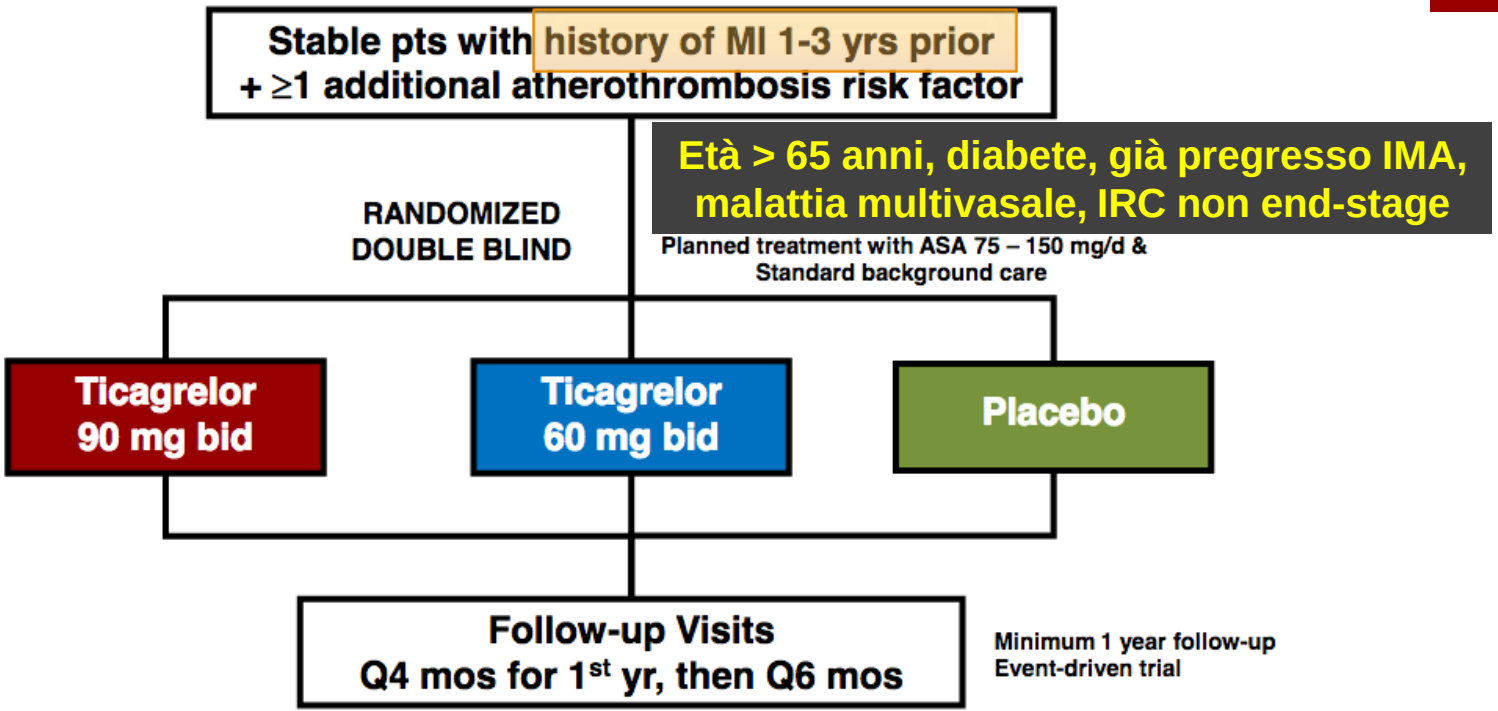




Greater benefit of prolonged DAPT in post-MI patients…

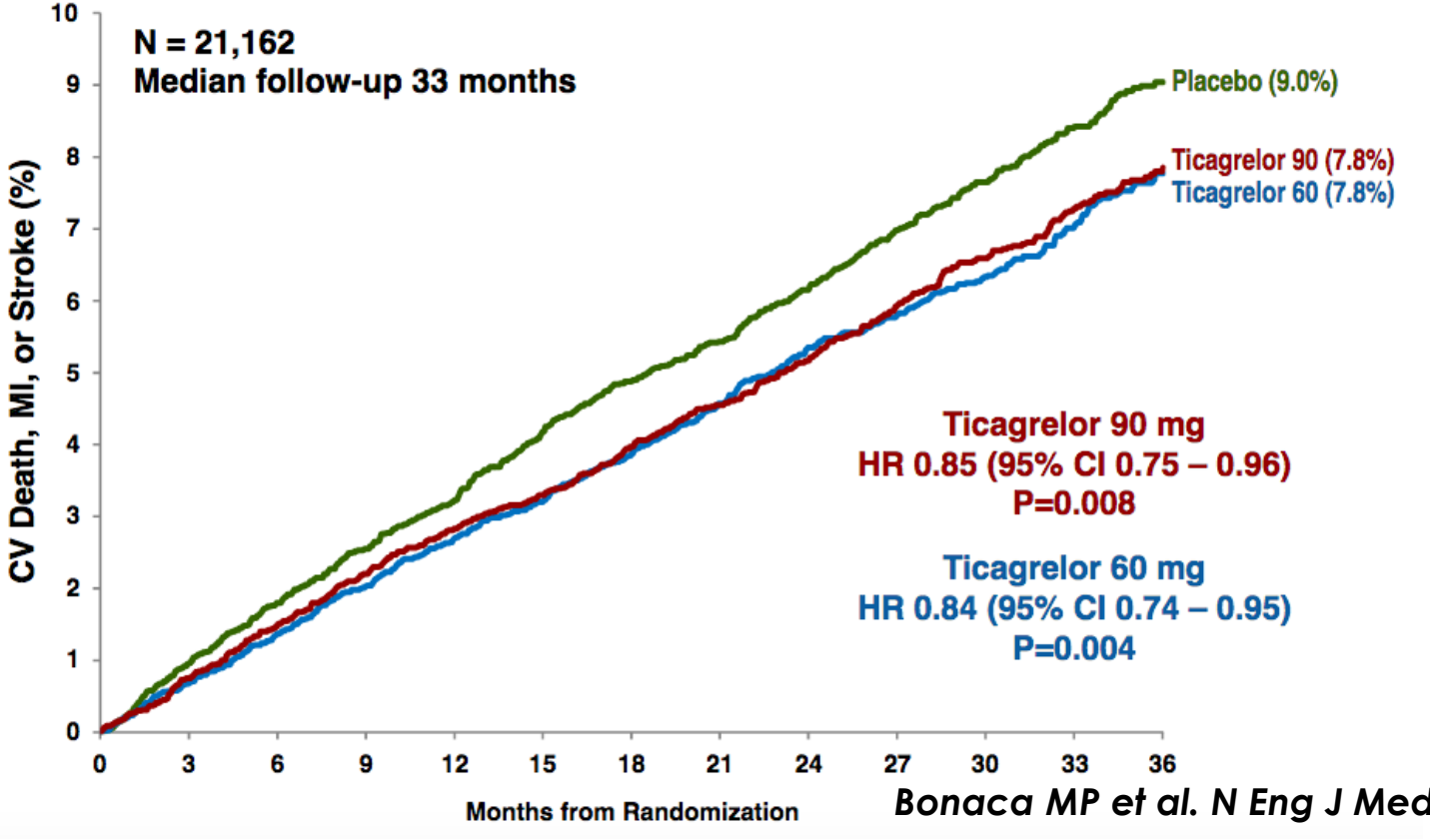
Yeh RW et al. J Am Coll Cardiol 2015; 65(20):2211-2221

Ticagrelor beyond 12 months: PEGASUS-TIMI 54 Study



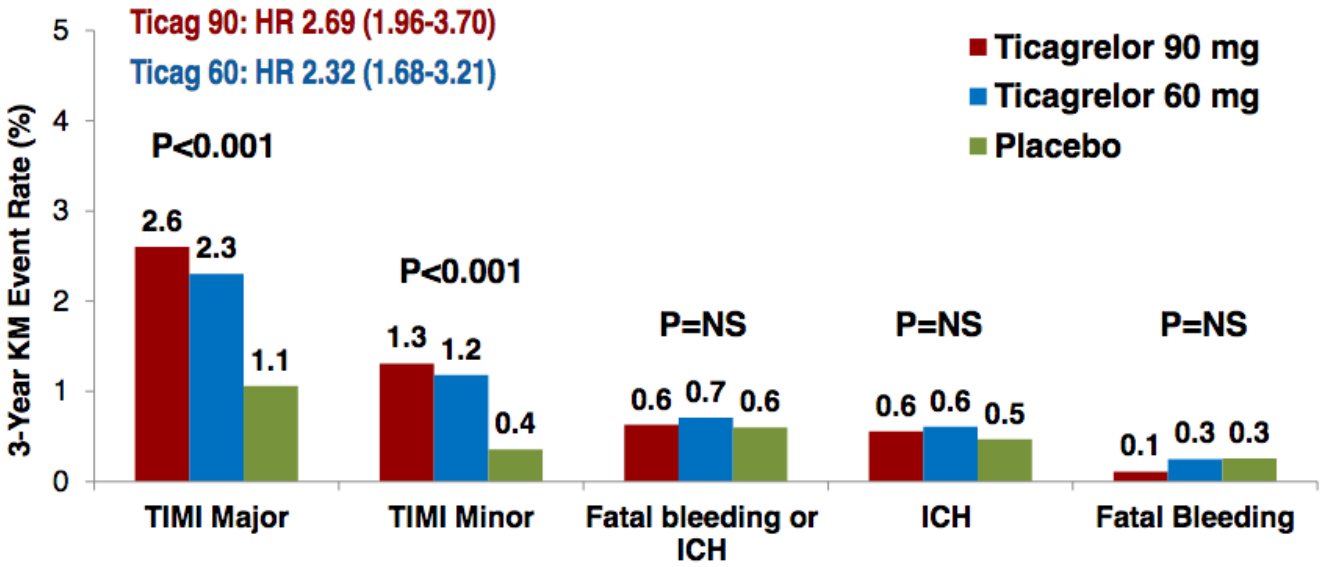
Bonaca MP et al. N Eng J Med 2015;372: 1191–1800

Ticagrelor beyond 12 months: PEGASUS-TIMI 54 Study



Bonaca MP et al. N Eng J Med 2015;372: 1191–1800

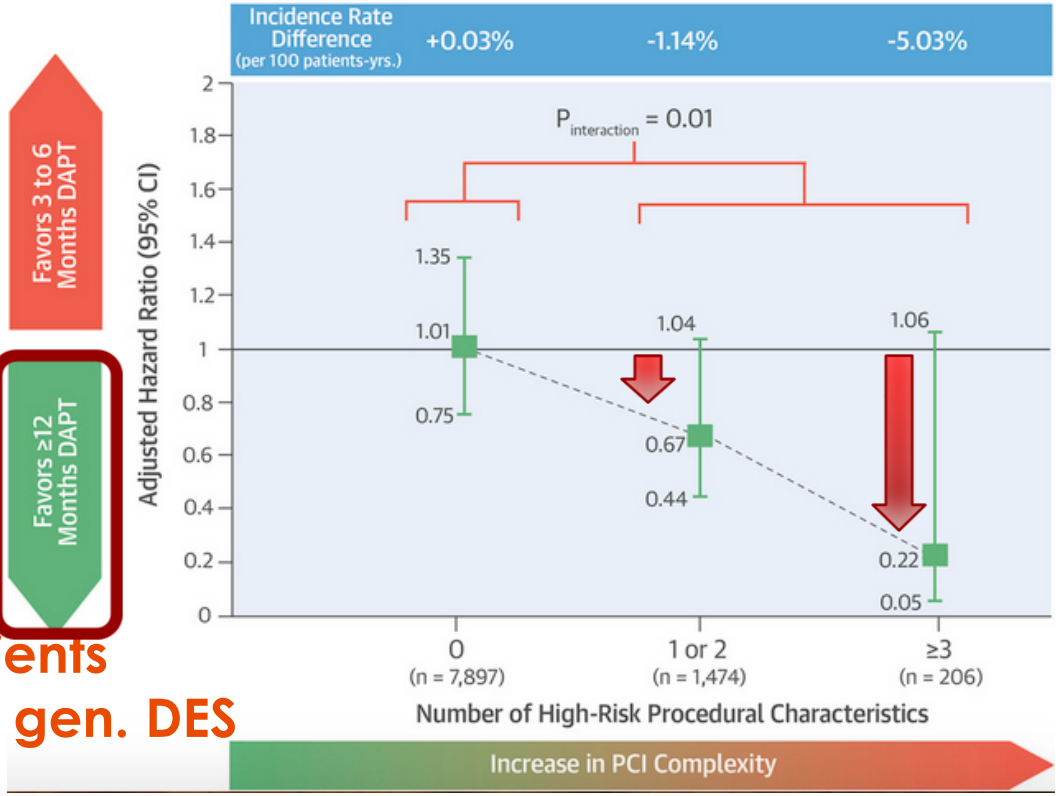
Ticagrelor beyond 12 months: PEGASUS-TIMI 54 Study



Trattando 10 000 pazienti con ticagrelor 90 mg x 2, si prevengono 40 eventi ischemici e si causano 41 eventi emorragici, per un risultato netto sfavorevole di +1 evento.

Al dosaggio di **60 mg x 2** invece, si stimano 42 eventi ischemici prevenuti e 31 eventi emorragici provocati, per un risultato netto favorevole di **-11 eventi**.

Procedural complexity



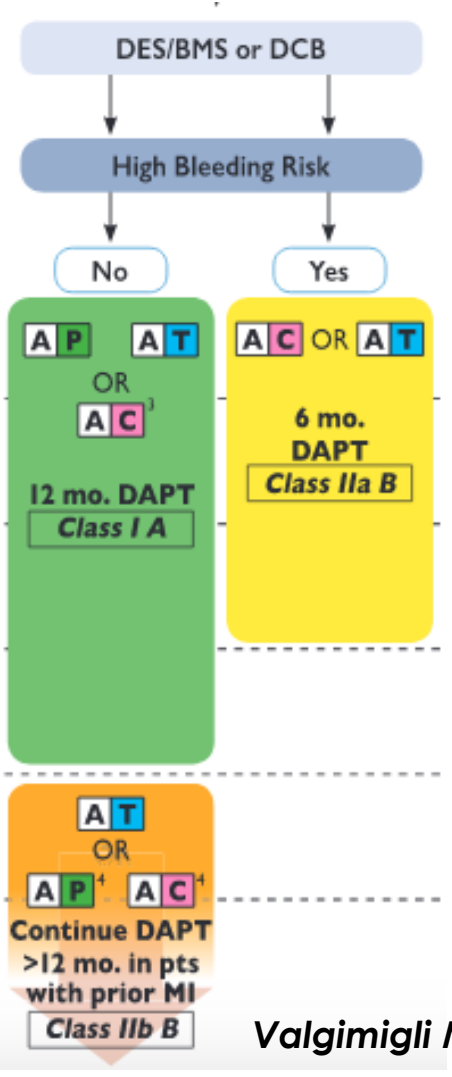
6 RCT
9577 patients
85% new gen. DES

Complex PCI:
3 vessels treated
≥3 stents implanted
≥3 lesions treated
bifurcation with 2 stents
total stent length >60 mm
CTOs

Giustino G et al. J Am Coll Cardiol. 2016;68(17):1851-1864

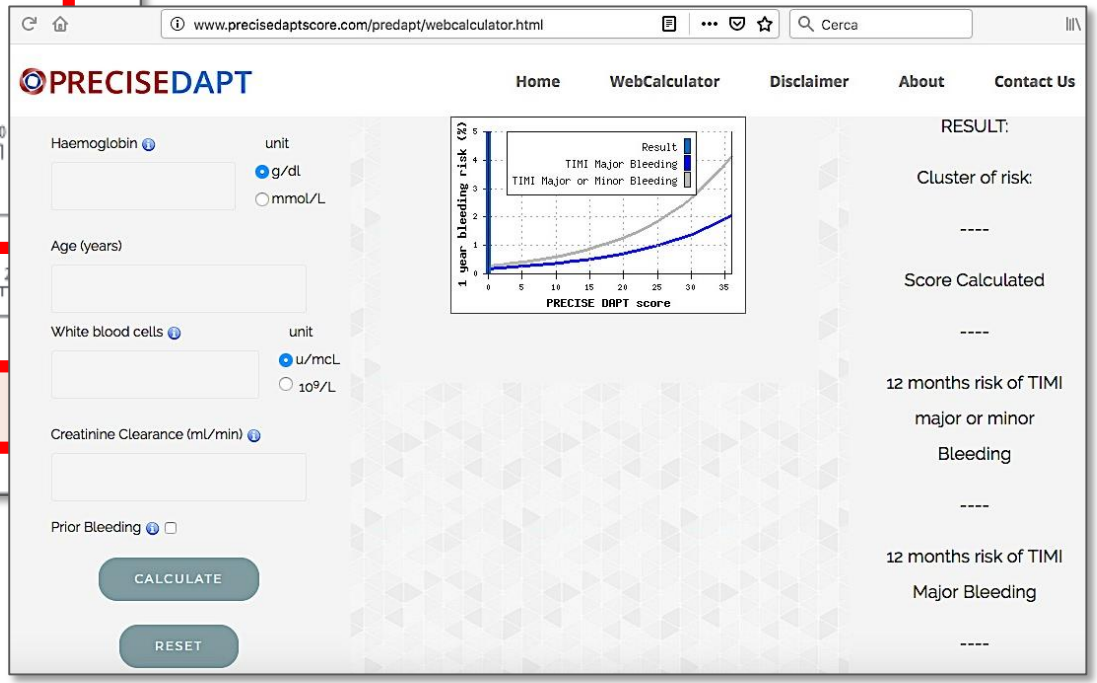
Choosing DAPT duration

ESC guidelines



Valgimigli M et al. Eur Heart J (2018)39, 213–254

	PRECISE-DAPT score[18]
Time of use	At the time of coronary stenting
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)
Score calculation[a]	HB ≥12 11-5 11 10-5 ≤10 WBC ≤5 8 10 12 14 16 18 ≥20 Age ≤50 60 70 80 ≥90 CrCl ≥100 80 60 40 20 0 Prior Bleeding No Score Points 0 2 4 6 8 10 12 14 16 18 20 22 24
Score range	0 to 100 points
Decision making cut-off suggested	Score ≥25 → Short DAPT Score <25 → Standard/long DAPT
Calculator	www.precisedaptscore.com



Valgimigli M et al. Eur Heart J (2018)39, 213–254

Conclusions

- 12 months DAPT duration remains a mainstay after ACS (don't stop prematurely unless absolutely necessary).
- Seriously consider > 12 months DAPT for
  - clinical factors (diabetes, PAD, myocardial infarction...)
  - anatomical factors (long lesions, left main, bifurcation, CTO)
  - technical / PCI-related factors (long and/or multiple stents)
- In high bleeding risk patients **at least 6 months** DAPT duration should be reasonable.
- In "very very" high bleeding risk patients consider 1 – 3 months DAPT...

Grazie per l'attenzione!