DAPT Dilemmas in ACS: Where to go- Shorter vs Longer Durations?

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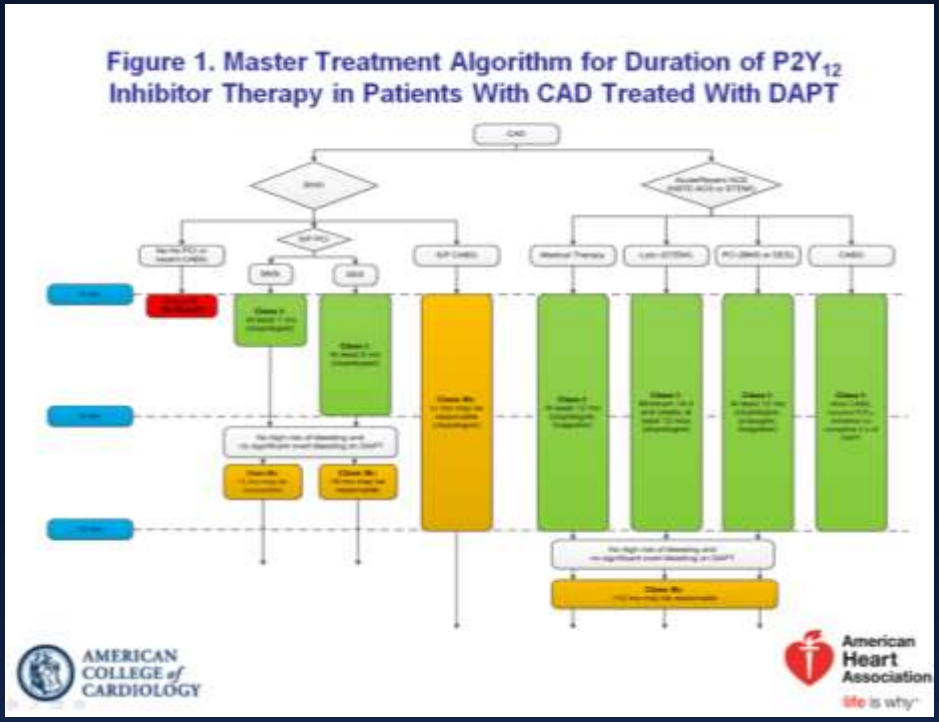
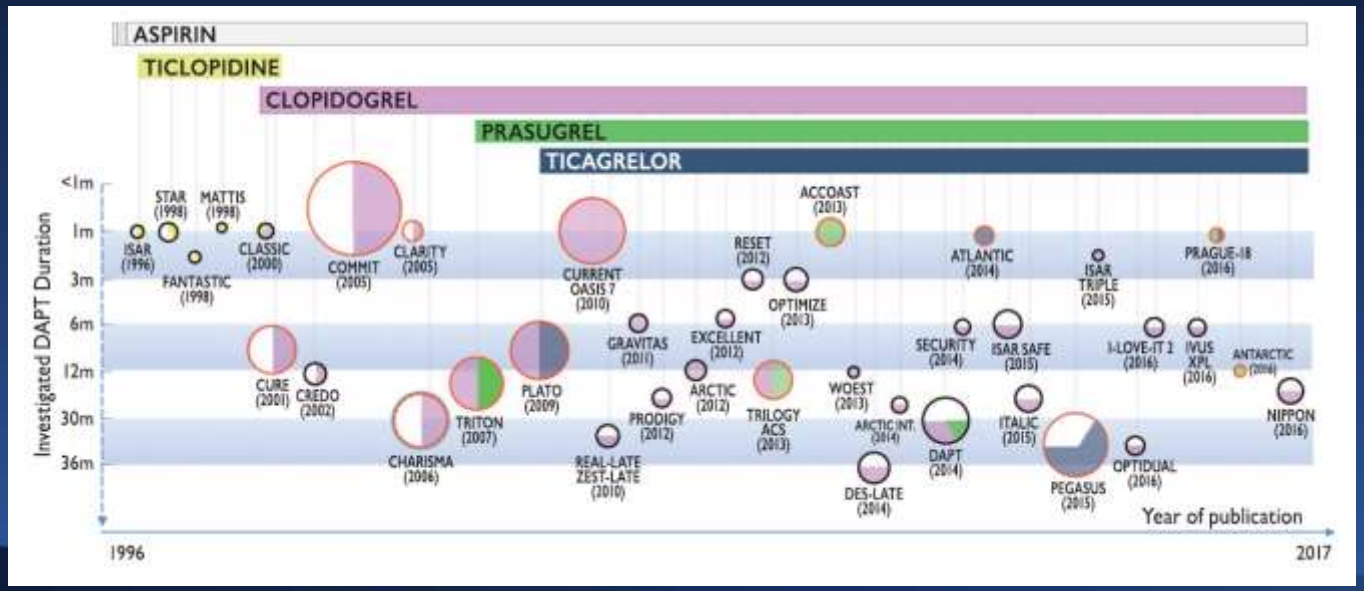
Conflict of interest

- None

DAPT Duration in ACS

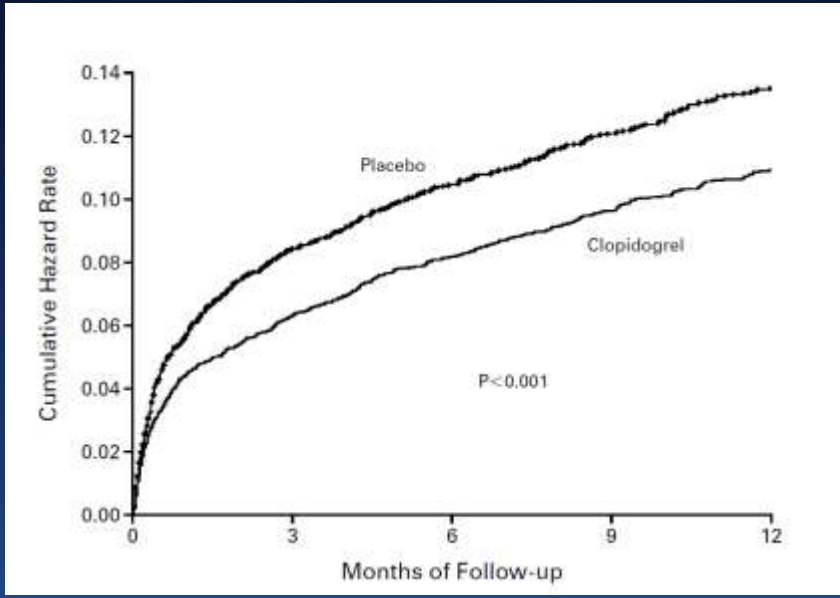


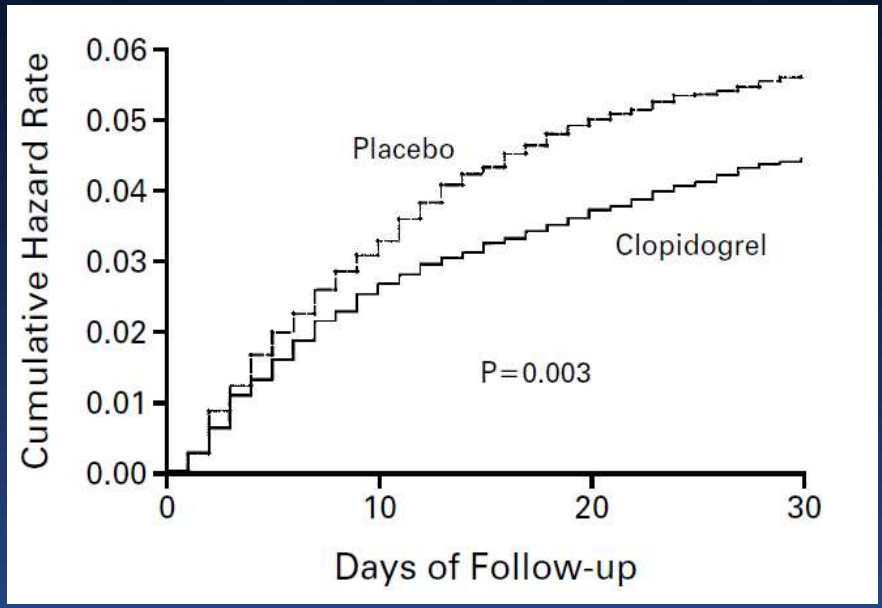


35 RCTs
225,00 patients

AHA/ACC guidelines, JACC 2016

CURE study





CURE Investigators; NEJM 2001

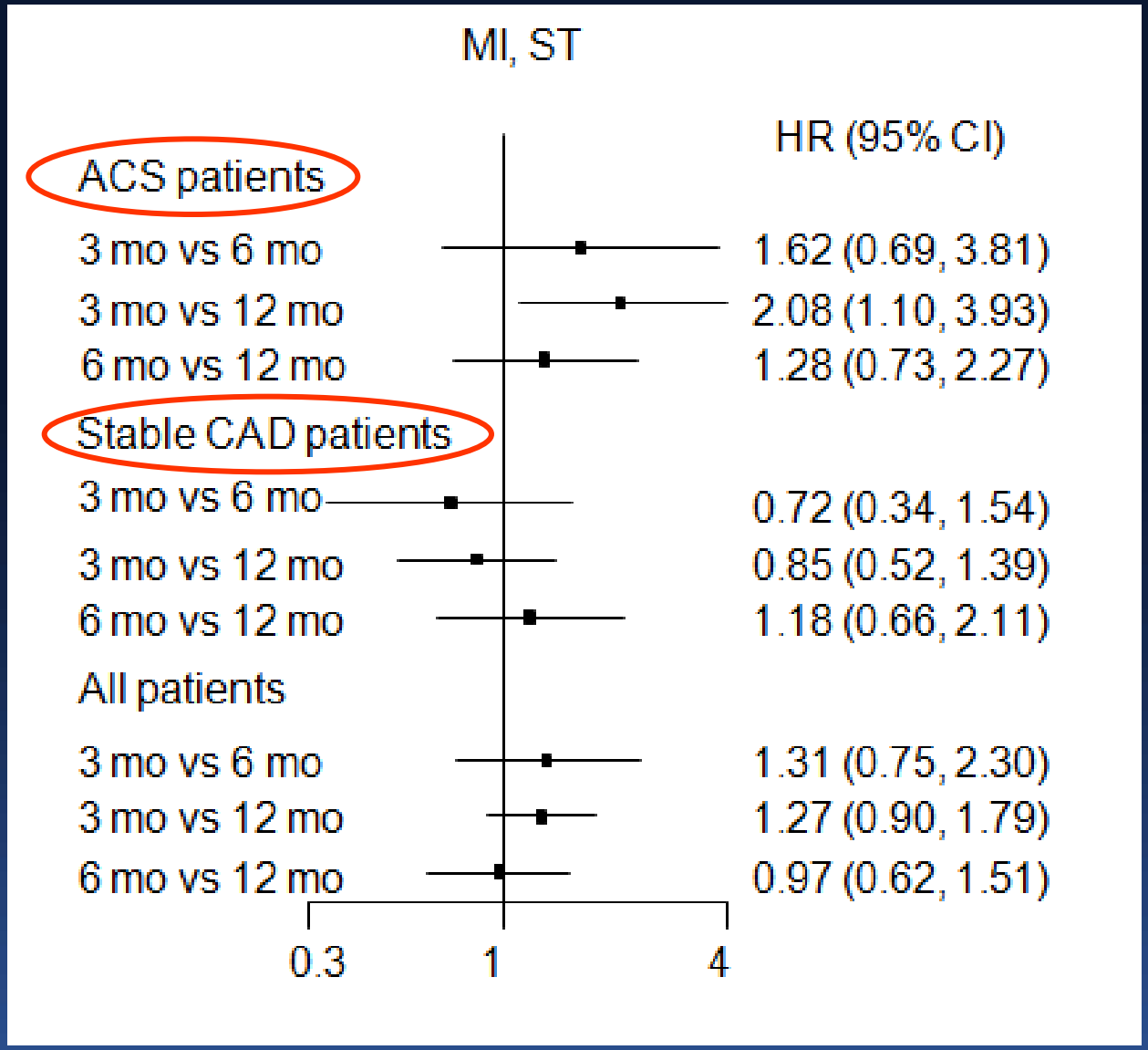
European Heart Journal Advance Access published January 21, 2017

European Heart Journal (2017) **0**, 1–10
doi:10.1093/eurheartj/ehw627

CLINICAL RESEARCH
Interventional cardiology

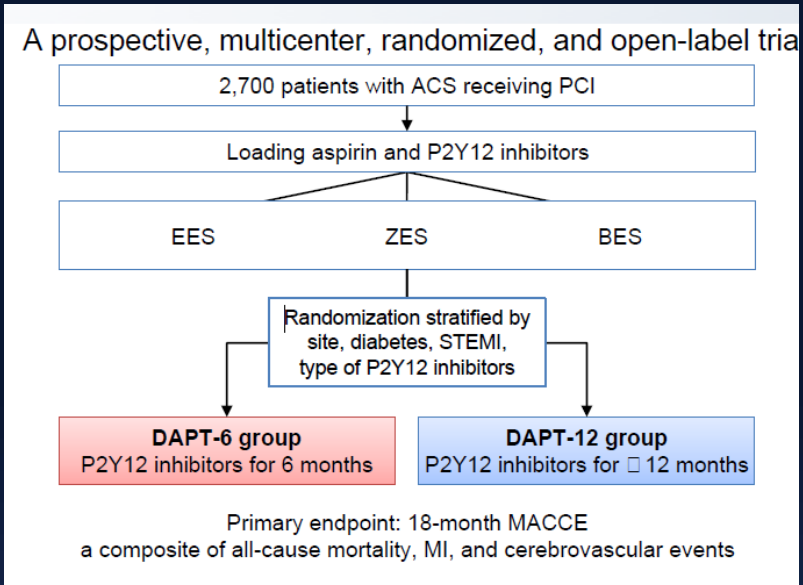
Three, six, or twelve months of dual antiplatelet therapy after DES implantation in patients with or without acute coronary syndromes: an individual patient data pairwise and network meta-analysis of six randomized trials and 11 473 patients

Tullio Palmerini[1], Diego Della Riva[1], Umberto Benedetto[2], Letizia Bacchi Reggiani[1], Fausto Feres[3], Alexandre Abizaid[3], Martine Gilard[4], Marie-Claude Morice[5], Marco Valgimigli[6], Myeong-Ki Hong[7], Byeong-Keuk Kim[7], Yangsoo Jang[7], Hyo-Soo Kim[8], Kyung Woo Park[8], Antonio Colombo[9], Alaide Chieffo[9], Diego Sangiorgi[1], Giuseppe Biondi-Zoccai[10], Philippe Généreux[11], Gianni D. Angelini[2], Maria Pufulete[2], Jonathon White[11], Deepak L. Bhatt[12], and Gregg W. Stone[11]*

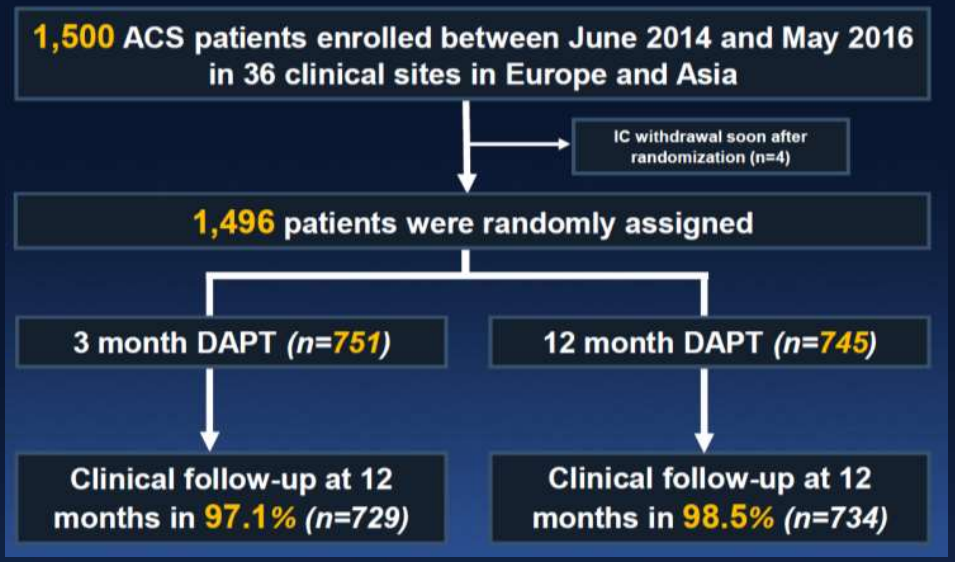


Palmerini et al; EHJ 2017

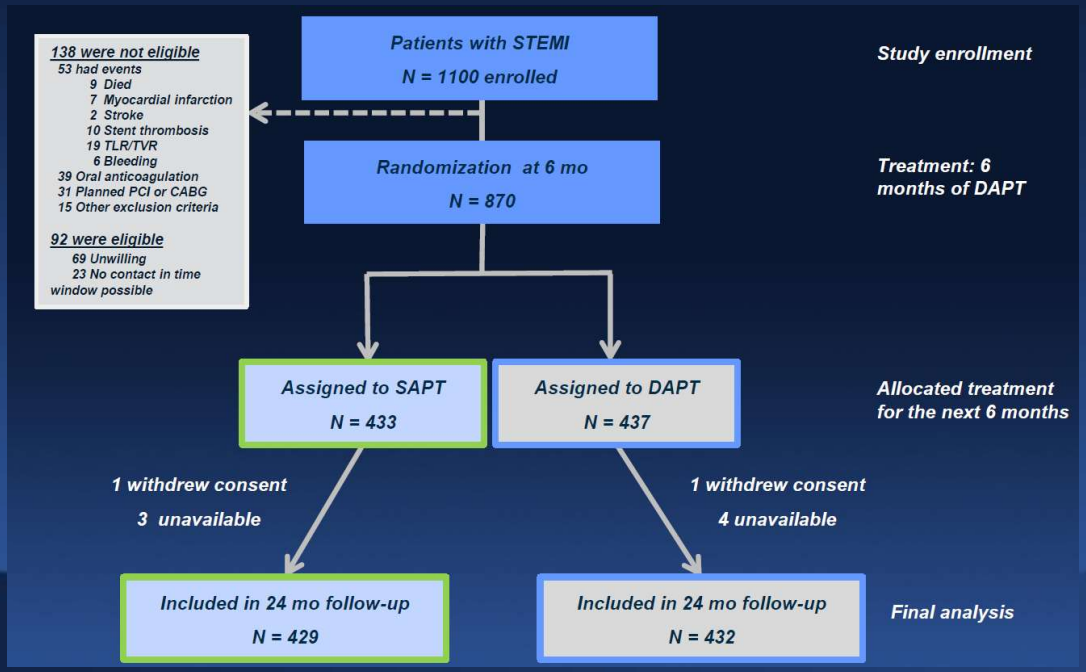
SMART DATE



REDUCE

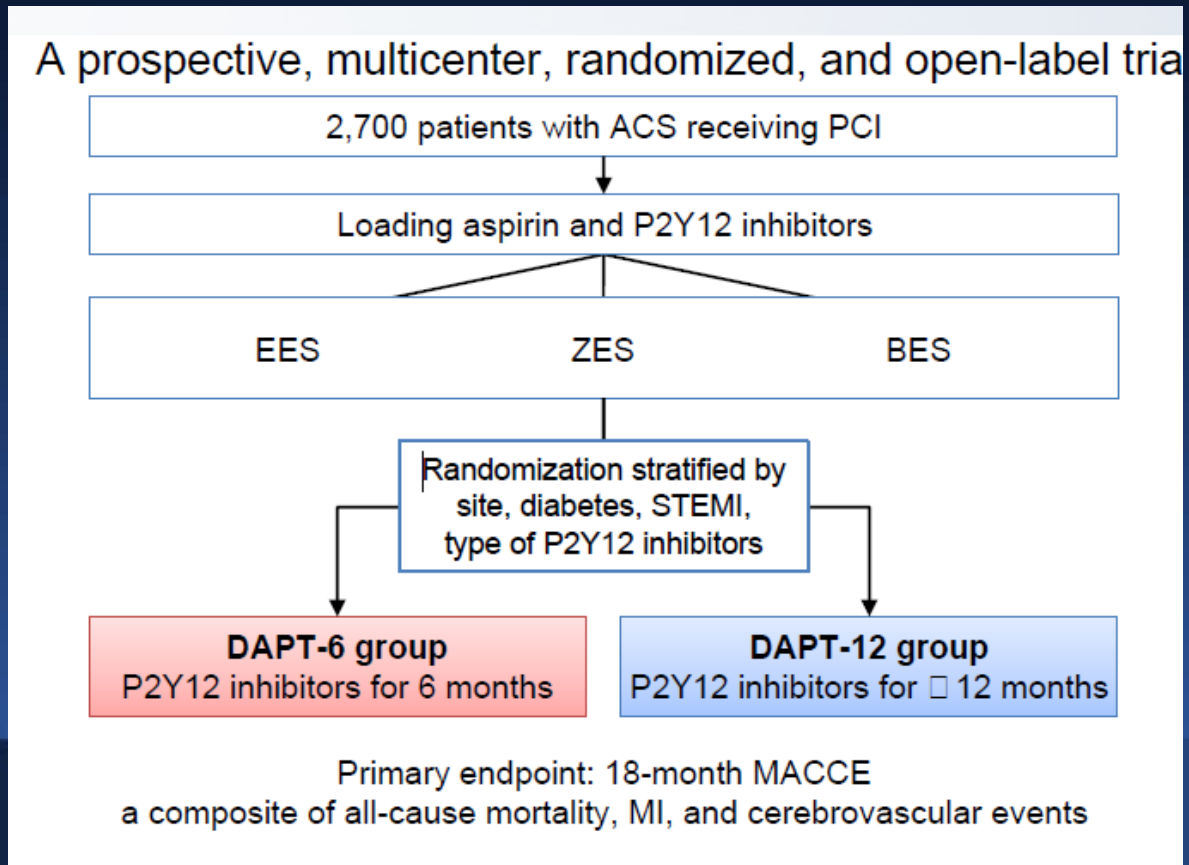


DAPT STEMI

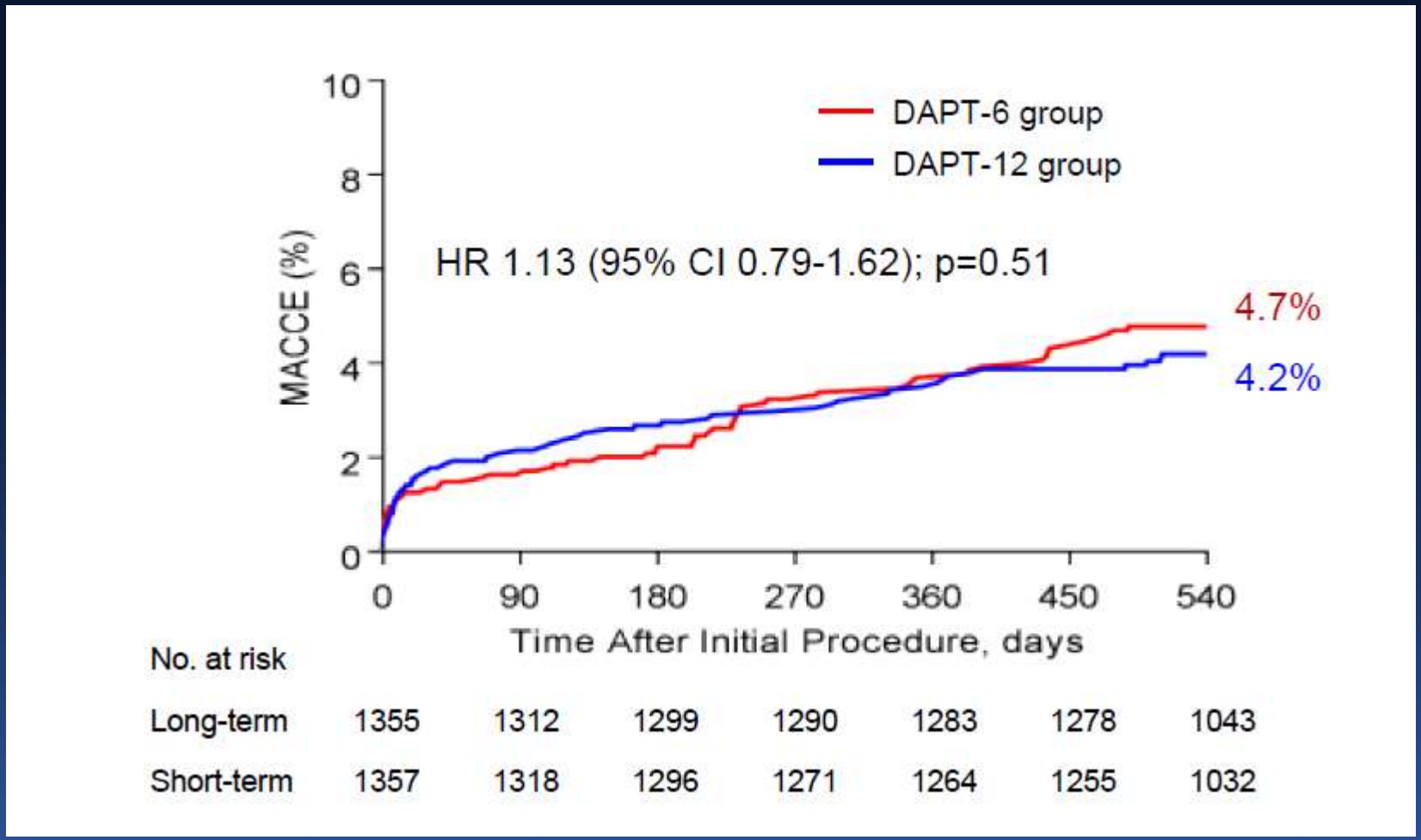


6-month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE): a randomised, open-label, non-inferiority trial

Joo-Yong Hahn, Young Bin Song*, Ju-Hyeon Oh, Deok-Kyu Cho, Jin Bae Lee, Joon-Hyung Doh, Sang-Hyun Kim, Jin-Ok Jeong, Jang-Ho Bae, Byung-Ok Kim, Jang Hyun Cho, Il-Woo Suh, Doo-il Kim, Hoon-Ki Park, Jong-Seon Park, Woong Gil Choi, Wang Soo Lee, Jihoon Kim, Ki Hong Choi Taek Kyu Park, Joo Myung Lee, Jeong Hoon Yang, Jin-Ho Choi, Seung-Hyuk Choi, Hyeon-Cheol Gwon, for the SMART-DATE investigators†*



Primary endpoint: death, MI or stroke



Hahn et al; Lancet 2018

Intention to treat analysis

	DAPT-6 group (n=1357)	DAPT-12 group (n=1355)	HR (95% CI)	p value
MACCE	63 (4.7%)	56 (4.2%)	1.13 (0.79-1.62)	0.51
Death	35 (2.6%)	39 (2.9%)	0.90 (0.57-1.42)	0.90
Myocardial infarction	24 (1.8%)	10 (0.8%)	2.41 (1.15-5.05)	0.02
Target vessel MI	14 (1.1%)	7 (0.5%)	2.01 (0.81-4.97)	0.13
Non-target vessel MI	10 (0.8%)	3 (0.2%)	3.35 (0.92-12.2)	0.07
Cerebrovascular accident (stroke)	11 (0.8%)	12 (0.9%)	0.·92 (0.41-2.08)	0.84
Cardiac death	18 (1.4%)	24 (1.8%)	0.75 (0.41-1.38)	0.36
Cardiac death or MI	39 (2.9%)	32 (2.4%)	1.22 (0.77-1.95)	0.40
Stent thrombosis	15 (1.1%)	10 (0.7%)	1.50 (0.68-3.35)	0.32
Bleeding BARC type 2-5	35 (2.7%)	51 (3.9%)	0.69 (0.45-1.05)	0.09
Major bleeding (BARC type 3,4,or 5)	6 (0.5%)	10 (0.8%)	0.60 (0.22-1.65)	0.33
Net adverse clinical and cerebral events	96 (7.2%)	99 (7.4%)	0.97 (0.73-1.29)	0.84

Hahn et al; Lancet 2018

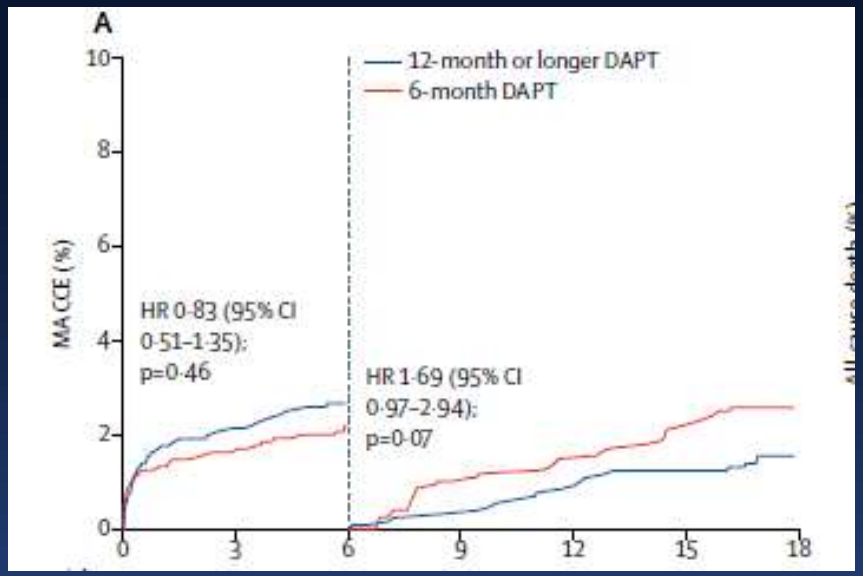
Per protocol analysis

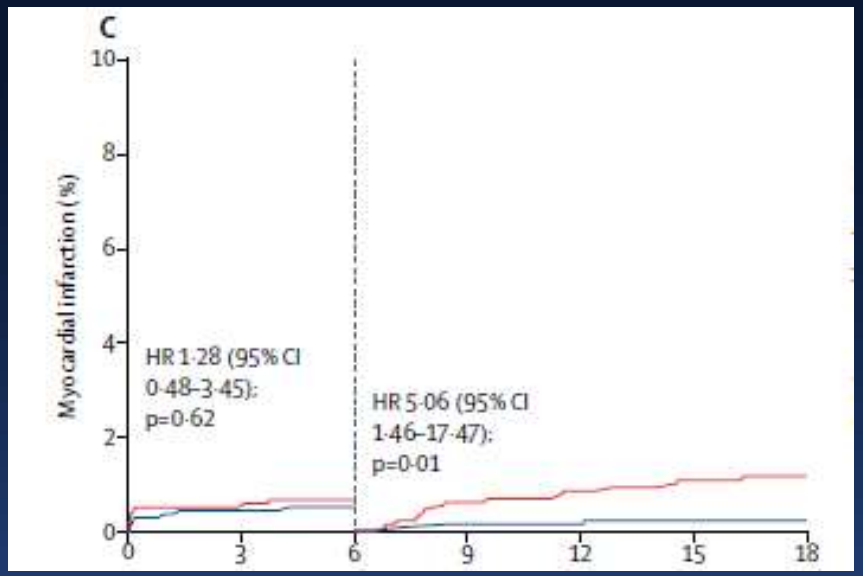
	DAPT-6 group (n=1000)	DAPT-12 group (n=1297)	HR (95% CI)	p value
MACCE	44 (4.5%)	52 (4.1%)	1.11 (0.74-1.66)	0.61
Death	29 (3.0%)	37 (2.9%)	1.03 (0.63-1.67)	0.92
Myocardial infarction	15 (1.6%)	10 (0.8%)	1.97 (0.88-4.38)	0.10
Target vessel MI	11 (1.1%)	7 (0.5%)	2.06 (0.80-5.31)	0.14
Non-target vessel MI	4 (0.4%)	3 (0.2%)	1.75 (0.39-7.81)	0.47
Cerebrovascular accident	6 (0.6%)	10 (0.8%)	0.79 (0.29-2.17)	0.64
Cardiac death	15 (1.5%)	22 (1.7%)	0.89 (0.46-1.72)	0.73
Cardiac death or MI	27 (2.8%)	30 (2.3%)	1.18 (0.70-1.98)	0.54
Stent thrombosis	13 (1.3%)	10 (0.8%)	1.70 (0.75-3.88)	0.21
Bleeding BARC type 2-5	22 (2.3%)	48 (3.8%)	0.60 (0.36-0.99)	0.046
Major bleeding (BARC type 3,4,or 5)	4 (0.4%)	10 (0.8%)	0.53 (0.17-1.68)	0.28
Net adverse clinical and cerebral events	65 (6.6%)	92 (7.2%)	0.92 (0.67-1.27)	0.62

** Defined as BARC type 3, 4 or 5*

Hahn et al; Lancet 2018

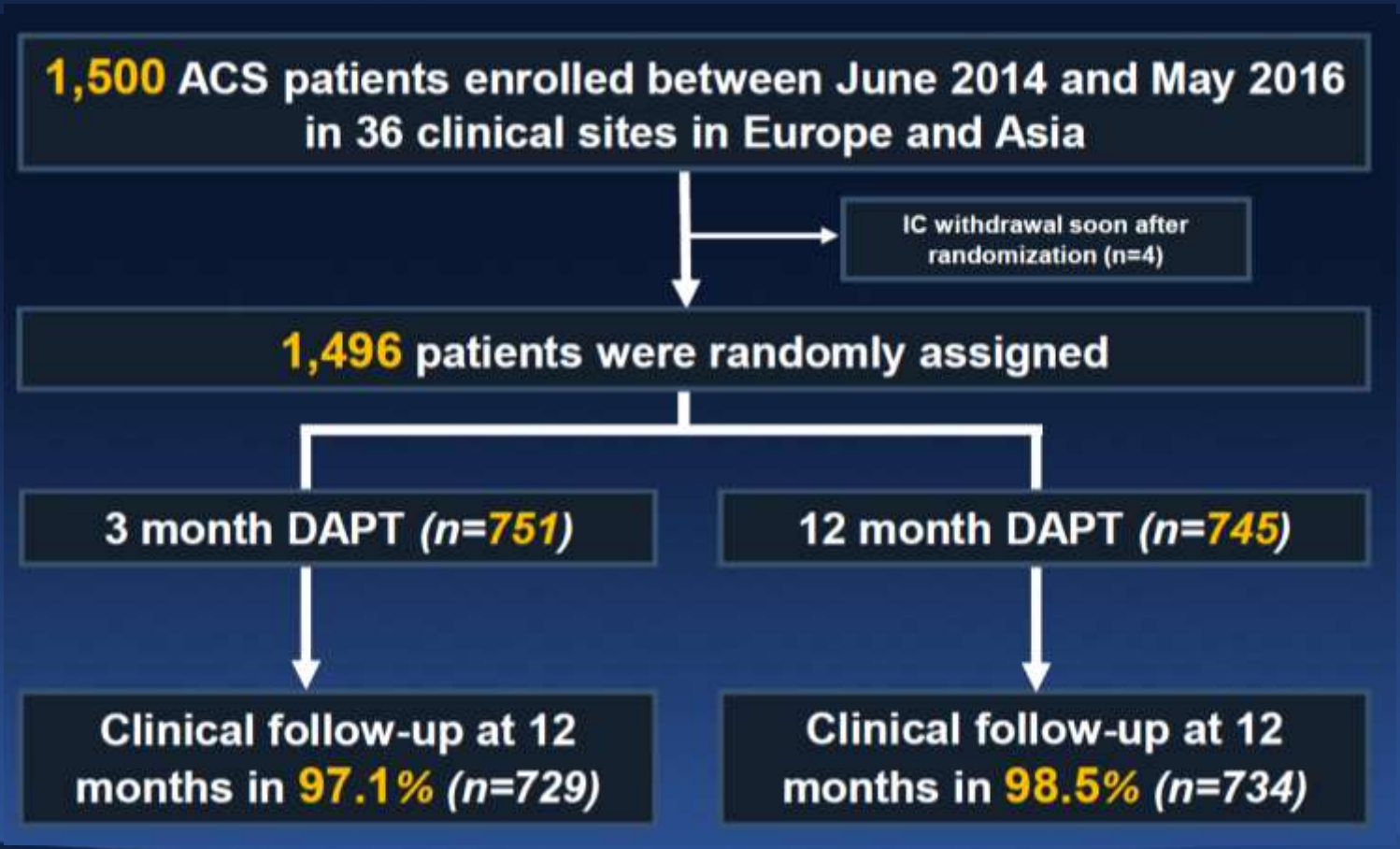
Landmark analysis





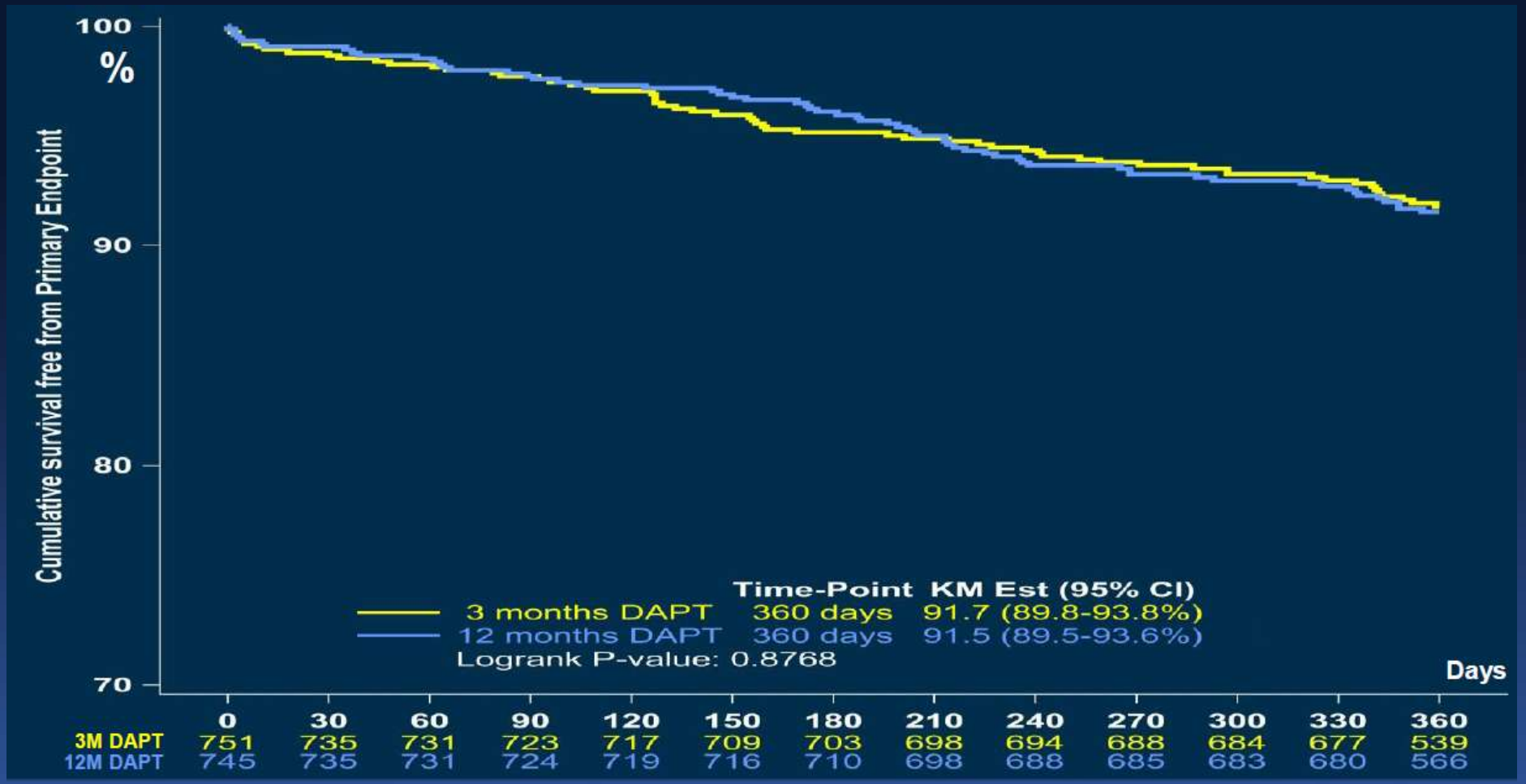
Hahn et al; Lancet 2018

REDUCE: A Randomized Trial of 3-Month vs 12-Month DAPT After Implantation of a Bioabsorbable Polymer-Based Metallic DES With a Luminal CD34+ Antibody Coating in Patients With ACS



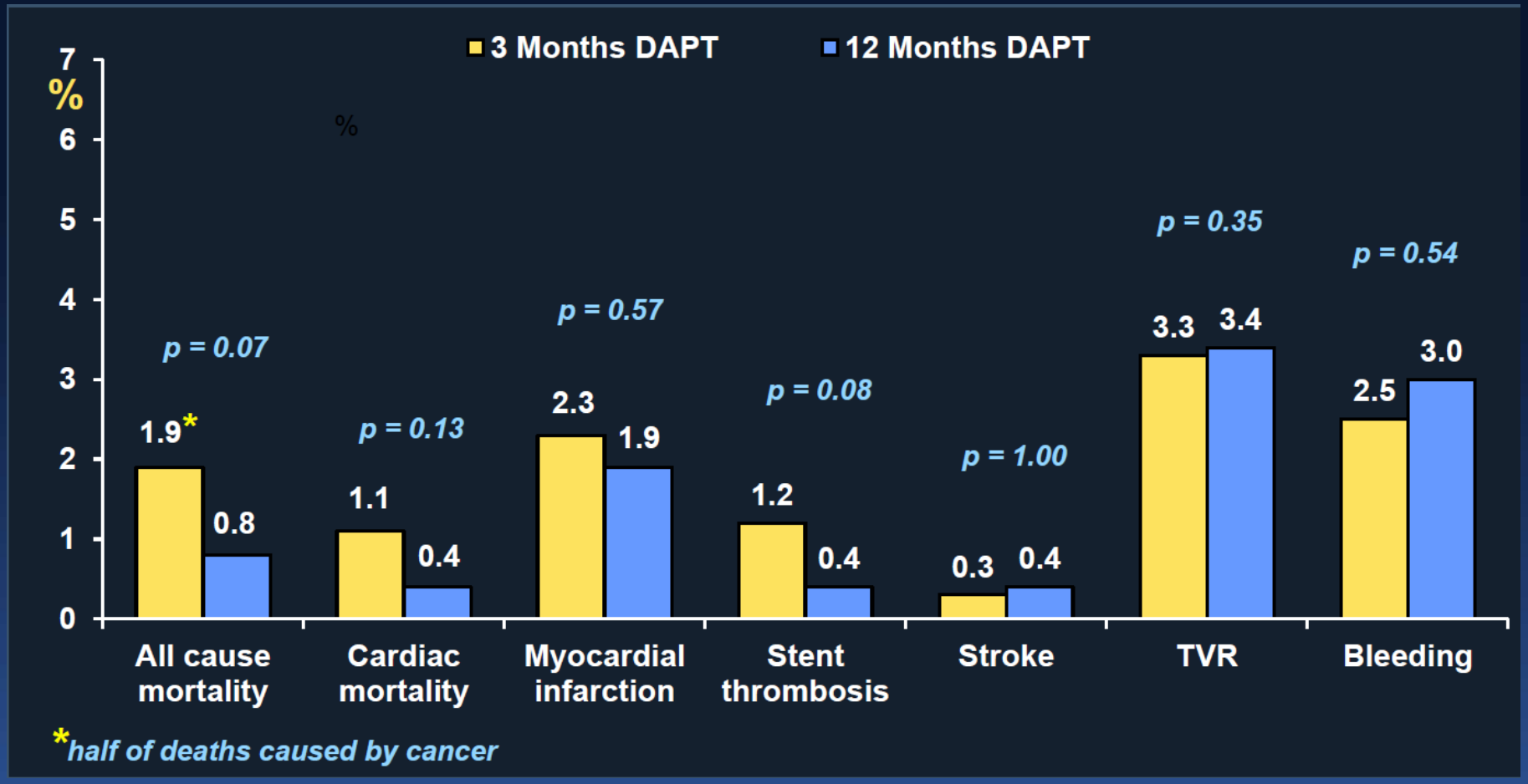
Suryapranata et al; TCT 2017

Primary endpoint: death, MI, stroke, TVR, bleeding



Suryapranata et al; TCT 2017

Secondary endpoint



Suryapranata et al; TCT 2017

DAPT STEMI design

Prospective, International, Randomized, Non-inferiority Trial
STEMI Patients undergoing primary PCI with a second-generation Zotarolimus-eluting stent (Resolute Integrity)

Enrollment took place in 17 centers in The Netherlands, Poland, Switzerland and Norway

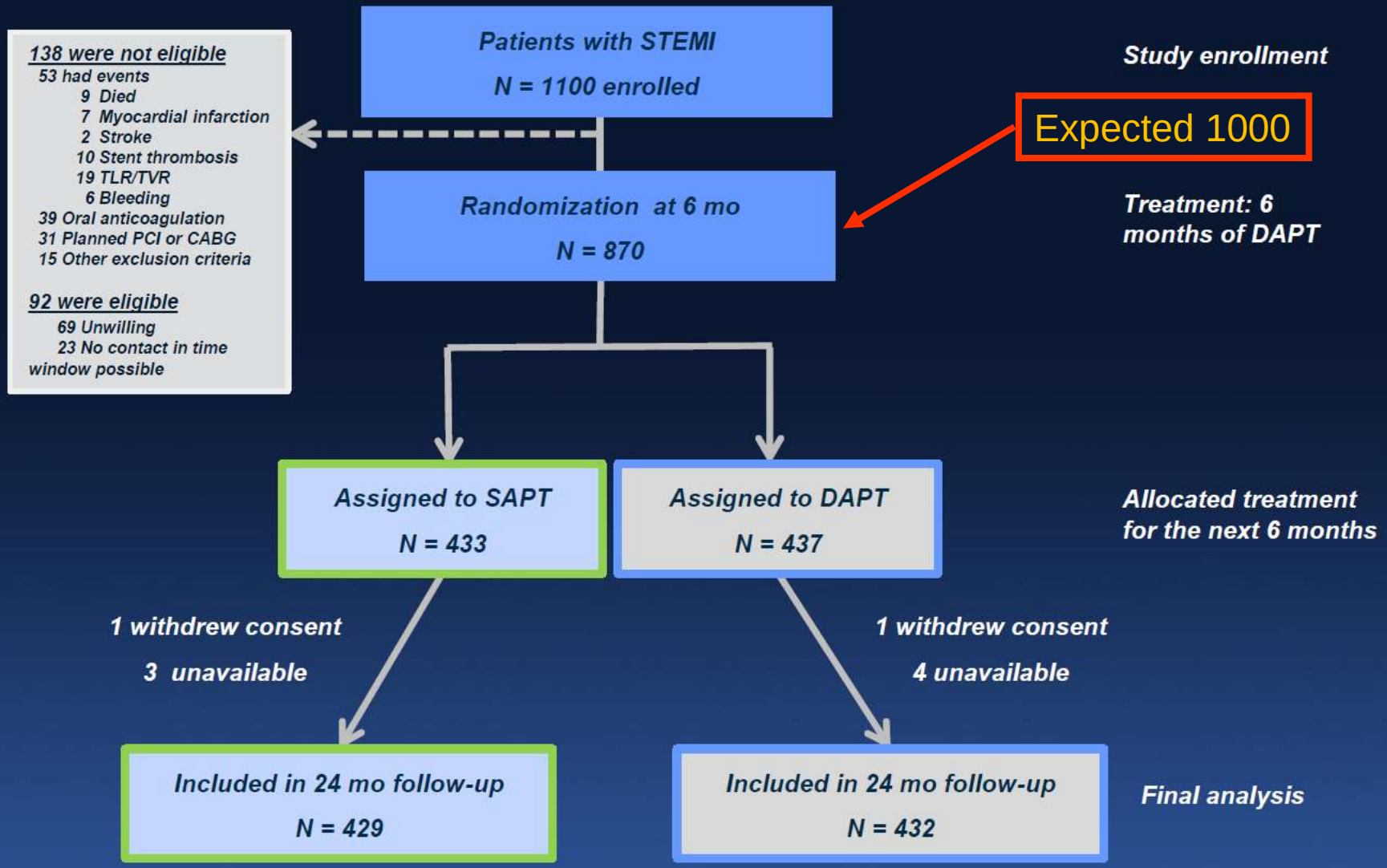
Kedhi, TCT 2017

Statistical assumption

- **The sample size:**
  - *α = 0.05 for a two-sided test* (0.025 for a one-sided test)
  - *Power of 85%*
  - Non-inferiority margin: *HR and upper 95% CI of 1.66*
  - The assumed *primary endpoint rate in both arms* was *15 %*
- The *sample size* needed was *1000 patients*
- To compensate for the patients who met a randomization exclusion criteria in the first 6 months *1100 patients were enrolled*

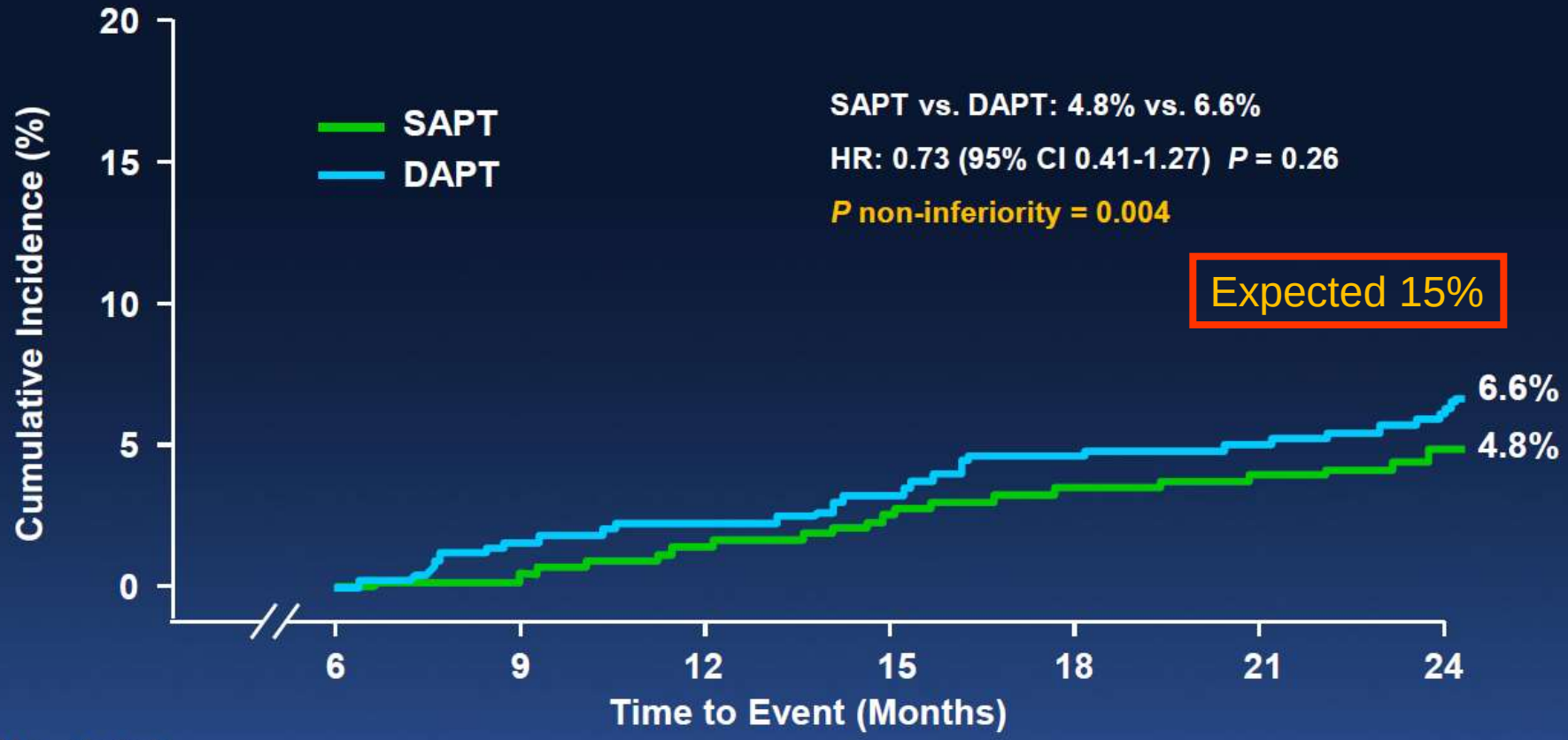
Kedhi, TCT 2017

Study flow



Kedhi, TCT 2017

Primary endpoint: death, MI, stroke, any revasc, TIMI major bleeding



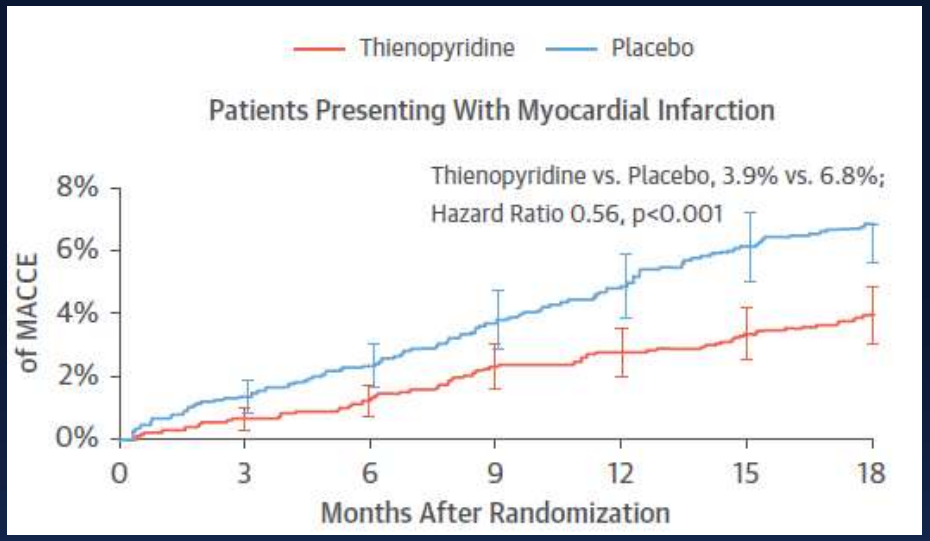
No. at risk							
SAPT	433	428	424	419	413	411	408
DAPT	437	430	426	421	412	409	403

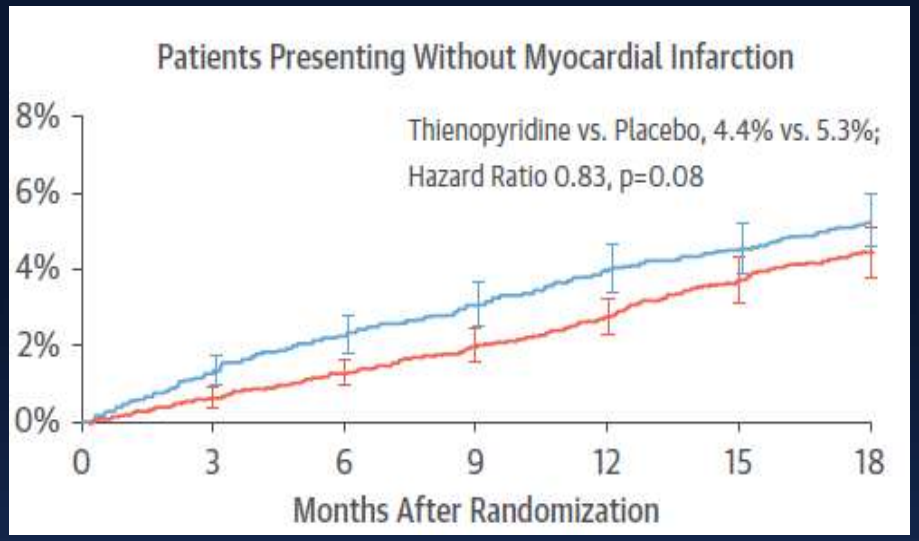
Kedhi, TCT 2017

Limitation of the DAPT STEMI trial

- The trial enrolled a lower than expected number of patients due to higher than expected rates of consent withdrawl
- The trial was underpowered because observed event rates were lower than expected
- The non inferiority margin was relatively high

DAPT trial: ACS vs non ACS

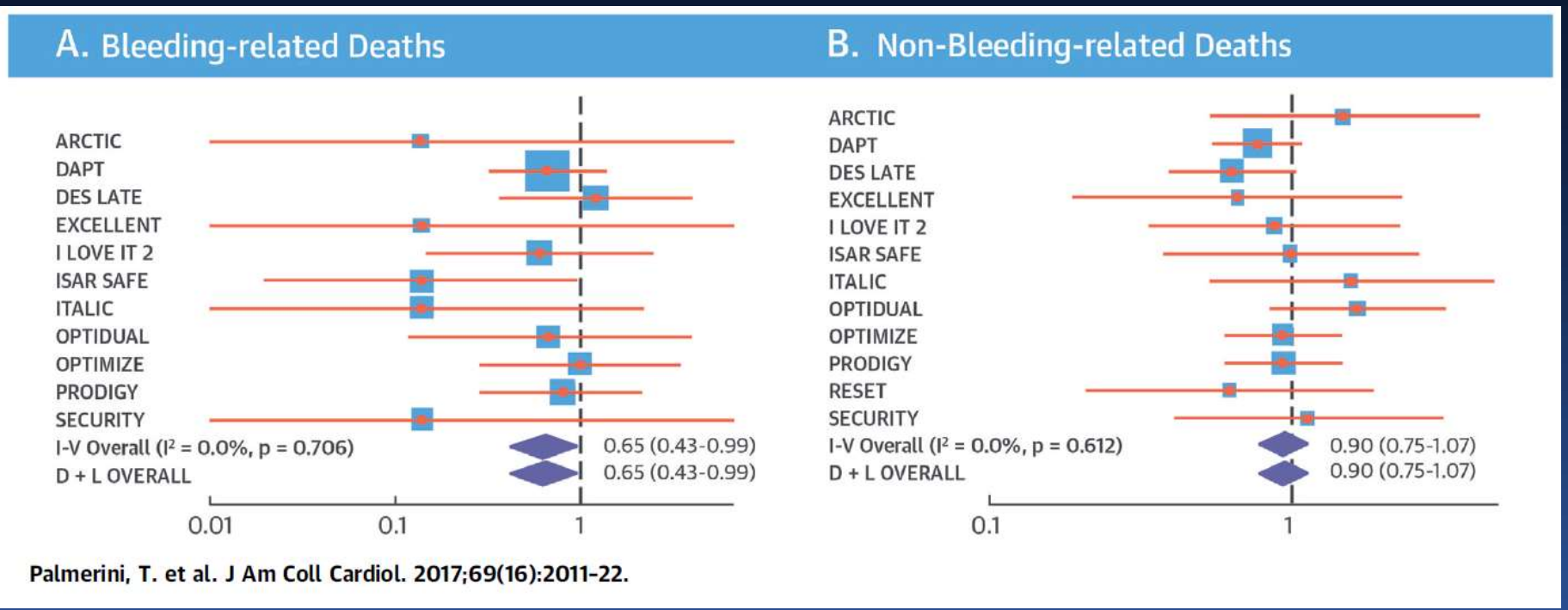




GUSTO moderate or severe bleeding					0.21
MI group	34 (1.9)	14 (0.8)	2.38 (1.27-4.43)	0.005	
No MI group	101 (2.6)	66 (1.7)	1.53 (1.12-2.08)	0.007	
GUSTO moderate bleeding					0.06
MI group	21 (1.2)	5 (0.3)	4.10 (1.55-10.87)	0.002	
No MI group	70 (1.8)	47 (1.2)	1.48 (1.03-2.15)	0.04	
GUSTO severe bleeding					0.86
MI group	13 (0.7)	9 (0.5)	1.41 (0.60-3.29)	0.43	
No MI group	31 (0.8)	20 (0.5)	1.54 (0.88-2.70)	0.13	

Yeh et al; JACC 2015

Bleeding-Related Deaths in Relation to the Duration of Dual-Antiplatelet Therapy After Coronary Stenting



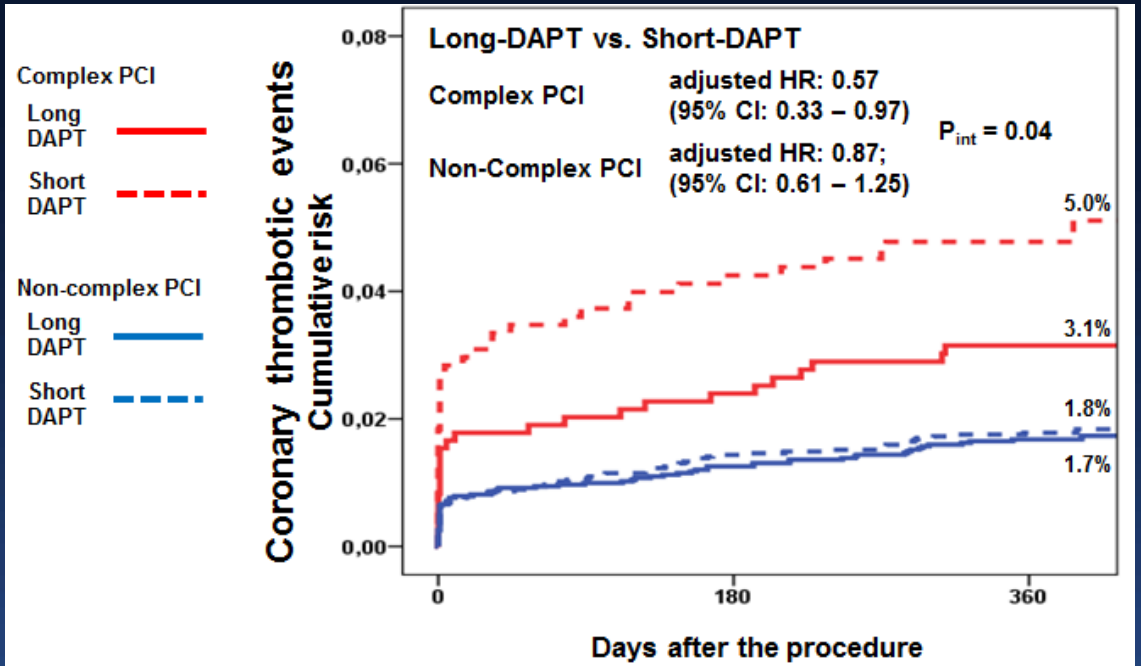
Palmerini, T. et al. J Am Coll Cardiol. 2017;69(16):2011-22.

Optimal DAPT duration after DES: a complex equation

$$R_{\mu\nu} - \frac{1}{2} R\, g_{\mu\nu} + \Lambda\, g_{\mu\nu} = \frac{8\pi G}{c^4} T_{\mu\nu}$$

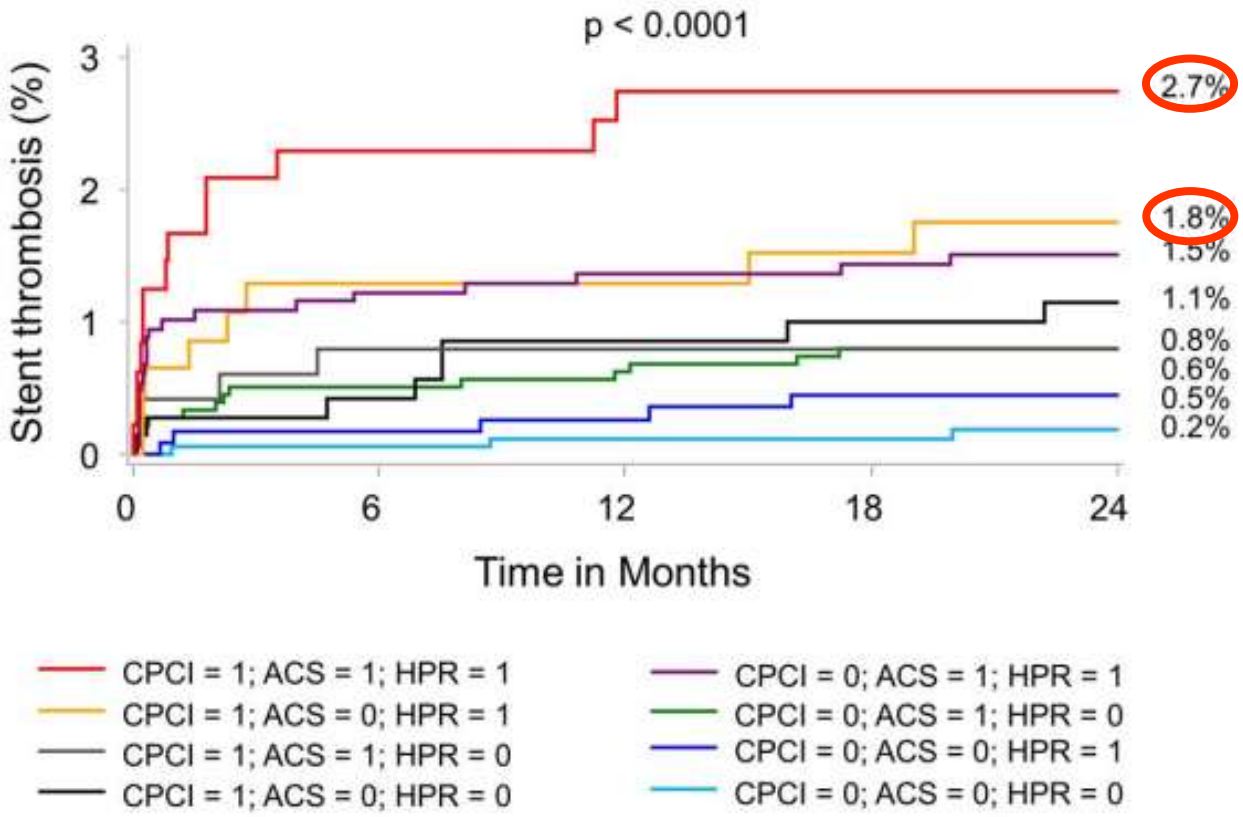
Ischemic risk vs Bleeding risk

Pooled analysis of EXCELLENT, ITALIC, OPTIMIZE, PRODIGY, RESET, SECURITY

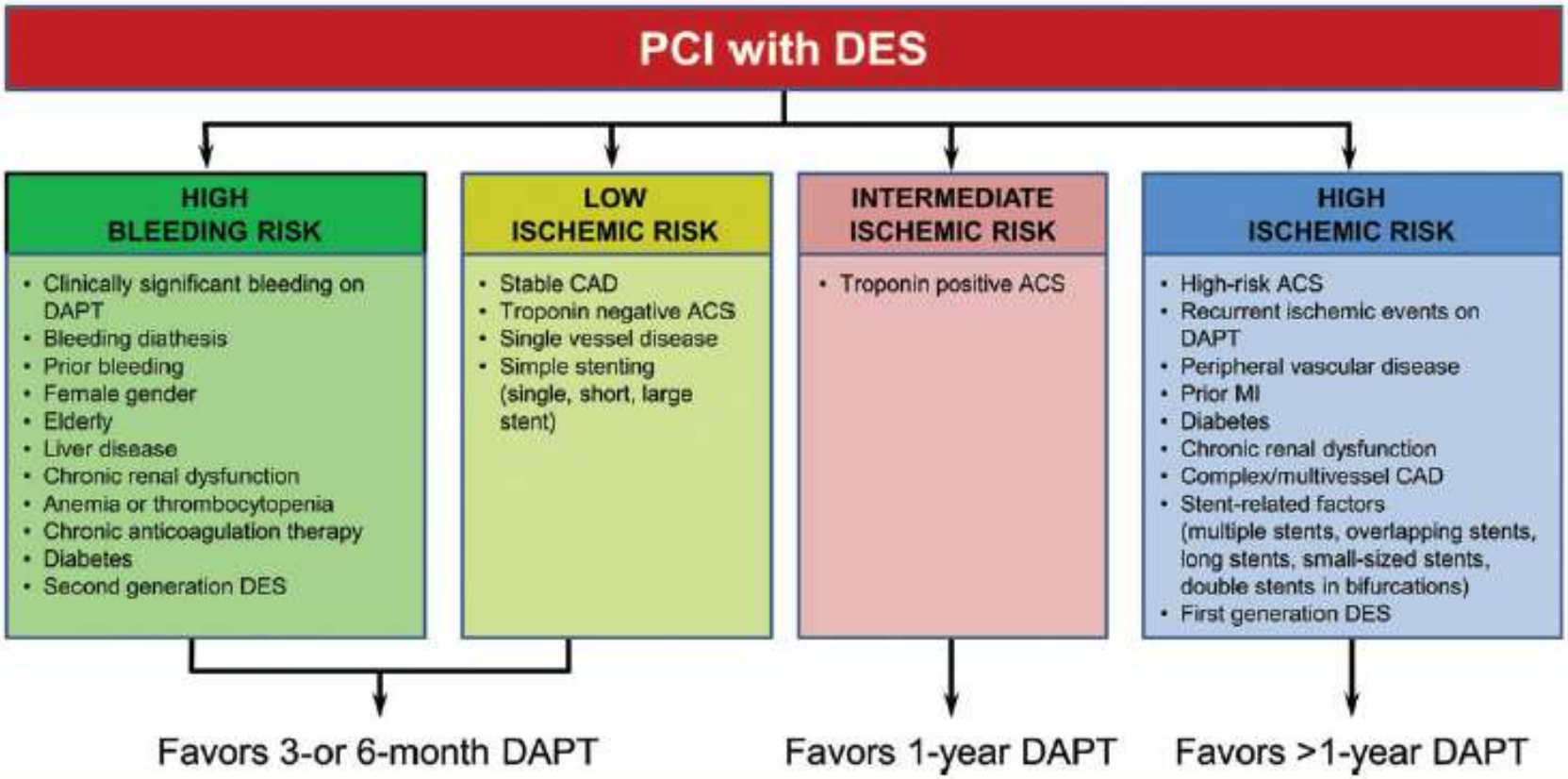


Giustino et al; JACC 2016

ADAPT DES study



Genereux et al; IJC in press



Palmerini and Stone; European Heart Journal 2016

Conclusions

- **In patients wih ACS prolonged DAPT significantly reduce the risk of ischemic events at the price of increased bleeding compared with abbreviated DAPT.**
- **A minimum of 1-year DAPT is recommended for patients with ACS, but in view of the trade off between bleeding and ischemic events, the duration of DAPT should be tailored according to patient risk profile.**