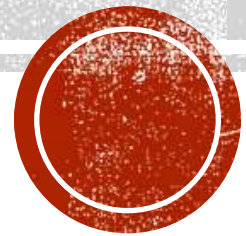
ΚΛΙΝΙΚΕΣ ΕΦΑΡΜΟΓΕΣ ΑΝΤΙΠΗΤΙΚΗΣ ΚΑΙ ΑΝΤΙΑΙΜΟΠΕΤΑΛΙΑΚΗΣ ΑΓΩΓΗΣ ΣΤΗ ΣΤΕΦΑΝΙΑΙΑ ΝΟΣΟ

ΚΑΤΣΙΑΝΗΣ ΑΝΤΩΝΙΟΣ



ΑΝΤΙΘΡΟΜΒΩΤΙΚΗ ΑΓΩΓΗ

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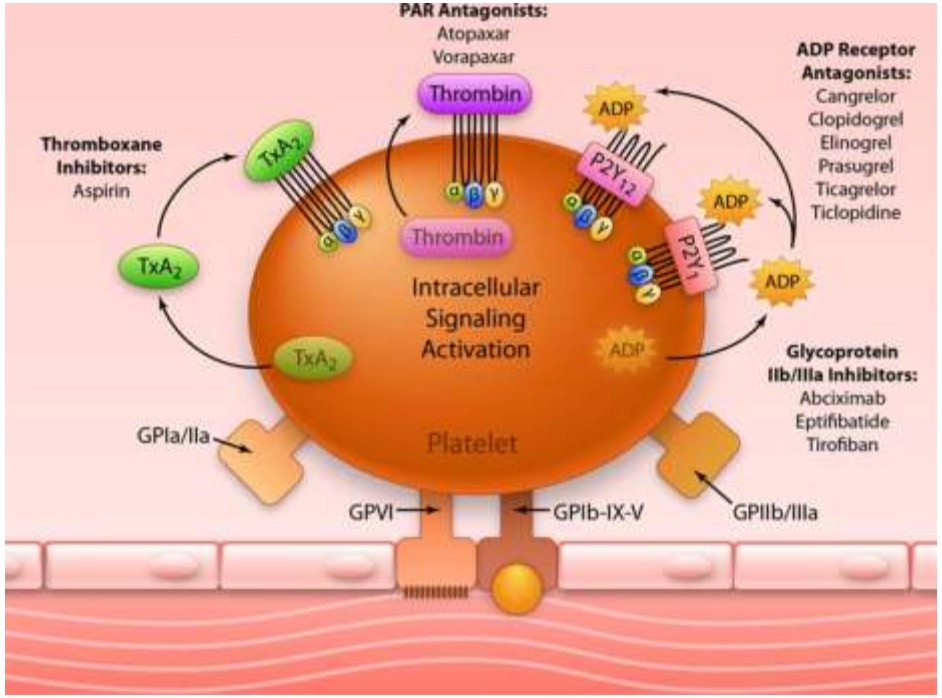

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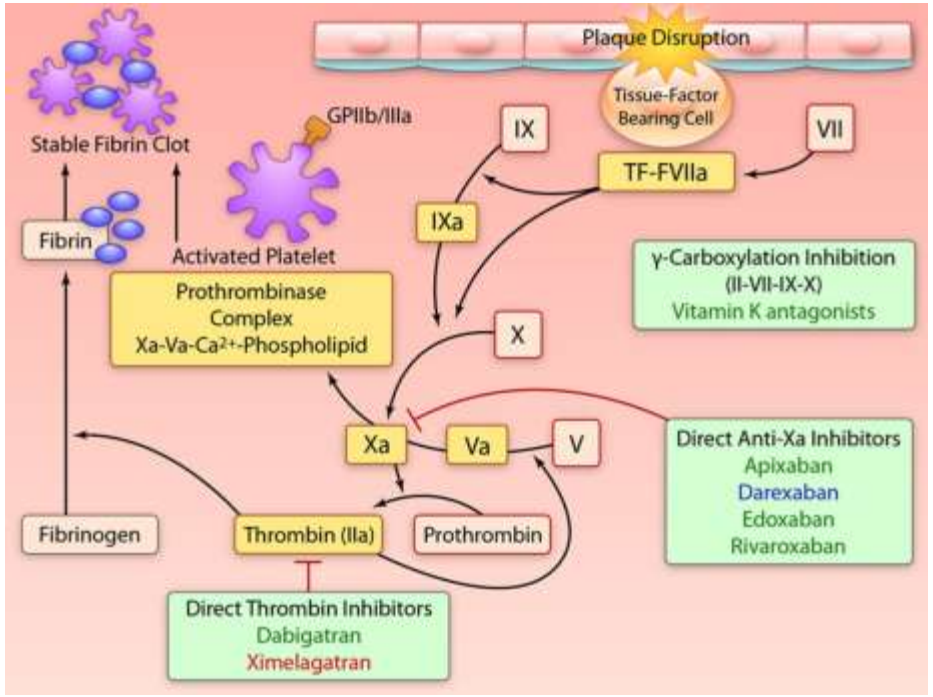
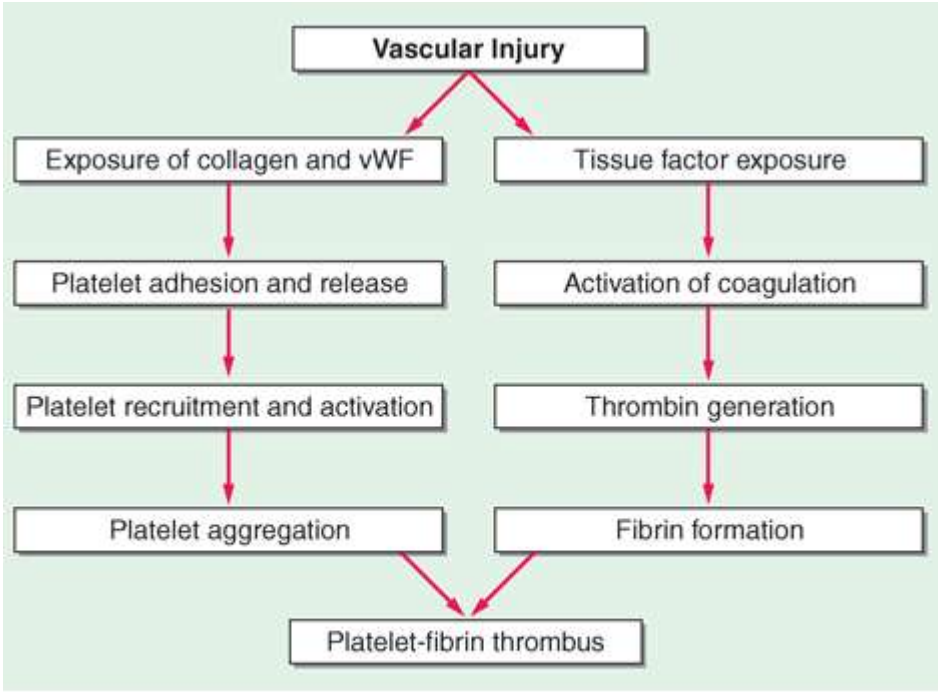


3) ΘΡΟΜΒΟΛΥΤΙΚΑ Ή ΙΝΩΔΟΛΥΤΙΚΑ ΦΑΡΜΑΚΑ

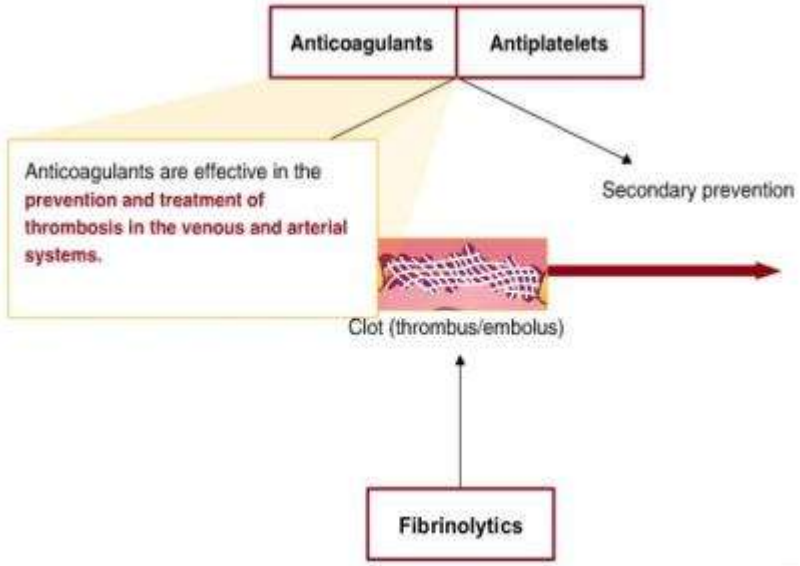
ΣΤΑΔΙΑ ΣΧΗΜΑΤΙΣΜΟΥ ΘΡΟΜΒΟΥ

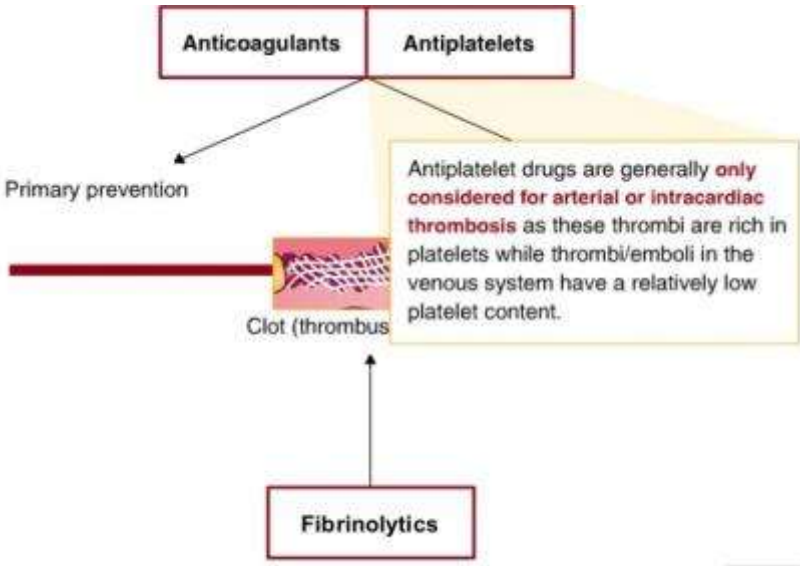
- Προσκόλληση αιμοπεταλίων
- Ενεργοποίηση αιμοπεταλίων
- Συσσώρευση αιμοπεταλίων
- Ενεργοποίηση καταρράκτη πήξης

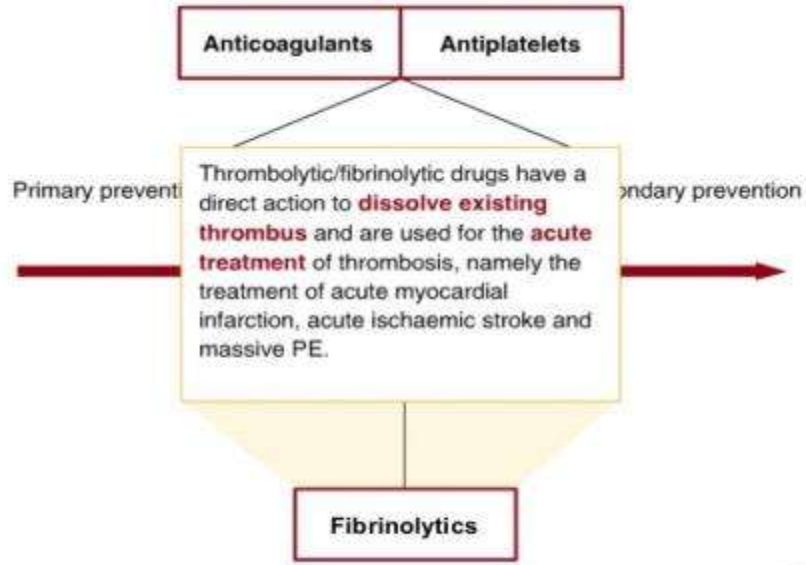


Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

ΘΕΣΕΙΣ ΔΡΑΣΗΣ ΑΝΤΙΘΡΟΜΒΩΤΙΚΩΝ







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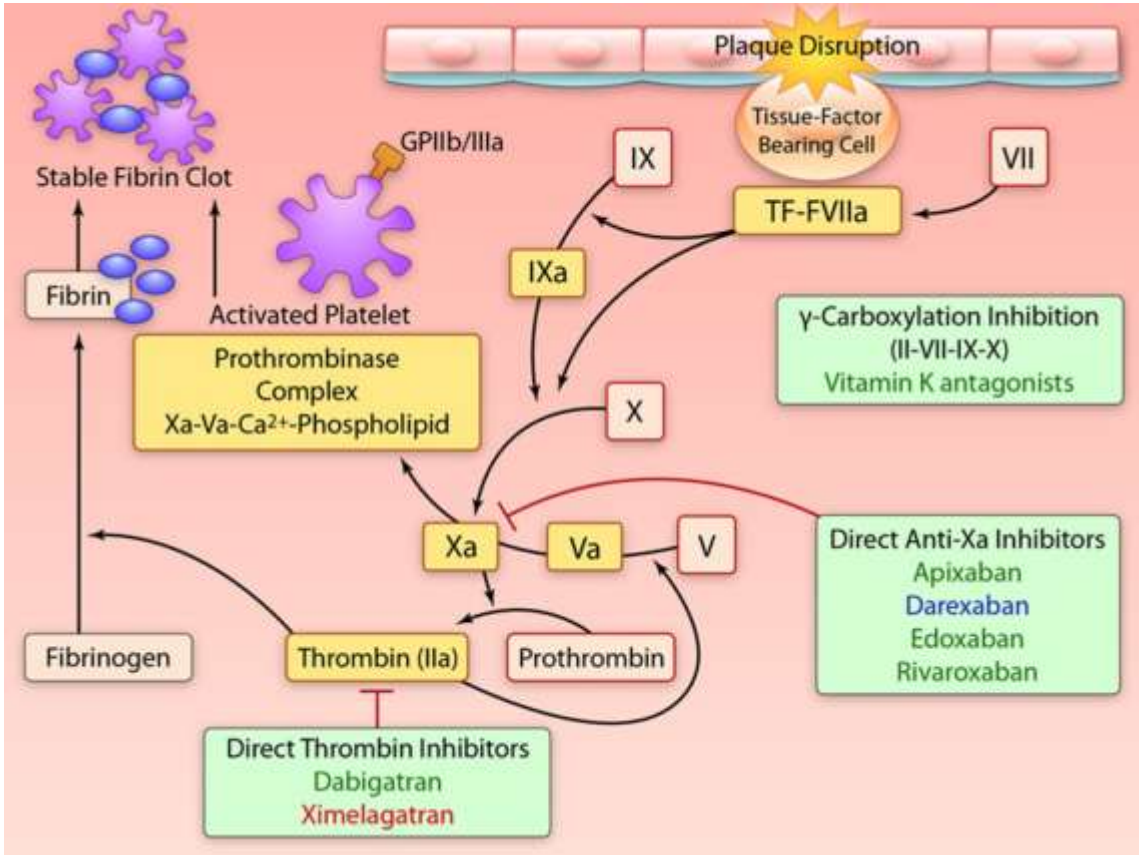

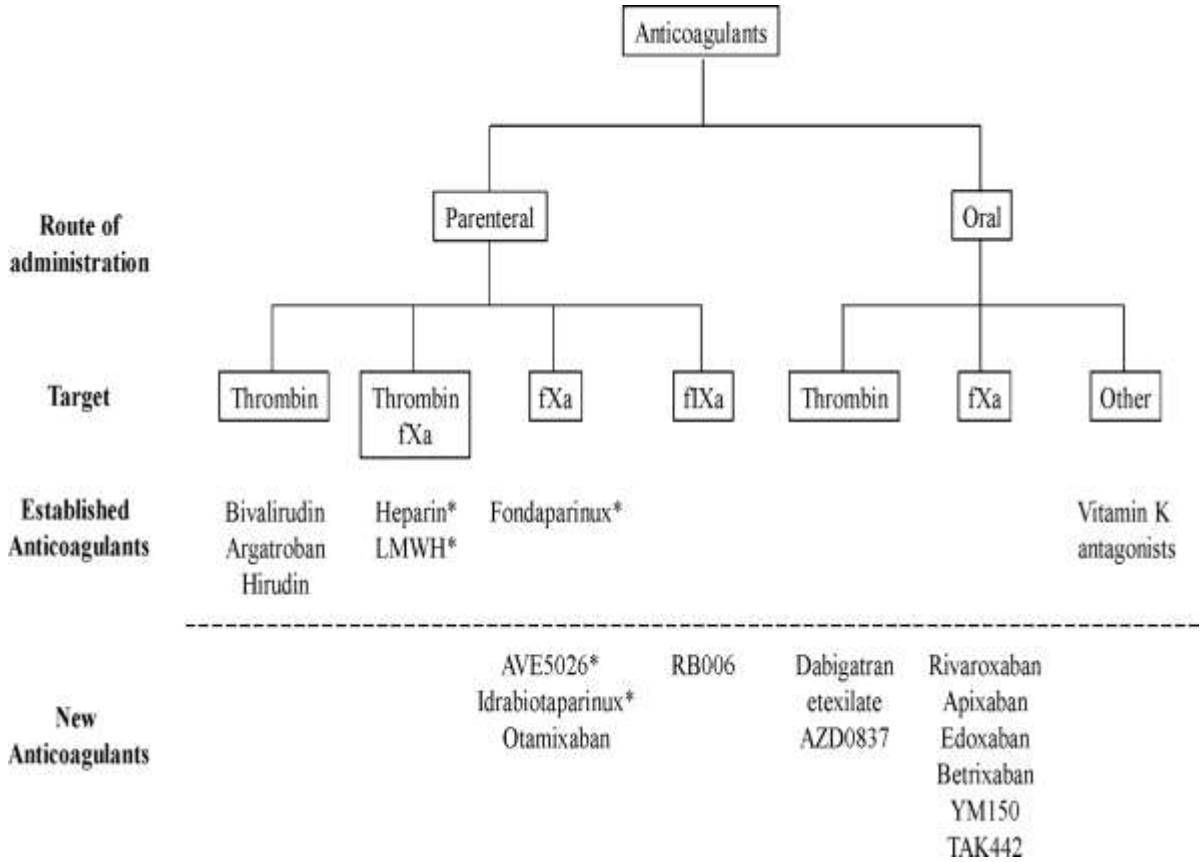

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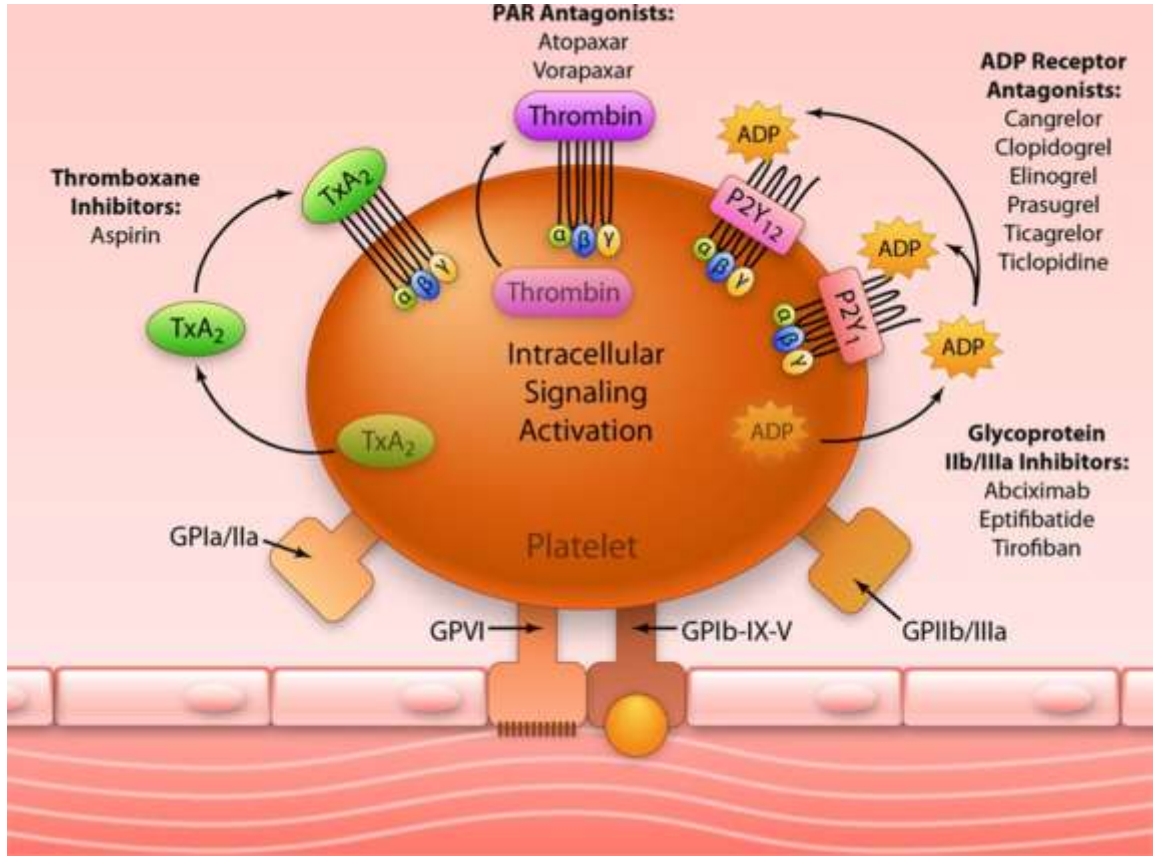
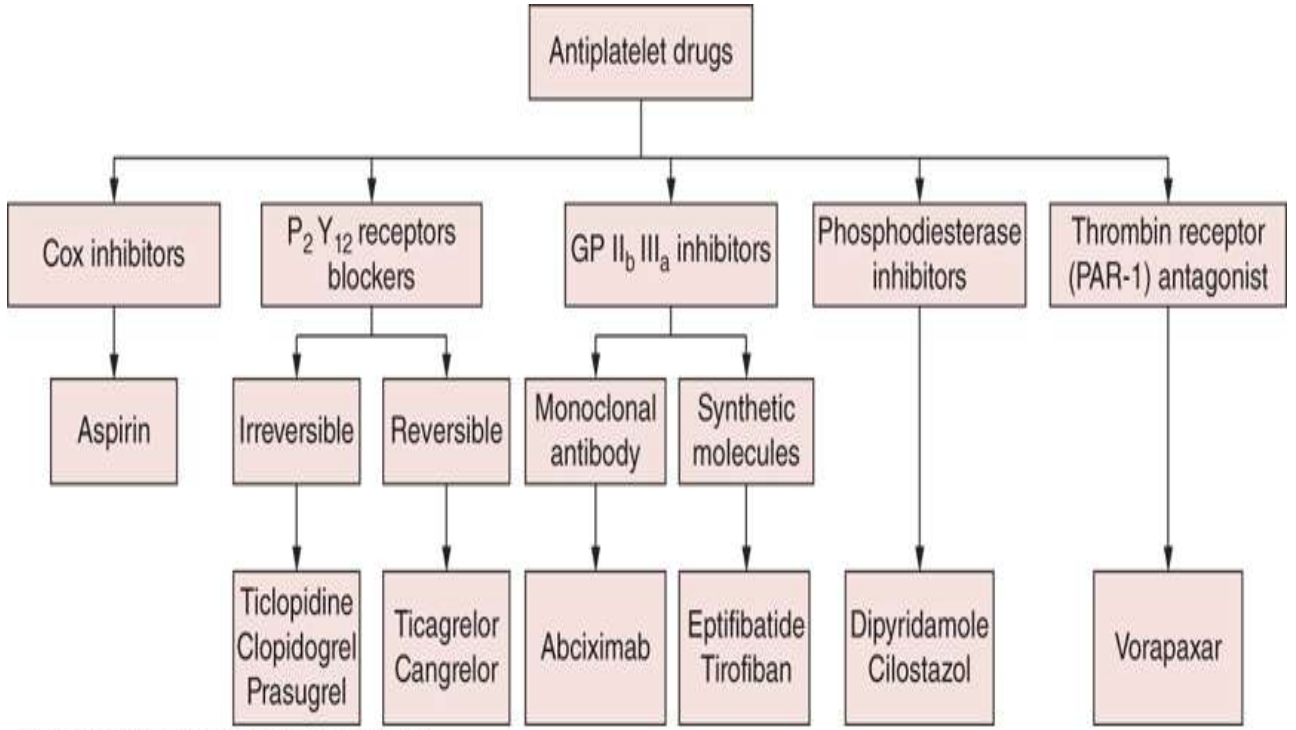
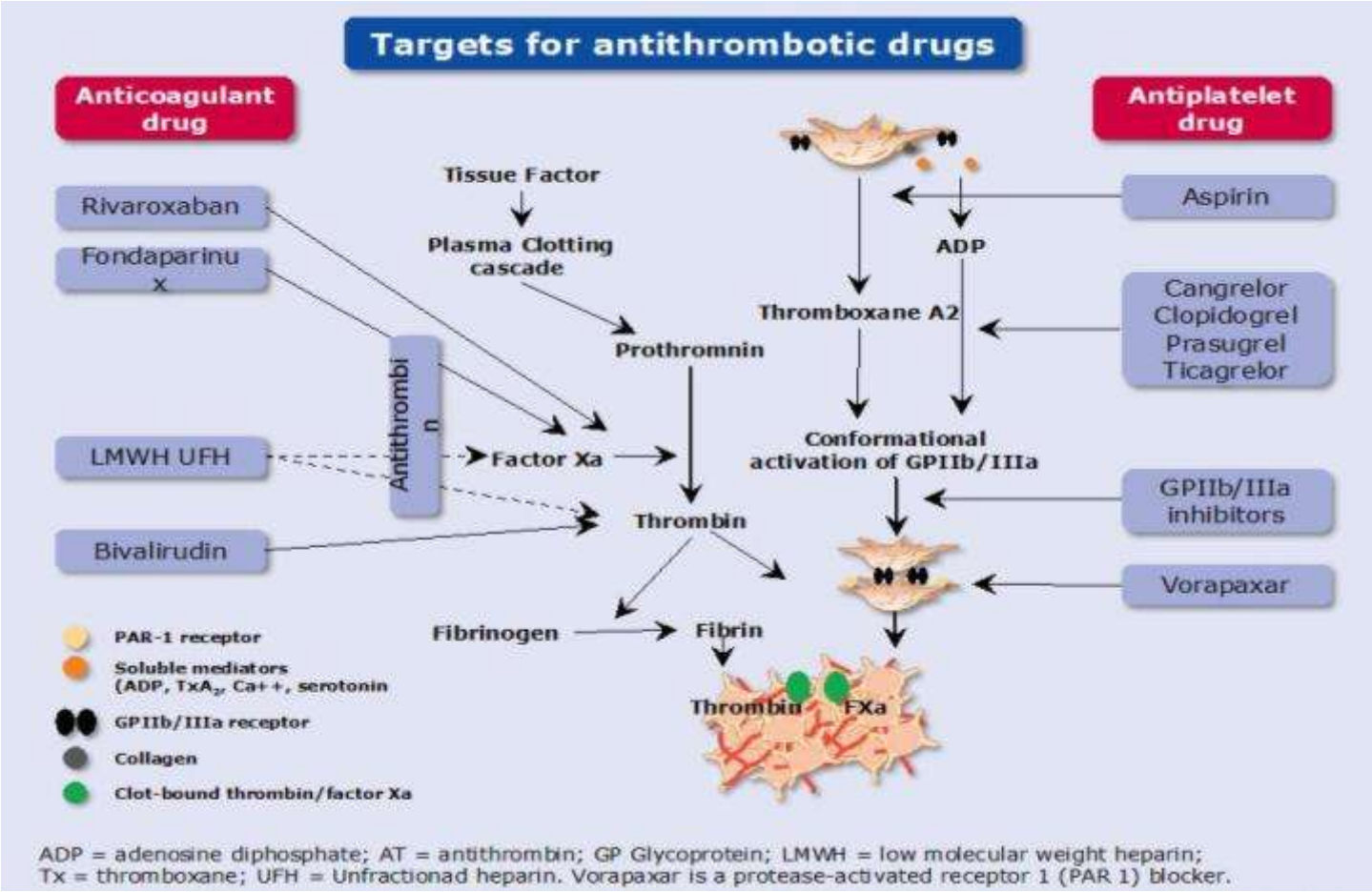




Source: Michael H. Crawford: Current Diagnosis & Treatment: Cardiology, Fifth Edition
www.cardiology.mhmedical.com

ΣΤΟΧΟΙ ΑΝΤΙΘΡΟΜΒΩΤΙΚΩΝ ΦΑΡΜΑΚΩΝ



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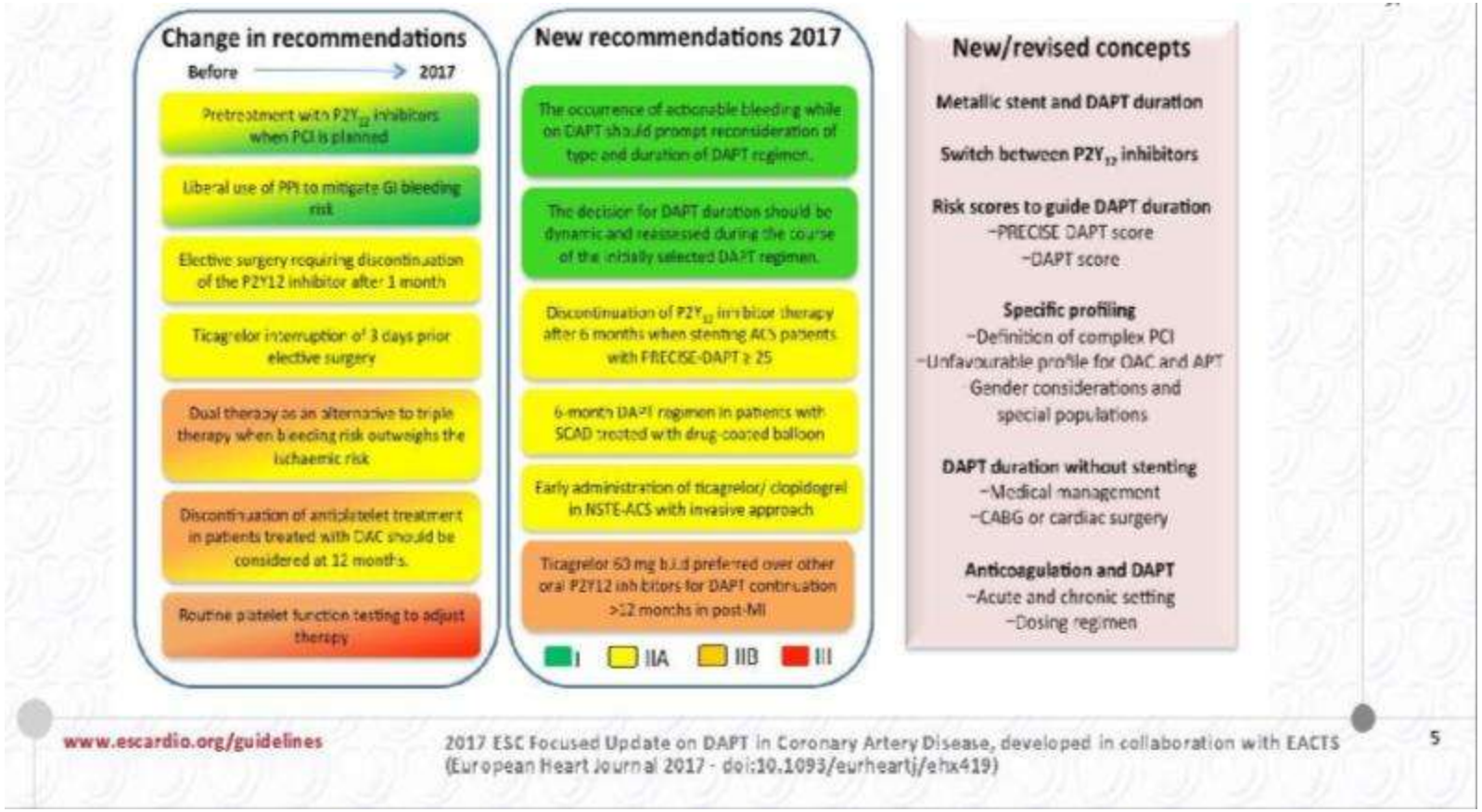
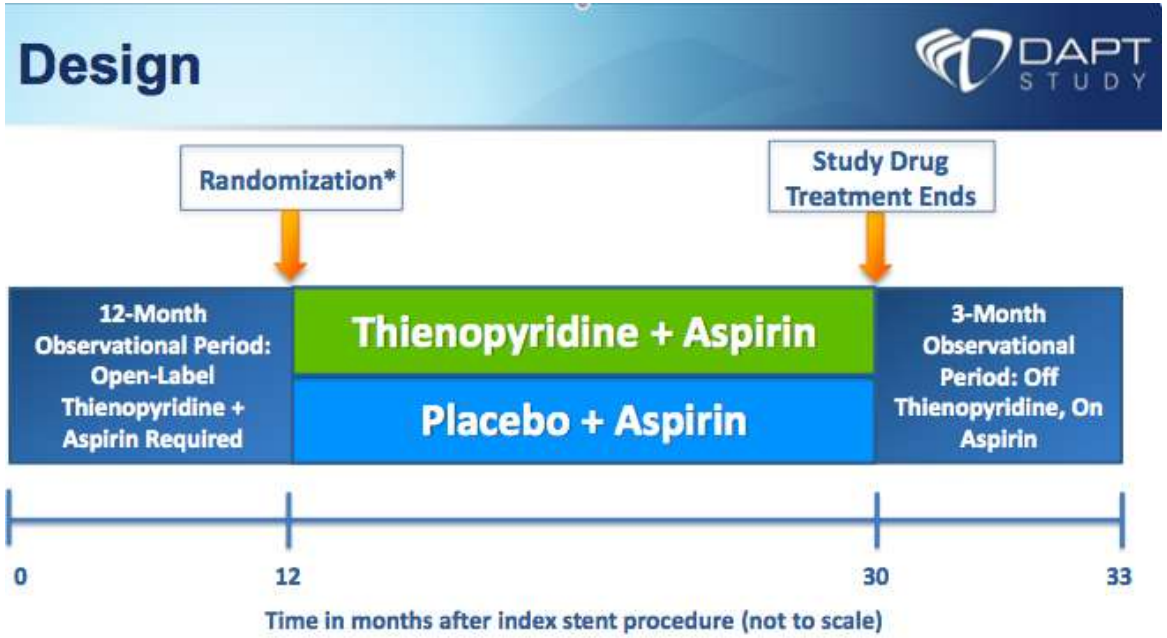


ΜΕΛΕΤΗ DAPT

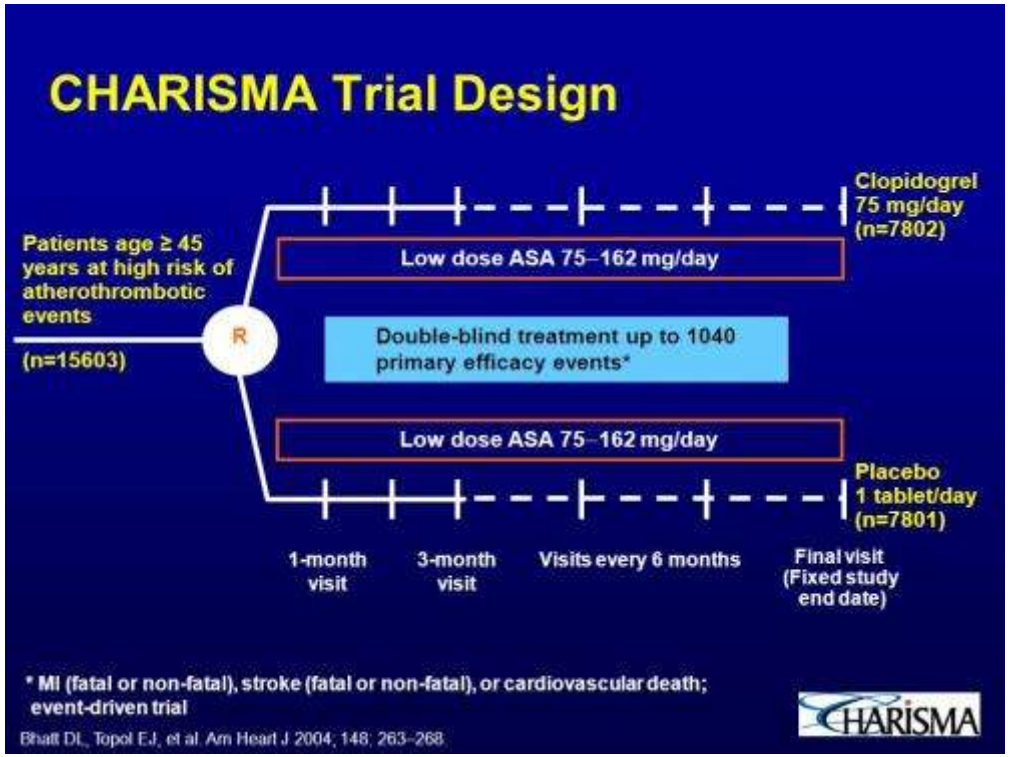


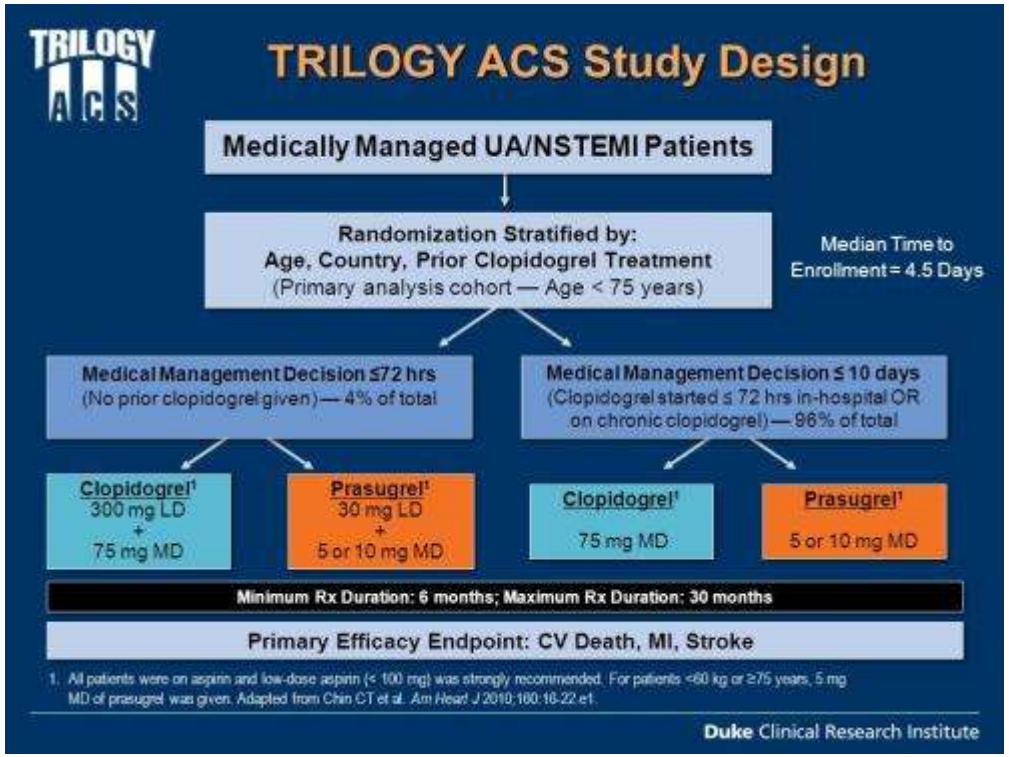
Enrolled: Subjects treated with FDA-approved DES or BMS. Subjects on oral anticoagulant therapy or with life expectancy < 3 years excluded.

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).

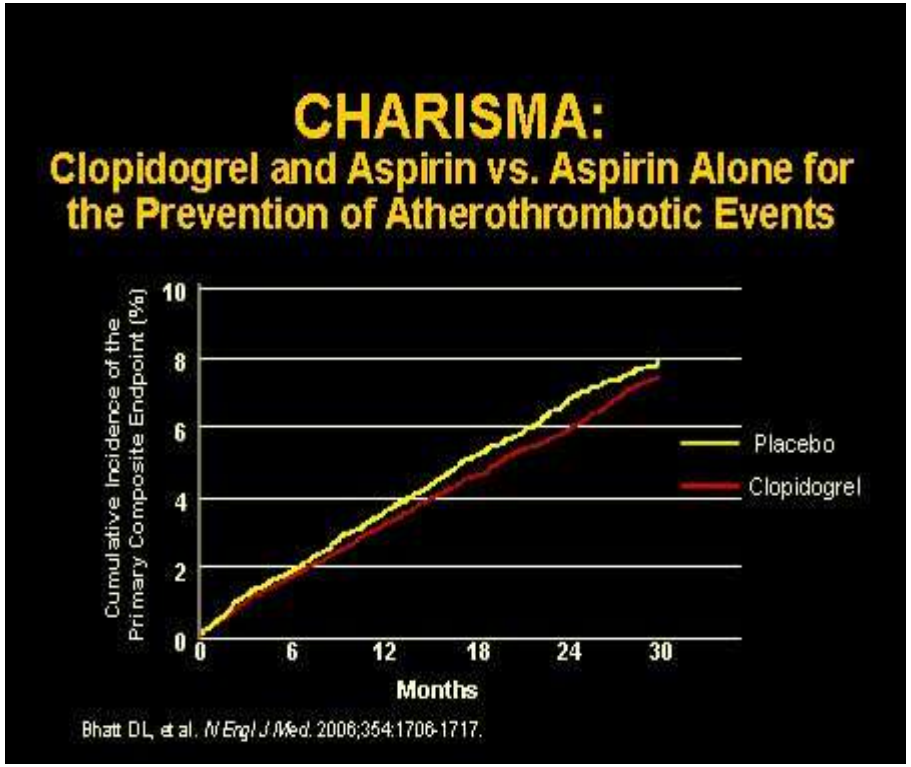
Mauri, Kereiakes et al AHJ 2010; 160(6): 1035-1041 ClinicalTrials.gov number NCT00977938

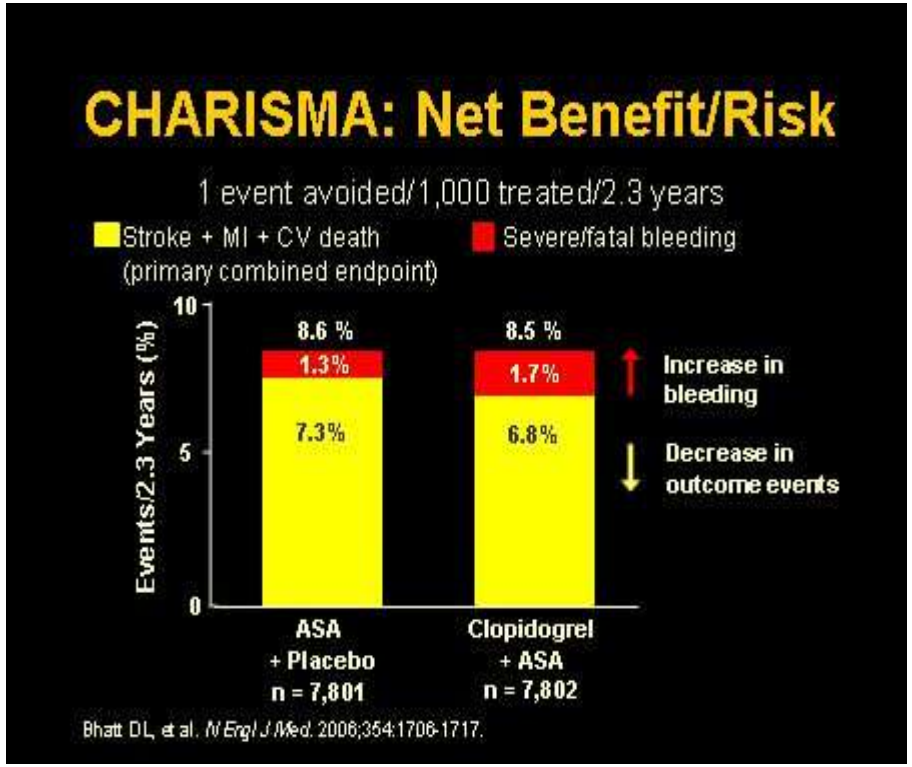
ΜΕΛΕΤΕΣ > 12 ΜΗΝΩΝ ΧΟΡΗΓΗΣΗΣ ASA + THIENOPYRIDINE





CHARISMA ΑΠΟΤΕΛΕΣΜΑΤΑ

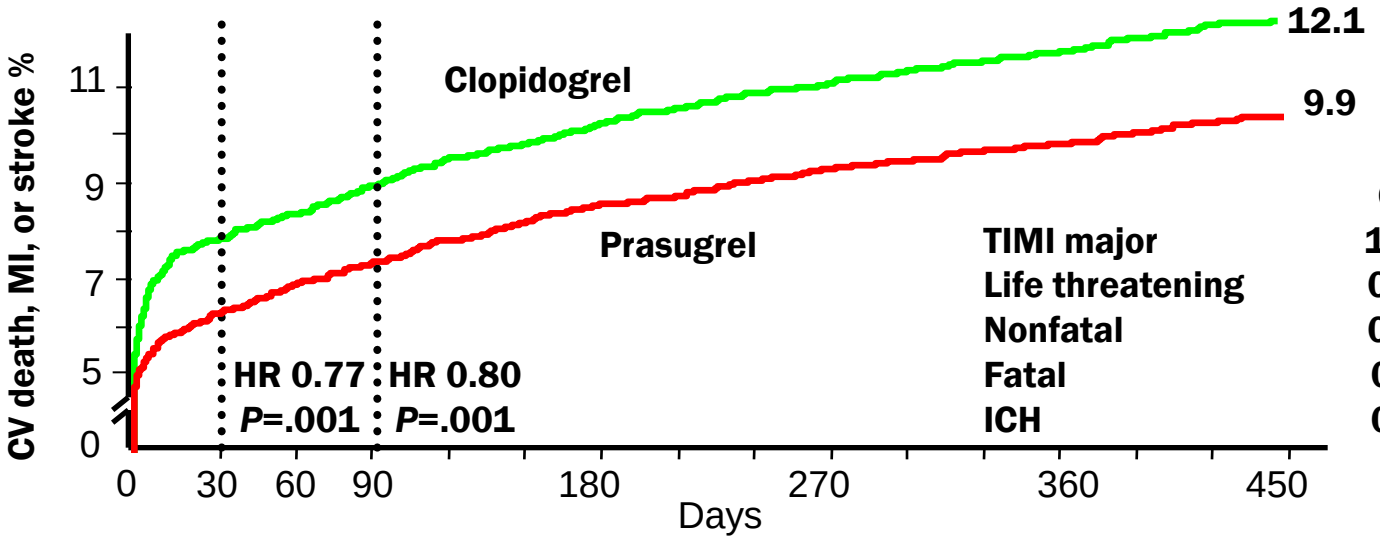




Prasugrel Evidence: Secondary Prevention

Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel (TRITON-TIMI 38)

13,608 patients with high-risk ACS scheduled for PCI randomized to clopidogrel (300 mg LD and 75 mg MD) or prasugrel (60 mg LD and 10 mg MD) for a median of 12 months



Bleeding Events

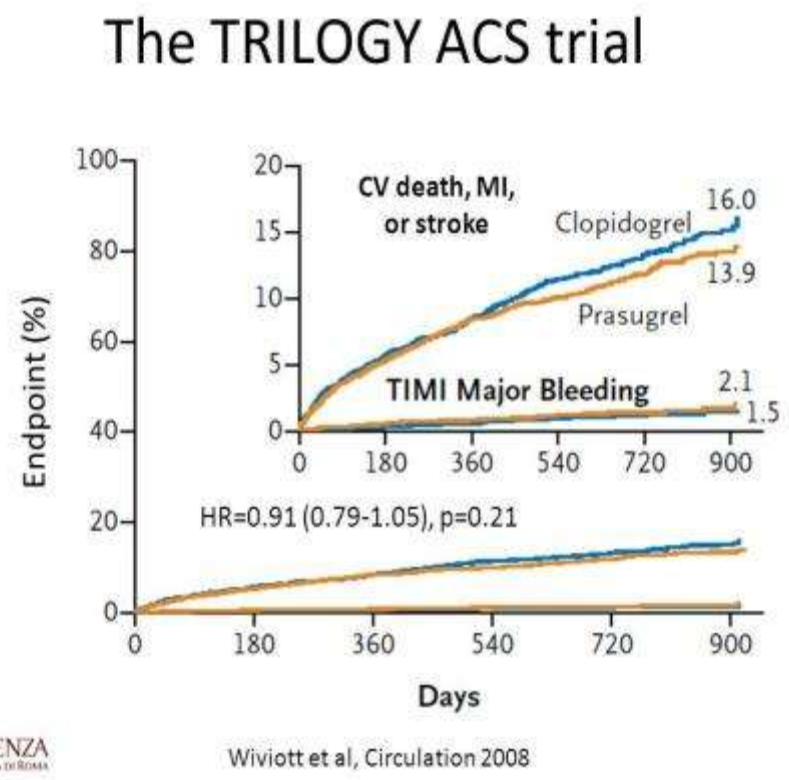
	C (%)	P (%)	*P-value*
TIMI major	1.8	2.4	0.03
Life threatening	0.9	1.4	0.01
Nonfatal	0.9	1.1	0.23
Fatal	0.1	0.4	0.002
ICH	0.3	0.3	0.74

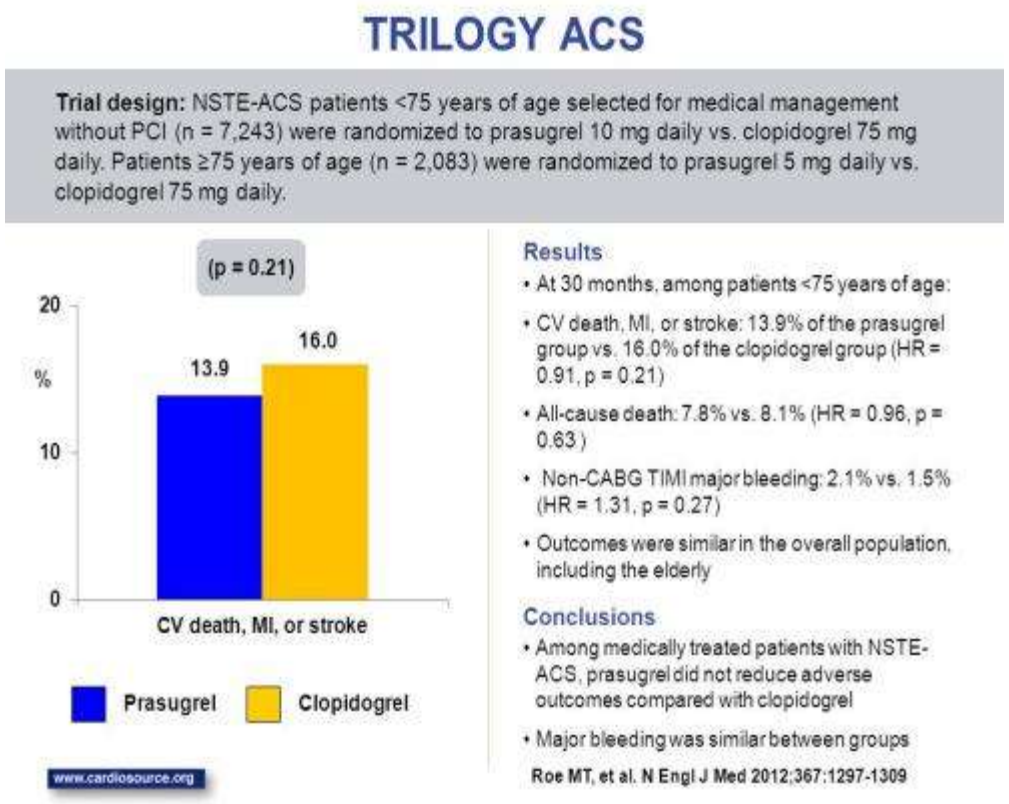
Prasugrel reduces ischemic events with a higher rate of bleeding

ACS=Acute coronary syndrome, ICH=Intracranial hemorrhage, LD=Loading dose, MD=Maintenance dose

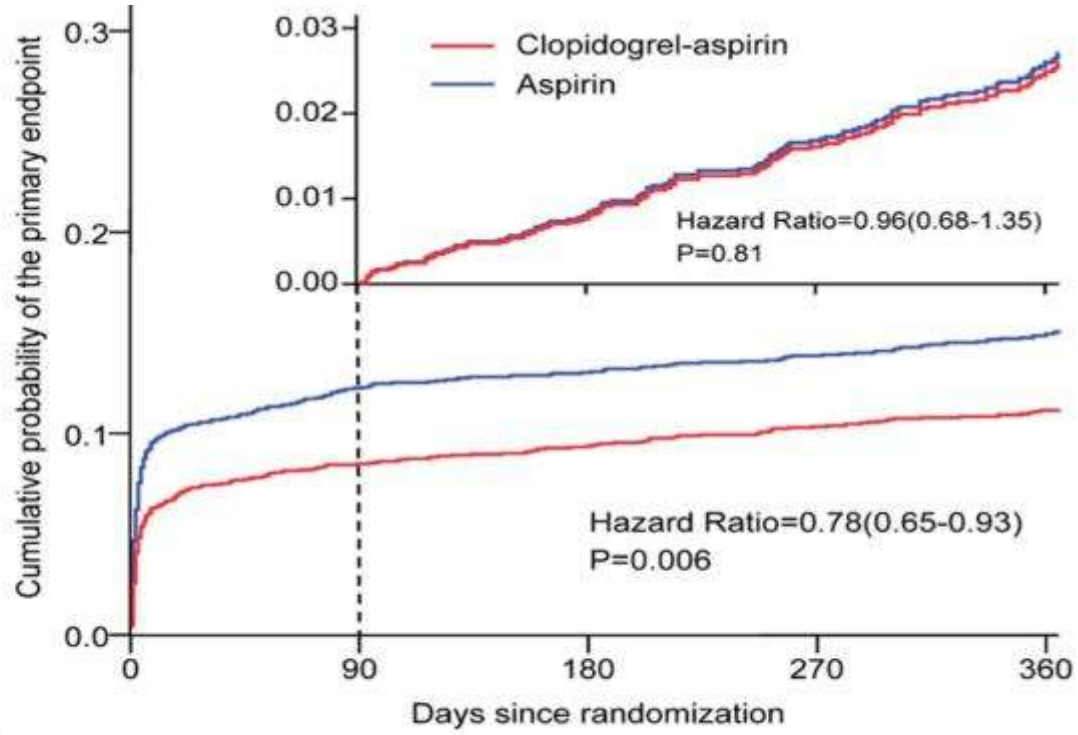
Source: Wiviott SD et al. *NEJM* 2007;357:2001-2015

TRILOGY ACS ΑΠΟΤΕΛΕΣΜΑΤΑ



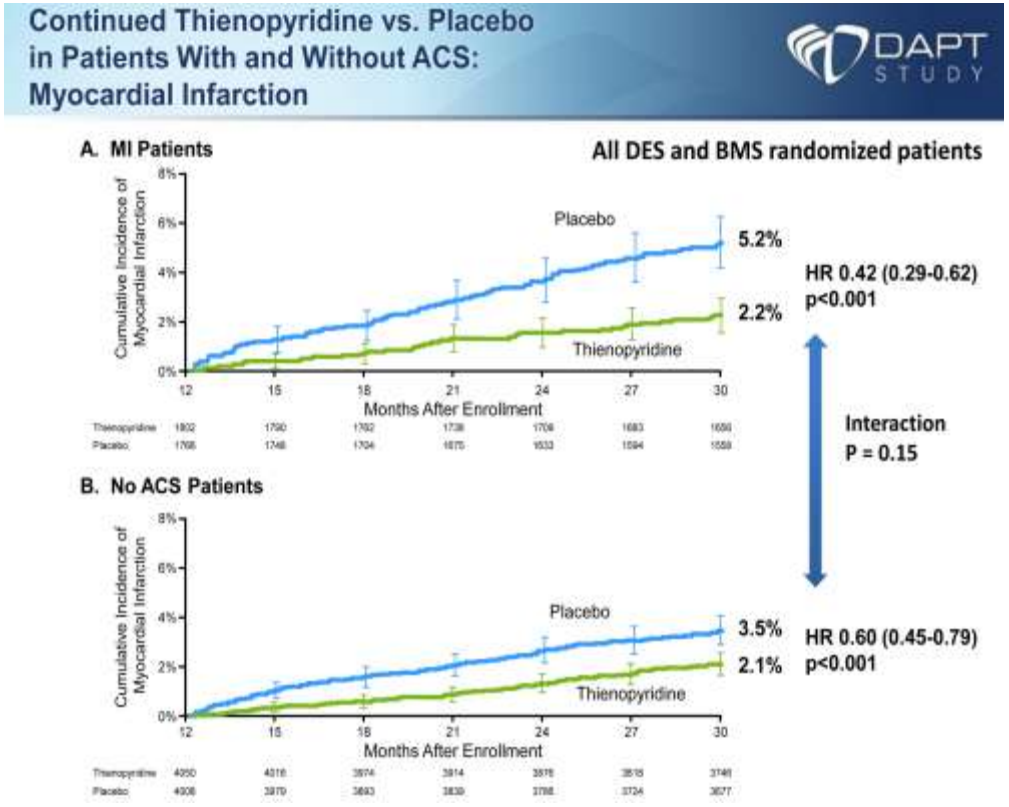


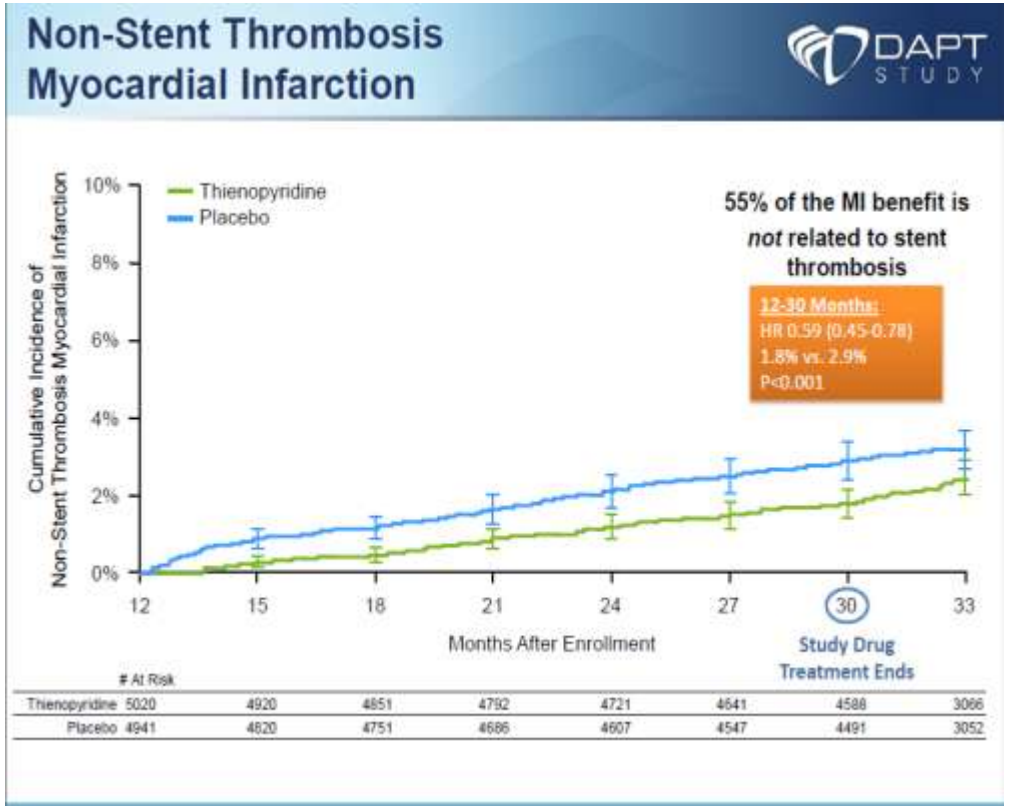
CURE TRIAL



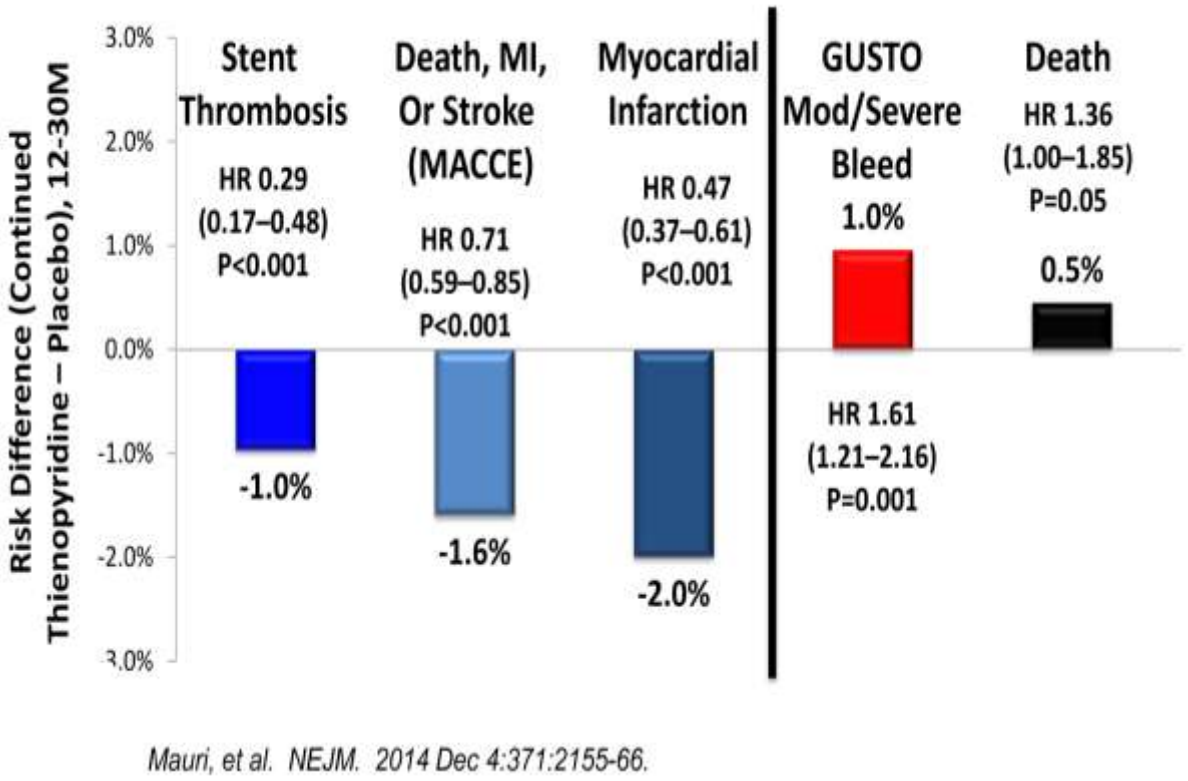
Number at risk					
Aspirin	2586	2260	2174	2149	1771
Clopidogrel-aspirin	2584	2346	2269	2240	1854

DAPT KAI MI

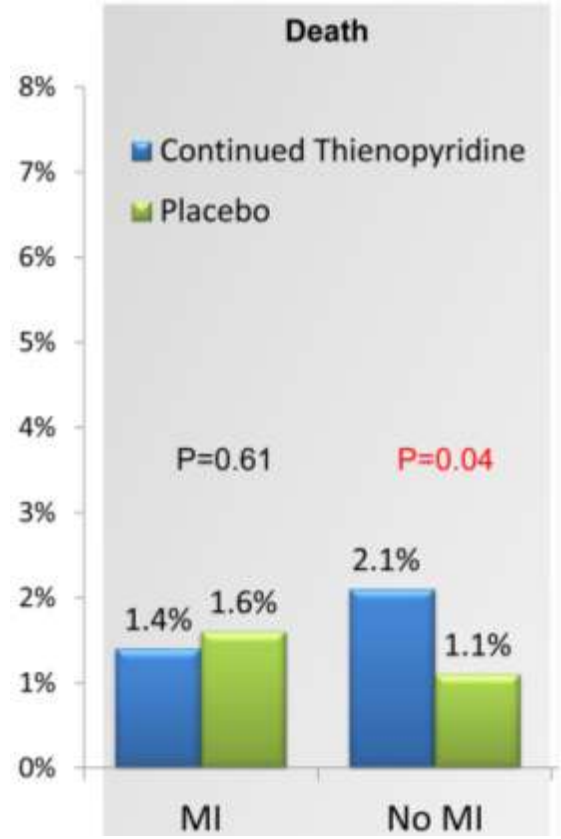

Continued Thienopyridine vs. Placebo in Patients With and Without ACS: Myocardial Infarction
DAPT STUDY
A. MI Patients
All DES and BMS randomized patients
Cumulative Incidence of Myocardial Infarction
Placebo
Thienopyridine
5.2%
2.2%
HR 0.42 (0.29-0.62)
p<0.001
Months After Enrollment
Interaction
P = 0.15
B. No ACS Patients
3.5%
2.1%
HR 0.60 (0.45-0.79)
p<0.001


Non-Stent Thrombosis Myocardial Infarction
DAPT STUDY
Cumulative Incidence of Non-Stent Thrombosis Myocardial Infarction
Thienopyridine
Placebo
55% of the MI benefit is not related to stent thrombosis
12-30 Months:
HR 0.59 (0.45-0.78)
1.8% vs. 2.9%
P<0.001
Months After Enrollment
Study Drug Treatment Ends
At Risk
Thienopyridine 5020 4920 4851 4792 4721 4641 4588 3066
Placebo 4941 4820 4751 4686 4607 4547 4491 3052

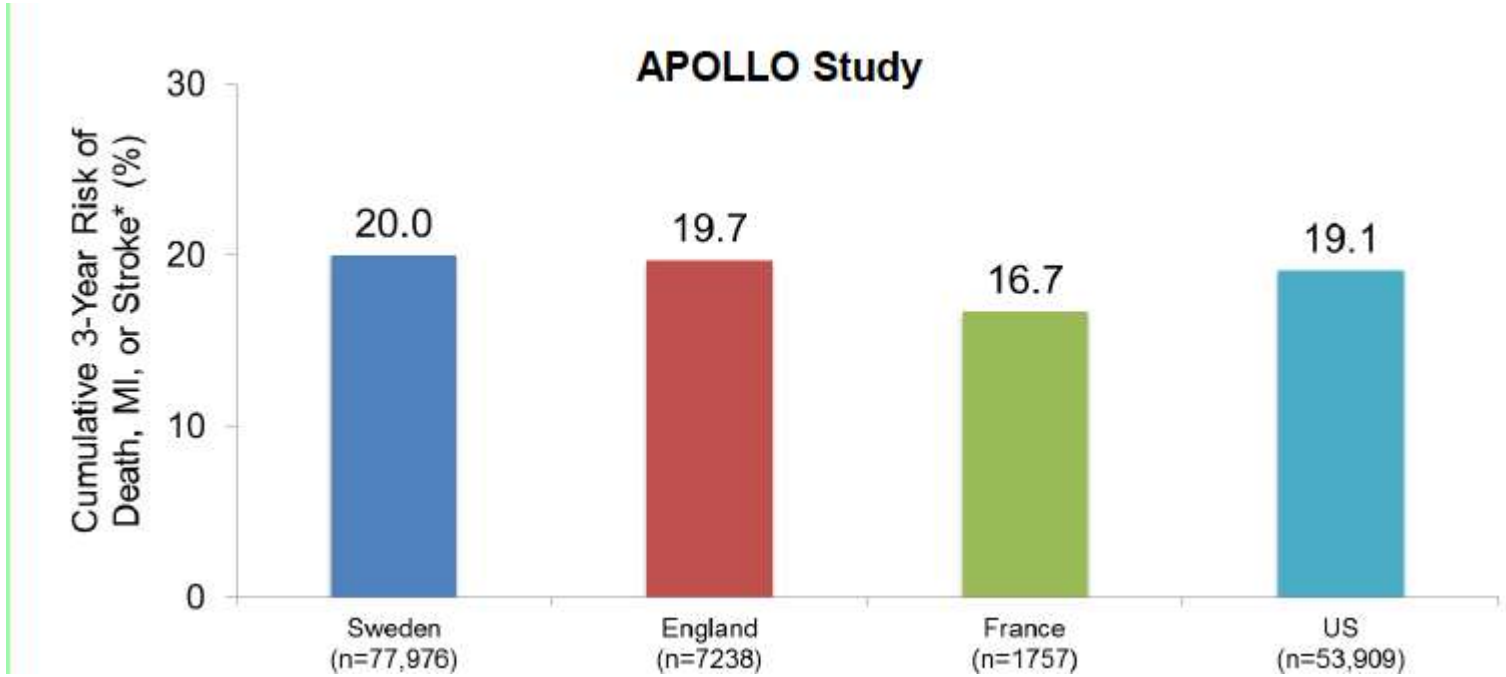
DAPT ΑΠΟΤΕΛΕΣΜΑΤΑ



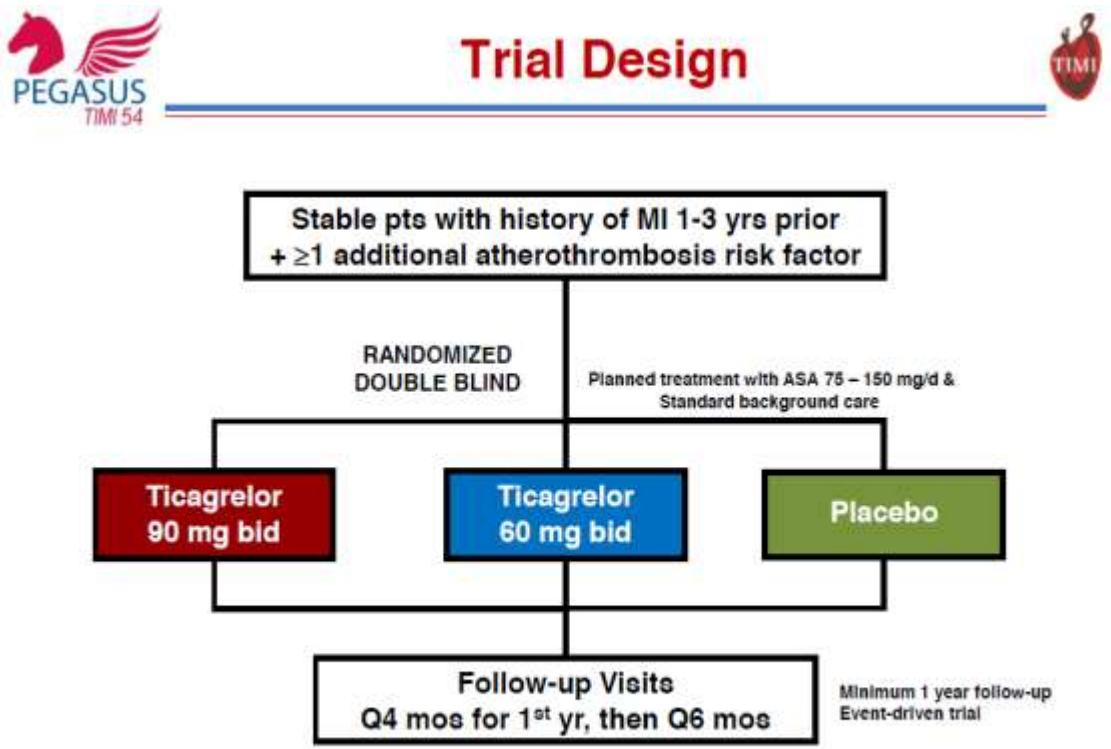
Mauri, et al. NEJM. 2014 Dec 4:371:2155-66.



ΑΥΞΗΜΕΝΟΣ ΚΑΡΔΙΑΓΓΕΙΑΚΟΣ ΚΙΝΔΥΝΟΣ ΣΤΗΝ 3ΕΤΙΑ ΜΕΤΑ ΕΜΦΡΑΓΜΑ



ΜΕΛΕΤΗ PEGASUS



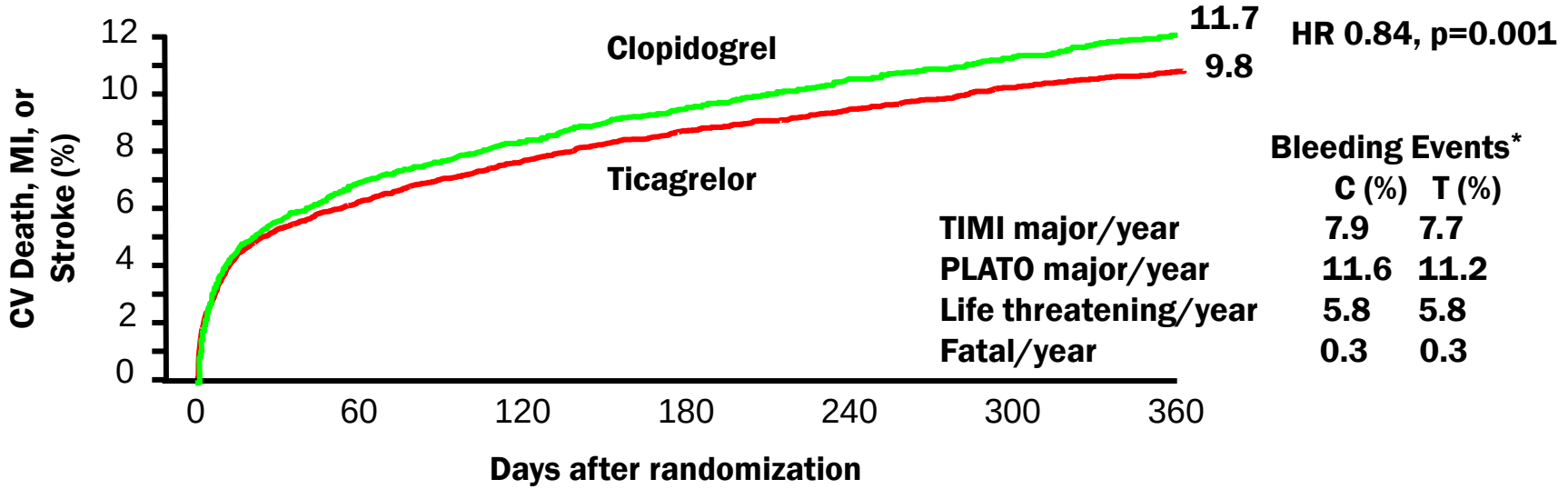
An Academic Research Organization of Brigham and Women's Hospital and Harvard Medical School

Bonaca MP et al. *Am Heart J* 2014;167:437-44

Ticagrelor Evidence: Secondary Prevention

Platelet Inhibition and Patient Outcomes (PLATO) Study

18,624 patients with a moderate to high risk ACS randomized to clopidogrel (300-600 mg LD and 75 mg MD) or ticagrelor (180 mg LD and 90 mg twice daily MD) for 12 months



Bleeding Events*

	C (%)	T (%)
TIMI major/year	7.9	7.7
PLATO major/year	11.6	11.2
Life threatening/year	5.8	5.8
Fatal/year	0.3	0.3

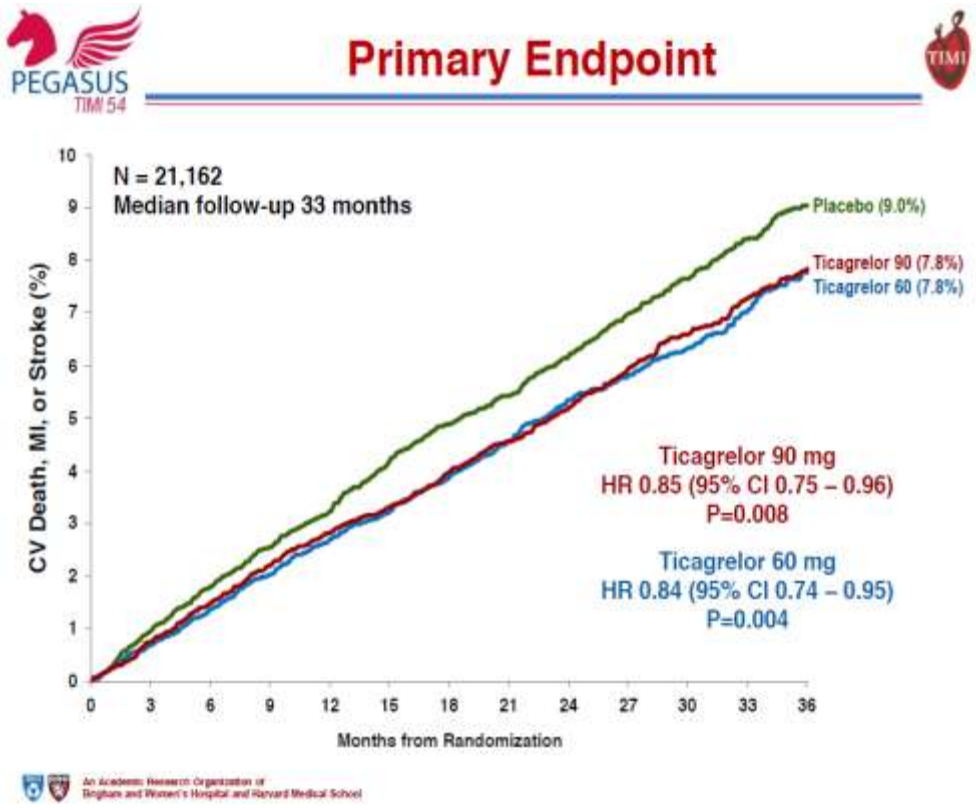
Ticagrelor reduces ischemic events with no higher rate of bleeding overall

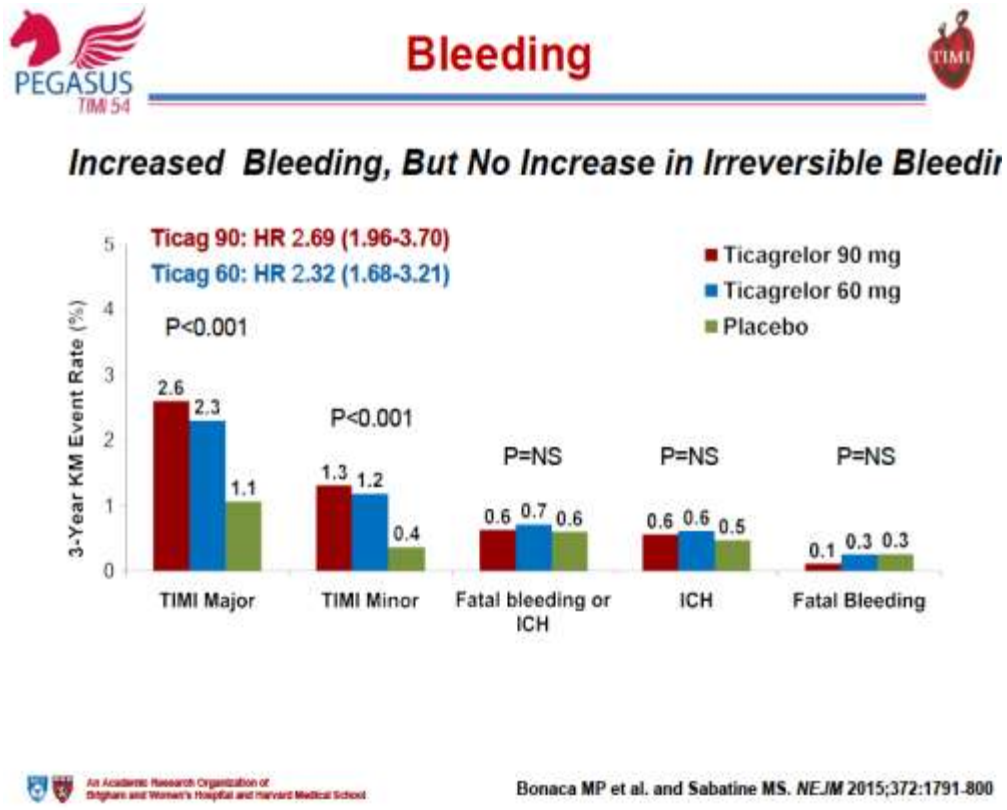
*No statistically significant differences were observed in bleeding rates overall

ACS=Acute coronary syndrome, CV=Cardiovascular, LD=Loading dose, MD=Maintenance dose

Source: Wallentin L et al. *NEJM* 2009;361:1045-1057

PEGASUS ΑΠΟΤΕΛΕΣΜΑΤΑ





Bonaca MP et al. and Sabatine MS. *NEJM* 2015;372:1791-800

European Heart Journal Advance Access published August 31, 2015

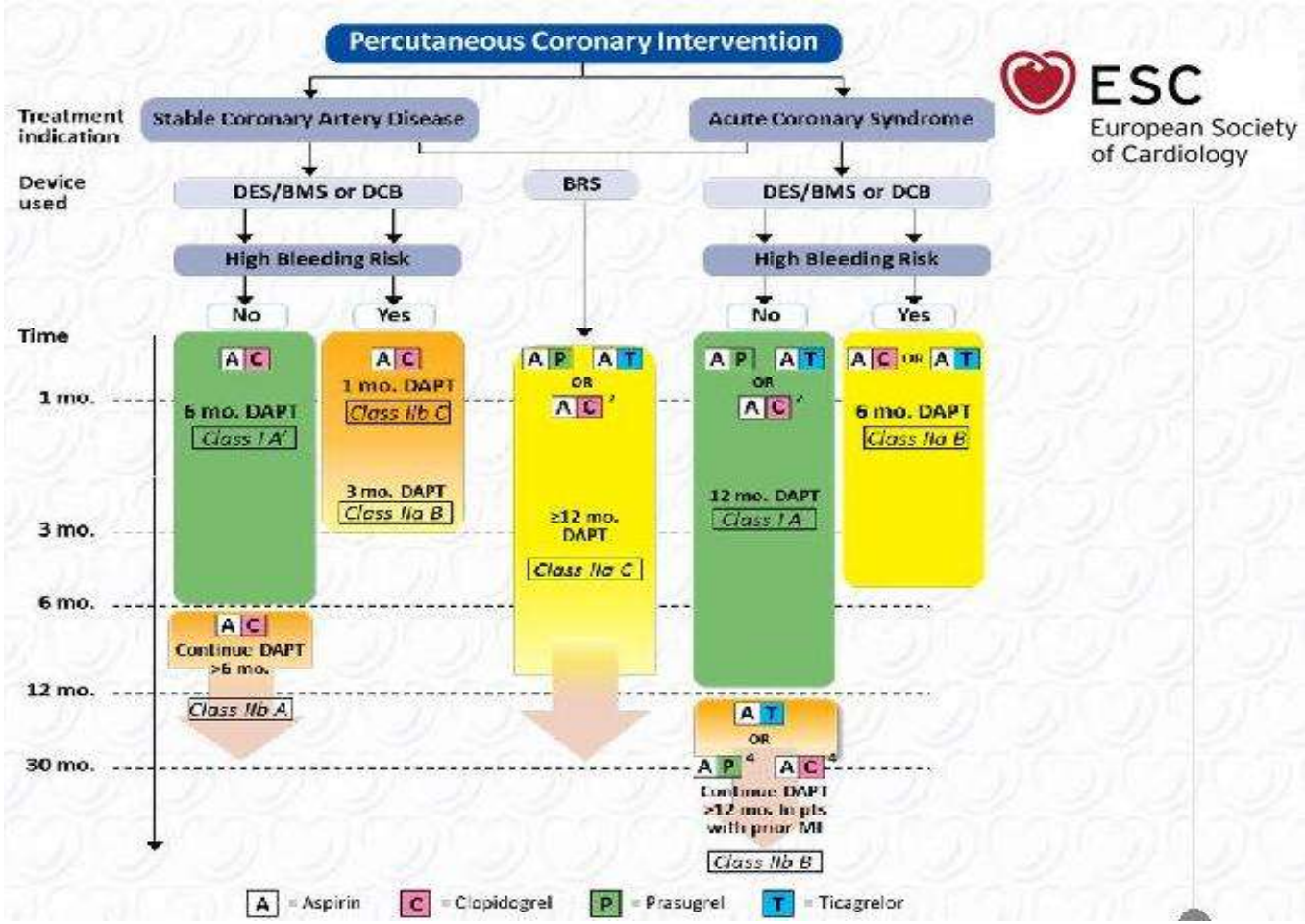
European Heart Journal
doi:10.1093/eurheartj/ehv443

FASTTRACK
ESC Clinical Trial Update

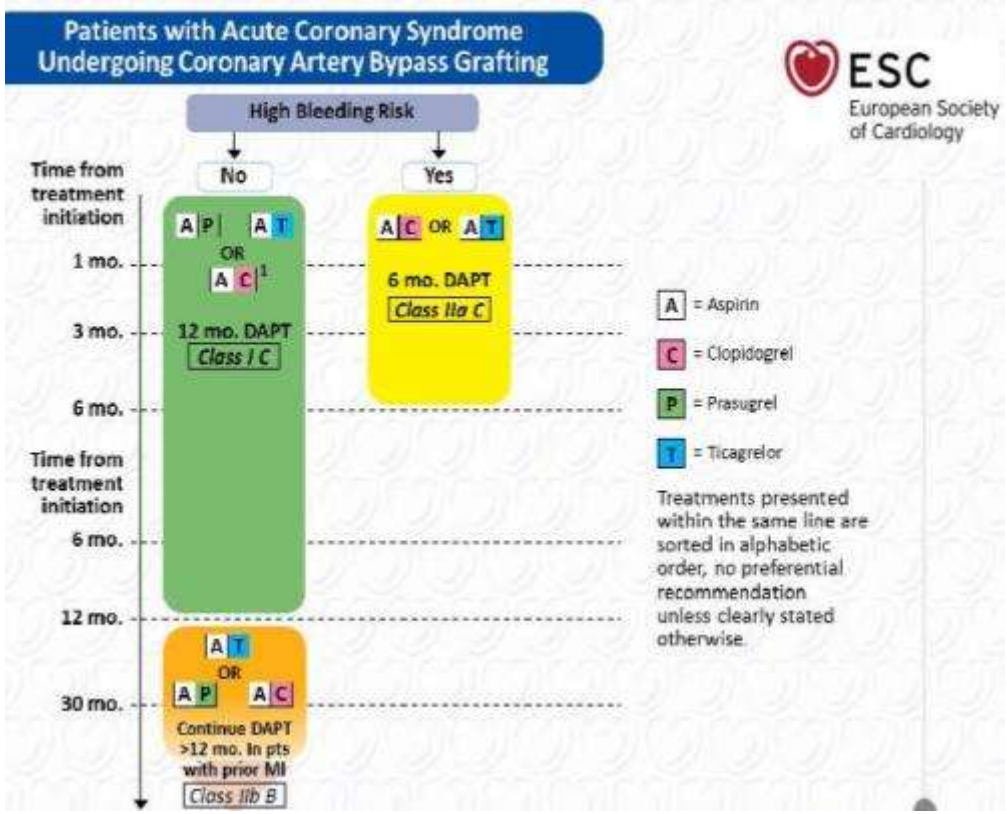
Long-term dual antiplatelet therapy for secondary prevention of cardiovascular events in the subgroup of patients with previous myocardial infarction: a collaborative meta-analysis of randomized trials

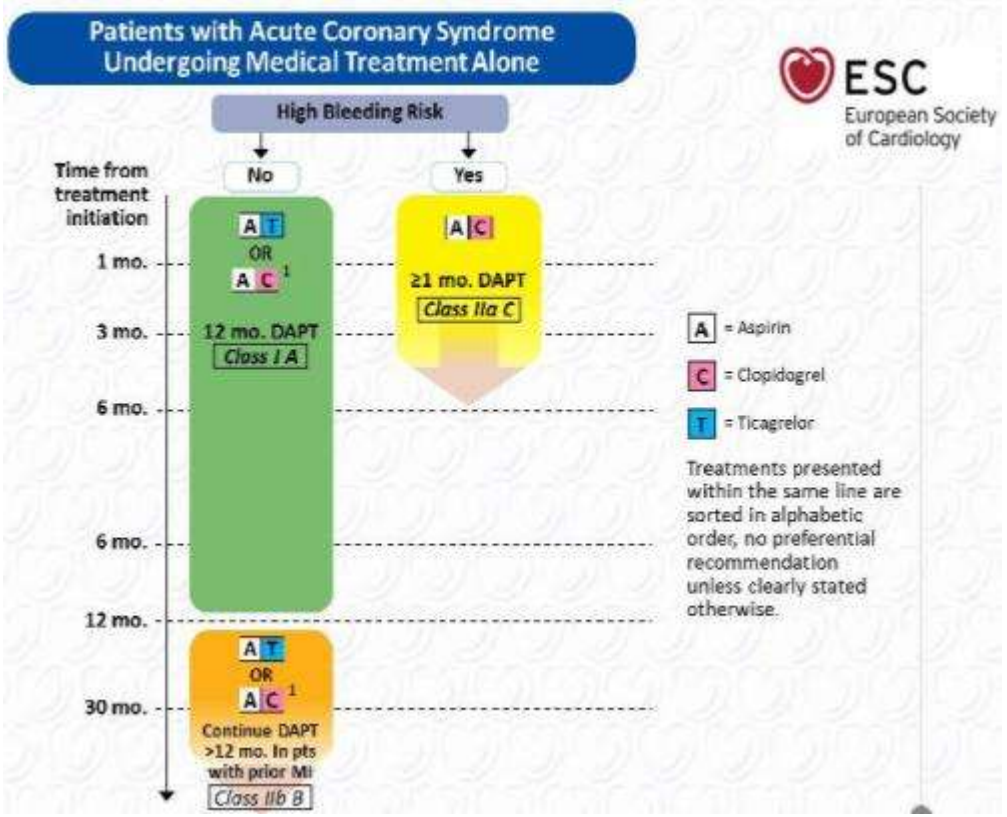
Jacob A. Udell[1,2*], Marc P. Bonaca[3], Jean-Philippe Collet[4], A. Michael Lincoff[5], Dean J. Kereiakes[6], Francesco Costa[7], Cheol Whan Lee[8], Laura Mauri[9], Marco Valgimigli[7,10], Seung-Jung Park[8], Gilles Montalescot[4], Marc S. Sabatine[3], Eugene Braunwald[3], and Deepak L. Bhatt[3*]

ΔΙΑΡΚΕΙΑ ΔΙΠΛΗΣ ΑΝΤΙΑΙΜΟΠΕΤΑΛΙΑΚΗΣ ΑΓΩΓΗΣ ΜΕΤΑ ΑΠΟ PCI



ΔΙΑΡΚΕΙΑ ΔΙΠΛΗΣ ΑΝΤΙΑΙΜΟΠΕΤΑΛΙΑΚΗΣ ΑΓΩΓΗΣ ΜΕΤΑ ΟΣΣ **ΧΩΡΙΣ PCI**





ΔΙΑΡΚΕΙΑ ΔΙΠΛΗΣ ΑΝΤΙΑΙΜΟΠΕΤΑΛΙΑΚΗΣ ΑΓΩΓΗΣ ΜΕΤΑ PCI

Risk scores validated for dual antiplatelet therapy duration decision-making

ESC European Society of Cardiology

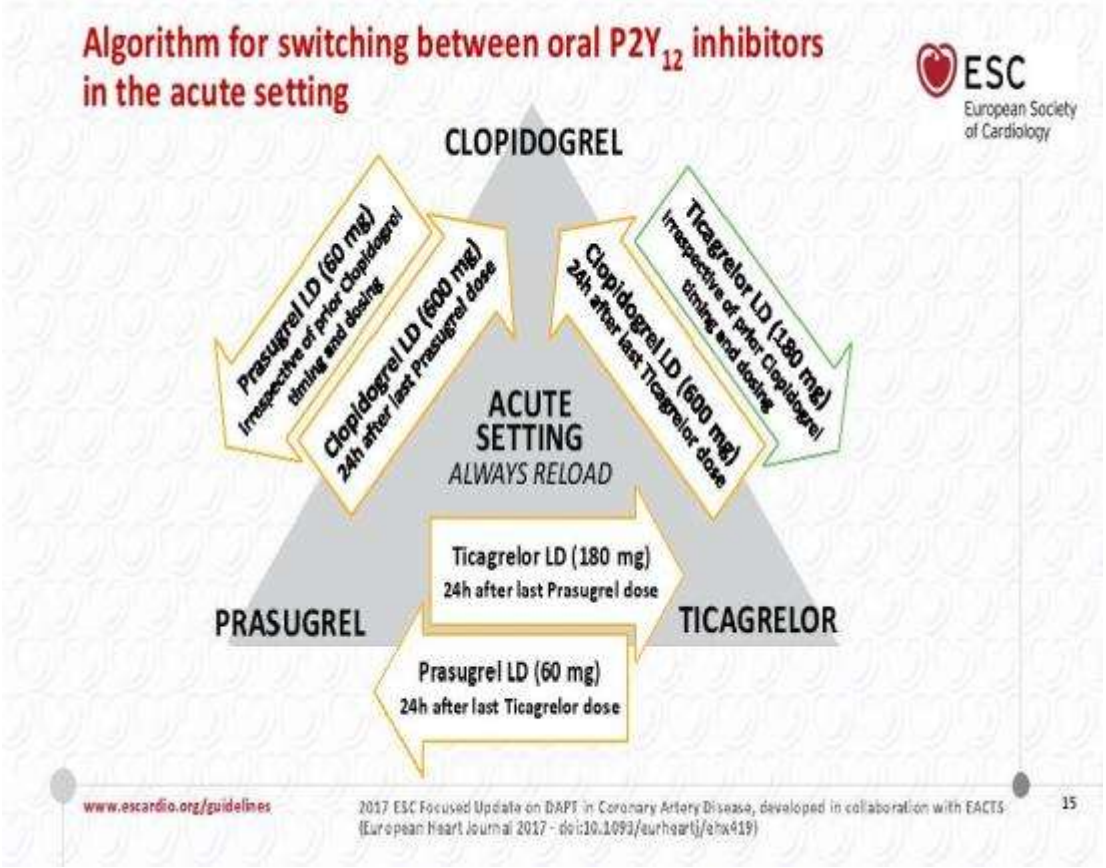
	PRECISE-DAPT score	DAPT score
Time of use	At the time of coronary stenting	After 12 months of uneventful DAPT
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)	Standard DAPT (12 months) vs. Long DAPT (30 months)
Score calculation	HB ≥2 11-5 11 10-5 ≤10 WBC ≤5 8 10 12 14 16 18 ≥20 Age ≤50 60 70 80 ≥90 CrCl ≥100 80 60 40 20 0 Prior Bleeding No Yes Score Points 0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30	Age ≥75 −2 pt 65 to <75 −1 pt <65 0 pt Cigarette smoking +1 pt Diabetes mellitus +1 pt MI at presentation +1 pt Prior PCI or prior MI +1 pt Paclitaxel-eluting stent +1 pt Stent diameter <3 mm +1 pt CHF or LVEF <30% +2 pt Vein graft stent +2 pt
Score range	0 to 100 points	−2 to 10 points
Decision making cut-off suggested	Score ≥25 → Short DAPT Score <25 → Standard/long DAPT	Score ≥2 → Long DAPT Score <2 → Standard DAPT
Calculator	www.precisedaptscore.com	www.daptstudy.org

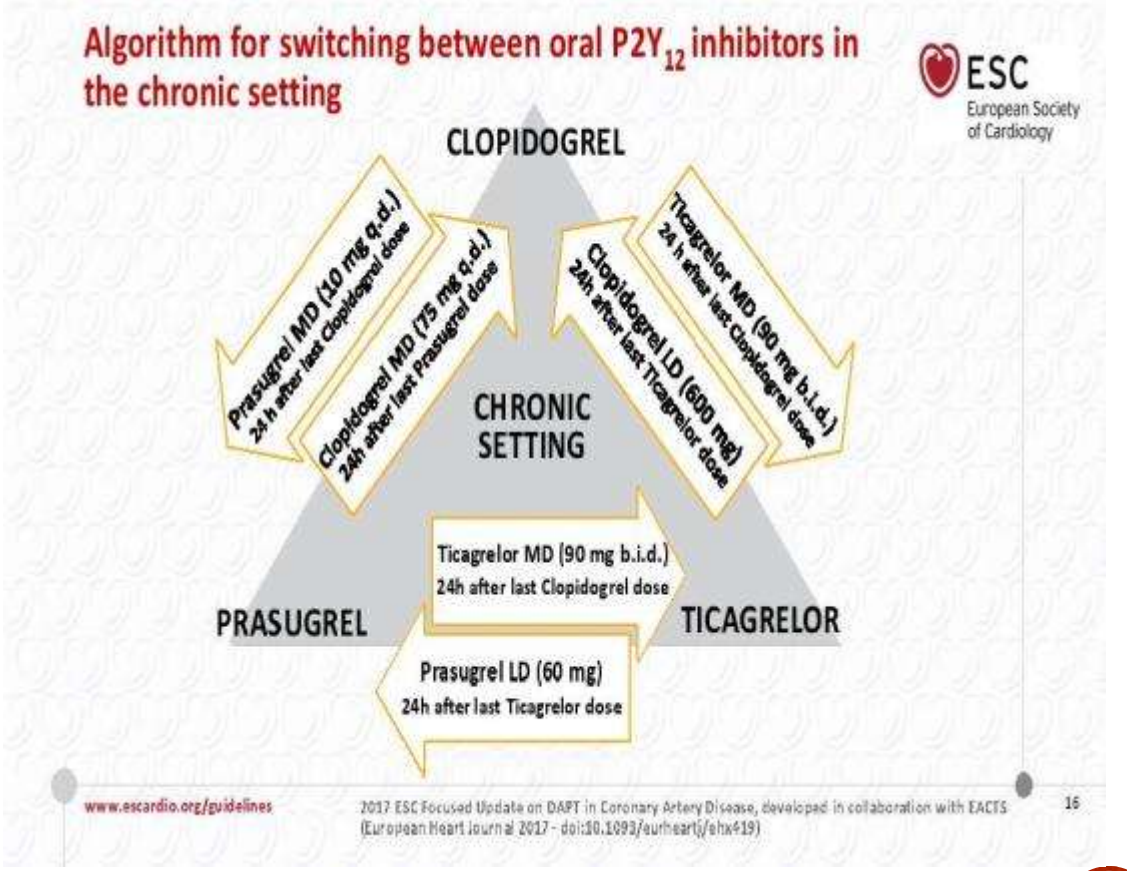
www.escardio.org/guidelines

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

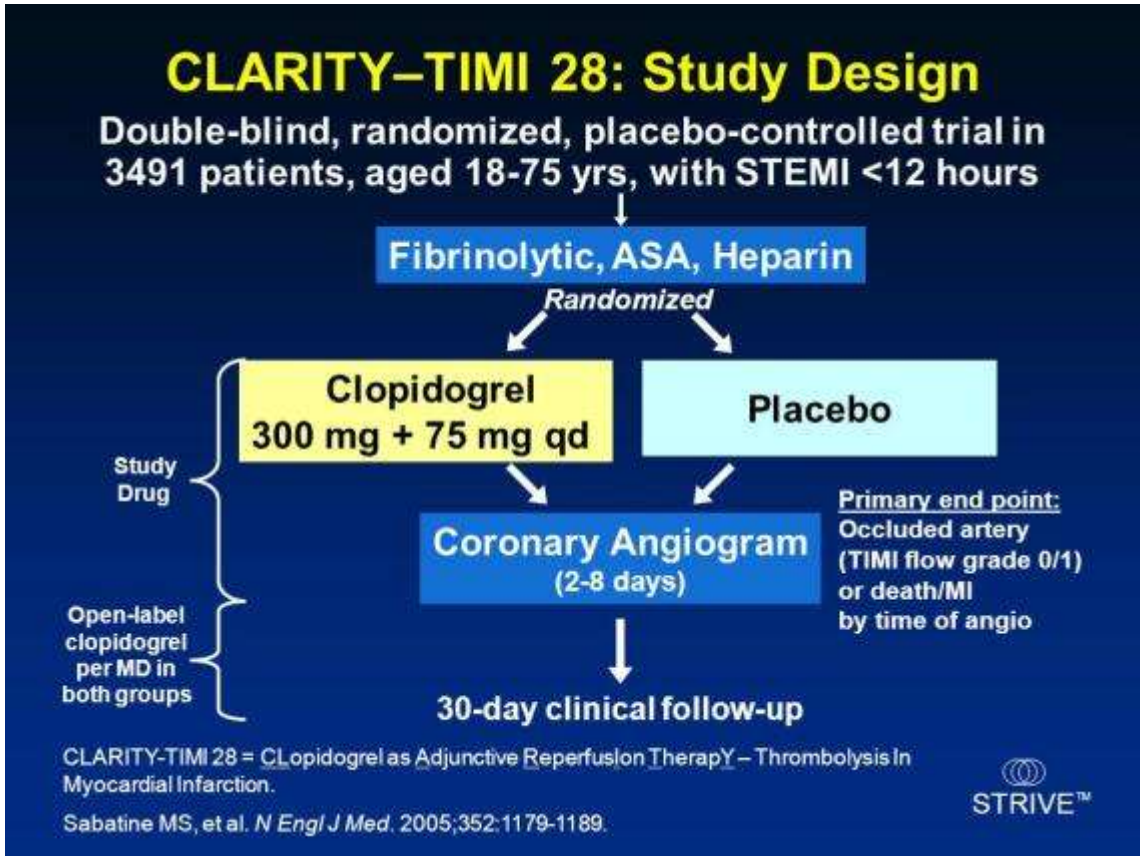
7

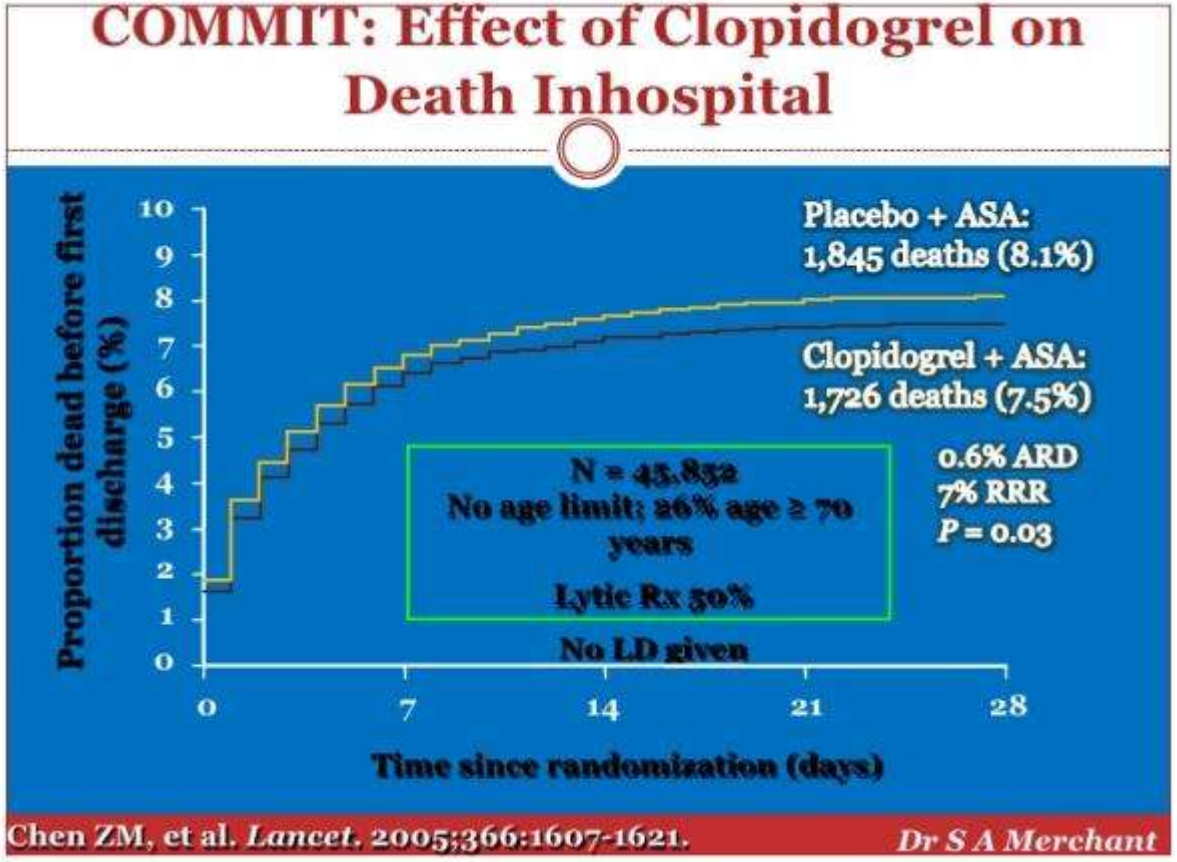
ΑΛΛΑΓΗ ΜΕΤΑΞΥ ΑΝΤΙΑΙΜΟΠΕΤΑΛΙΑΚΩΝ





ΑΛΛΑΓΗ ΑΠΟ CLOPIDOGREL ΜΕΤΑ ΑΠΟ ΘΡΟΜΒΟΛΥΘΕΝ STEMI





ΑΛΛΑΓΗ ΑΠΟ **CLOPIDOGREL** ΜΕΤΑ ΑΠΟ ΘΡΟΜΒΟΛΥΘΕΝ **STEMI**

ESC

- **TICAGRELOR 180 mg 48** ώρες μετά
- ΔΕΝ δίνεται κάποια οδηγία για την Πρασουγκρέλη

ACC / AHA

- **PRASUGREL 60 mg 24** ώρες μετά και εφ' όσον γίνει τοποθέτηση **stent**
- ΔΕΝ δίνεται κάποια οδηγία για την Τικαγκρελόρη

*Το 1ο 24ωρο από τη χορήγηση θρομβόλυσης χορηγούμε μόνο την ασπιρίνη και την κλοπιδογρέλη (**max 300 mg**), ασχέτως αν γίνει διαδερμική στεφανιαία παρέμβαση ή ακολουθηθεί συντηρητική (φαρμακευτική) αντιμετώπιση*

CANGRELOR

Cangrelor
The CHAMPION PHOENIX Trial

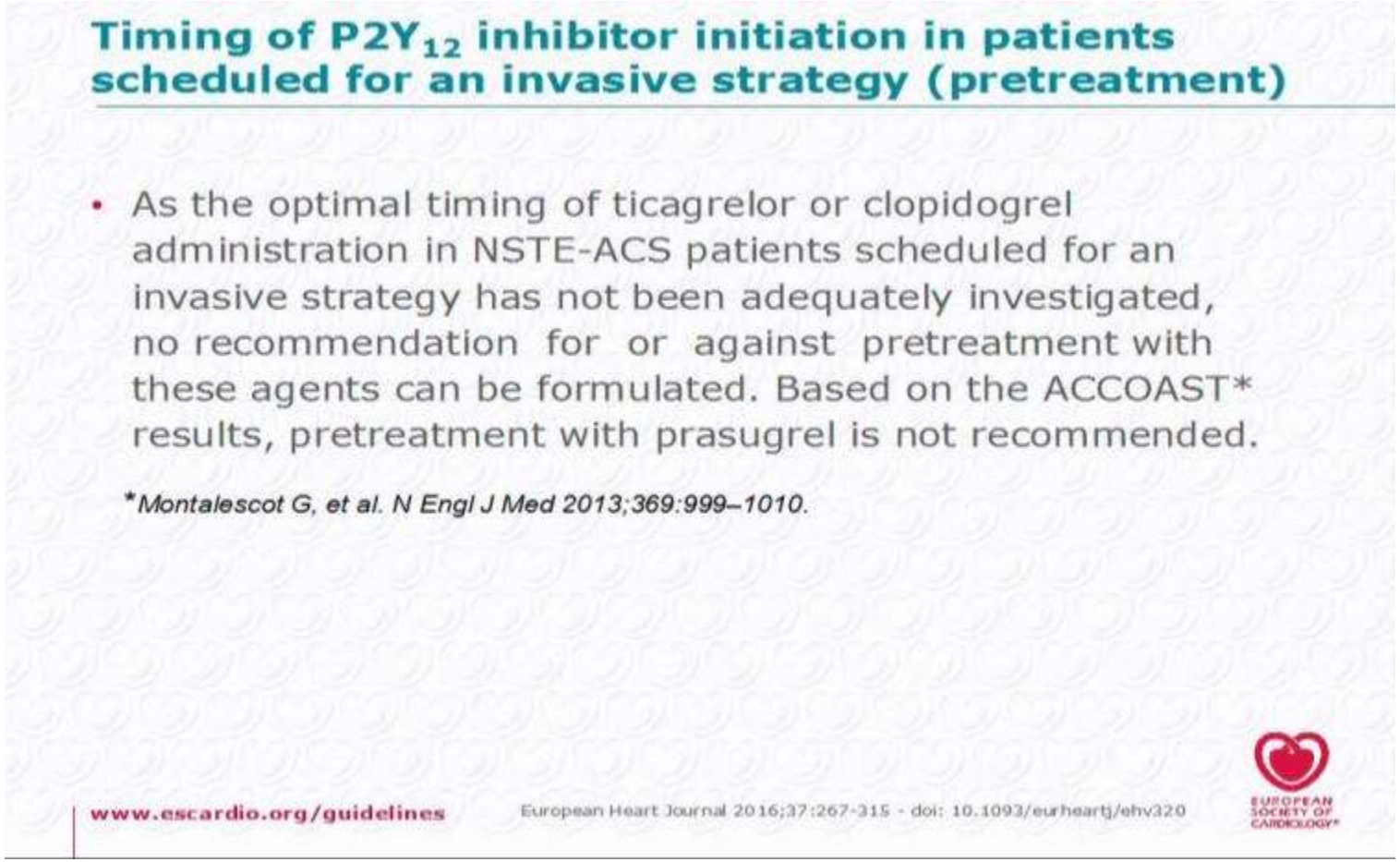
- Inclusion criteria
  - Patients with coronary atherosclerosis who required PCI for stable angina, a NSTE-ACS, or STEMI and did not receive pretreatment with platelet inhibitors
- High-risk characteristics included
  - Long (> 20 mm)
  - Bifurcation (DS ≥ 50%)
  - Angulated (mod/sev)
  - Calcified (mod/sev)
  - Left main (DS ≥ 50%)
  - Multilesion PCI
  - Eccentric
  - Thrombus
  - Tortuous

Bhatt DL, et al. *N Engl J Med*. 2013;368:1303-1313.

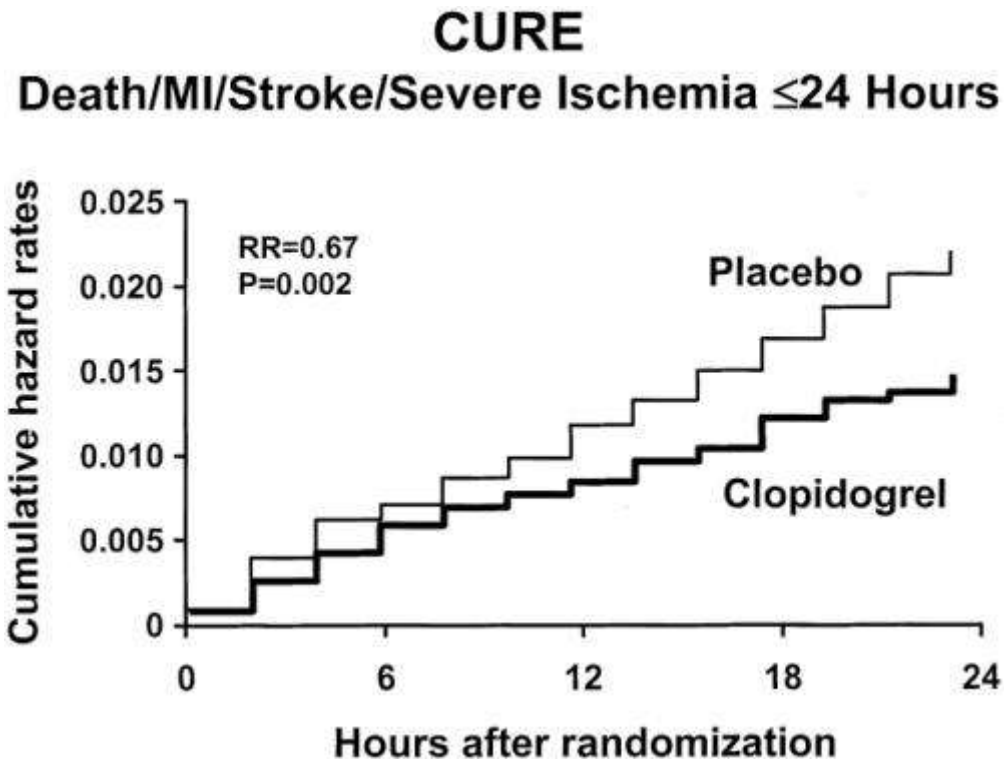
Mechanism of Action: $P2Y_{12}$ Agents

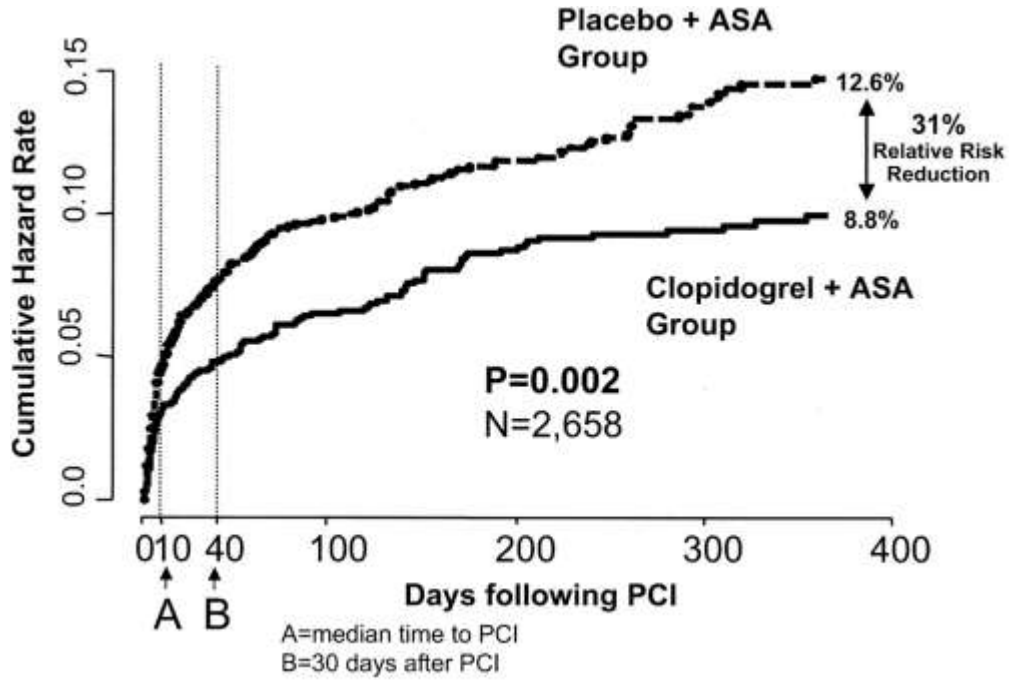
- Clopidogrel binds to the ADP binding site
- Prasugrel binds to the ADP binding site
- Ticagrelor blocks the ADP receptors of subtype $P2Y_{12}$, but in contrast to the other antiplatelet drugs, ticagrelor has a binding site different from ADP, making it an allosteric antagonist, and the blockage is reversible
- Cangrelor appears to bind at same ADP binding site as clopidogrel and prasugrel

NSTEMI


Timing of P2Y12 inhibitor initiation in patients scheduled for an invasive strategy (pretreatment)
• As the optimal timing of ticagrelor or clopidogrel administration in NSTE-ACS patients scheduled for an invasive strategy has not been adequately investigated, no recommendation for or against pretreatment with these agents can be formulated. Based on the ACCOAST* results, pretreatment with prasugrel is not recommended.
*Montalescot G, et al. N Engl J Med 2013;369:999–1010.
www.escardio.org/guidelines
European Heart Journal 2016;37:267-315 - doi: 10.1093/eurheartj/ehv320
EUROPEAN SOCIETY OF CARDIOLOGY®

CURE TRIAL


CURE
Death/MI/Stroke/Severe Ischemia ≤24 Hours
Cumulative hazard rates
0.025
0.020
0.015
0.010
0.005
0
RR=0.67
P=0.002
Placebo
Clopidogrel
0
6
12
18
24
Hours after randomization

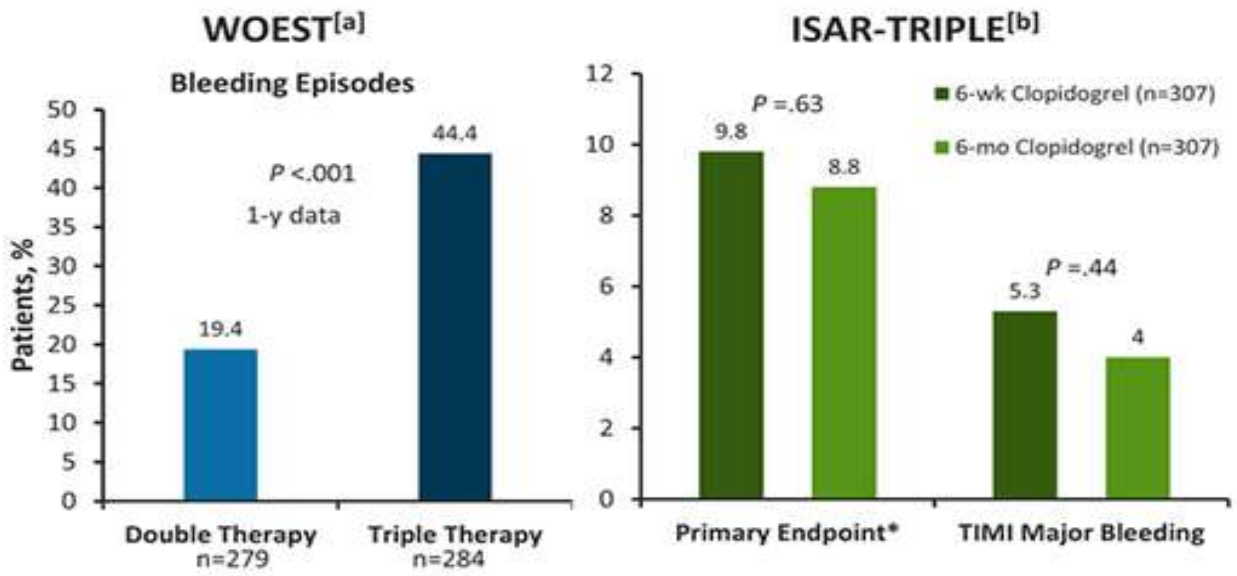

Placebo + ASA Group
12.6%
31%
Relative Risk Reduction
8.8%
Clopidogrel + ASA Group
P=0.002
N=2,658
Cumulative Hazard Rate
0.15
0.10
0.05
0.0
0
10
40
100
200
300
400
A
B
Days following PCI
A=median time to PCI
B=30 days after PCI

ΑΣΘΕΝΕΙΣ ΜΕ NSTEMI ΥΠΟ ΑΝΤΙΠΗΚΤΙΚΗ ΑΓΩΓΗ

- Anticoagulant doses adjusted to bodyweight and renal function, especially in women and elderly patients.
- Radial approach preferred.
- Proton pump inhibitors in patients on DAPT at higher than average risk of gastrointestinal bleeds (i.e. history of gastrointestinal ulcer/haemorrhage, anticoagulant therapy, chronic NSAIDs/corticosteroid use, or two or more among age ≥65 years, dyspepsia, gastrooesophageal reflux disease, *Helicobacter pylori* infection, and chronic alcohol use).
- In patients on OAC
  - PCI performed without interruption of VKAs or NOACs.
  - In patients on VKAs, do not administer UFH if INR value >2.5.
  - In patients on NOACs, regardless of the timing of the last administration of NOACs, add additional low-dose parenteral anticoagulation (e.g. enoxaparin 0.5 mg/kg i.v. or UFH 60 IU/kg).
  - Aspirin indicated but avoid pretreatment with $P2Y_{12}$ inhibitors.
  - GPIIb/IIIa inhibitors only for bailout of periprocedural complications.

ΤΡΙΠΛΗ ΑΝΤΙΘΡΟΜΒΩΤΙΚΗ ΑΓΩΓΗ

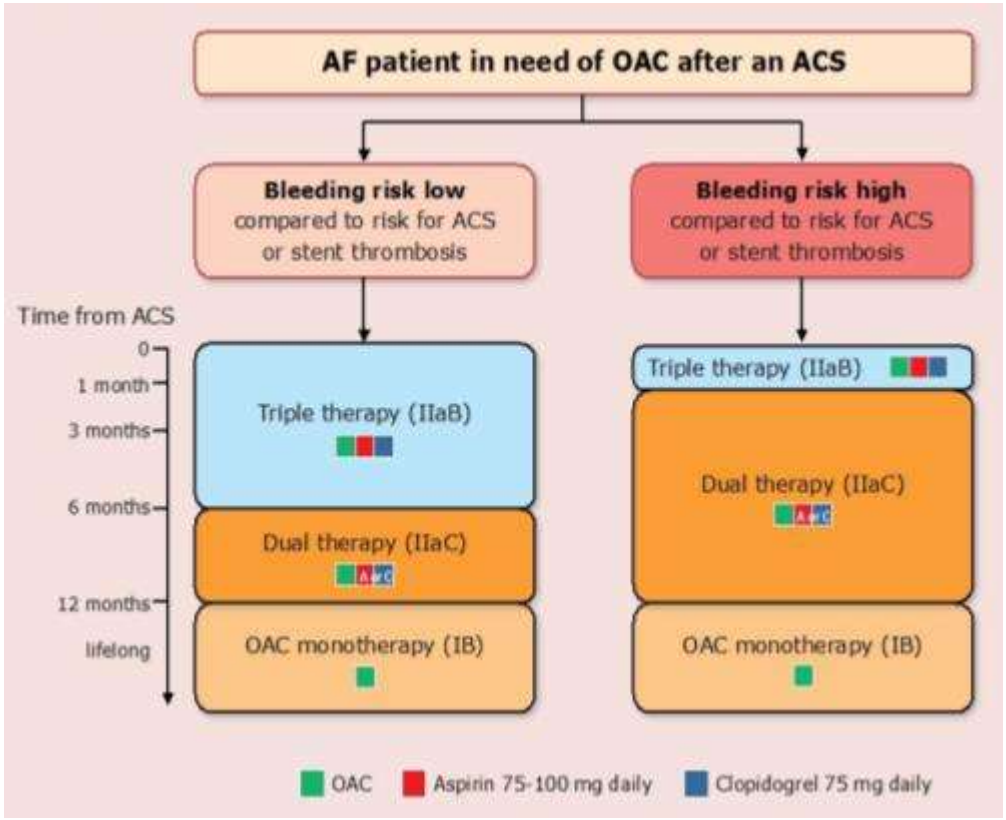
WOEST and ISAR-TRIPLE

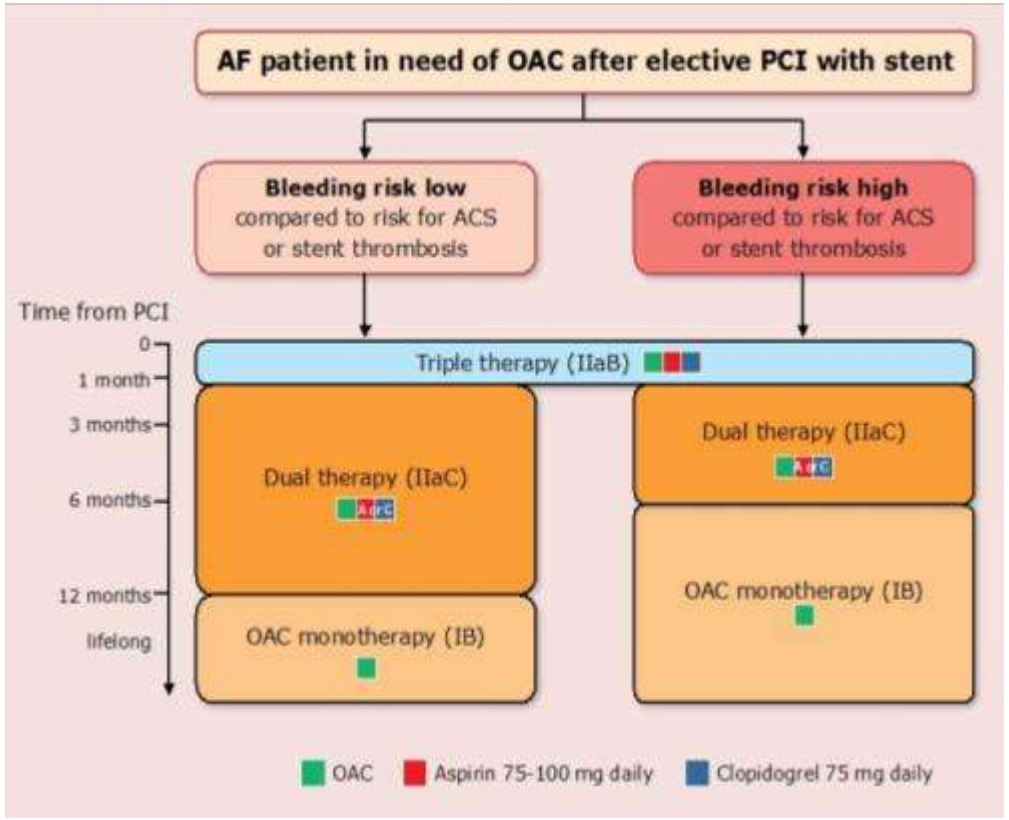


*Composite of death, MI, definite stent thrombosis, stroke, or TIMI major bleeding at 9 mo.

a. Dewilde WJ, et al. *Lancet*. 2013;381:1107-1115; b. Fielder KA, et al. *J Am Coll Cardiol*. 2015;65:1619-1629.

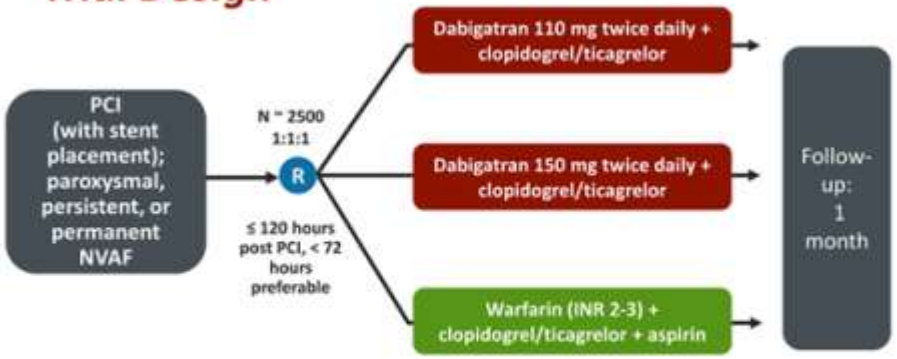
ΟΔΗΓΙΕΣ ΣΕ ΑΣΘΕΝΕΙΣ ΜΕ ΣΤΕΦΑΝΙΑΙΑ ΝΟΣΟ ΚΑΙ ΚΟΛΠΙΚΗ ΜΑΡΜΑΡΥΓΗ





RE - DUAL

RE-DUAL-PCI
Trial Design

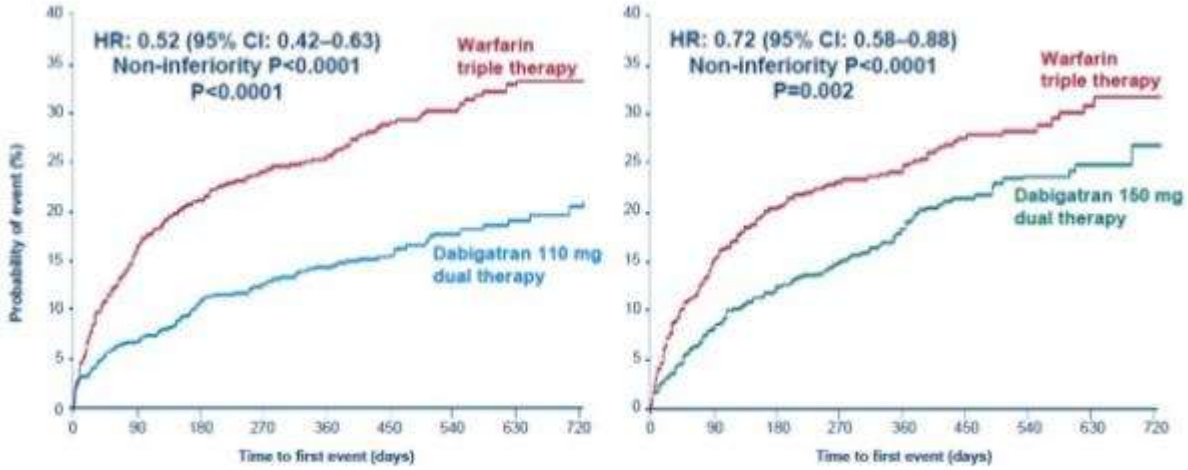


- Primary outcome measure: Time to first ISTH major bleeding or CRNM bleeding event
- Secondary endpoints: Composite of all cause death or thrombotic events (MI, or stroke/SE) and unplanned revascularization

Cannon CP, et al. *Clin Card*. 2016; 39:555-564.

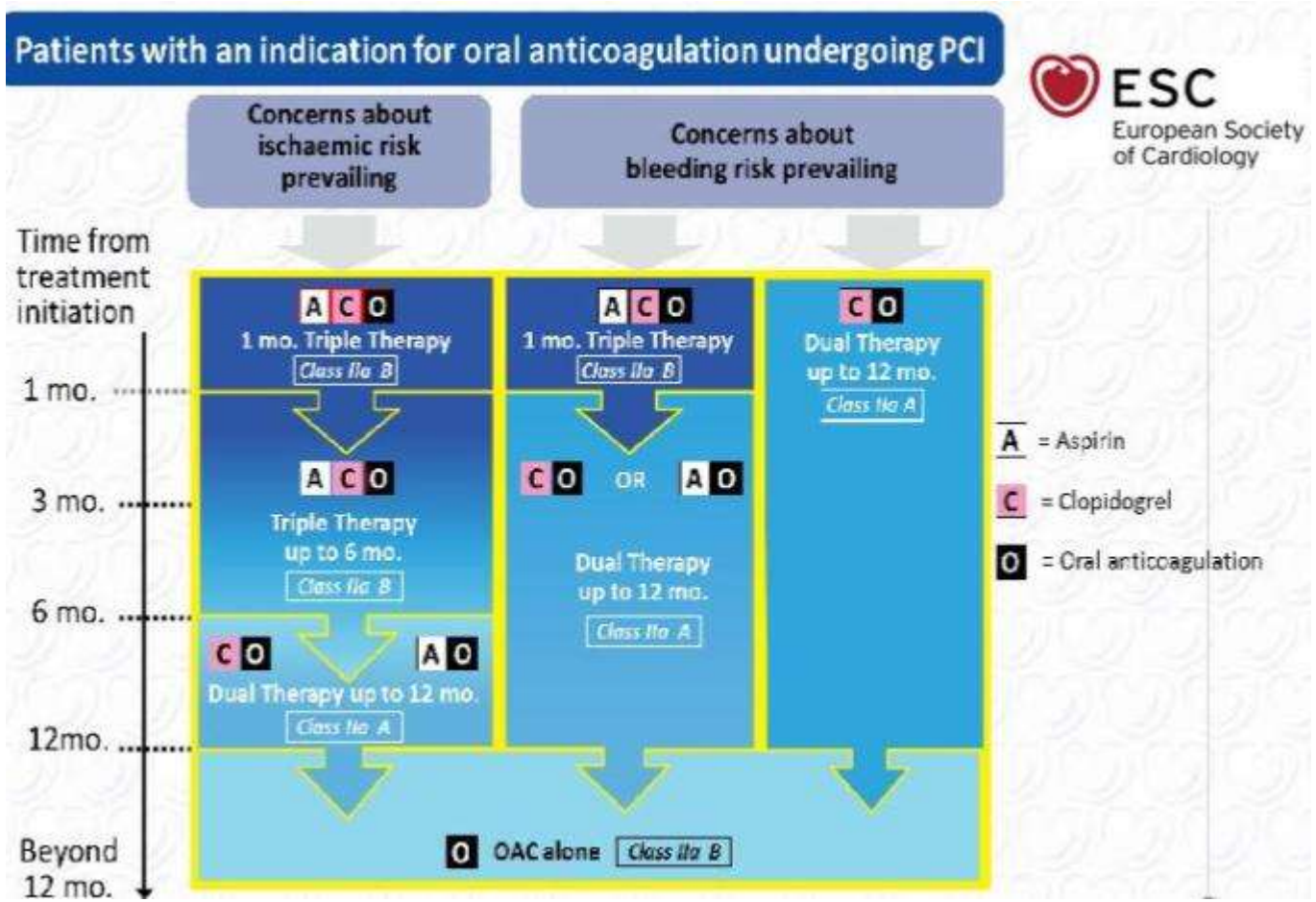
Primary Endpoint: Time to first ISTH major or clinically relevant non-major bleeding event

RE-DUAL PCI



Full analysis set presented. HRs and Wald CIs from Cox proportional-hazard model. For the dabigatran 110 mg vs warfarin comparison, the model is stratified by age, non-elderly vs elderly (<70 or ≤70 in Japan and <80 or ≤80 years old elsewhere). For the dabigatran 150 mg vs warfarin comparison, an unstratified model is used; elderly patients outside the USA are excluded. Non-inferiority P value is one sided (alpha=0.025). Wald two-sided P value from (stratified) Cox proportional-hazard model (alpha=0.05)

ΑΓΩΓΗ ΣΕ ΑΣΘΕΝΕΙΣ ΜΕ ΕΝΔΕΙΞΗ ΛΗΨΗΣ ΑΝΤΙΠΗΚΤΙΚΟΥ



ΤΡΙΠΛΗ ΑΓΩΓΗ ΜΕ DOAC

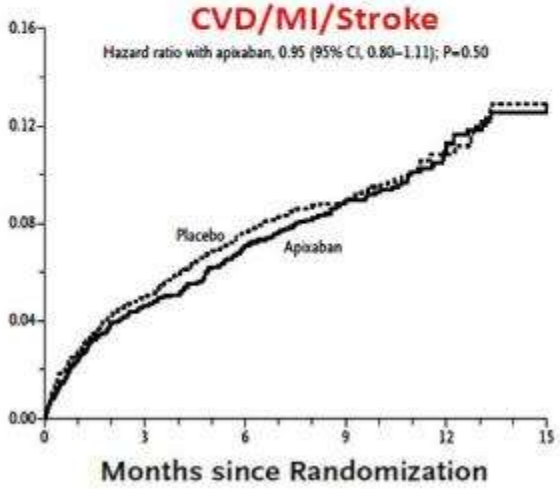
Apixaban with Antiplatelet therapy after Acute Coronary Syndrome (APPRAISE-2)

- Randomized, double-blind controlled clinical trial comparing apixaban, at dose of 5 mg twice daiy with placebo in addition to standard antiplatelet therapy in pts with a recent ACS and at least 2 additional RF for recurrent ischemic events

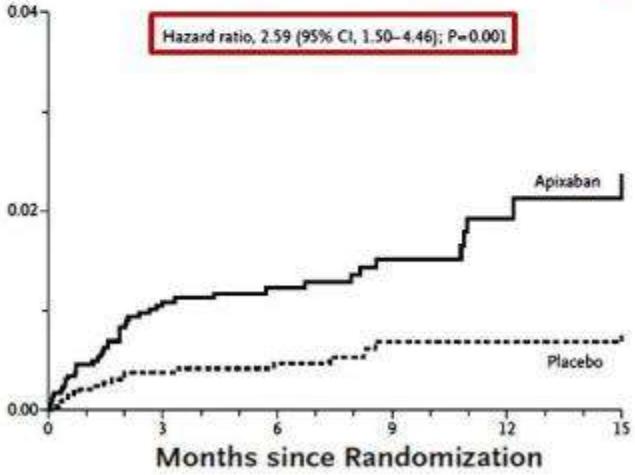
RESULTS

The trial was terminated prematurely after recruitment of 7392 patients because of an increase in major bleeding events with apixaban in the absence of a counterbalancing reduction in recurrent ischemic events. With a median follow-up of 241 days,

Probability of CVD/MI/Stroke



Probability of TIMI major bleeding

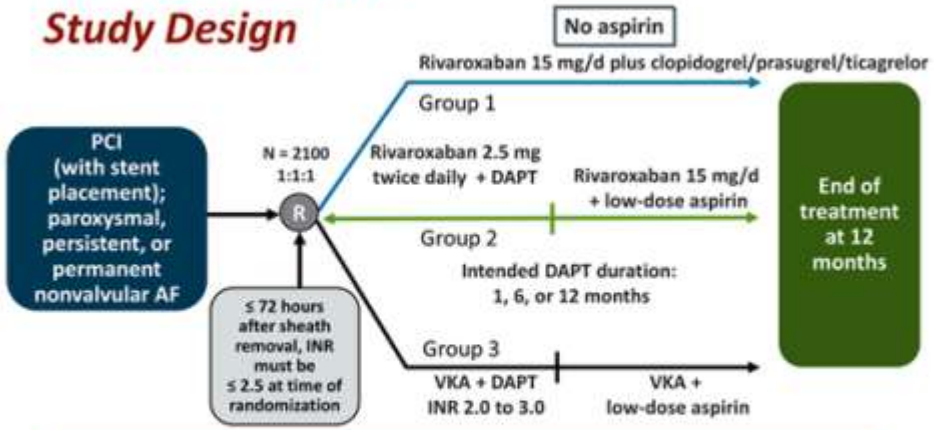


N Engl J Med 2011;365:699-708.

PIONEER

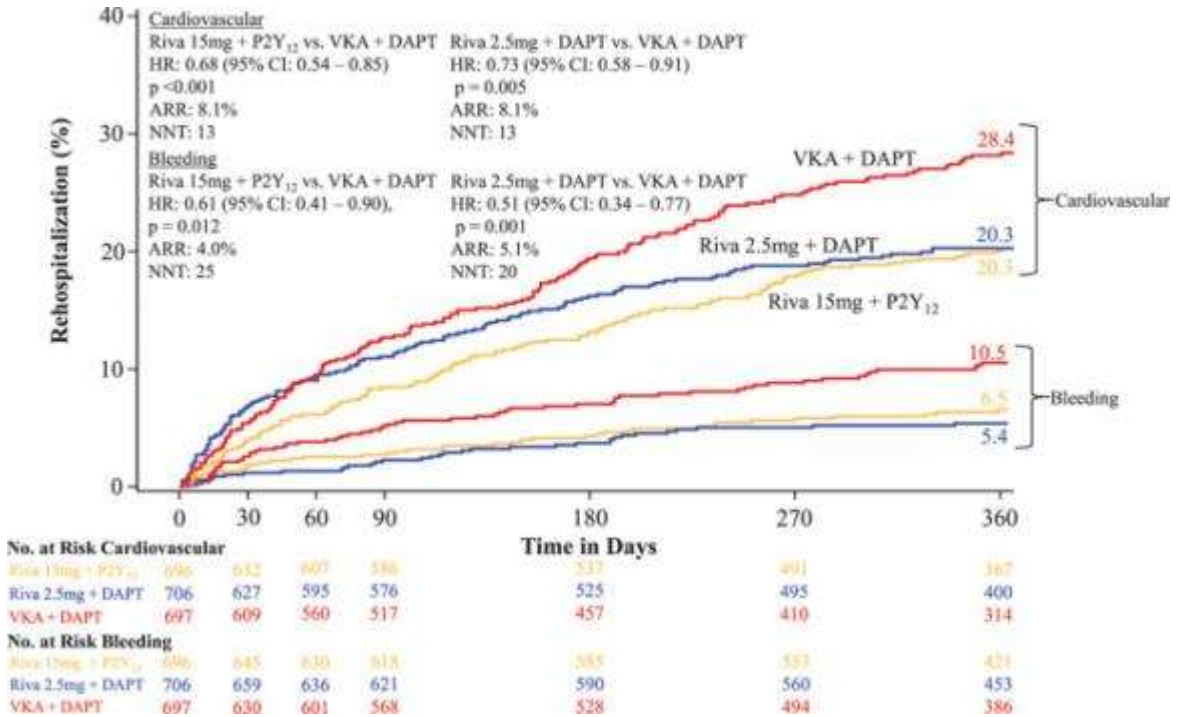
PIONEER AF-PCI

Study Design



- Primary outcome measure: Clinically significant bleeding (composite of TIMI major or minor bleeding or bleeding requiring medical attention)
- Secondary outcome measure: MACE (composite of death from CV causes, MI, or stroke

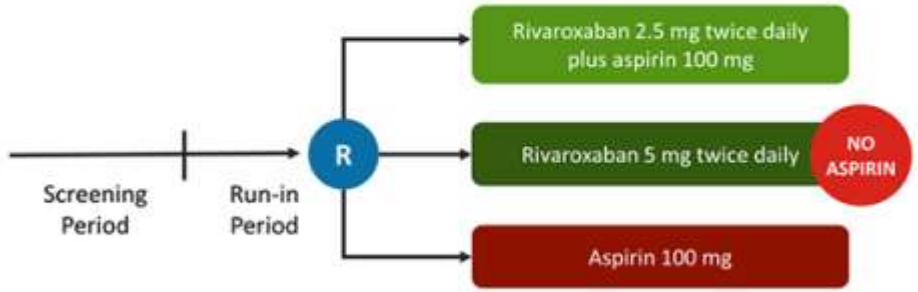
Gibson CM, et al. *Am Heart J.* 2015;169:472-478.



COMPASS

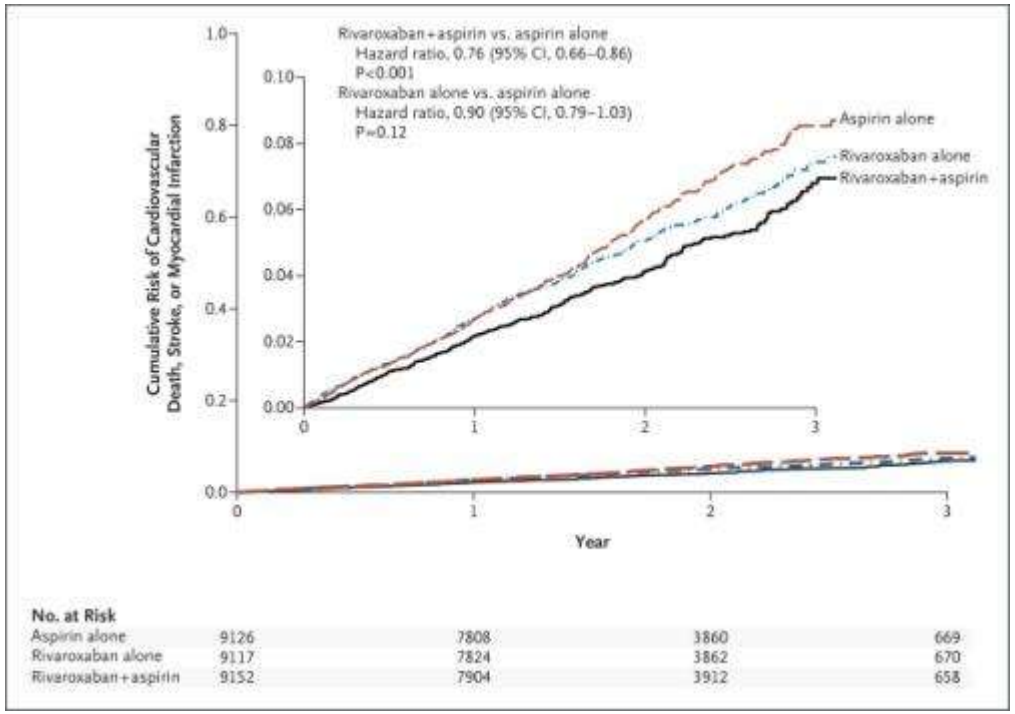
COMPASS
Trial Design (cont)

Rivaroxaban With or Without Aspirin vs Aspirin in Patients With CAD and/or PAD

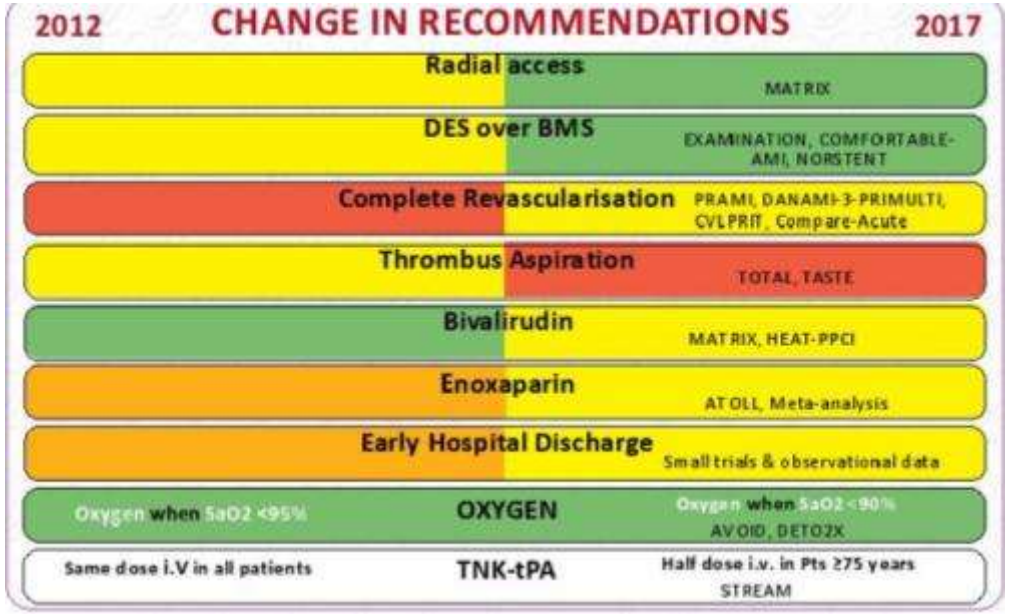


Primary Outcome: MI, Stroke, CV Death
Mean Follow-Up: 3 to 4 y

ClinicalTrials.gov NCT01776424.



ΣΥΝΟΨΗ

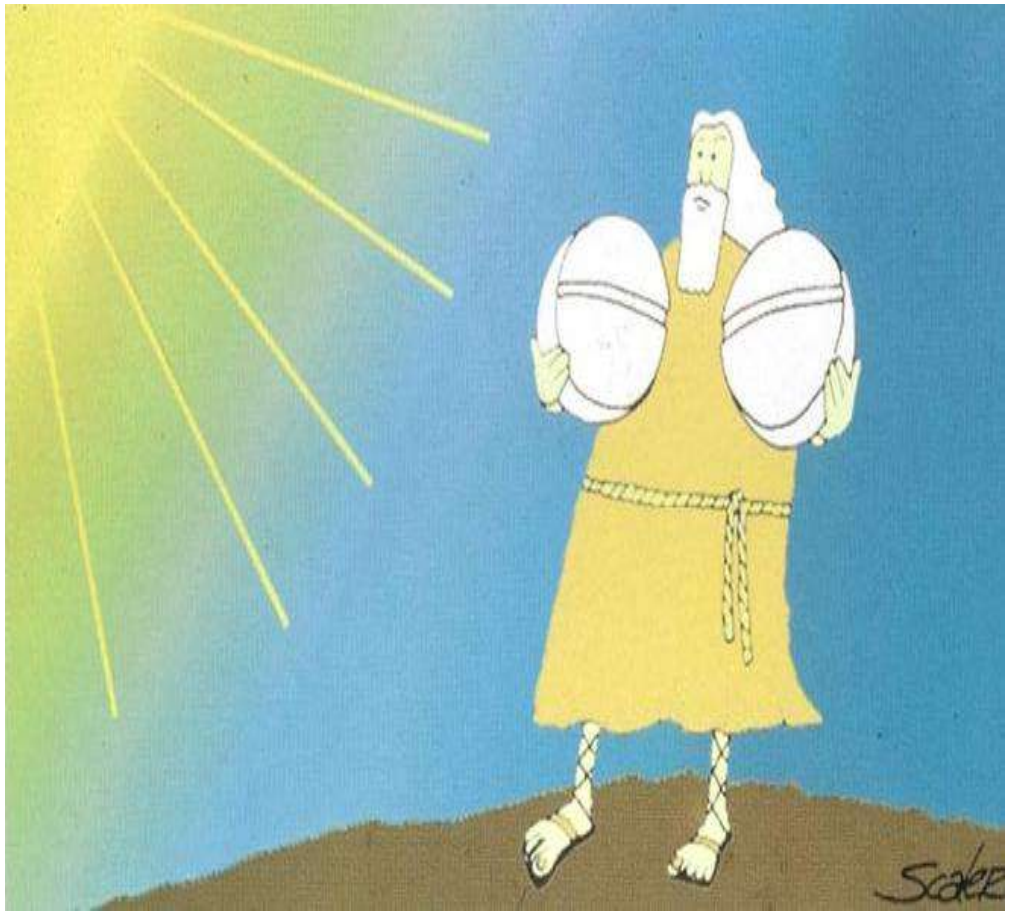

2012
CHANGE IN RECOMMENDATIONS
2017
Radial access
MATRIX
DES over BMS
EXAMINATION, COMFORTABLE-AMI, NORSTENT
Complete Revascularisation
PRAMI, DANAMI-3-PRIMULTI, CVLPRIT, Compare-Acute
Thrombus Aspiration
TOTAL, TASTE
Bivalirudin
MATRIX, HEAT-PPCI
Enoxaparin
ATOLL, Meta-analysis
Early Hospital Discharge
Small trials & observational data
Oxygen when SaO2 <95%
OXYGEN
Oxygen when SaO2 <90%
AVOID, DETO2X
Same dose i.V in all patients
TNK-tPA
Half dose i.v. in Pts ≥75 years
STREAM


2017 NEW RECOMMENDATIONS
• Additional lipid lowering therapy if LDL >1.8 mmol/L (70 mg/dL) despite on maximum tolerated statins. IMPROVE-IT, FOURIER
• Complete revascularization during index primary PCI in STEMI patients in shock. Expert opinion
• Cangrelor if P2Y12 inhibitors have not been given. CHAMPION
• Switch to potent P2Y12 inhibitors 48 hours after fibrinolysis. Expert opinion
• Extend Ticagrelor up to 36 months in high-risk patients. PEGASUS-TIMI 54
• Use of polypill to increase adherence. FOCUS
• Routine use of deferred stenting. DANAMI 3-DEFER
I
IIa
IIb
III

ΕΥΧΑΡΙΣΤΩ ΠΟΛΥ

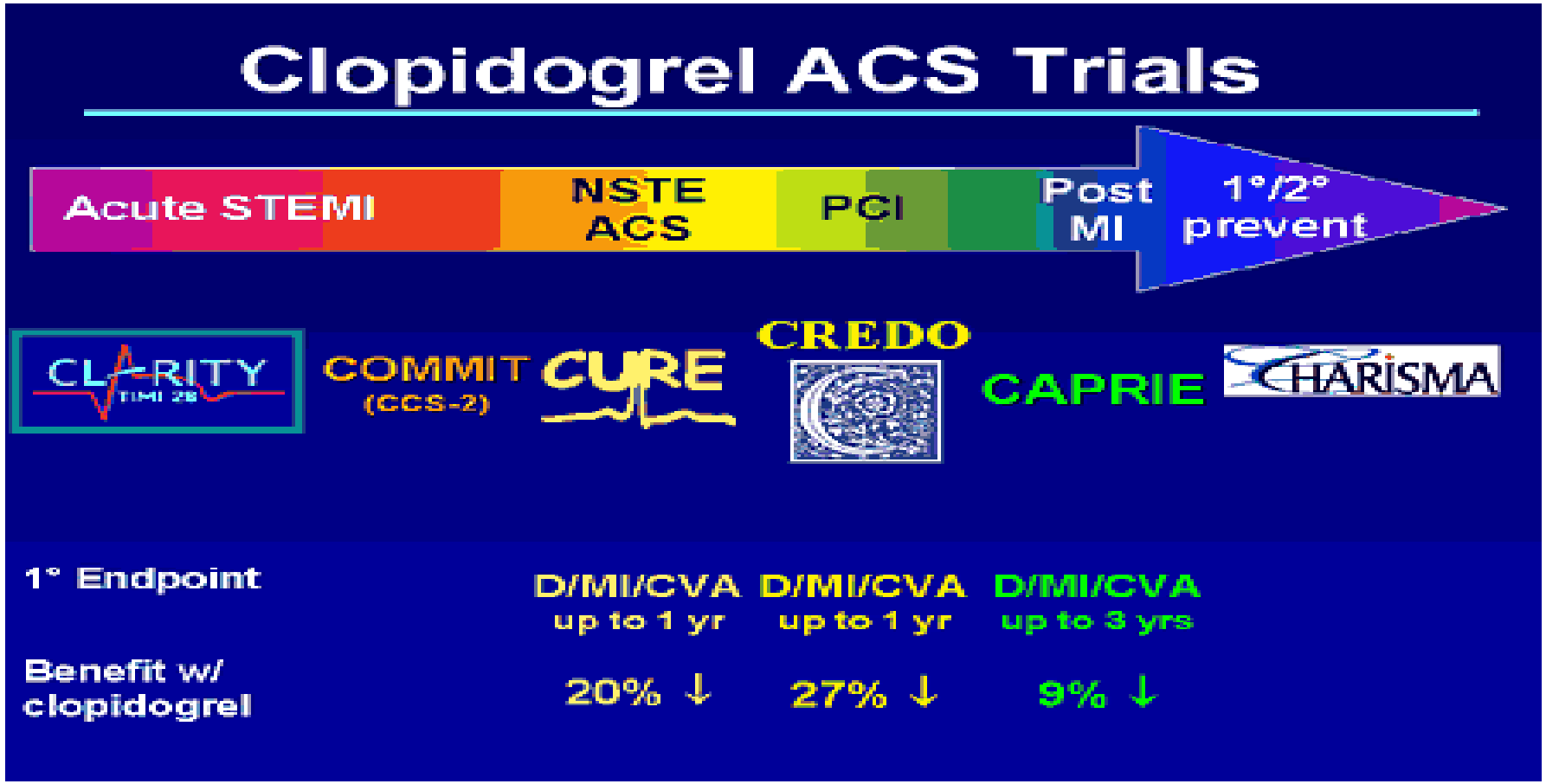
ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ ΣΑΣ

ΑΣΠΙΡΙΝΗ



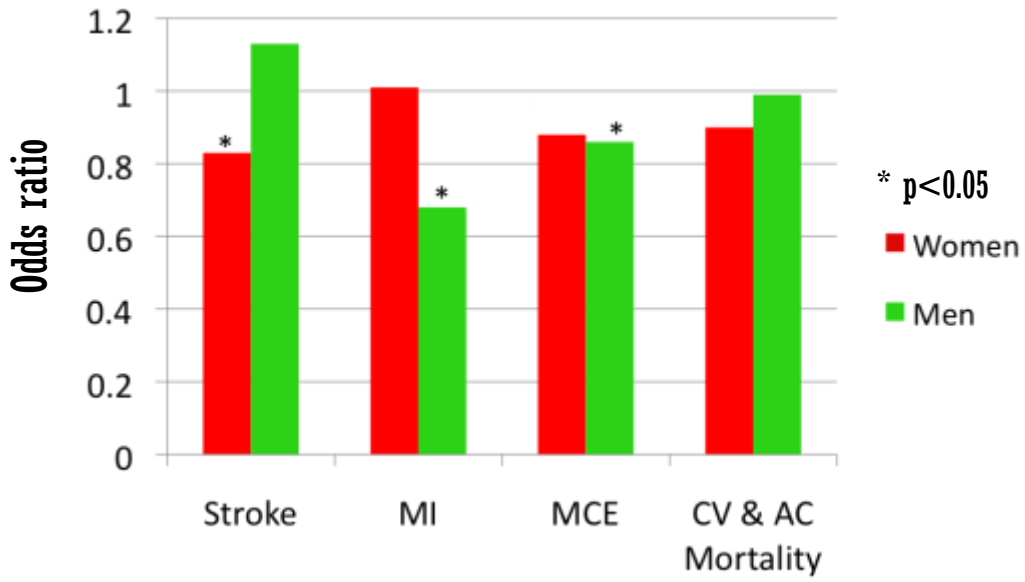

DEMAND
BAYER
ASPIRIN
Unless you see the "Bayer Cross" on package or on tablets you are not getting the genuine Bayer Aspirin proved safe by millions and prescribed by physicians over twenty-seven years for
Colds
Neuritis
Toothache
Neuralgia
Headache
Lumbago
Rheumatism
Pain, Pain
DOES NOT AFFECT THE HEART

ASPIRIN + CLOPIDOGREL

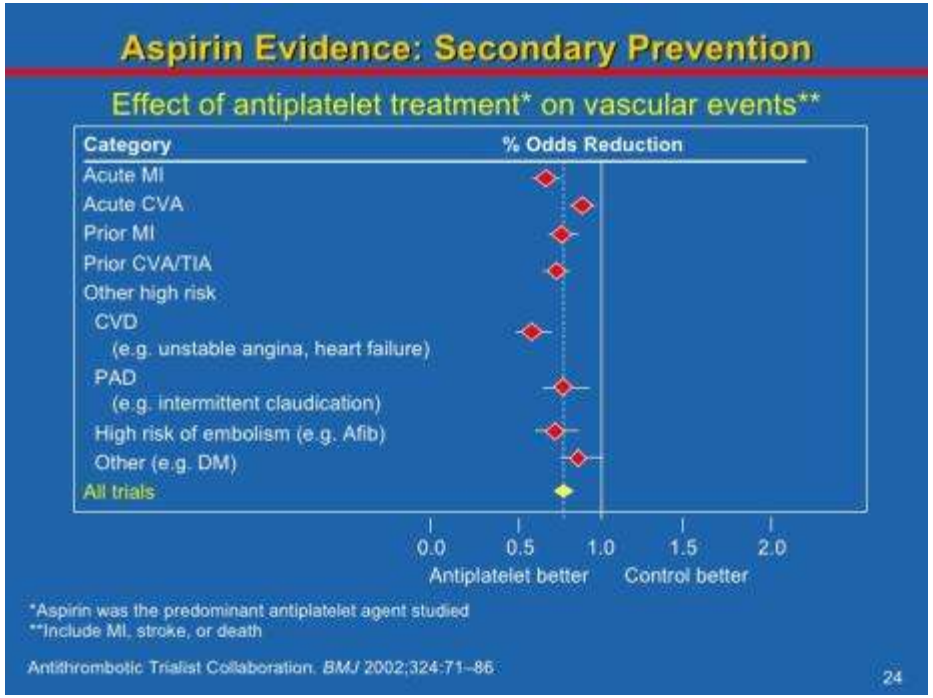


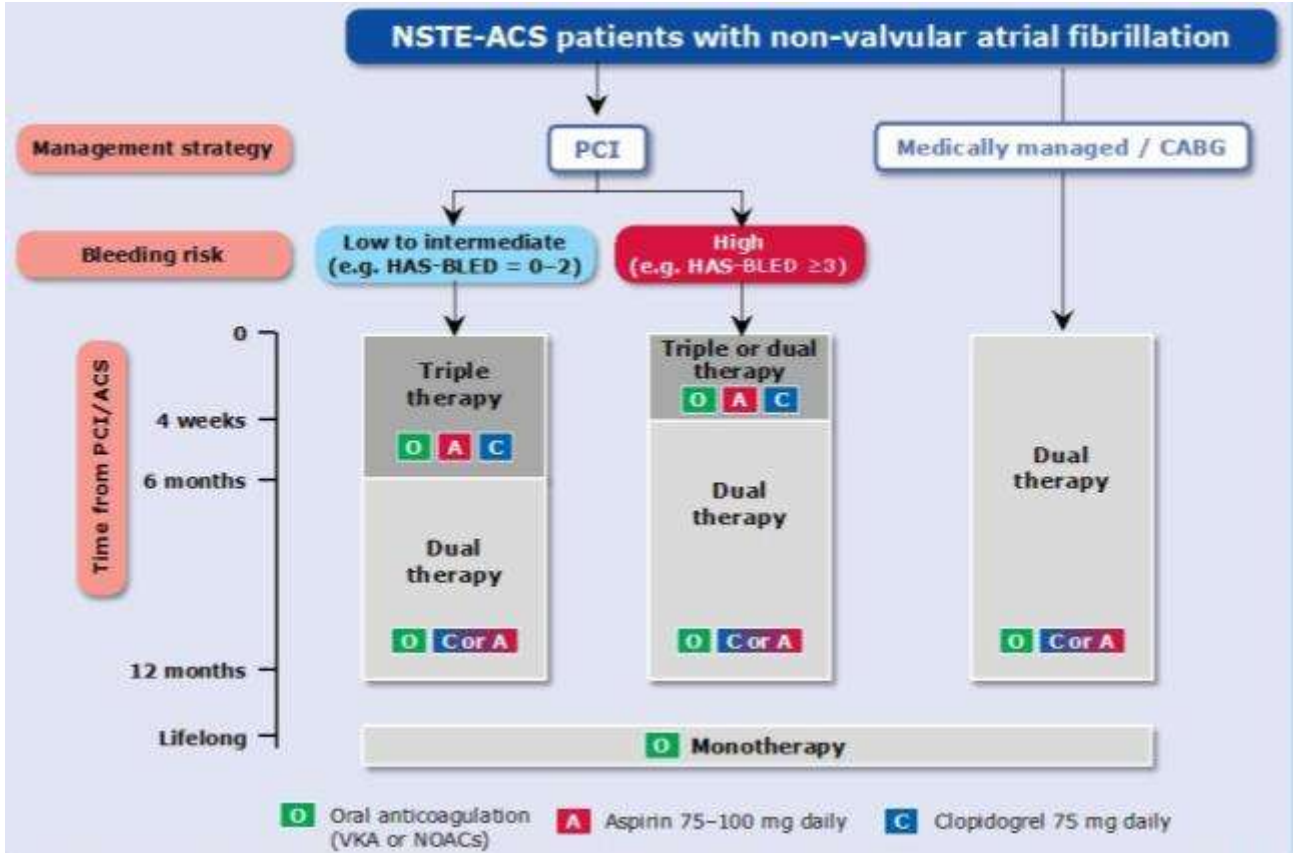
ASPIRIN

Primary prevention

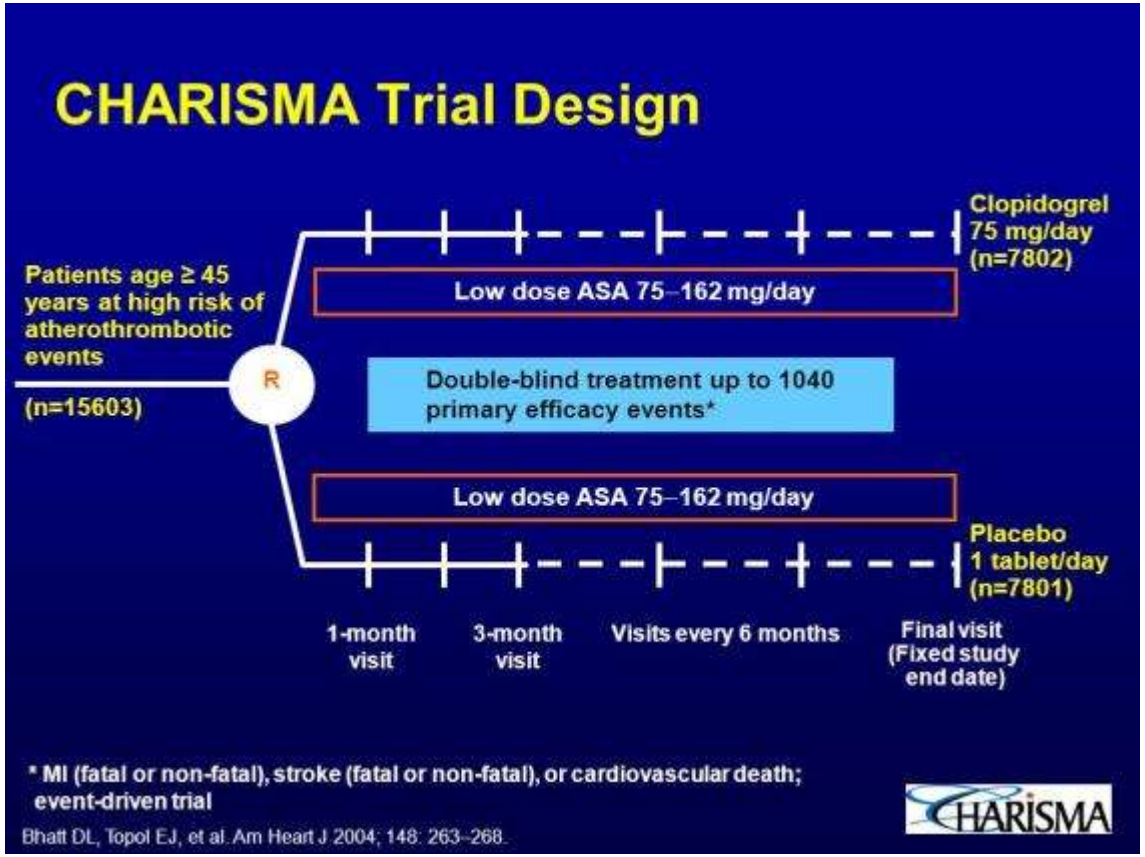


Secondary prevention

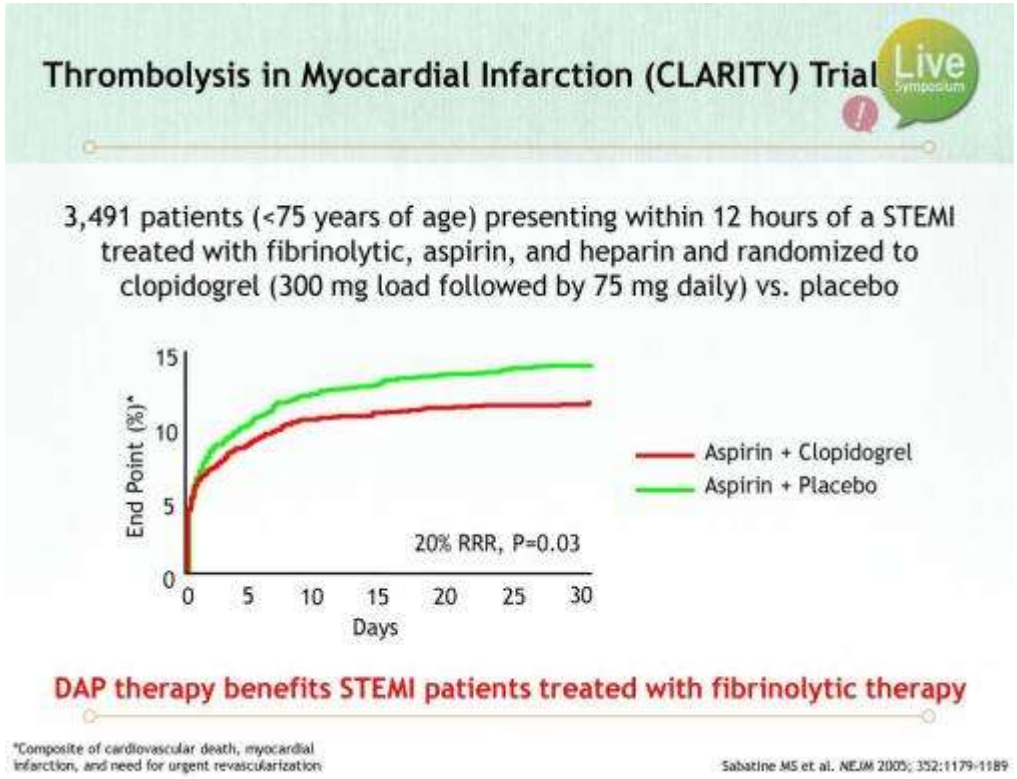


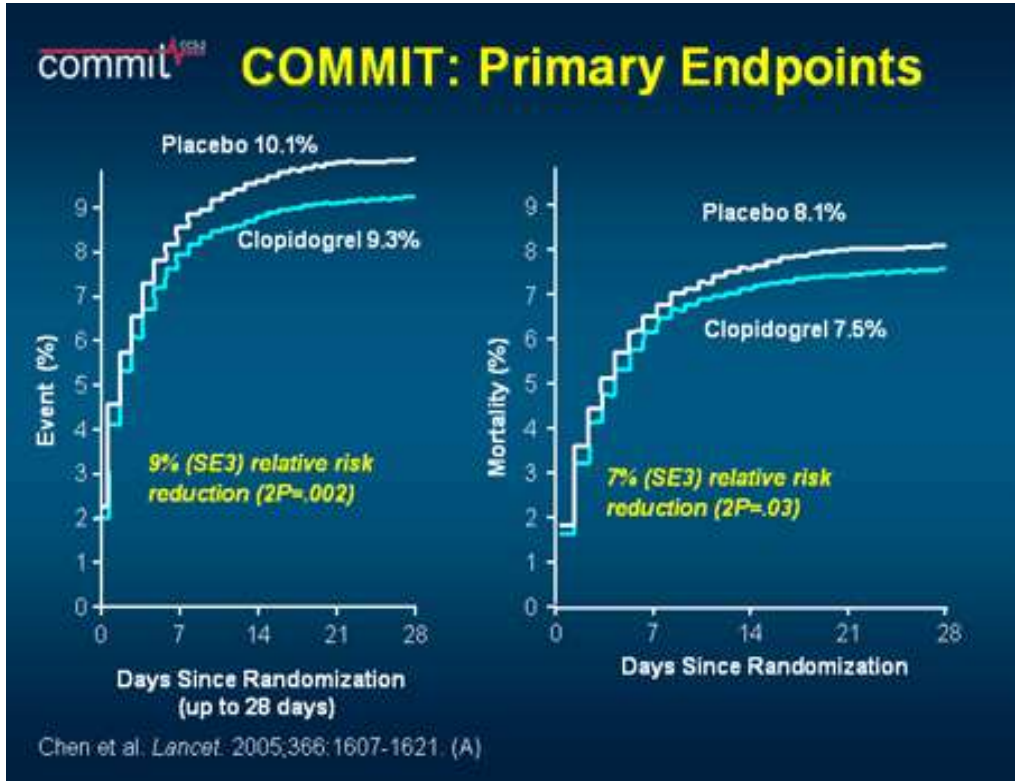

NSTE-ACS patients with non-valvular atrial fibrillation
Management strategy
PCI
Medically managed / CABG
Bleeding risk
Low to intermediate (e.g. HAS-BLED = 0–2)
High (e.g. HAS-BLED ≥3)
Time from PCI/ACS
0
4 weeks
6 months
12 months
Lifelong
Triple therapy
O A C
Dual therapy
O C or A
Triple or dual therapy
O A C
Dual therapy
O C or A
Dual therapy
O C or A
O Monotherapy
O Oral anticoagulation (VKA or NOACs)
A Aspirin 75–100 mg daily
C Clopidogrel 75 mg daily

ΜΕΛΕΤΗ CHARISMA

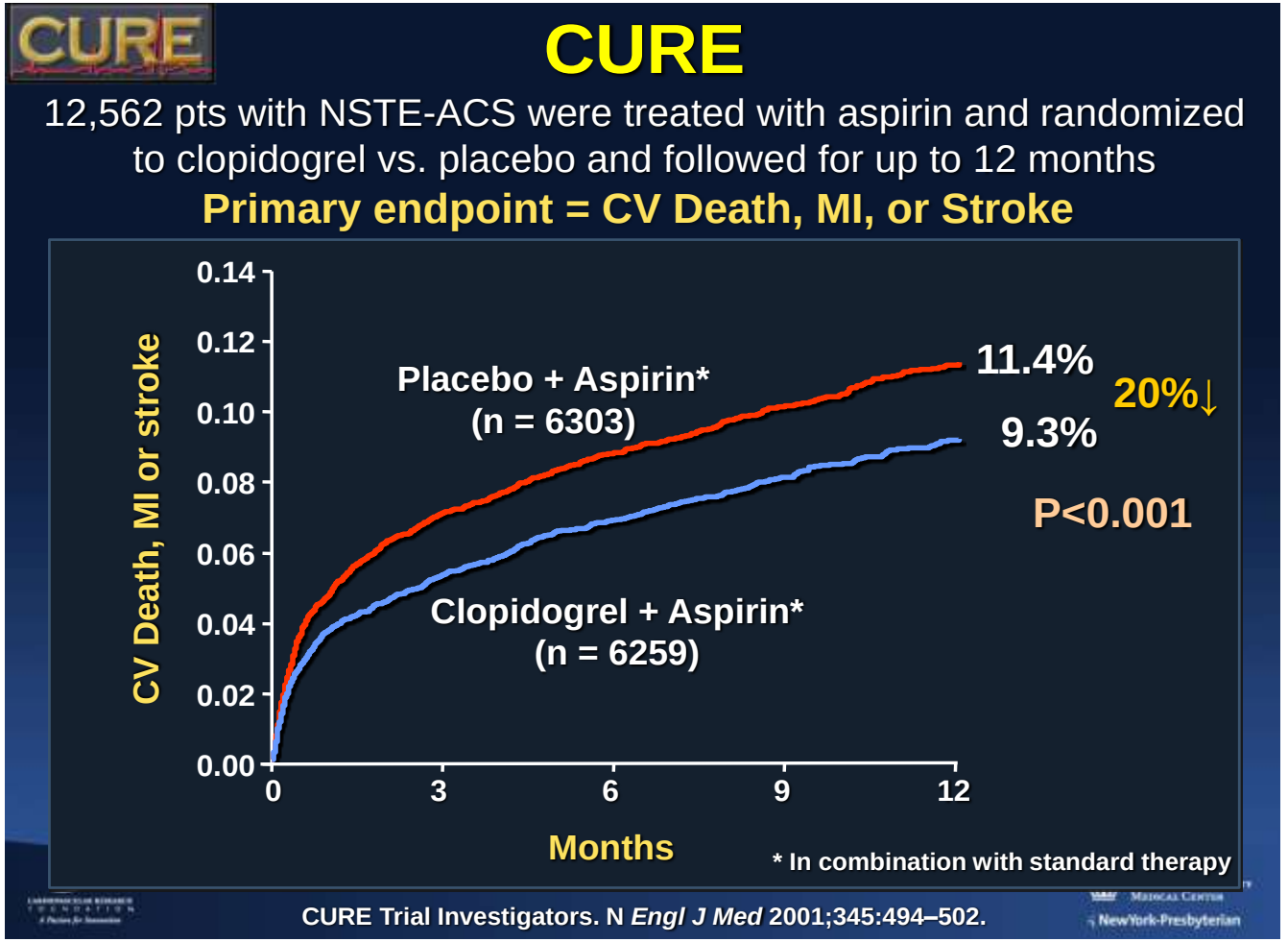


ΑΣΘΕΝΕΙΣ ΜΕΤΑ ΘΡΟΜΒΟΛΥΣΗ

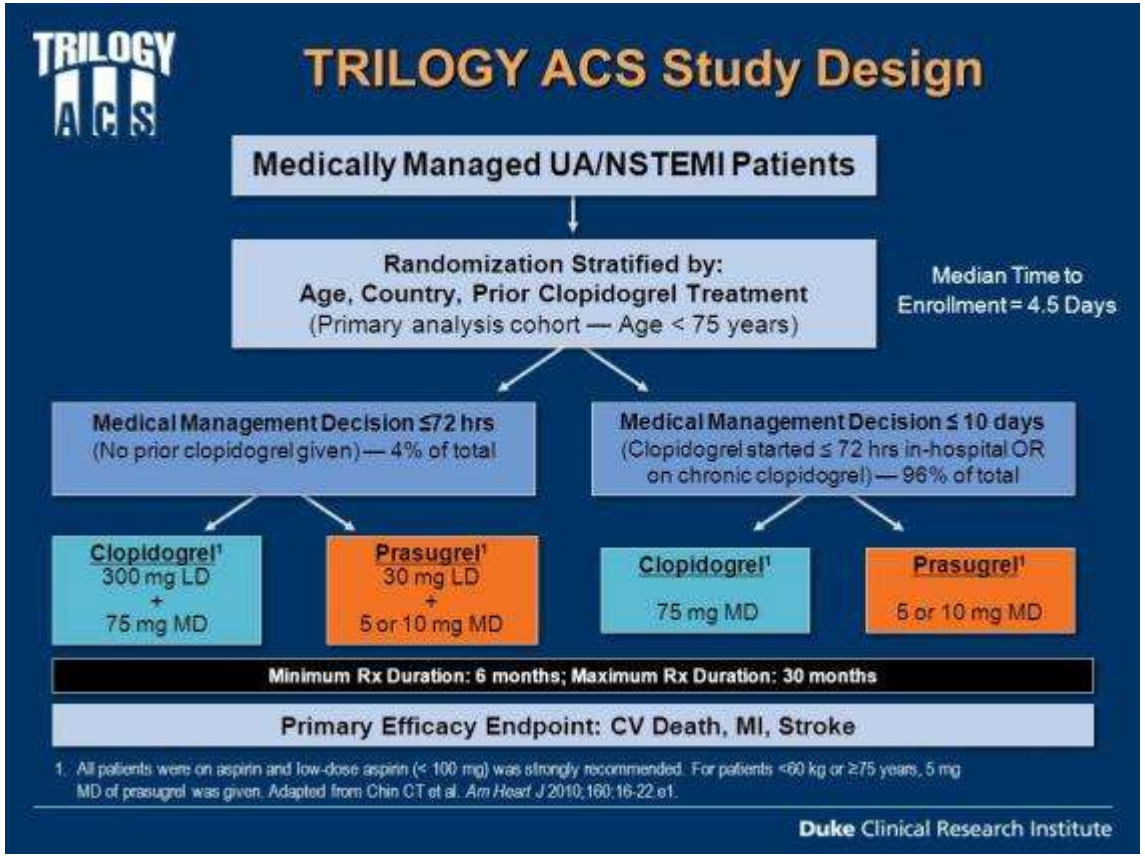




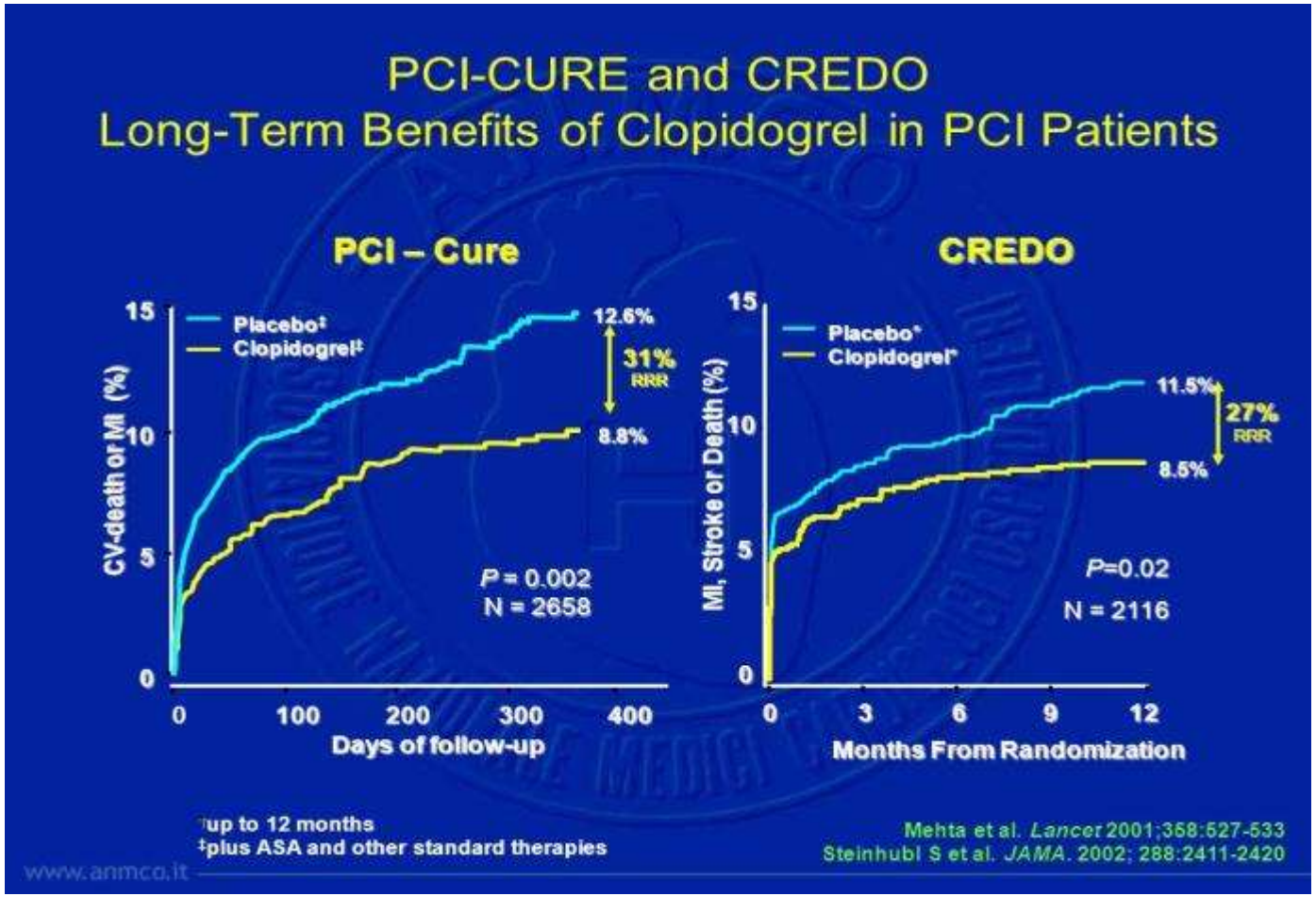
ΑΣΘΕΝΕΙΣ ΜΕ NSTEMI



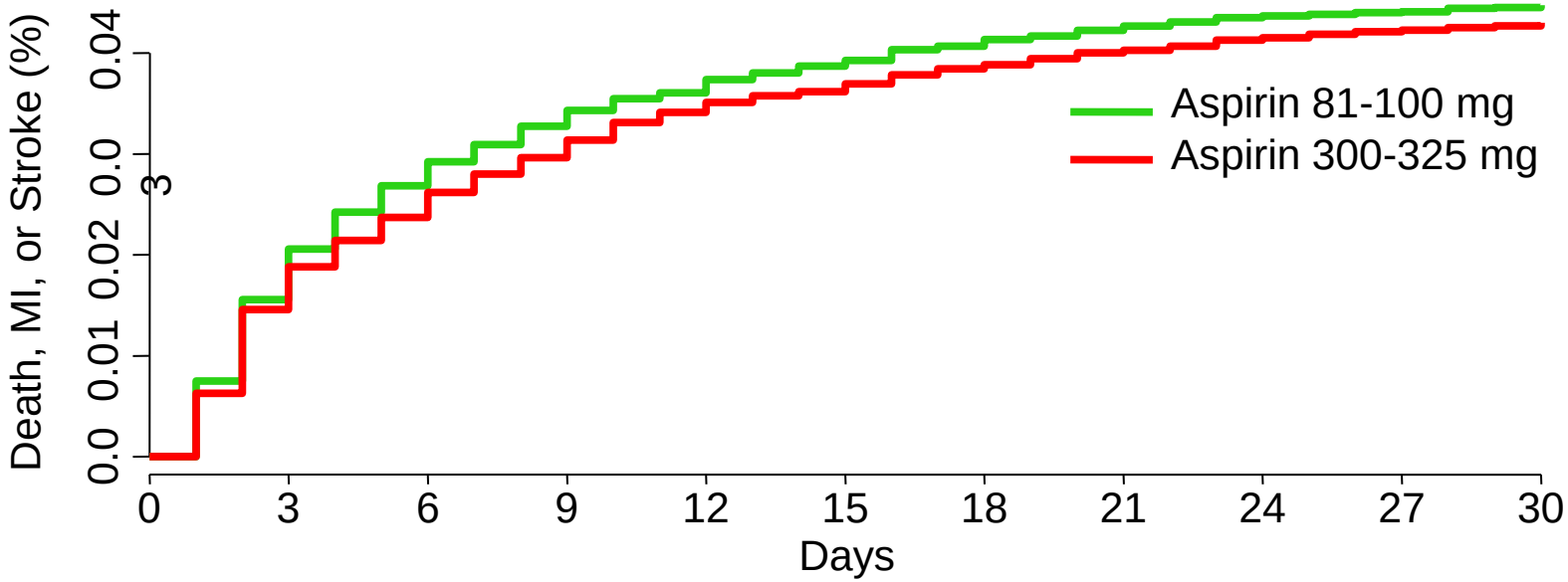
ΜΕΛΕΤΗ TRILOGY ACS

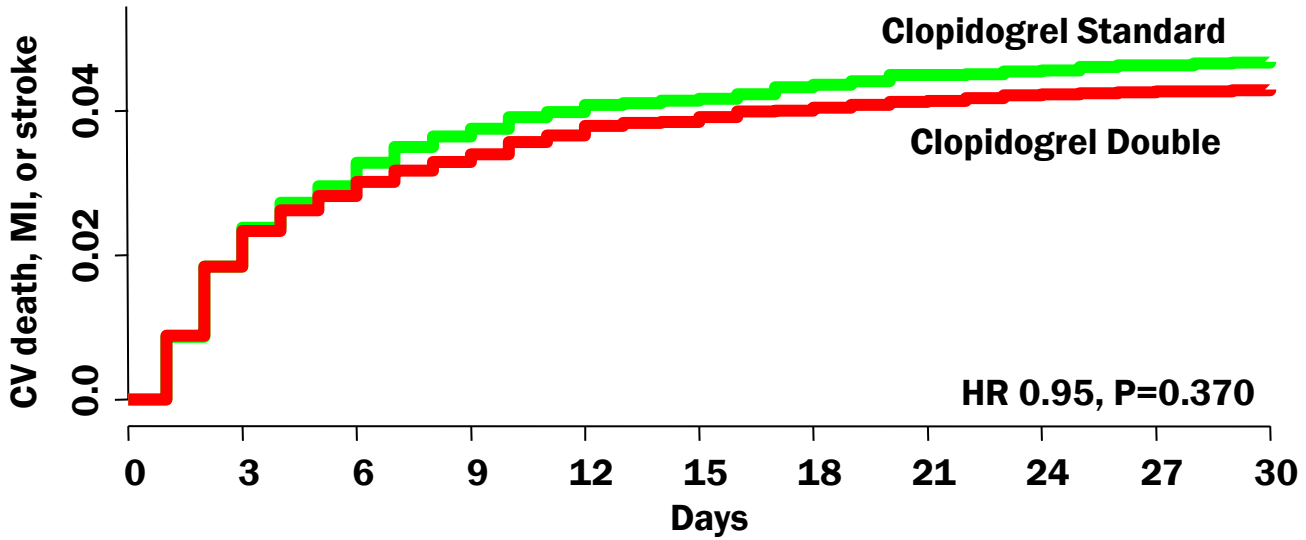


ΑΣΘΕΝΕΙΣ ΜΕΤΑ PCI



CURRENT – OASIS 7





Type of Bleeding	D (%)	S (%)
TIMI Major	1.7	1.3
CURRENT Major*	2.5	2.0
Fatal	0.13	0.11
ICH	0.03	0.05
CABG-related	1.0	0.9

ΜΕΛΕΤΗ CAPRIE