La terapia antiaggregante dopo il 12 mese da una SCA: connessione tra ospedale e territorio

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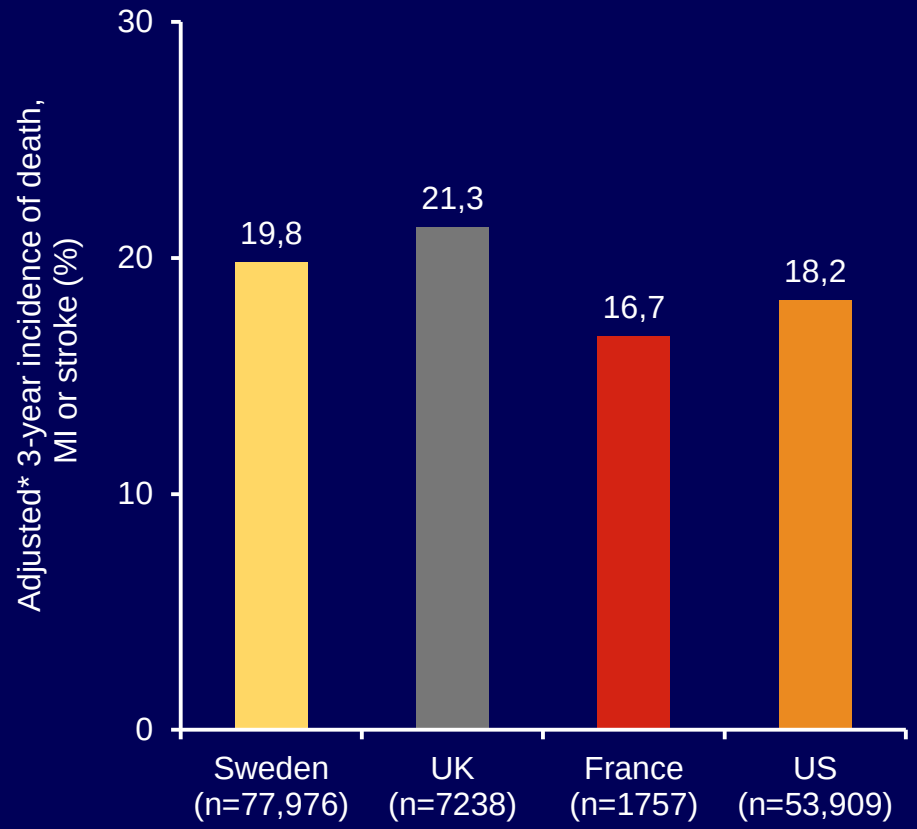
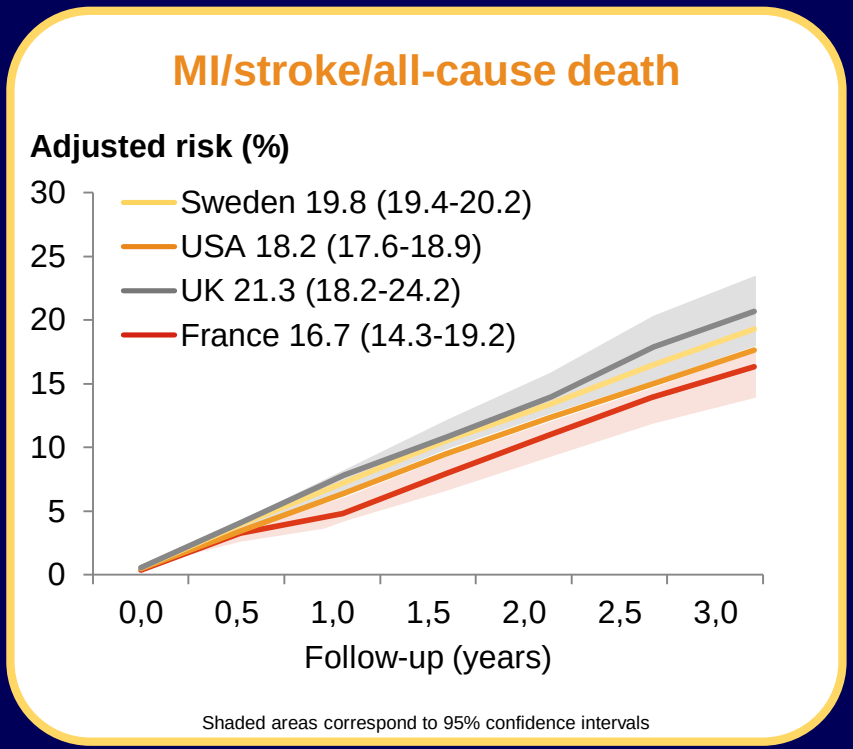
~1 in 5 patients were event free for the first year post-MI suffered an MI, stroke or death within 3 years

APOLLO 4-country analysis: adjusted incidence*[Rapsomaniki 2014]





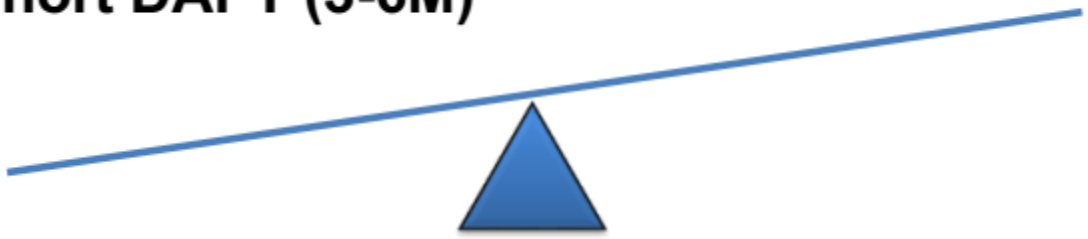
MI, myocardial infarction.

*Adjusted for differences in study populations; MI, myocardial infarction. Shaded areas / figures in brackets [95%CI]

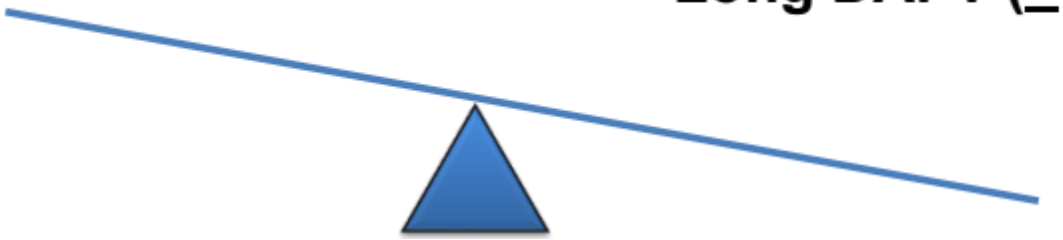
1. Rapsomaniki E *et al*. ESC Late Breaking Registry presentation 2014.

Risk vs. Benefit of DAPT

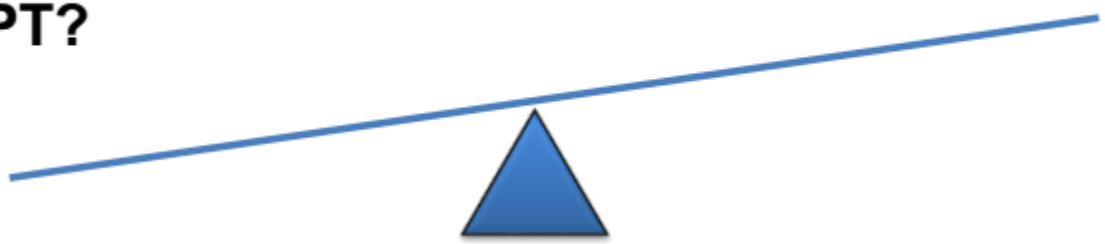
Short DAPT (3-6M)



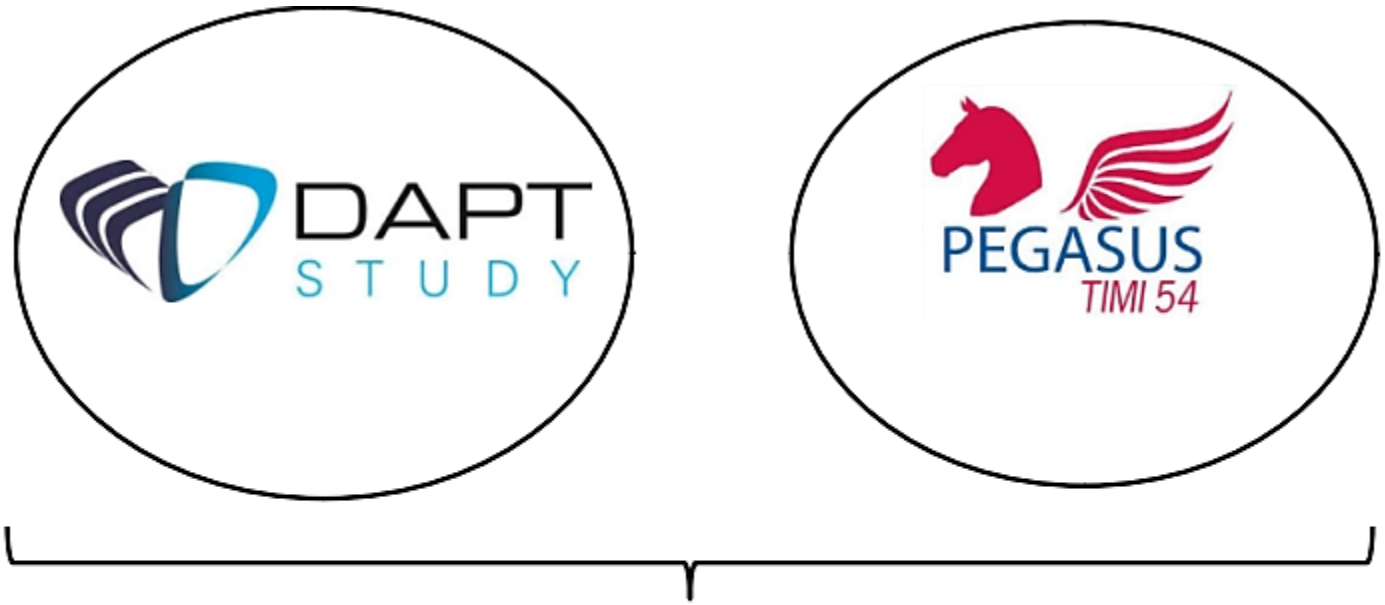
Long DAPT (≥12M)



Short DAPT
Or Long DAPT?



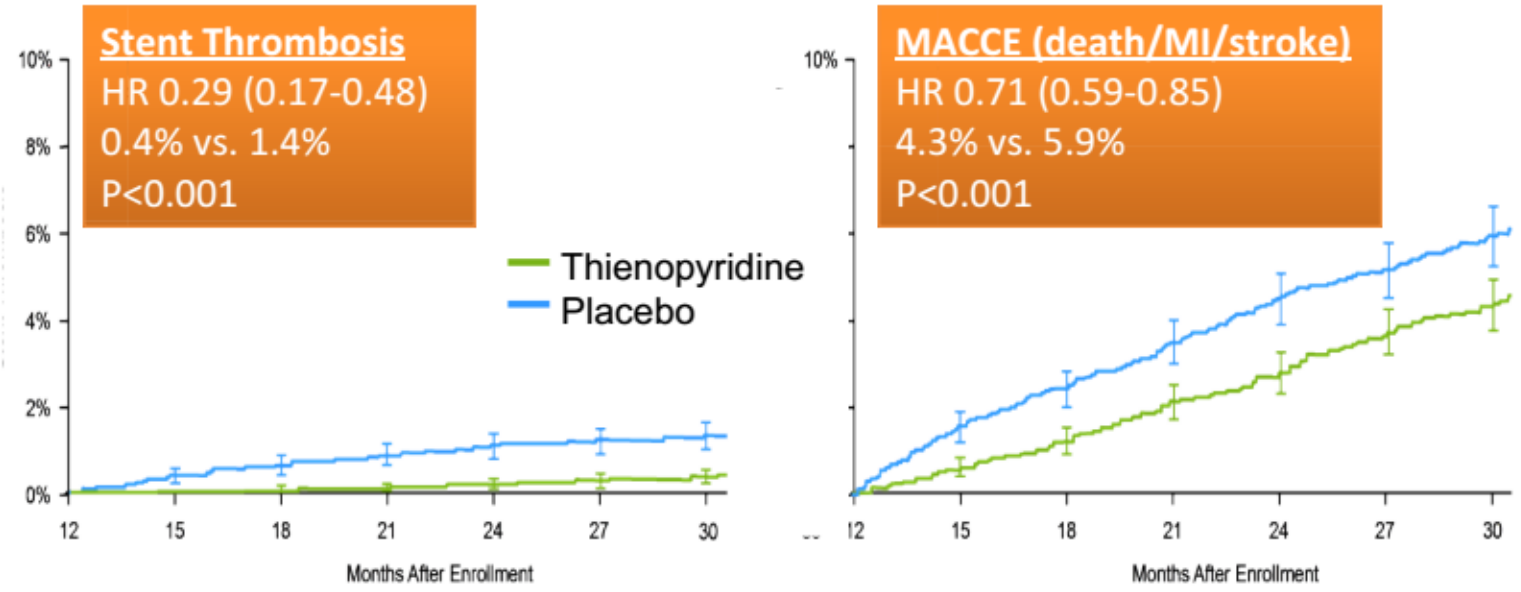
Antiplatelet Therapy Trials



Common Question: Does Ischemic Benefit outweigh Bleeding Risk of Late Dual Antiplatelet Therapy (1 or more years after stent, or MI)

Primary Results: Continued Thienopyridine vs Placebo 12 months after DES

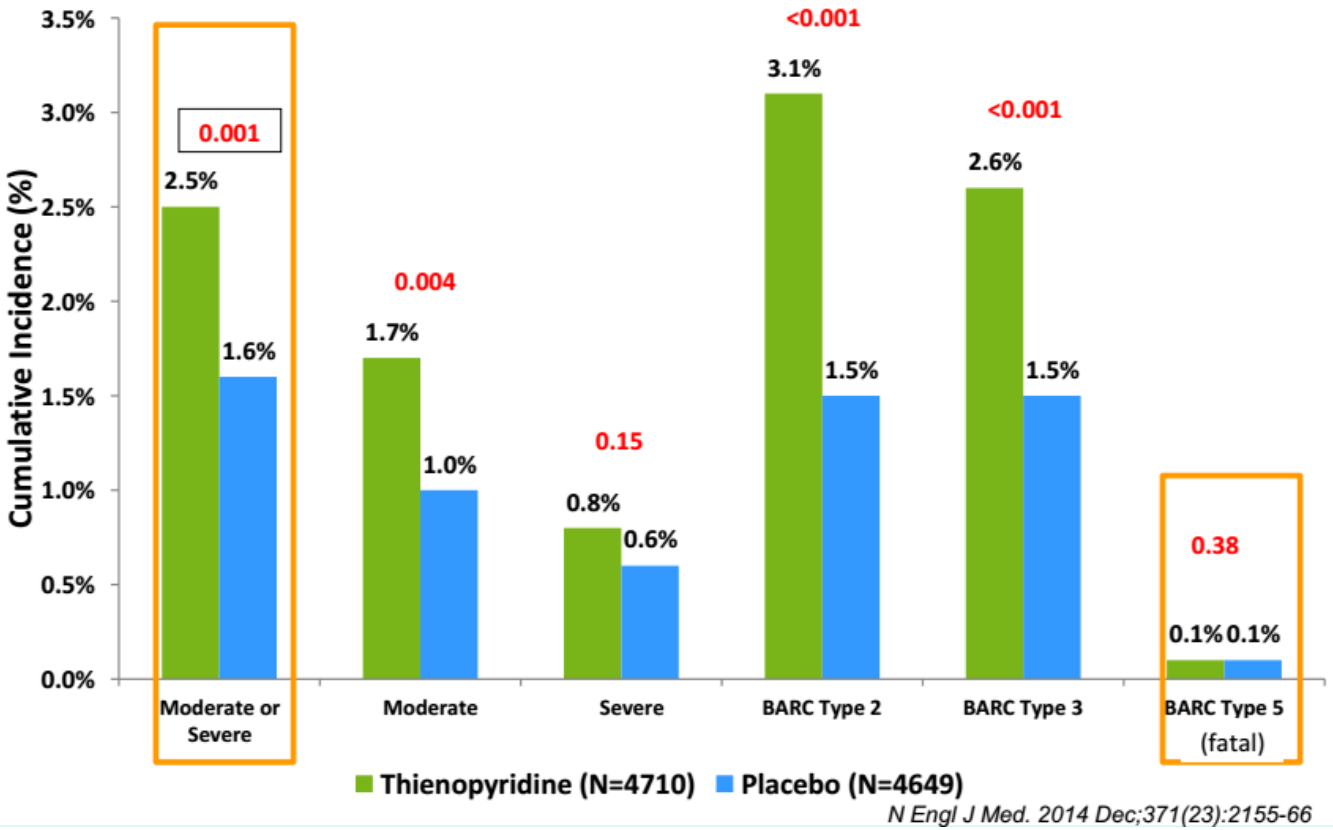
- N= 11648 total, 9961 DES treated randomized, 452 sites worldwide
- Continuing dual antiplatelet therapy beyond 12 months after coronary stenting reduced ischemic complications



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

DAPT STUDY

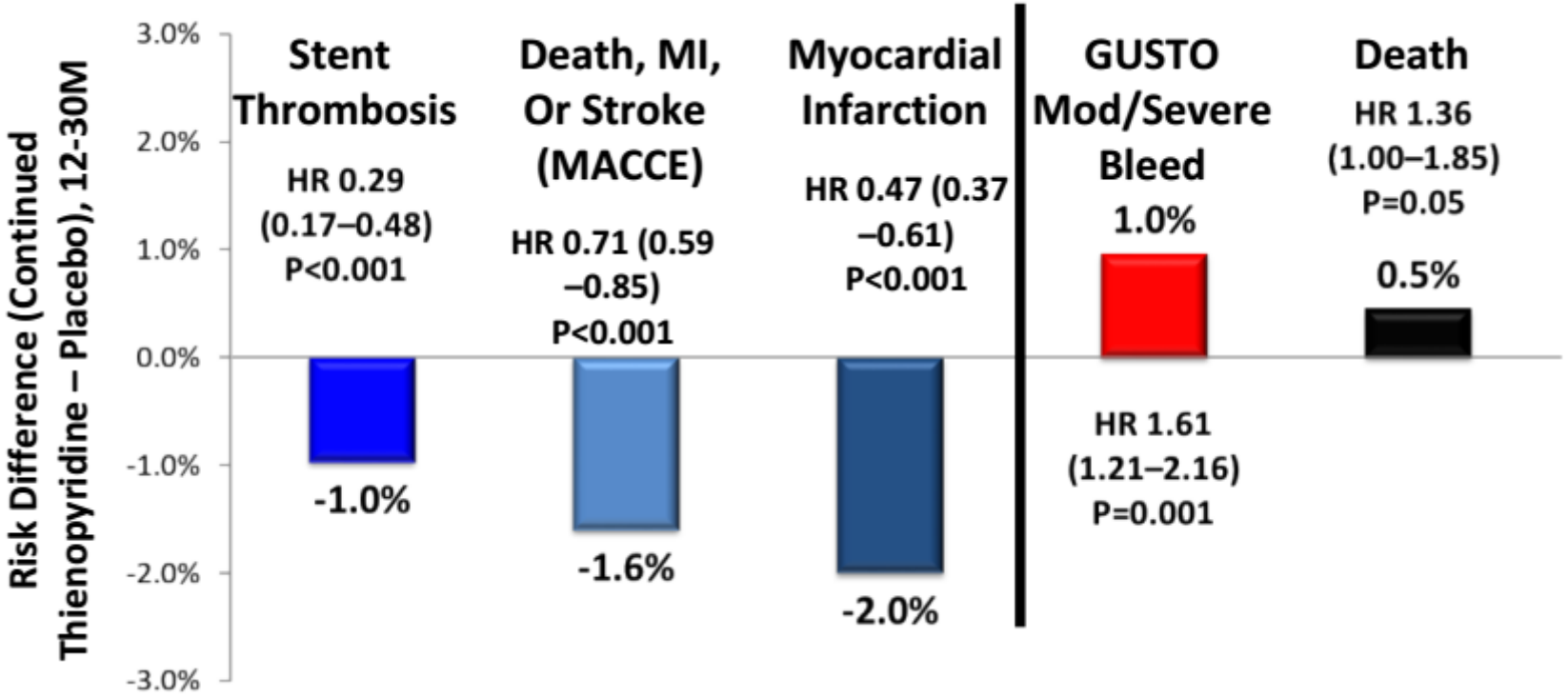
Primary Safety End Point (Moderate or Severe Bleeding): 12-30 Months



N Engl J Med. 2014 Dec;371(23):2155-66

DAPT STUDY

Continued Thienopyrine vs Placebo 1 year after PCI (N=11648)

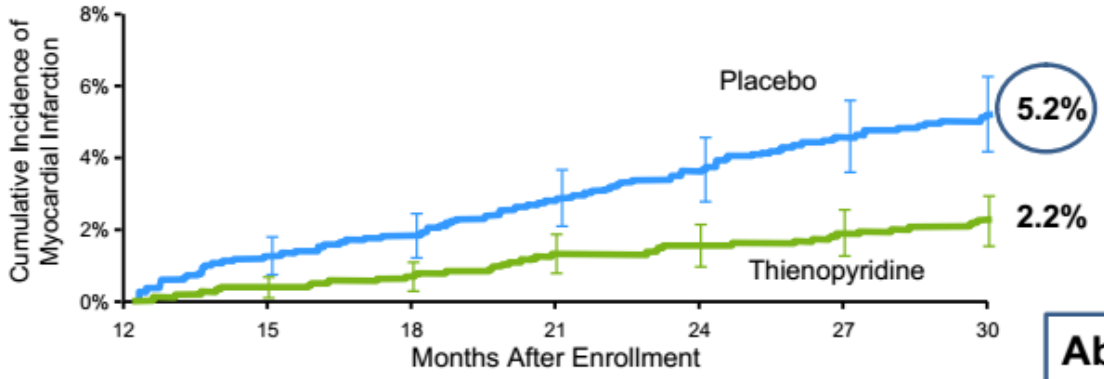


Mauri et al. NEJM. 2014 Dec 4:371:2155-66.

DAPT STUDY

Effect of Continued DAPT on MI by ACS presentation 1 year prior to randomization

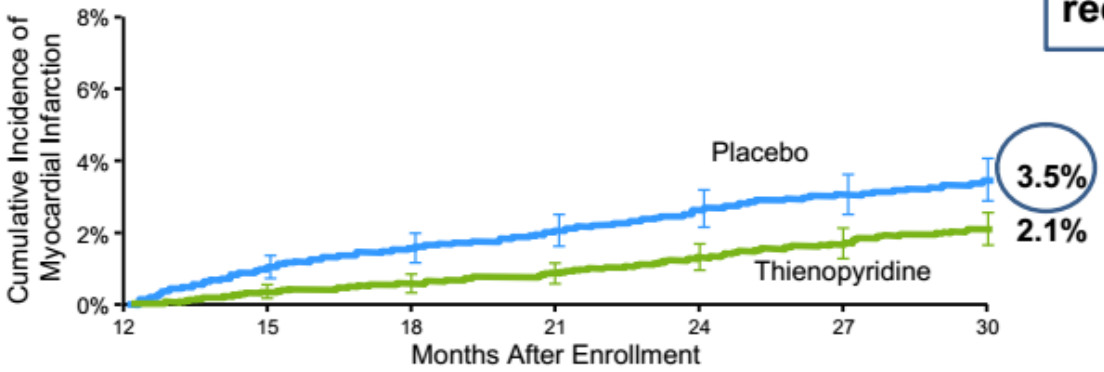
ACS Patients N=3576



HR 0.42 (0.29-0.62)
p<0.001

Absolute reduction greater in ACS, relative reduction similar

Non-ACS Patients N=8072

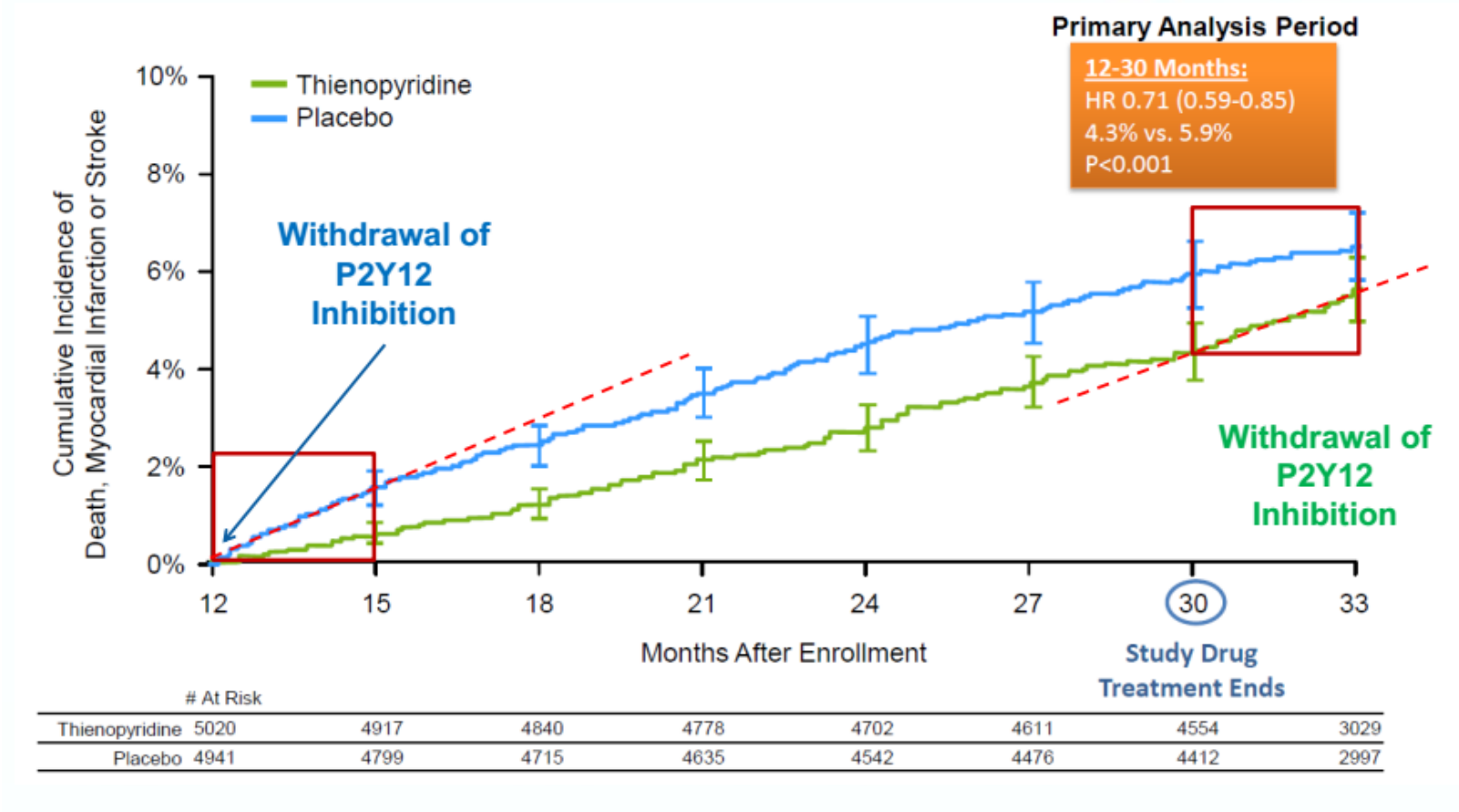


HR 0.60 (0.45-0.79)
p<0.001
P int =NS

Yeh et al., J Am Coll Cardiol. 2015 May 26

DAPT STUDY

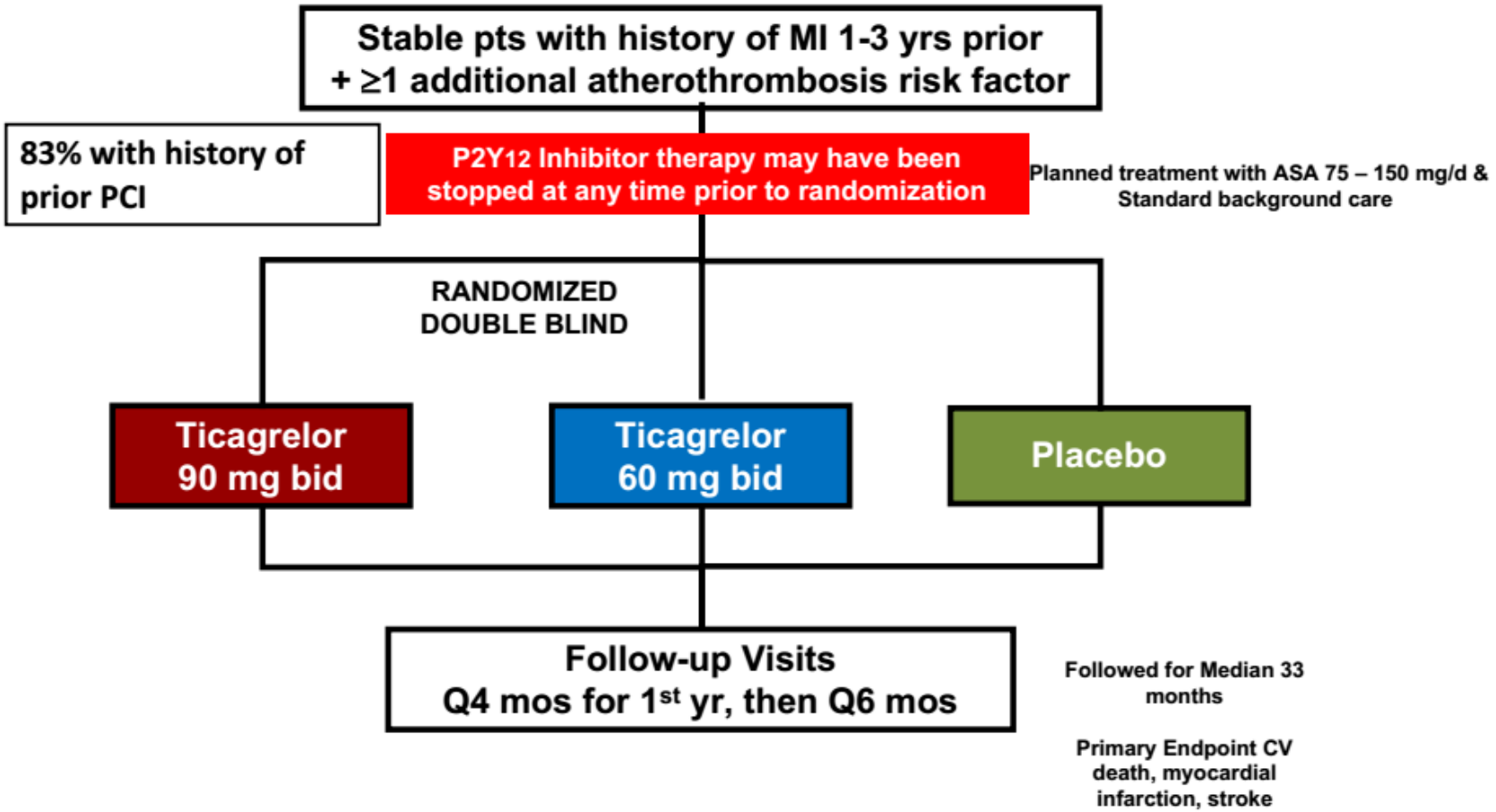
DAPT: Withdrawal of Thienopyridine 12 Months after Coronary Stenting



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

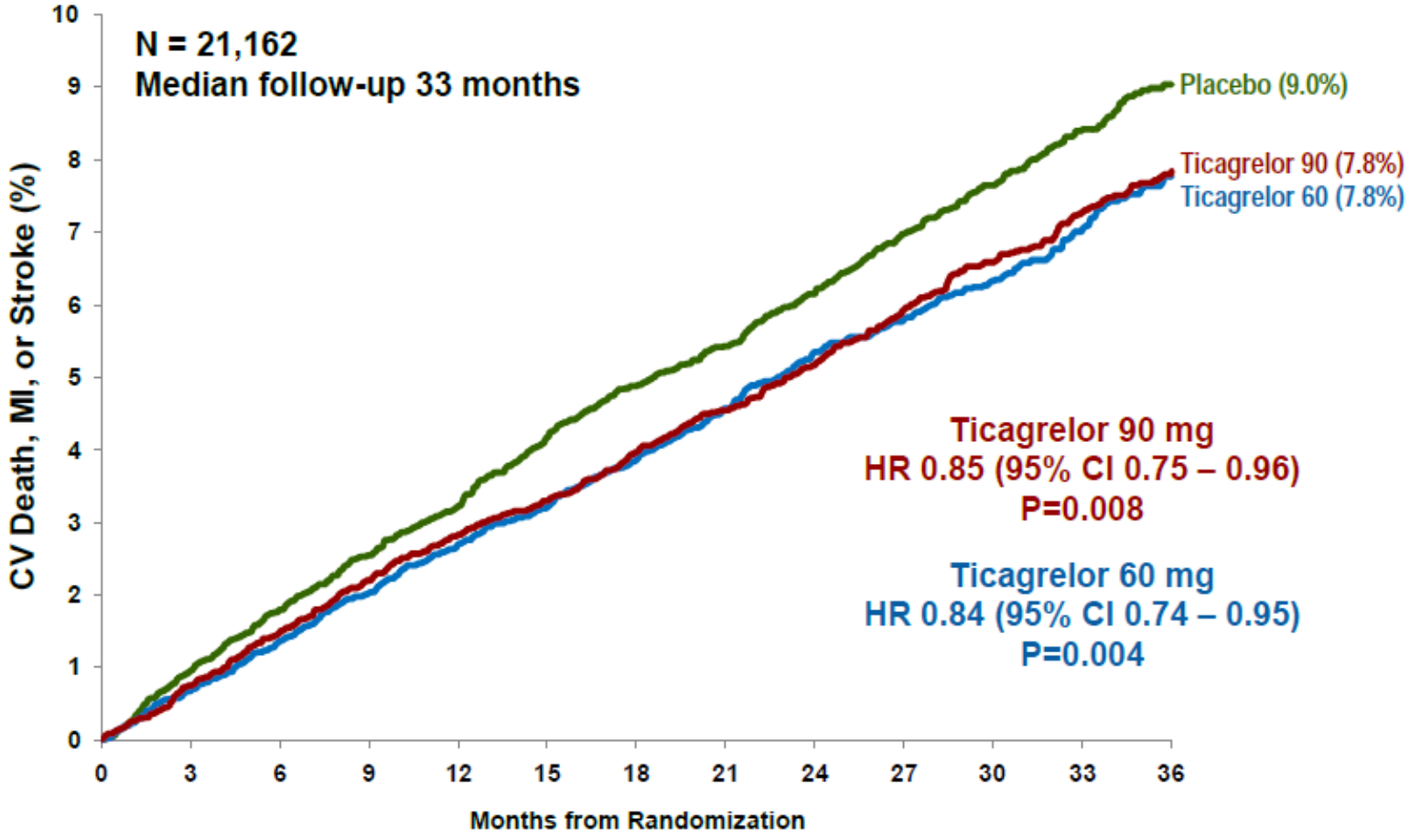
Mauri et al. NEJM 2014

Ticagrelor vs Placebo 1-3 y after MI



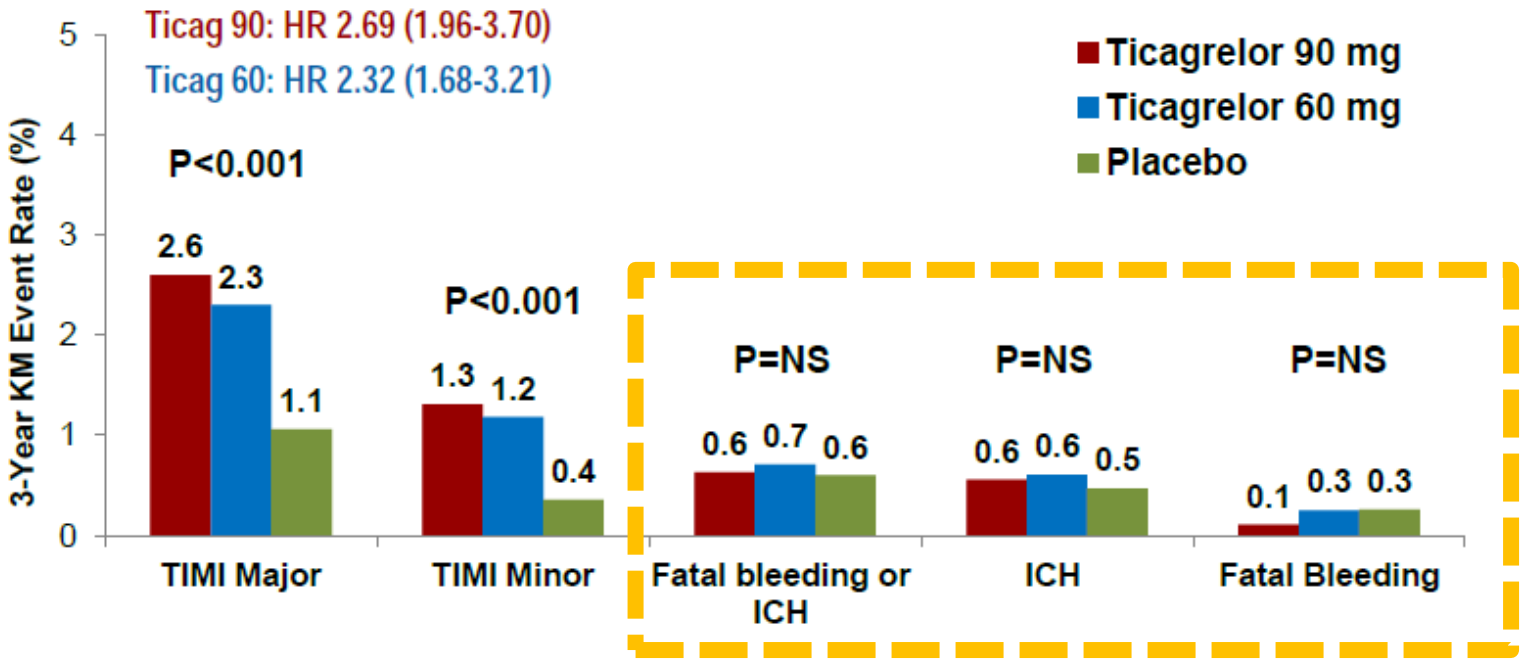
Bonaca MP et al. NEJM 2015

Primary Endpoint



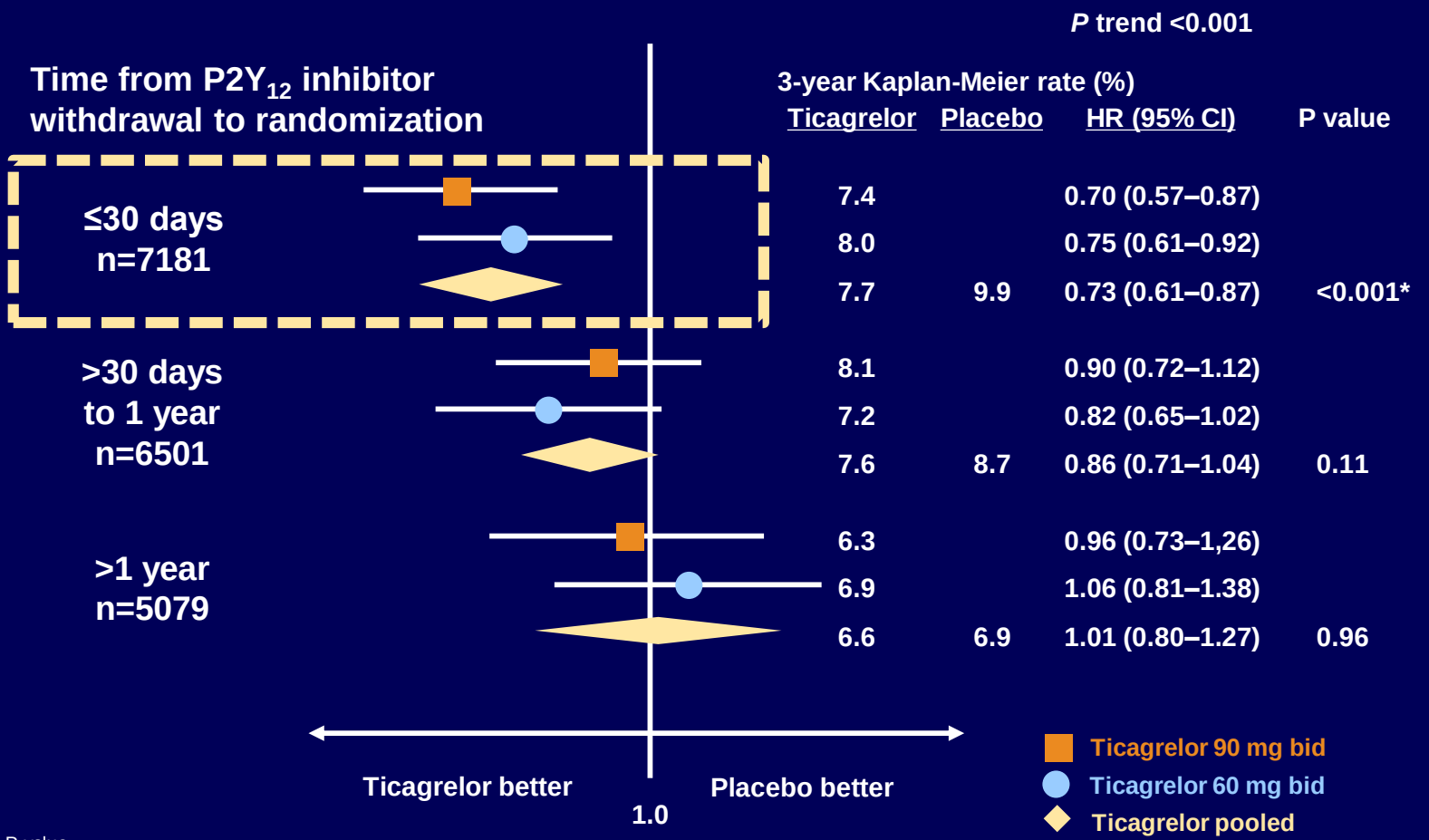
Bonaca et al. NEJM 2015 May 7;372(19):1791-800

Bleeding



Bonaca et al. NEJM 2015 May 7;372(19):1791-800

PEGASUS-TIMI 54: Effect of Ticagrelor on the Composite of CV Death, MI and Stroke at 3 years by Time from $P2Y_{12}$ Withdrawal



*Indicates nominal P value

Bonaca MP *et al. Eur Heart J* 2016;37:1133–1142

Efficacy and safety with ticagrelor in patients with prior myocardial infarction in the approved European label

Subgroup analysis from PEGASUS-TIMI 54

Background

- The CHMP-EMA approved European label recommends that after the initial 1-year treatment with ticagrelor 90 mg bid in ACS patients, treatment with ticagrelor 60 mg bid may be started without interruption as continuation therapy
  - Treatment can also be initiated up to 2 years from the MI, or within 1 year after stopping previous ADP receptor inhibitor treatment
- This subgroup analysis reports on the efficacy and bleeding safety in the PEGASUS-TIMI 54 sub-population recommended for treatment in the European label

*Age ≥65 years, diabetes mellitus, second prior MI, multivessel CAD or chronic non-end-stage renal disease

Ticagrelor EU label http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/001241/human_med_001398.jsp&mid=WC0b01ac058001d125
Dellborg M et al. *Eur Heart J* 2017;38(suppl):794–795. Abs P3670 (Presented at ESC 2017)

Methods

≤2 years from their qualifying MI OR ≤1 year from prior ADP receptor inhibitor treatment

- PEGASUS-TIMI 54 randomized 21,162 patients who had an MI 1–3 years earlier to ticagrelor, at a dose of 90 or 60 mg bid, or placebo (on a background of low dose ASA 75–150 mg daily)
- **More than 75% of the study population (16,153 patients) were ≤2 years from their qualifying MI or ≤1 year from prior ADP receptor inhibitor treatment**
- Out of these, 5388 were randomized to ticagrelor 60 mg bid and 5391 to placebo
- Hazard ratios, 95% confidence intervals and two-sided *P* values were generated using the Cox proportional hazards model. The cumulative proportions of patients with events at 36 months were calculated by the Kaplan–Meier method

Dellborg M et al. *Eur Heart J* 2017;38(suppl):794–795. Abs P3670 (Presented at ESC 2017)

PEGASUS-TIMI 54 EU label population

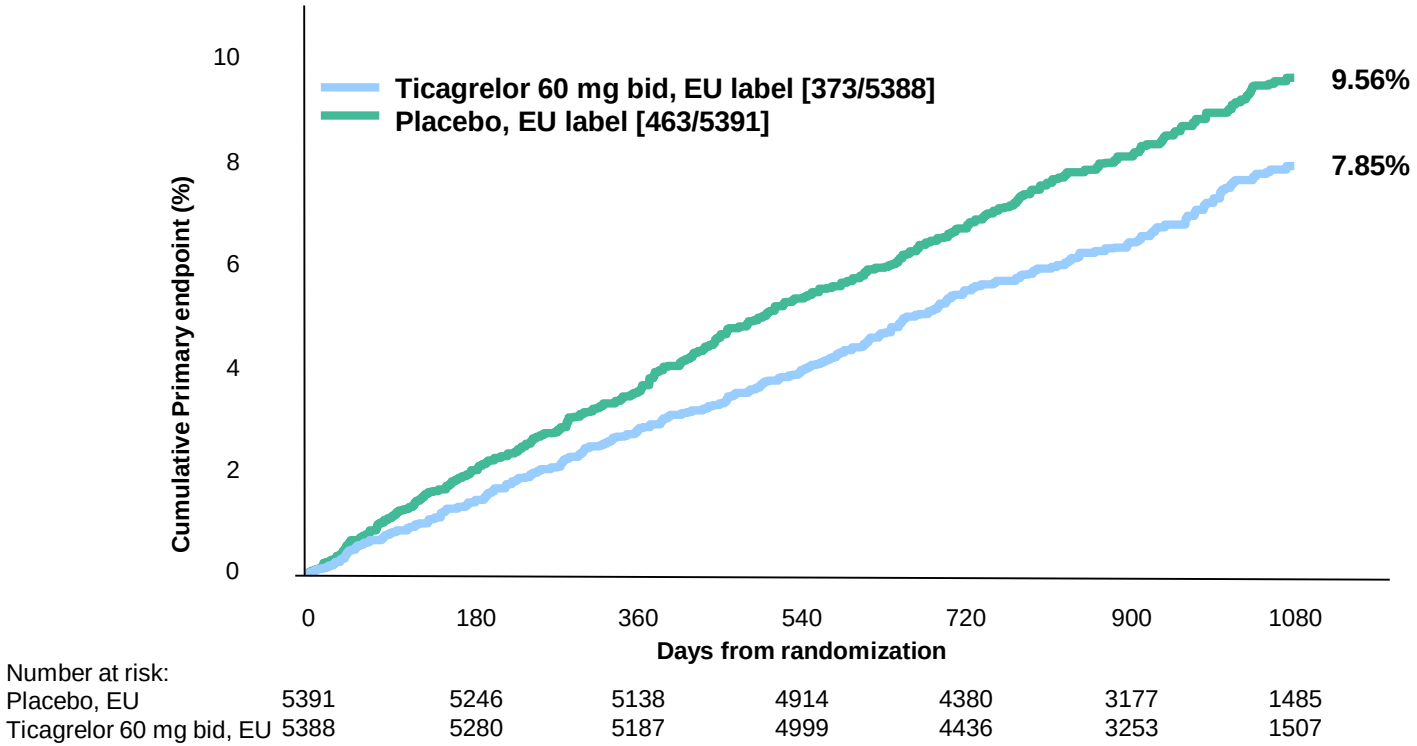
Primary and secondary outcomes – patients with ≤2 years from qualifying MI or ≤1 year from prior ADP receptor inhibitor treatment (efficacy cohort)

Outcome	Ticagrelor 60 mg bid N=5388		Placebo N=5391		Hazard ratio (95% CI)	*P* value
	n	3 year KM%	n	3 year KM%		
Composite of CV death, MI or stroke	373	7.9	463	9.6	0.80 (0.70–0.91)	0.001
CV death	119	2.6	167	3.6	0.71 (0.56–0.90)	0.0041
MI	230	4.8	274	5.6	0.83 (0.70–0.99)	0.041
Stroke	71	1.5	95	2.0	0.74 (0.55–1.01)	0.058
All-cause mortality	206	4.4	256	5.4	0.80 (0.67–0.96)	0.018

Dellborg M et al. *Eur Heart J* 2017;38(suppl):794–795. Abs P3670 (Presented at ESC 2017)

PEGASUS-TIMI 54 EU label population

- **Primary endpoint by time since qualifying MI and prior ADP receptor inhibitor**



The EU label subgroup includes patients with ≤2 years from qualifying MI or ≤1 year from last dose of prior ADP receptor inhibitor treatment to randomization. All patients received low dose ASA (75–150mg daily)

Dellborg M et al. *Eur Heart J* 2017;38(suppl):794–795. Abs P3670
(Presented at ESC 2017)

PEGASUS-TIMI 54 EU label population

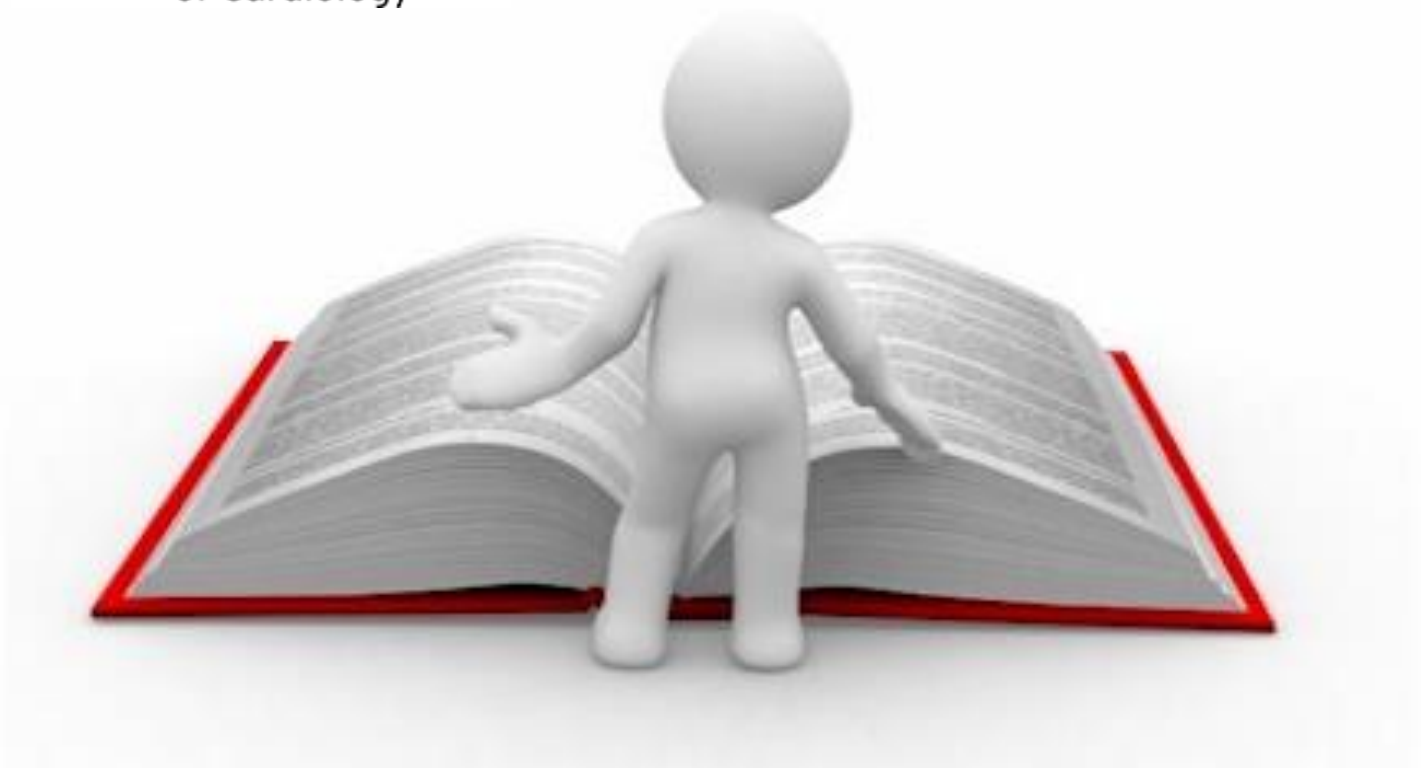
- **Major bleeding events – patients with ≤2 years from qualifying MI or ≤1 year from prior ADP receptor inhibitor treatment (safety cohort)**

Outcome	Ticagrelor 60 mg bid N=5322		Placebo N=5331		Hazard ratio (95% CI)	*P* value
	n	3 year KM%	n	3 year KM%		
TIMI major bleeding	94	2.5	43	1.1	2.36 (1.65–3.39)	<0.0001
Fatal or intracranial bleeding	27	0.8	25	0.7	1.17 (0.68–2.01)	0.58

Dellborg M et al. *Eur Heart J* 2017;38(suppl):794–795. Abs P3670 (Presented at ESC 2017)

What Guidelines say?

ESC
European Society
of Cardiology



Dual antiplatelet therapy duration in patients with acute coronary syndrome treated with percutaneous coronary intervention *(continued)*

ESC European Society of Cardiology

Recommendations	Class	Level
In patients with ACS who have tolerated DAPT without a bleeding complication, continuation of DAPT for longer than 12 months may be considered.	IIb	A
In patients with MI and high ischaemic risk who have tolerated DAPT without a bleeding complication, ticagrelor 60 mg *b.i.d.* for longer than 12 months on top of aspirin may be preferred over clopidogrel or prasugrel.	IIb	B

2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS
(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

From Clinical Trials to Clinical Practice…

DAPT STUDY

PEGASUS TIMI 54

Position paper ANMCO: Gestione della dimissione ospedaliera

Mauro Mennuni[1] (Coordinatore), Michele Massimo Gulizia[2] (Coordinatore), Gianfranco Alunni[3], Antonio Francesco Amico[4], Francesco Maria Bovenzi[5], Roberto Caporale[6], Furio Colivicchi[7], Andrea Di Lenarda[8], Giuseppe Di Tano[9], Sabrina Egman[10], Francesco Fattirolli[11], Domenico Gabrielli[12], Giovanna Geraci[13], Giovanni Gregorio[14], Gian Francesco Mureddu[15], Federico Nardi[16], Donatella Radini[8], Carmine Riccio[17], Fausto Rigo[18], Marco Sicuro[19], Stefano Urbinati[20], Guerrino Zuin[18]

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G Ital Cardiol 2016;17(9):657-686

La «*Buona*» Dimissione

Tabella 25. Standard educativi da completare prima della dimissione per il paziente con sindrome coronarica acuta.

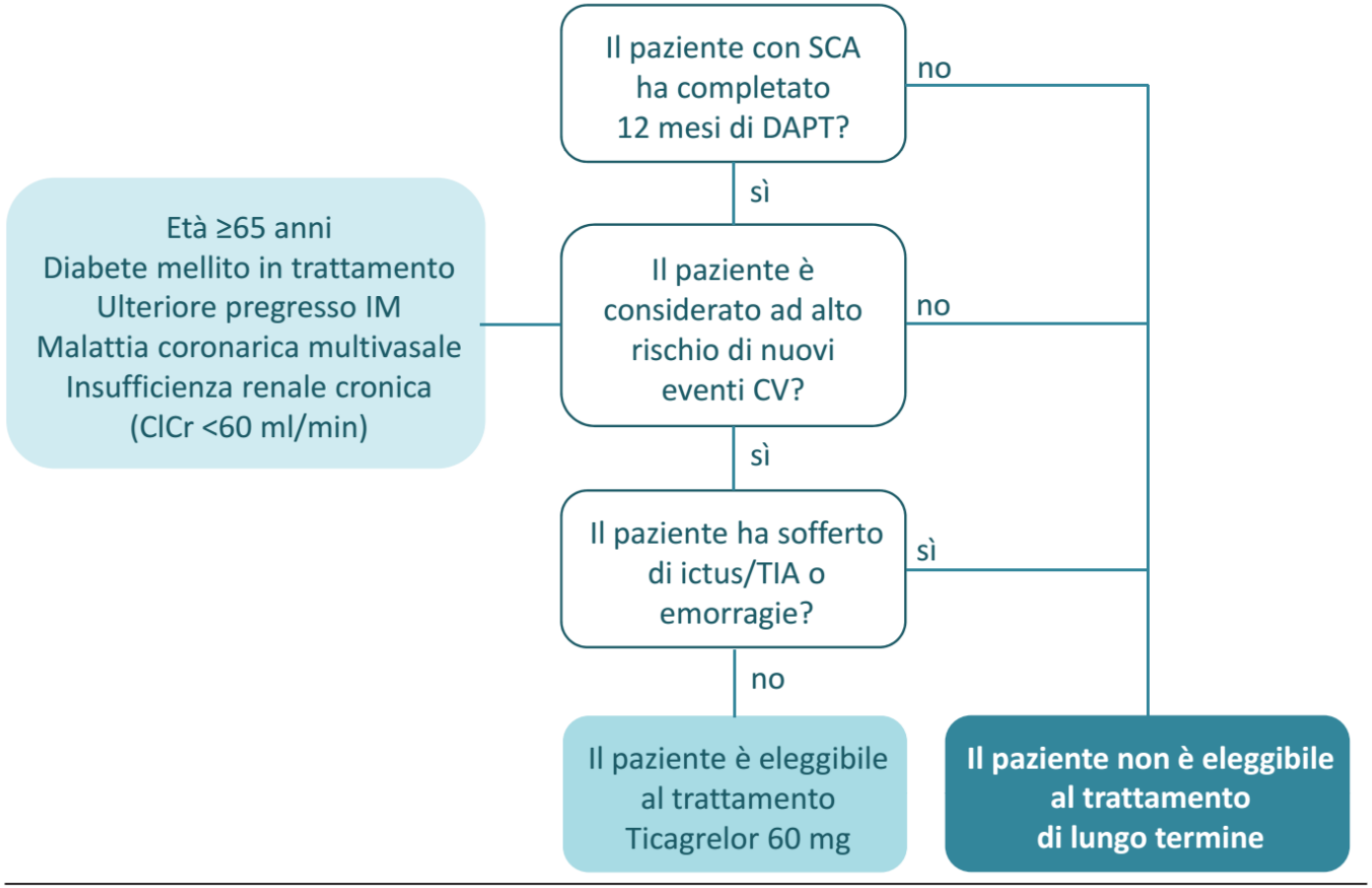
- Spiegazione
  - della diagnosi e delle procedure da effettuare
  - dei farmaci, del loro dosaggio, della loro azione; uso dei nitrati perlinguali
  - delle conseguenze gravi della sospensione dei farmaci
  - del piano d'azione in caso di recidiva di dolore toracico
  - dell'importanza del follow-up
  - dei fattori di rischio e importanza della loro correzione
  - del fumo come fattore di rischio cardiovascolare
- Riesame
  - delle indicazioni dietetiche
  - del programma di esercizi fisici domiciliari
  - dell'importanza della riabilitazione
- Tempistica
  - del ritorno al lavoro
  - della guida di veicoli
  - dell'attività sessuale
- Il paziente ha compreso e condiviso il piano di cura

Tabella 17. Informazioni da raccogliere per la ricognizione terapeutica.

- Nome commerciale e/o principio attivo
- Forma farmaceutica
- Dosaggio
- Posologia giornaliera
- Data di inizio e durata della terapia
- Data e ora dell'ultima dose assunta
- Via di somministrazione
- Trattamenti a carattere sperimentale
- Assunzione di omeopatici, fitoterapici e integratori
- Presenza di allergie o intolleranze
- Terapie pregresse ed eventuali effetti indesiderati
- Assunzione di alimenti (pompelmo, caffè, tè, frutta e verdura) che possano interferire con la terapia
- Peso e altezza del paziente
- Eventuale assunzione di alcool, fumo e uso di droghe
- Utilizzo di dispositivi medici medicati
- Ogni altro dato ritenuto significativo

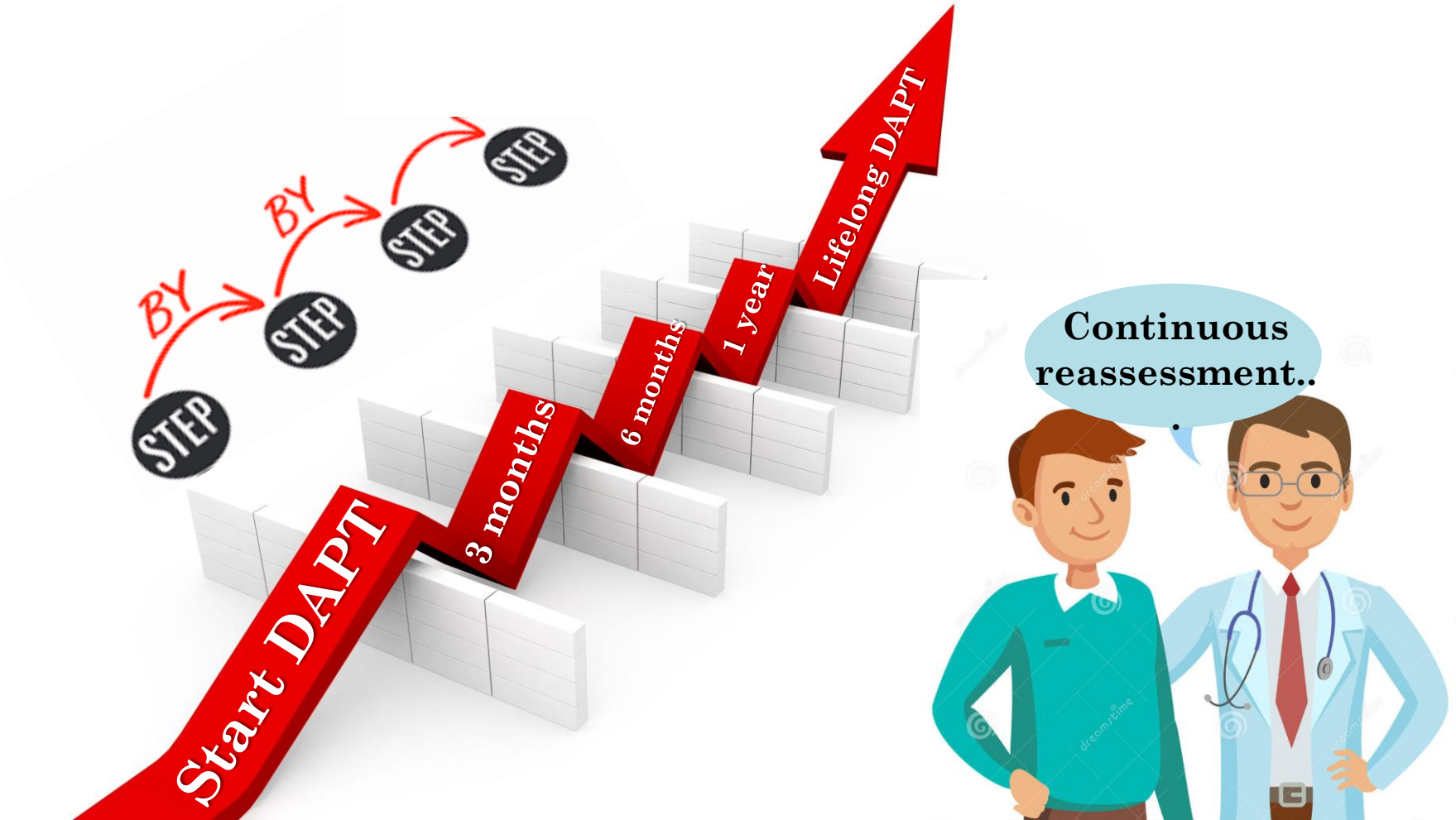
G Ital Cardiol 2016;17(9):657-686

Flow-chart decisionale

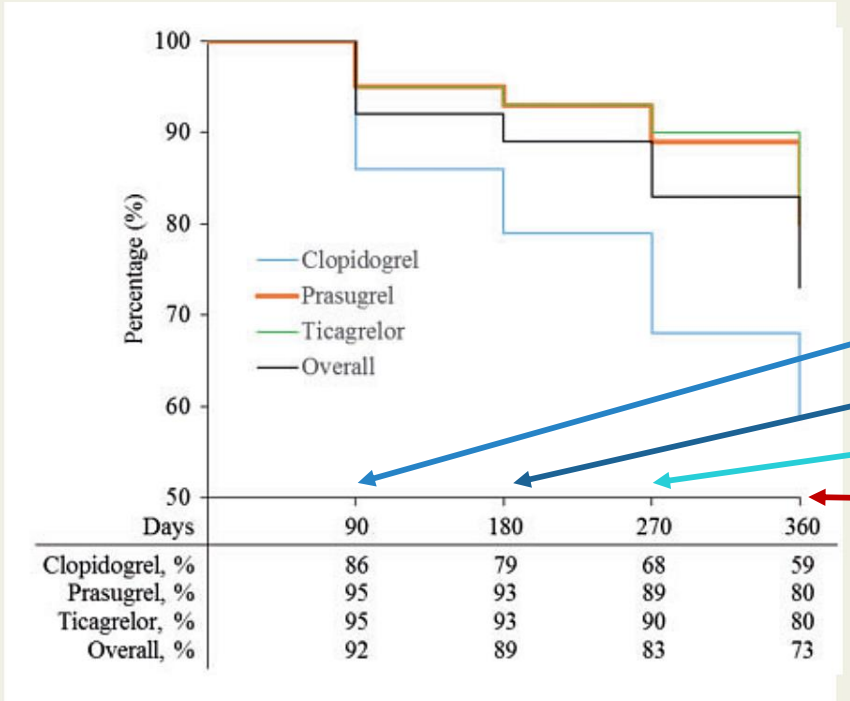


G Ital Cardiol (Rome). 2018 May;19(5):263-331.

The risk for bleeding is dynamic and could change over time…



Real-world insights on treatment duration of antiplatelets in ACS



Days	90	180	270	360
Clopidogrel, %	86	79	68	59
Prasugrel, %	95	93	89	80
Ticagrelor, %	95	93	90	80
Overall, %	92	89	83	73

Figure 2 Persistence of medication during the treatment course for the analysed population ($n = 295$), by OAP type and overall. *n*, number of patients; OAP, oral antiplatelet.

Proportion of patients still using oral antiplatelets:

After 90 days = 92%

After 180 days = 89%

After 270 days = 83%

After 360 days = 73%

Claeys et al. EHJ Cardiov Pharm (2017) 3, 189–197

Real-world insights on treatment duration of antiplatelets in ACS

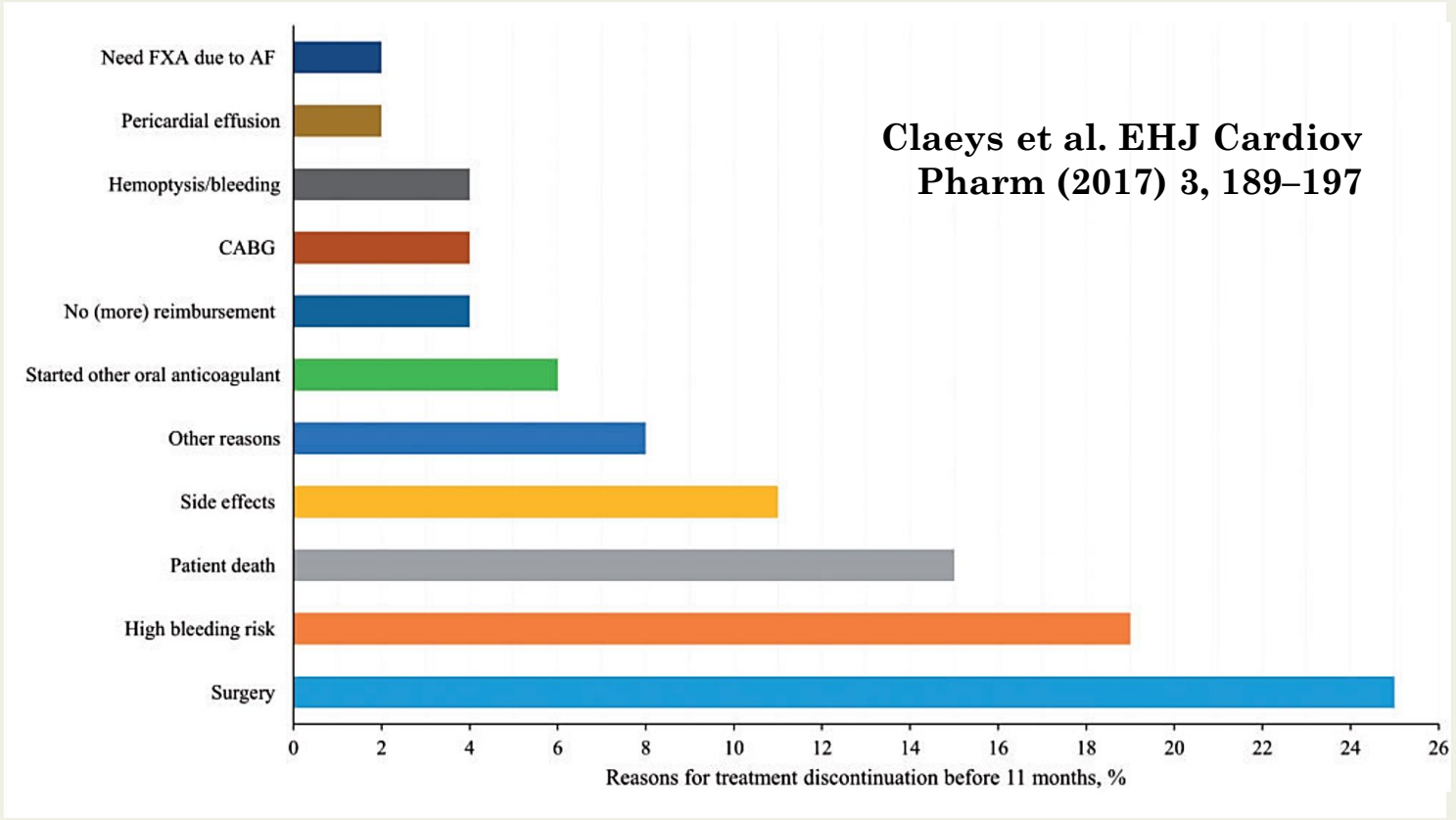
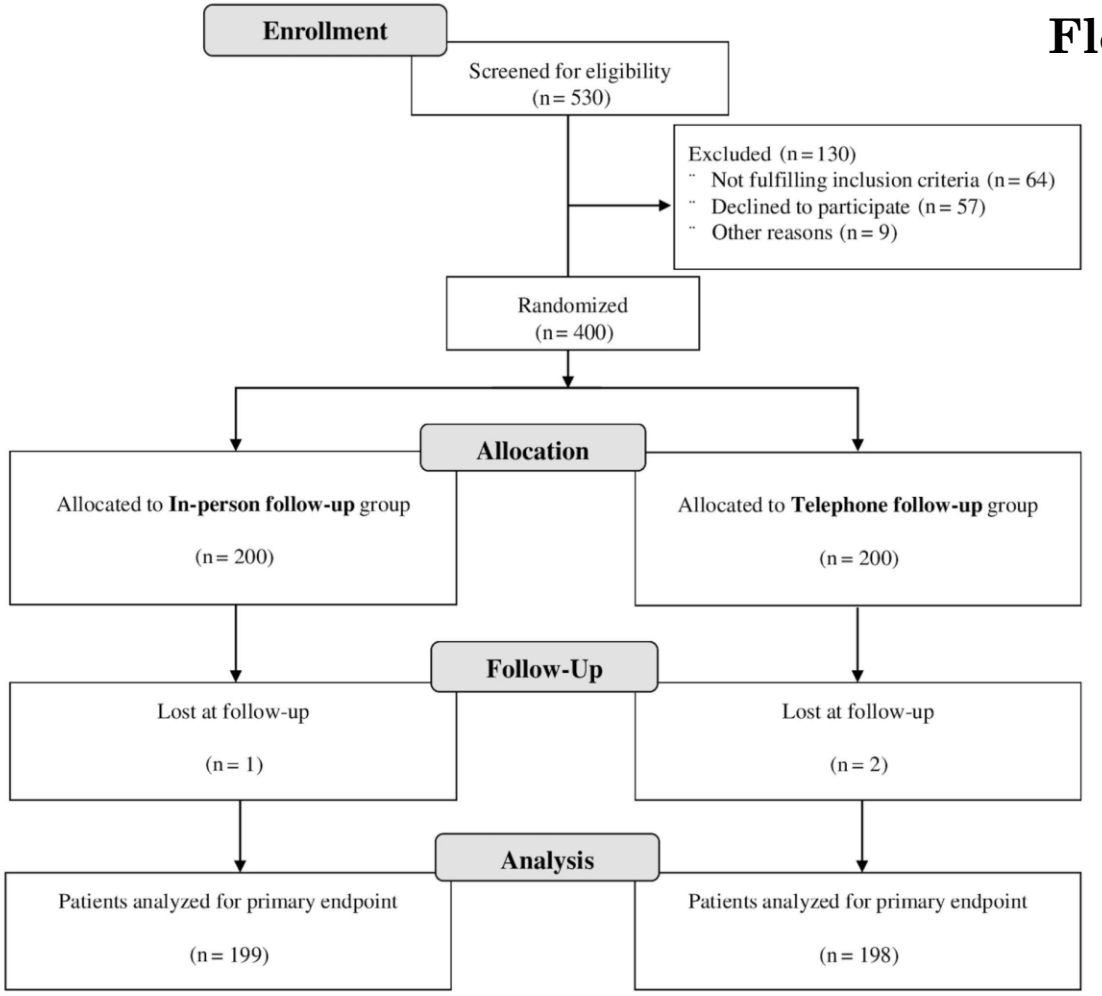


Figure 3 Reasons for stopping OAP treatment before 11 months. OAP, oral antiplatelet; CAGB, coronary artery bypass graft; FXA, coagulation factor X; AF, atrial fibrillation. Note: Other reasons were: standard practice; palliative care; no objective reasons/reasons related to patient.

Improving Adherence to Ticagrelor in Patients After Acute Coronary Syndrome: Results from the Progress Trial

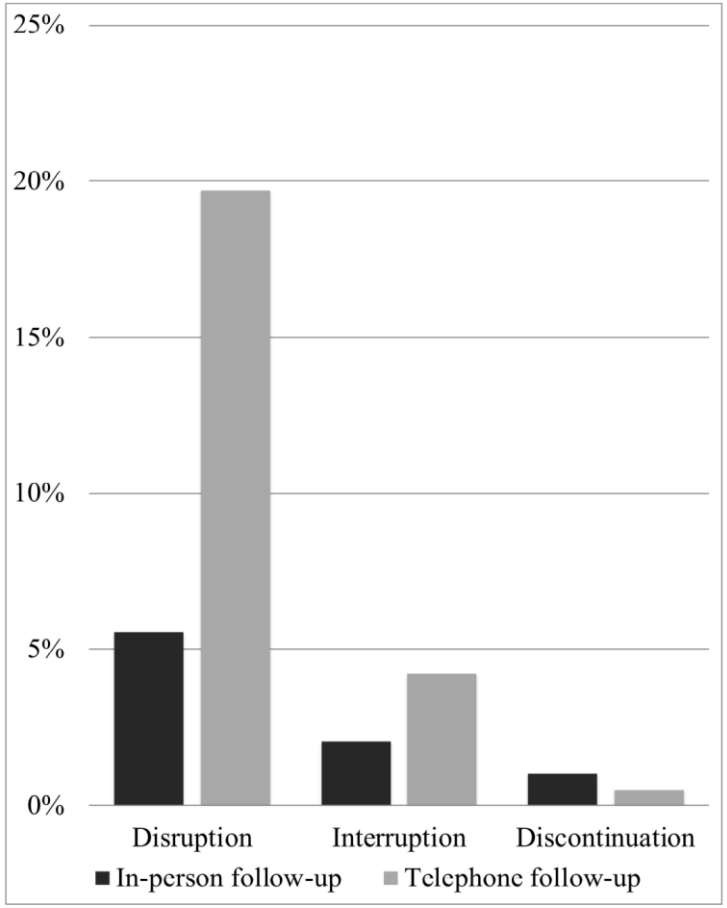
Mario Crisci[1], Felice Gragnano[2], Marco Di Maio[2], Vincenzo Diana[2], Elisabetta Moscarella[2], Ivana Pariggiano[2], Dario Di Maio[2], Claudia Concilio[2], Vittorio Taglialatela[3], Fabio Fimiani[2], Arturo Cesaro[2], Plinio Lorenzo Cirillo[3] and Paolo Calabrò[2,*]

Flow-chart of the study

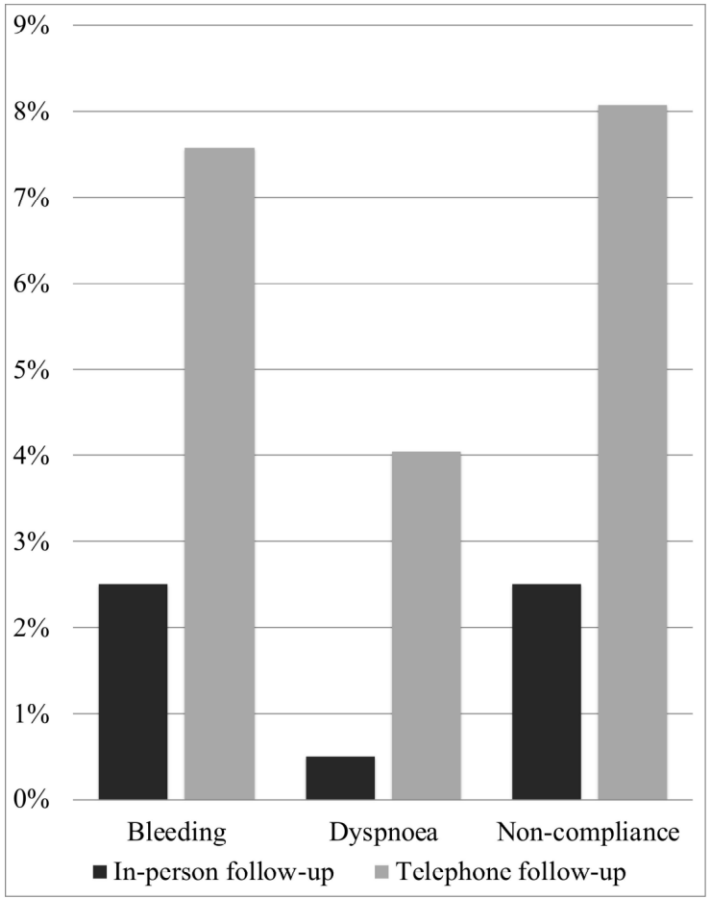


Crisci M, Calabro' P, et al. CVP 2019

Efficacy of in-person follow-up for improving Ticagrelor adherence



Rate of disrutpion, interruption and discontinuation of Ticagrelor in study groups



Causes of Ticagrelor disruption

So…how long is long enough?

- Acute Coronary Syndrome history is associated with a greater benefit vs risk for longer DAPT than all comers with PCI or CAD.
- Nonetheless, the patient course, and individual characteristics should be considered in order to balance risk and benefit.
- A more careful (in-person) follow-up strategy can effectively improve the adherence to antiplalet agents at long-term follow-up-
- Clinicians must remain aware and vigilant that risk scores, although useful, cannot be considered a clear-cut decision rule or a substitute for case-by-case critical judgment.

GRAZIE DELL'ATTENZIONE

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