Dual Anti-Platelet Therapy
DAPT

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Why DAPT?

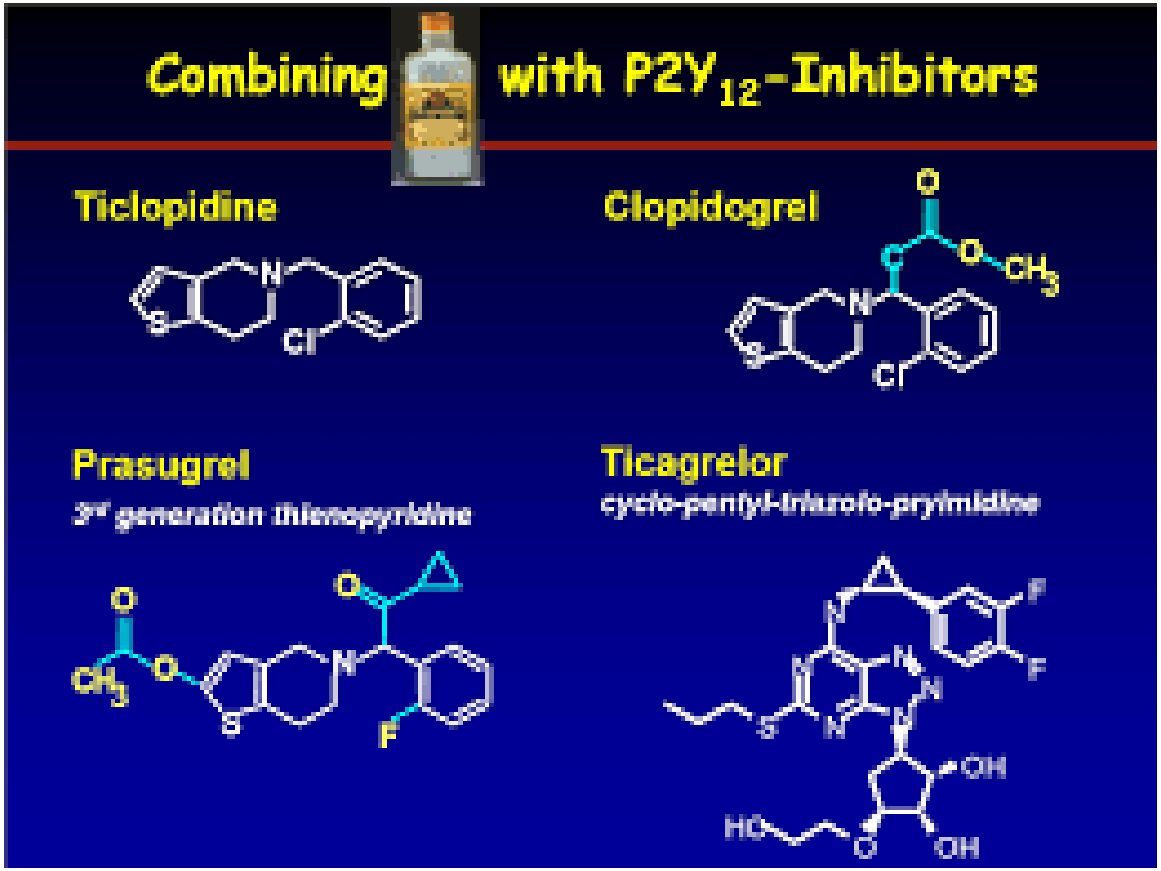
Cornerstone of treatment - ACS and PCI

- To prevent local thrombotic complications related to stent implantation

and

- To reduce systemic athero thrombotic events

What is DAPT?



DAPT- combination of Aspirin and a P2Y12 receptor inhibitor

P2Y12 inhibitors

- Three generations of thienopyridines , a family of non direct, orally administered antiplatelet agents that irreversibly block the platelet ADP $P2Y_{12}$ receptor, are approved currently for clinical use.
- Non-thienopyridines- direct, reversible inhibitors namely ticagrelor, cangrelor and elinogrel

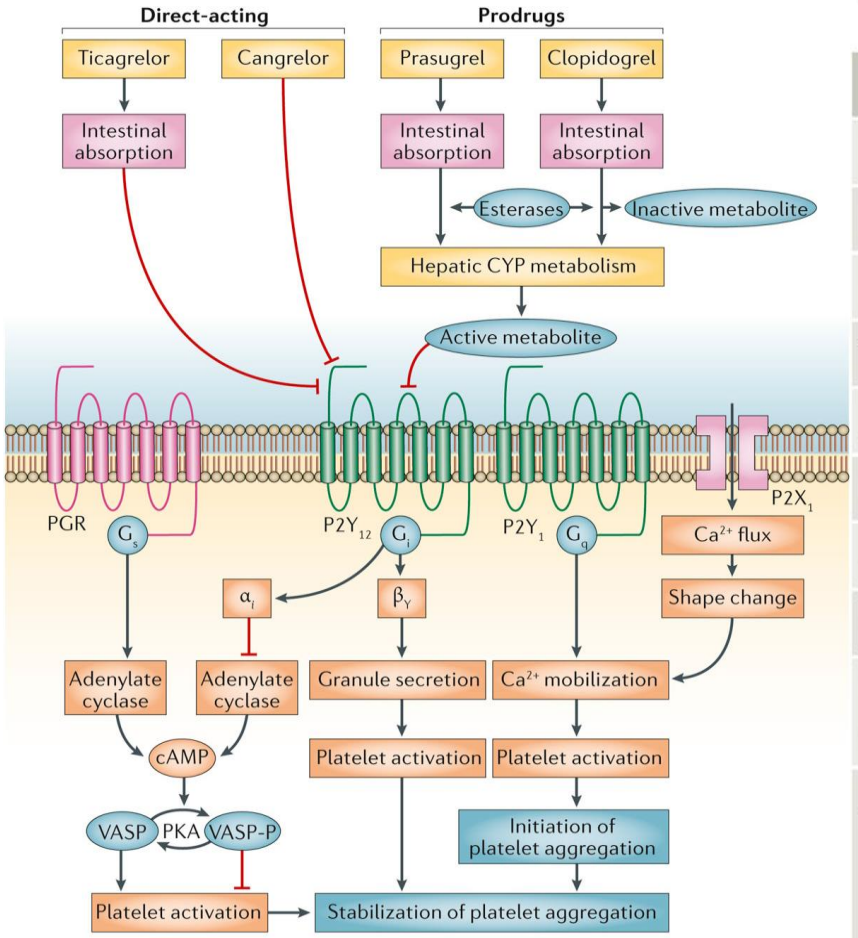
- 3 different oral P2Y12 receptor inhibitors are available
  - 2 have obtained the indication for ACS (**clopidogrel and ticagrelor**)
  - 1 for ACS with planned percutaneous coronary intervention (PCI) (**prasugre**l).
- **In addition, an intravenous direct acting P2Y12 inhibitor, cangrelor, has been recently approved by US and European regulatory agencies for patients undergoing PCI**

History of DAPT

- **Ticlopidine** was the first to receive regular FDA approval in ***1991*** to reduce ischemic events in CAD patients

  -Ticlopidine for 2-4 weeks after BMS implantation (ISAR and STARS study)
- **Clopidogrel** was approved by the U.S. FDA in ***1997*** to reduce ischemic event following CAPRIE study
- **Prasugrel** was cleared by FDA in ***2009*** only for use in the context of PCI following the TRITON-TIMI 38 trial
- **Ticagrelor** received regulatory approval in Europe and US for use to reduce thrombotic events in patients of ACS in ***2011*** after PLATO trial
- **Cangrelor** was approved by the US FDA for reducing thrombotic events in patients undergoing PCI in ***2015*** based on the CHAMPION-PHOENIX study

Pharmacological properties of P2Y12 inhibitors



Nature Reviews | Cardiology

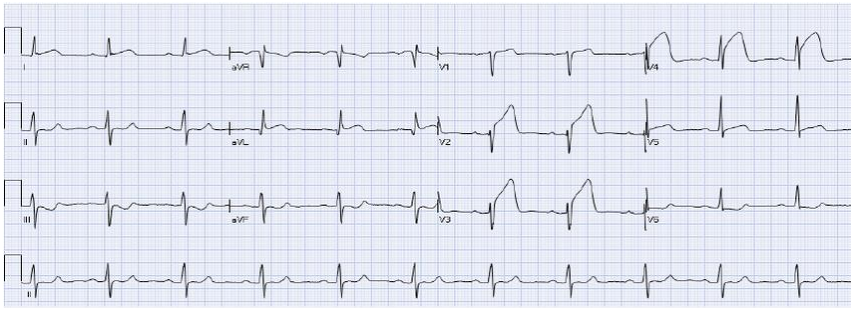
Table 1 | Pharmacological properties of $P2Y_{12}$-receptor inhibitors

Property	Clopidogrel	Prasugrel	Ticagrelor	Cangrelor
Receptor blockade	Irreversible	Irreversible	Reversible	Reversible
Prodrug	Yes	Yes	No	No
Half-life	~6 h	~7 h	8–12 h	3–5 min
Type of binding	Competitive	Competitive	Noncompetitive	Undetermined*
Administration route	Oral	Oral	Oral	Intravenous
Frequency	Once daily	Once daily	Twice daily	Bolus plus infusion
Onset of action	2–8 h	30 min to 4 h	30 min to 4 h	~2 min
Offset of action	5–7 days	7–10 days	3–5 days	30–60 min
Drug interaction with CYP enzymes	CYP2C19	No	CYP3A	No
Approved settings	ACS (invasively or noninvasively managed) and PCI in stable CAD	PCI in patients with ACS	ACS (invasively or noninvasively managed)	PCI in patients with or without ACS

*The binding site of cangrelor at the $P2Y_{12}$-receptor level is not clearly defined; nevertheless, cangrelor is associated with high levels of receptor occupancy preventing ADP signalling. Abbreviations: ACS, acute coronary syndromes; CAD, coronary artery disease; CYP, cytochrome P450; PCI, percutaneous coronary intervention.

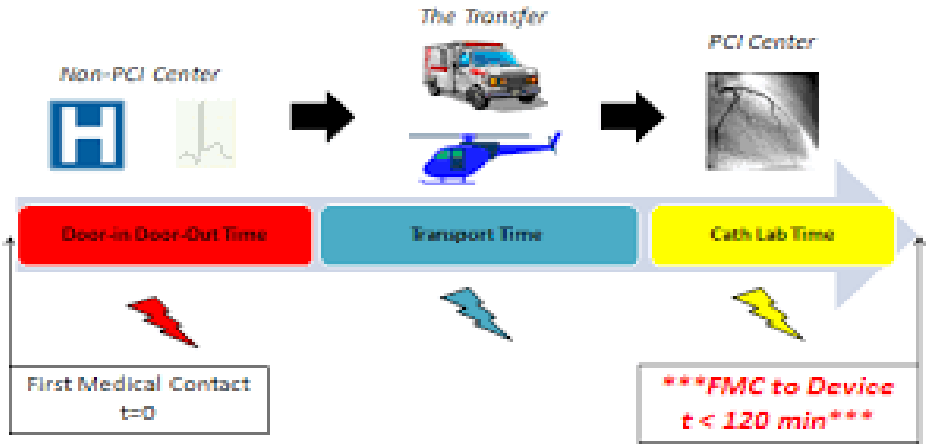
Case scenario-1

- A 56 year old male, HTN, smoker had typical chest pain of 6 hours duration. Vitals stable. ECG was taken and tele-transmitted to me from the ambulance for further advice.

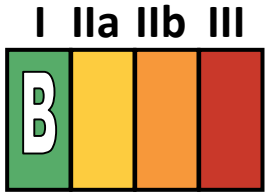


ECG showed acute anterior STEMI

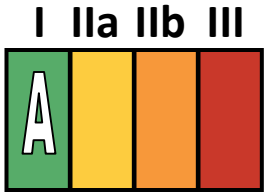
Advised shift for primary PCI



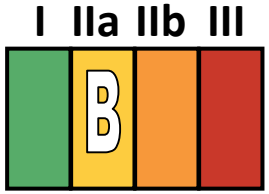
Antiplatelet Therapy to Support Primary PCI for STEMI



Aspirin 162 to 325 mg should be given before primary PCI.



After PCI, aspirin should be continued indefinitely.

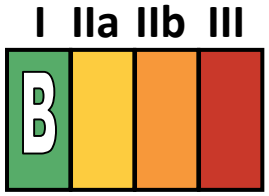


It is reasonable to use 81 mg of aspirin per day in preference to higher maintenance doses after primary PCI.

Antiplatelet Therapy to Support Primary PCI for STEMI

A loading dose of a $P2Y_{12}$ receptor inhibitor should be given as early as possible or at time of primary PCI to patients with STEMI. Options include:

- Clopidogrel 600 mg; or Prasugrel 60 mg; or Ticagrelor 180 mg

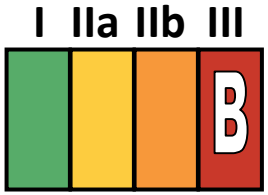


$P2Y_{12}$ inhibitor therapy should be given for 1 year to patients with STEMI who receive a stent (BMS or DES) during primary PCI using the following maintenance doses:

- Clopidogrel 75 mg daily; or Prasugrel 10 mg daily; or Ticagrelor 90 mg twice a day*

*The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.

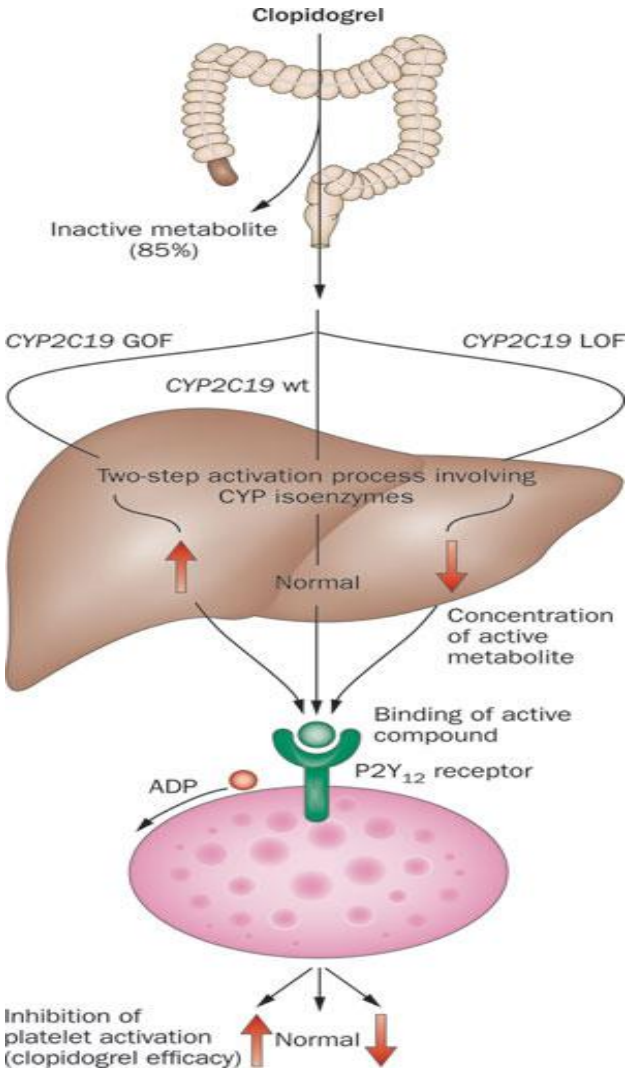
Continuation of a $P2Y_{12}$ inhibitor beyond 1 year may be considered in patients undergoing DES placement.



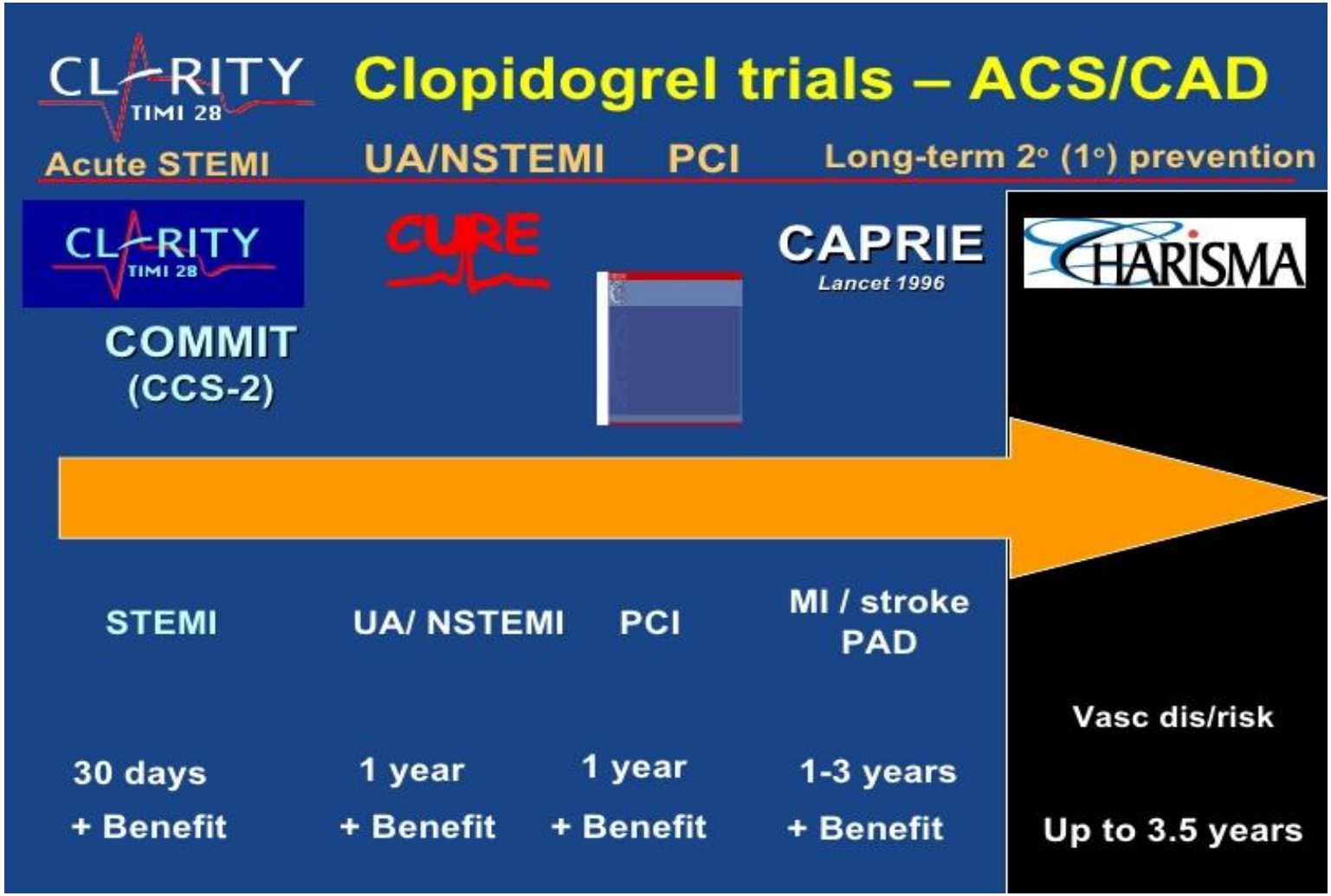
Harm

Prasugrel should not be administered to patients with a history of prior stroke or transient ischemic attack.

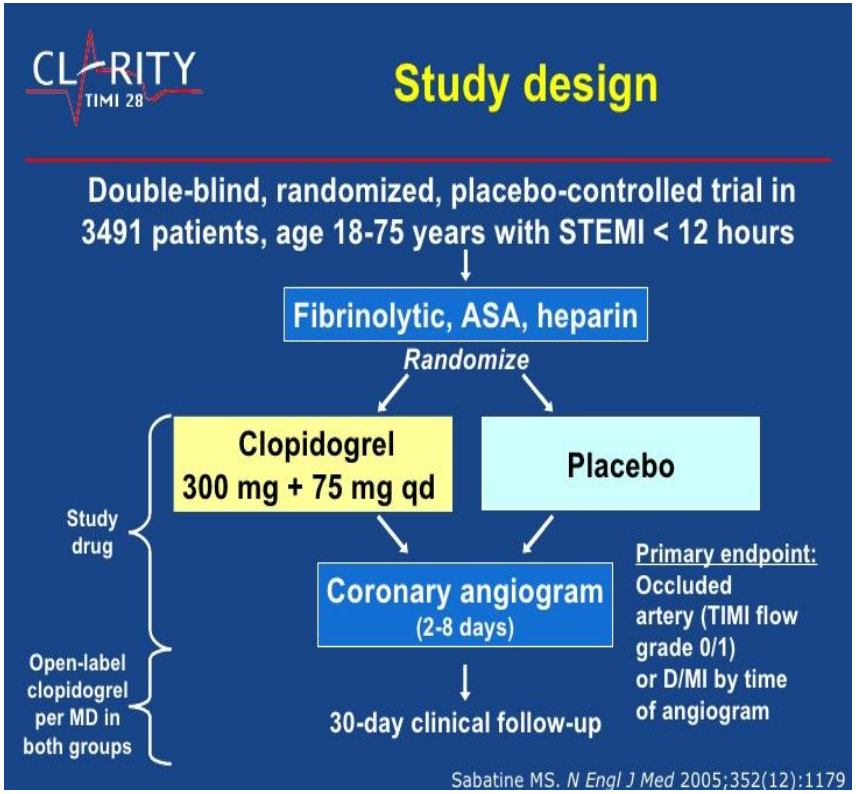
Clopidogrel

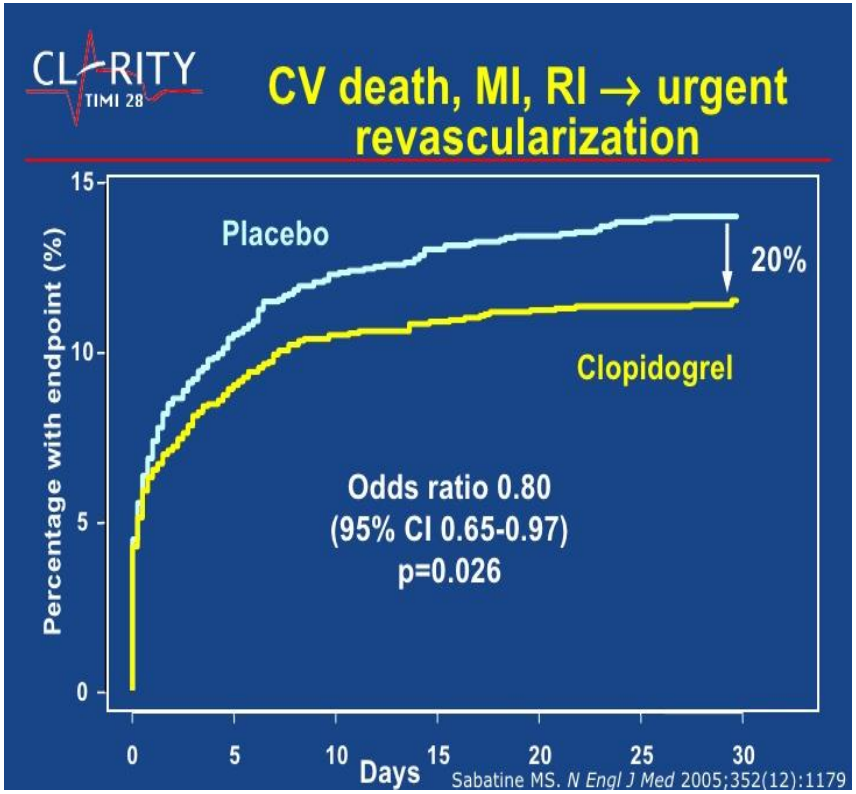


- Clopidogrel -2nd generation thienopyridine.
- Prodrug
- Must be metabolized by CYP450 enzymes to produce the active metabolite.
- The active metabolite selectively inhibits the binding of ADP to its platelet P2Y12 receptor and the subsequent ADP-mediated activation of the glycoprotein GPIIb/IIIa complex, thereby inhibiting platelet aggregation
- This action is irreversible. Platelets affected for the remainder of their lifespan (about 7 to 10 days).
- Platelet aggregation induced by agonists other than ADP is also inhibited by blocking the amplification of platelet activation by released ADP

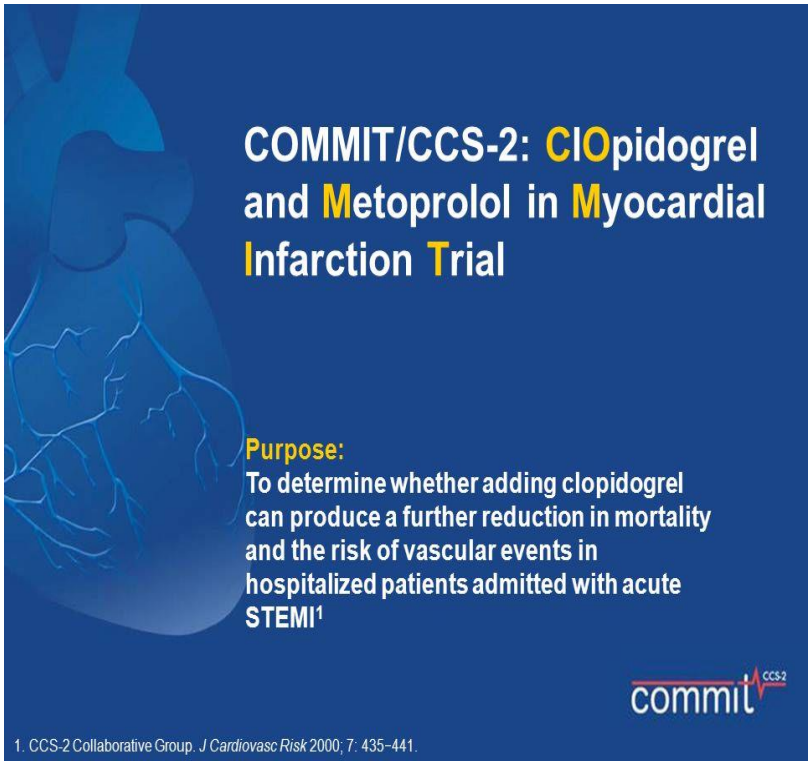

CLARITY TIMI 28
Clopidogrel trials – ACS/CAD
Acute STEMI
UA/NSTEMI
PCI
Long-term 2° (1°) prevention
CLARITY TIMI 28
COMMIT (CCS-2)
CURE
CAPRIE
Lancet 1996
CHARISMA
STEMI
UA/ NSTEMI
PCI
MI / stroke PAD
Vasc dis/risk
30 days + Benefit
1 year + Benefit
1 year + Benefit
1-3 years + Benefit
Up to 3.5 years

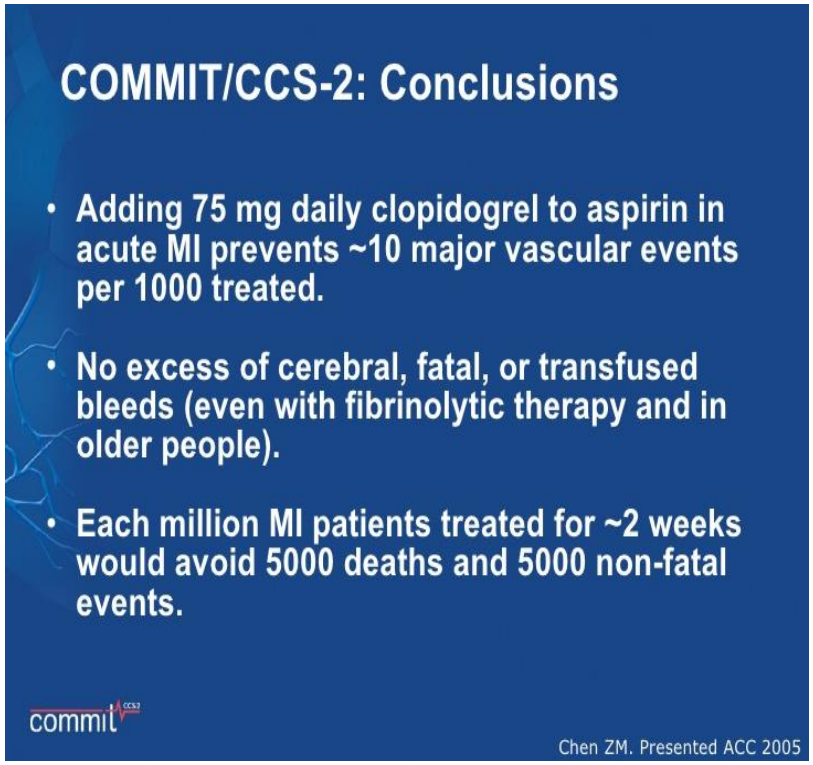
CLARITY-TIMI 28 TRIAL



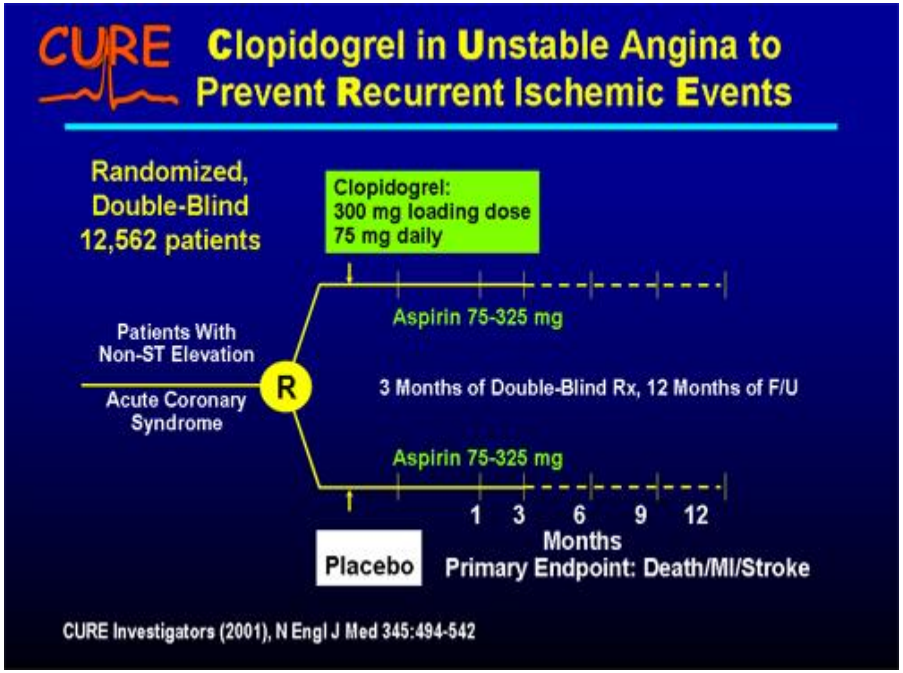


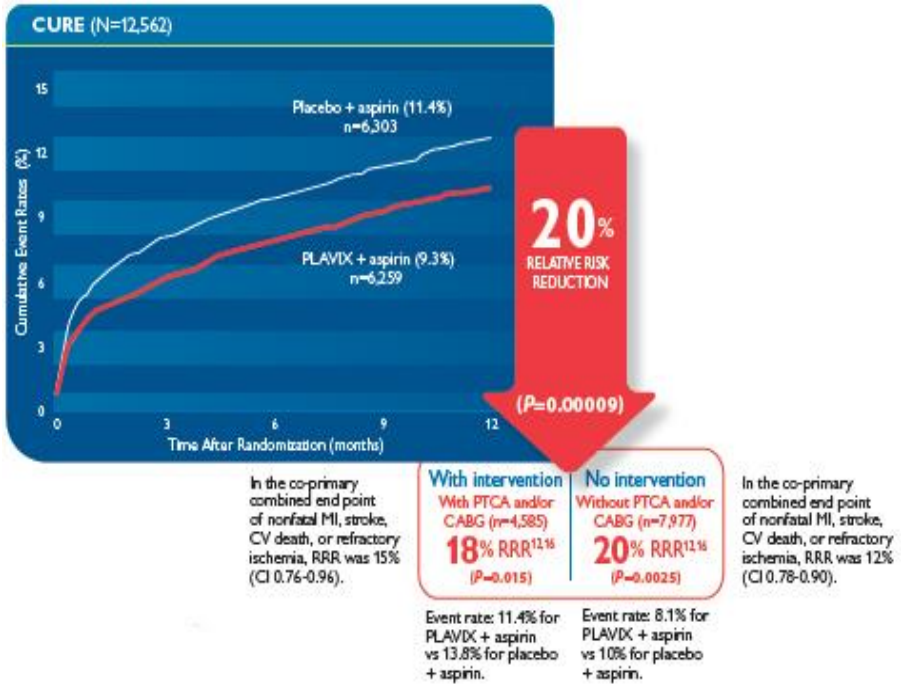
COMMIT/CCS-2 TRIAL





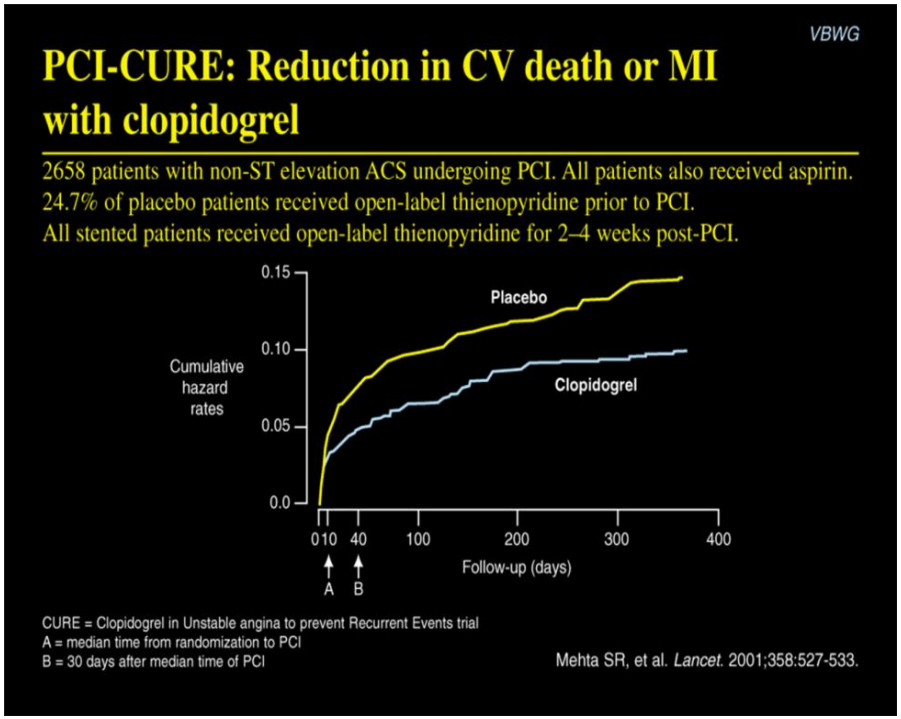
Clopidogrel-DAPT
CURE trial

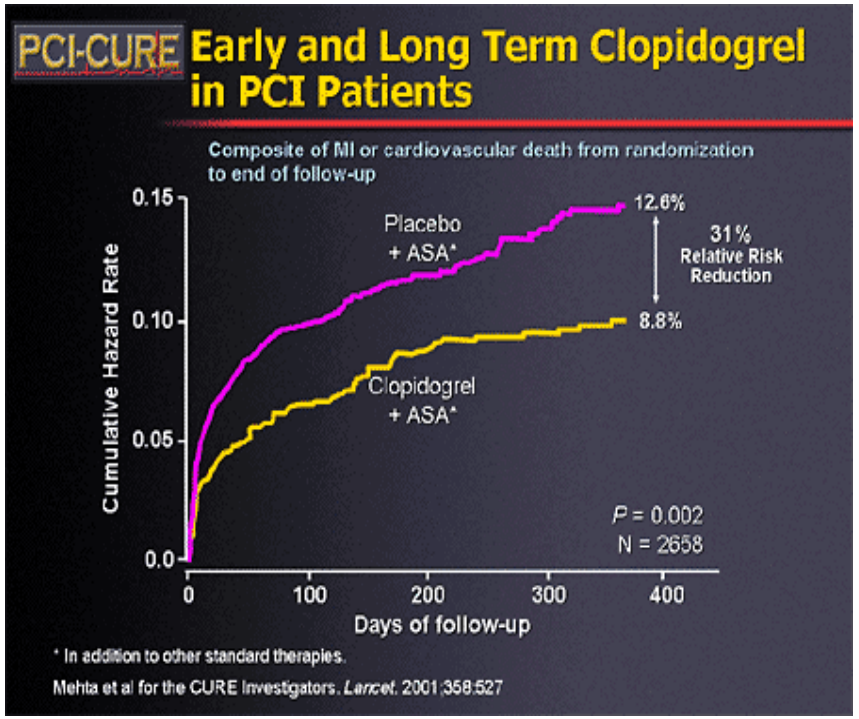




CURE trial and demonstrated a clinical benefit, in an ACS population Death, MI, or stroke was reduced by 20% in patients (95% CI, 10% to 28%; *P*<0.001).

PCI-CURE





In the **PCI-CURE** trial, a predefined post randomization subgroup of patients undergoing PCI, the relative risk reduction associated with clopidogrel was 31% (95% CI, 13% to 46%;*P*=0.002).

Pre-hospital antiplatelet therapy Clopidogrel

Conclusions:

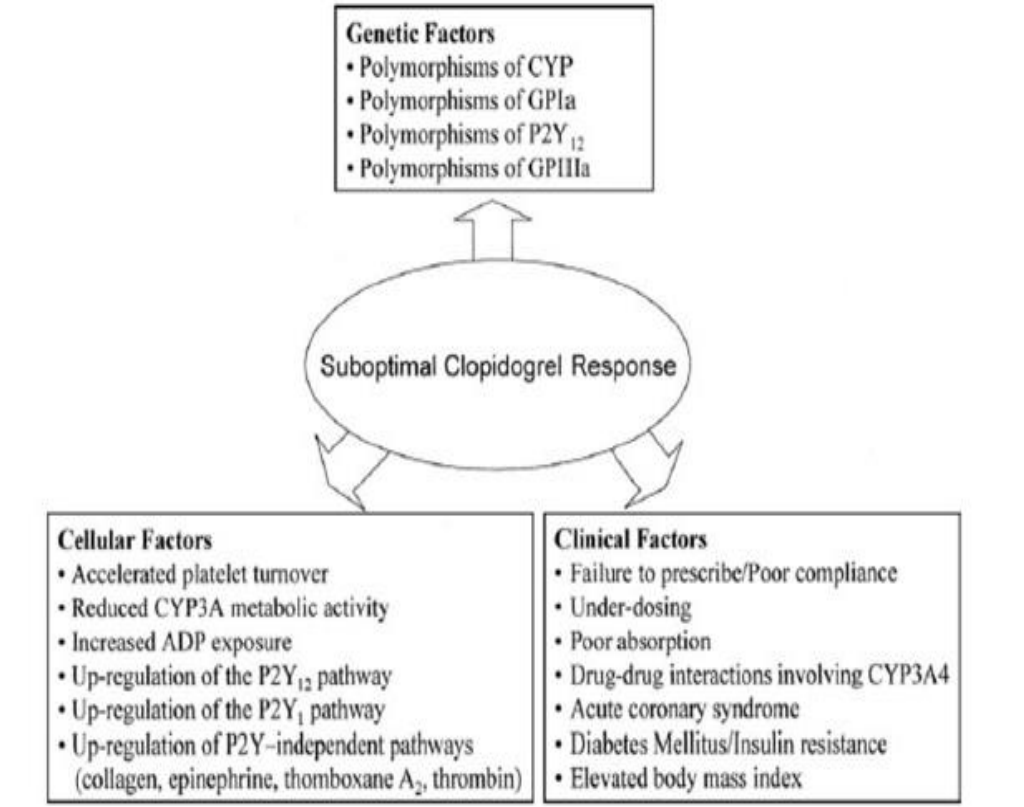
Addition of clopidogrel to medical reperfusion of STEMI with fibrinolysis, heparin, and aspirin before reaching the hospital is feasible in medically equipped ambulances without an apparent increase in bleeding. Furthermore, prehospital clopidogrel tended to show better early coronary patency compared to placebo, a result consistent with that observed in patients randomized in-hospital in the CLARITY-TIMI 28 trial.

Various studies and meta-analyses suggested that pre-treatment with clopidogrel in patients with STEMI could reduce the rate of ischemic events without excess bleeding, but its effectiveness may be limited by its slow onset of action and the variable response

Drawbacks with clopidogrel

PHARMACOKINETICS & DOSAGES

- Inactive prodrug; requires in vivo oxidation by hepatic &/or intestinal cyp 3A4 & 2C19
- Onset of action: within hours
- Steady state: b/w 3-7 days
- 300 mg LD: within 4-6 hours
- 600 mg LD: within 2 hours
- Cessation for 5 days is recommended prior to CABG



Proposed mechanisms leading to variability in individual responsiveness to clopidogrel[1]. ADP-Adenosine diphosphate; CYP-cytochrome P450; GP-gly

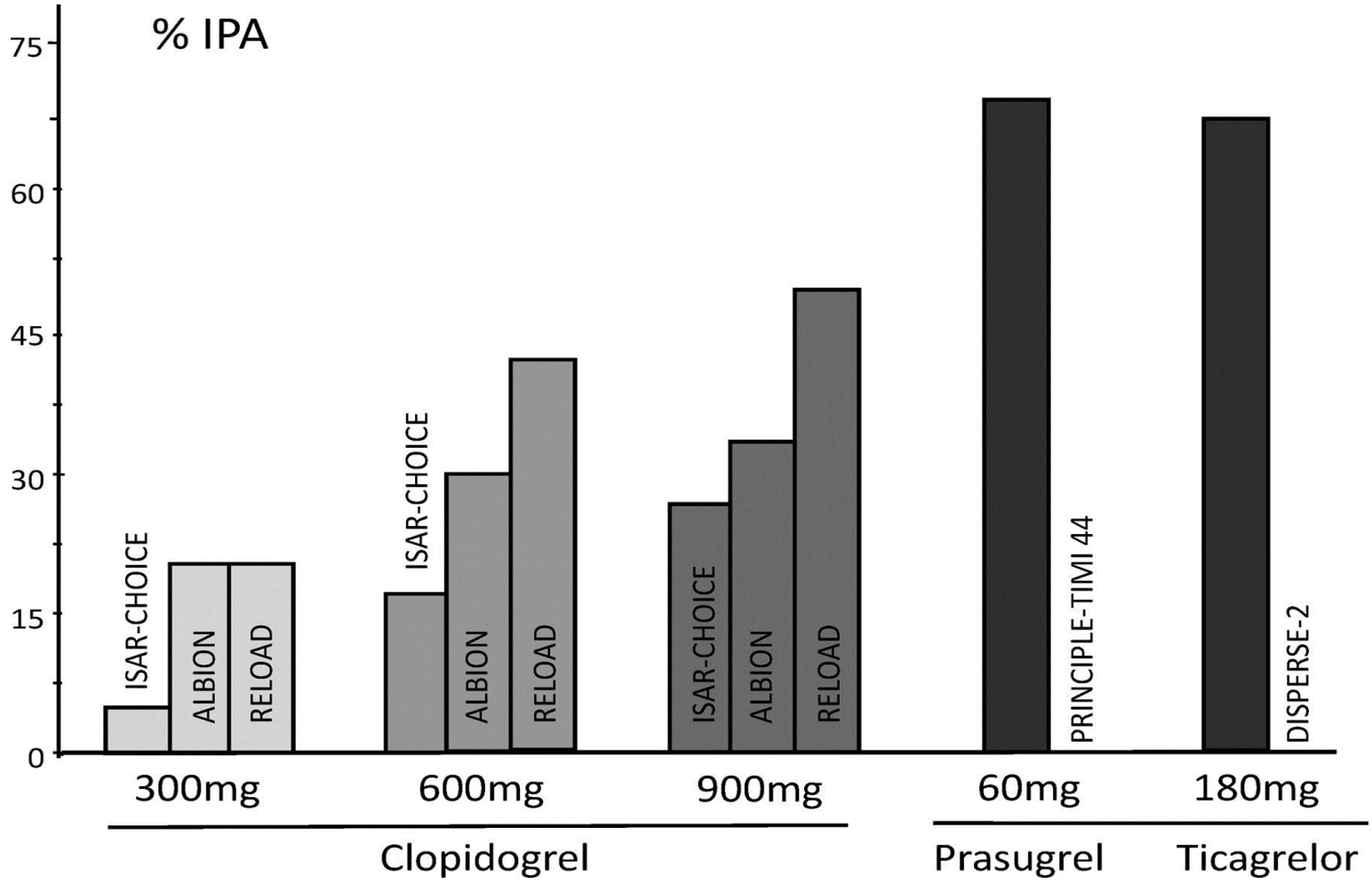
The percentage of "low responders" or "resistant" patients ranges from 5% to 40% across studies

Clinical effects of LD >300 mg

Trial	Year	N0.	Population	LD-CLOPI	Clinical End Point	inference
ARMYDA	2005	255	Elective PCI and NSTE-ACS	300 mg vs.. 600 mg	Death, MI, or TVR at 30 days	52% R.R reduction
Cuisset et.al	2006	292	NSTE-ACS	300 mg vs. 600 mg	Death, stent thrombosis, recurrent ACS, and stroke at 30 days	decreased the rate of MACE (5% versus 12%; P0.02)
Bonello et al	2009	429	Elective PCI and NSTE-ACS	600 mg vs. repeated bolus of 600 mg	Stent thrombosis at 30 days	improve prognosis stent thrombosis (0.5% versus 4.2%; P0.01), bleeding (4% versus 5%).
ARMYDA-RELOAD	2010	503	Elective PCI and NSTE-ACS	Placebo vs. 600 mg in patients under chronic clopidogrel therapy	Death, MI, or TVR at 30 days	MACE no different , no increasedbleeding.ACS subgroup did benefit (6.4 versus 16.3%; P0.033),
CURRENT-OASIS 7	2010	25 086	NSTE-ACS	300 mg vs. 600 mg	Death, MI, and stroke at 30 days	patients with ACS who underwent PCI, the double-dose regimen led to a nominal 25% decrease in CV events (3.9% versus 4.5%

600 mg loading dose is associated with reduced resistance and increased responsiveness to clopidogrel, as well as a greater magnitude of platelet inhibition and faster onset-of-action

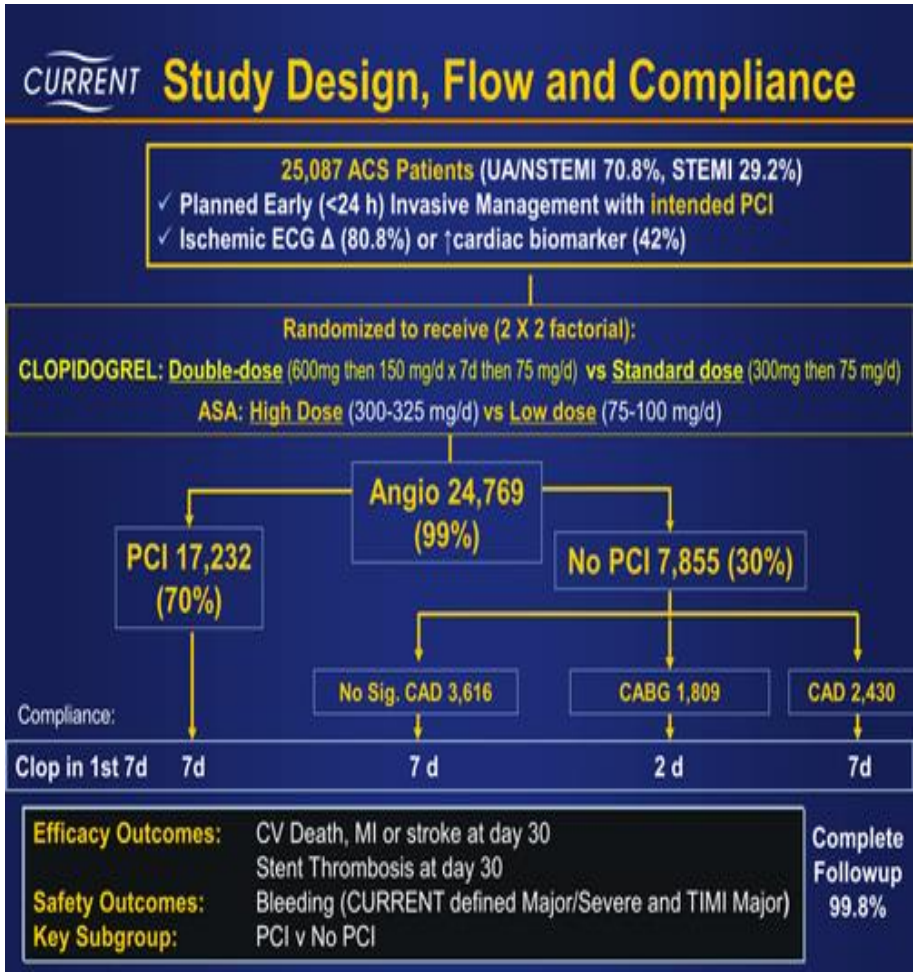
Inhibition of platelet aggregation (%) obtained 4 hours after loading when measured with 20 µmol /L ADP with light transmittance aggregometry in patients with ACS [IPA=(RPA at baseline−RPA at H4)−RPA at baseline].

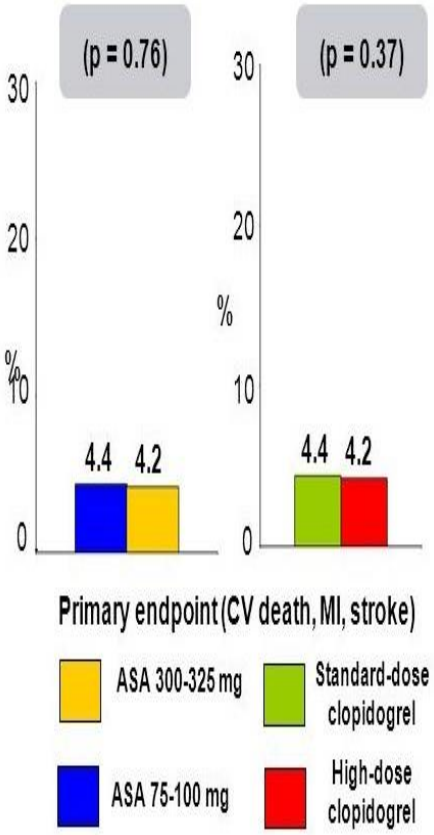


Johanne Silvain et al. Circ Cardiovasc Interv. 2011;4:95-103

Doses greater than 900 i.e.1200 mg were tested tin PRINC and PREPAIR trials and showed to have the maximum platelet inhibition

CURRENT OASIS-7 trial





Results

- No difference in primary endpoint between aspirin arms; benefit noted in high-dose arm on high-dose clopidogrel ($p = 0.04$)
- No difference in primary endpoint between clopidogrel arms, but significant interaction with aspirin dose; benefit noted in high-dose arm undergoing PCI ($p < 0.05$)
- Major bleeding similar in both aspirin arms, but higher in high-dose clopidogrel arm ($p = 0.01$)

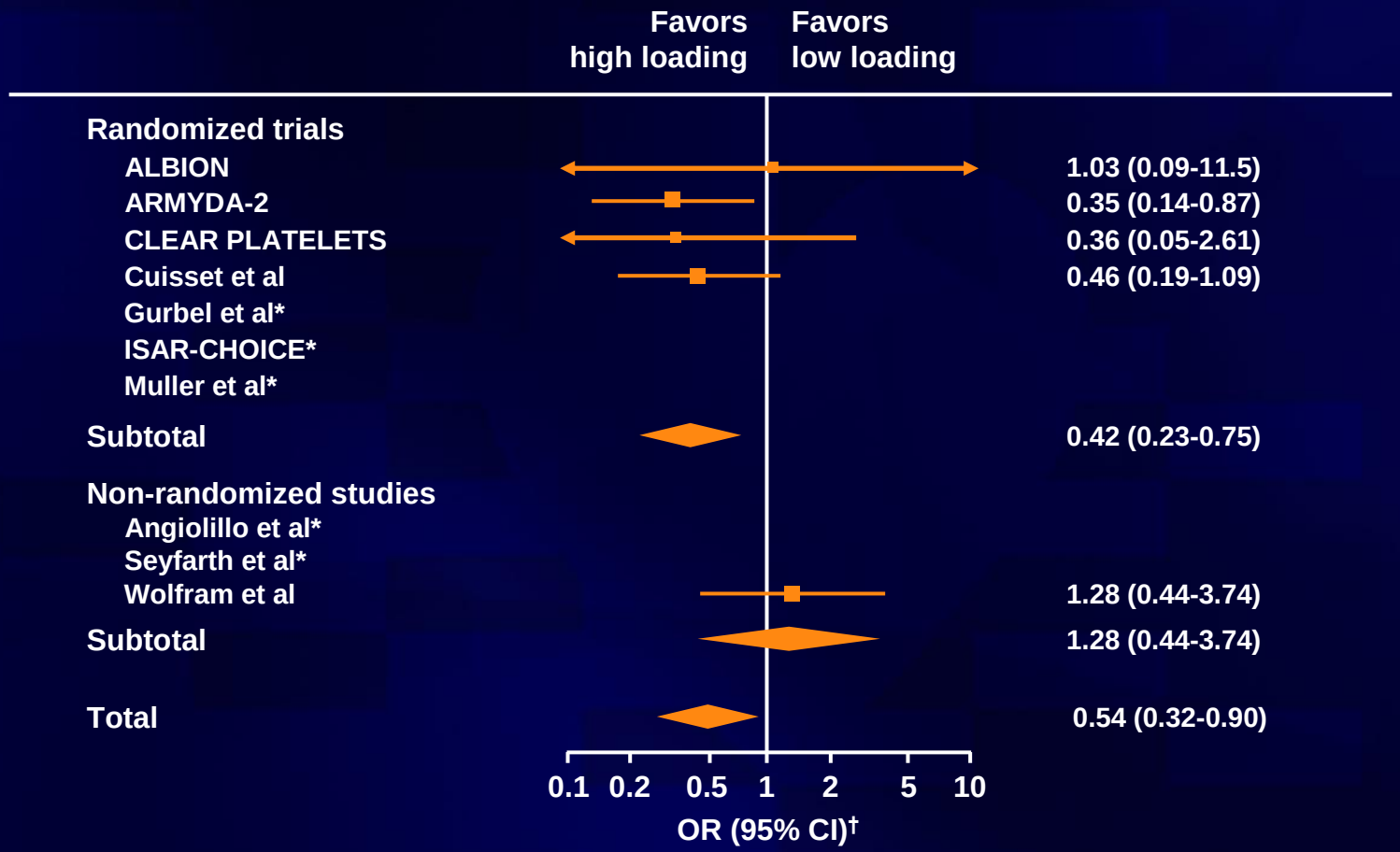
Conclusions

- High-dose aspirin and high-dose clopidogrel associated with significant clinical benefit at 30 days in ACS patients; more in PCI subgroup
- Bleeding complications were higher with high-dose clopidogrel, but not with aspirin
- Important findings; likely to be in future guidelines

In the subgroup of patients undergoing PCI, the high dose strategy was associated with a decrease in the rates of ischemic outcomes (3.9% versus 4.5%; hazards ration [HR], 0.85; *P*=0.036), and reduced the risk of stent thrombosis by 30%, at the expense, of a significant increase in major bleedings.

Clopidogrel 600 mg vs 300 mg loading dose

Meta-analysis; N = 1567; Primary endpoint: Cardiac death or MI at 1 month



*No events in either group
†Peto fixed-effect method

Lotrionte M et al. *Am J Cardiol*. 2007;100:1199-206.

Current recommendations for Clopidogrel in STEMI

ESC guidelines and ACC/AHA 2013 Guidelines for STEMI :

- loading dose of 300- 600 mg followed by a maintenance dose of 75 mg/day, in patients with ACS, including those undergoing PCI

a. Adjunct to fibrinolytic therapy:

- 300mg LD in patients ≤ 75 mg; and 75 mg in patients ≥ 75 yrs (class IA)
- 75 mg MD for atleast 14 days and up to 1 yr (class IA;C)

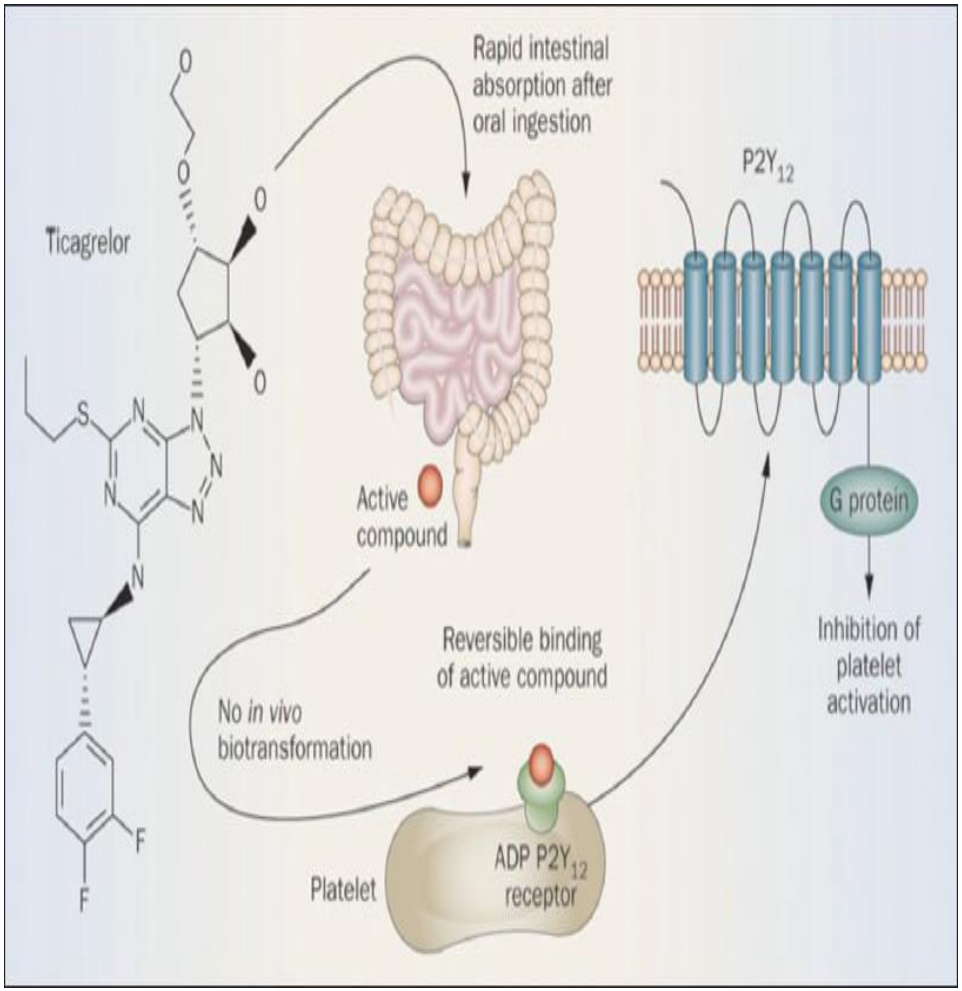
b. Adjunct to PCI:

- 600mg LD 4-8 hours prior to PCI (class IA)
- MD of 75 mg for 1 year (class IB)

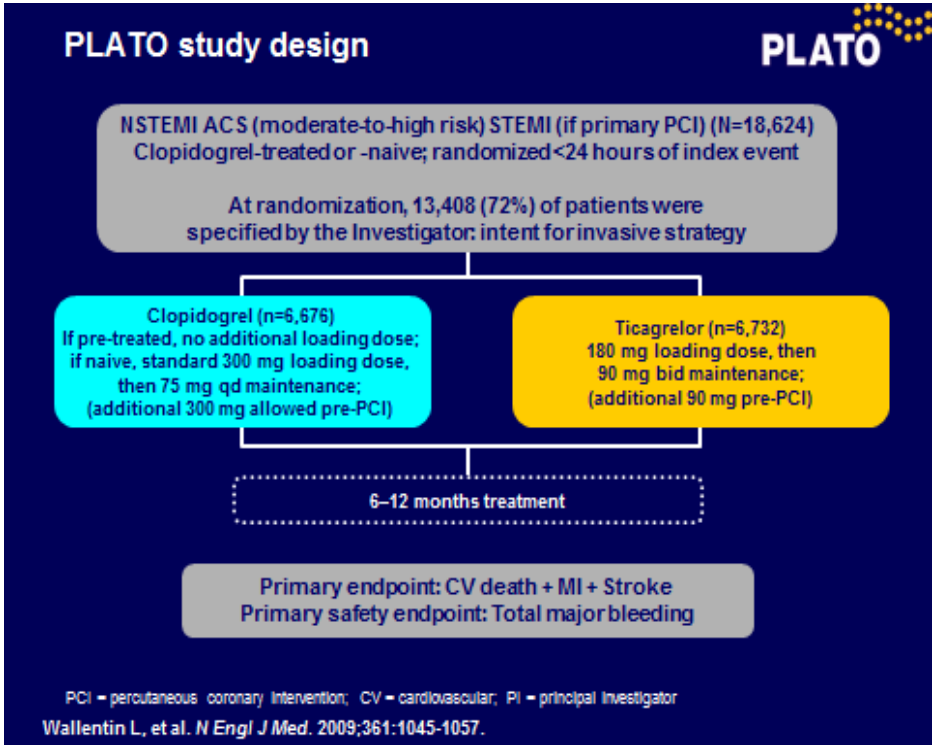
c. Adjunct to PCI after fibrinolytic therapy:

Ticagrelor- First choice

- Direct acting reversible blocker of P2Y12 platelet receptor
- Half life of approx 12 hours.
- Inhibit P2Y12 mediated platelet aggregation completely



Pivotal Trial-PLATO



PLATO RESULTS

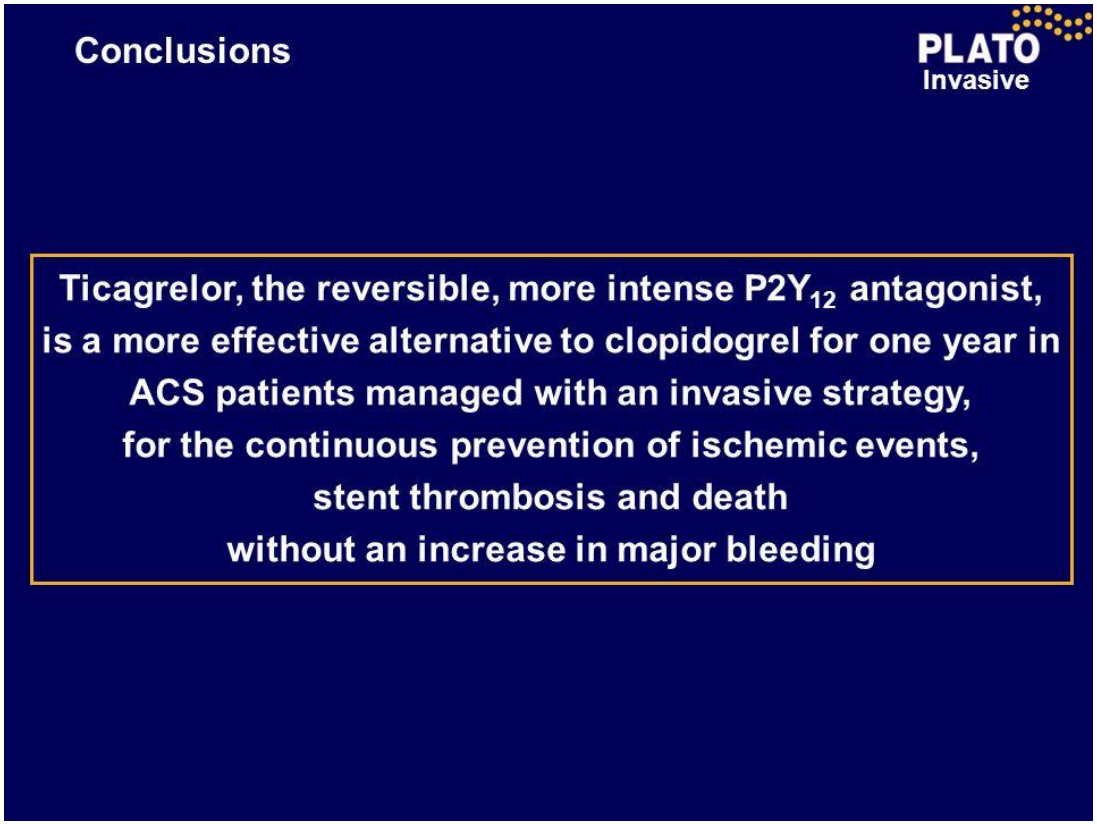
Positive results

- Primary end point fell significantly by 16%
- 16% reduction in MI
- 21% reduction in CV death
- 22% relative reduction in mortality
- Rate of stent thrombosis reduced significantly from 1.9% to 1.3%
- Greater clinical efficacy in non-invase, STEMI, previous clopidogrel patients

Negative results

- No benefit in sub group in whom aspirin dose was high
- 0.7% absolute (19% relative) higher incidence of non-CABG major bleed
- Moderate to minor dyspnoea was more common
- Ventricular pauses exceeding 5 sec occurred more frequently

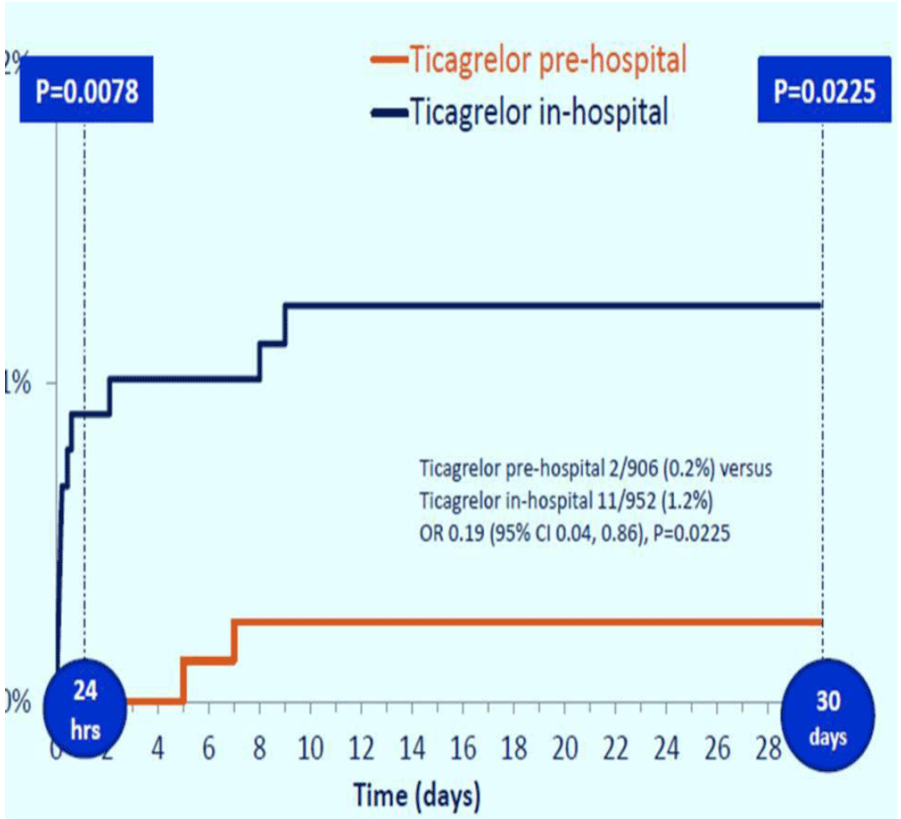
PLATO-conclusion



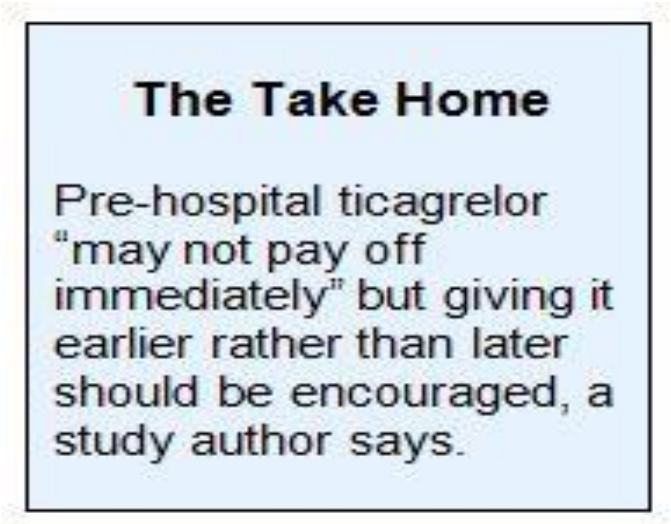
ACC/AHA guidelines 2013/ESC GUIDELINES

- **180 mg LD as early as possible or at the time of PCI (class IB)**
- **90 mg twice a day as MD**

Pre-hospital Ticagrelor



Prehospital administration of ticagrelor in patients with acute STEMI appeared to be safe but did not improve pre-PCI coronary reperfusion



- The new oral $P2Y_{12}$-receptor antagonists inhibit platelet function in less than 1 hour, which is compatible with transfer times for primary PCI

Switch over:
Clopidogrel to Ticagrelor
HOW?

P2Y12 switching regimens

Only evidence-PLATO TRIAL

- 46% of ticagrelor subjects had received clopidogrel mainly as loading dose, subsequently ticagrelor loading dose of 180 mg within 24 hours
- Suggestion: Acute phase (within 24 hours of onset of chest pain) administer loading dose of 180 mg9unless active bleeding) regardless of the timing of clopidogrel dose

SHIFT-0VER study: Switch From Ongoing Clopidogrel Treatment to Ticagrelor in Patients With Acute Coronary Syndrome

- Randomized, single-blinded, single center study
- Aspirin-treated patients with ACS (n = 50) receiving clopidogrel were randomly assigned to either ticagrelor 90 mg (no LD) plus 90 mg twice daily or 180-mg LD plus 90 mg Bd
- At 2 hours after the first dose, residual platelet aggregation was significantly reduced in both arms, with no difference between groups;

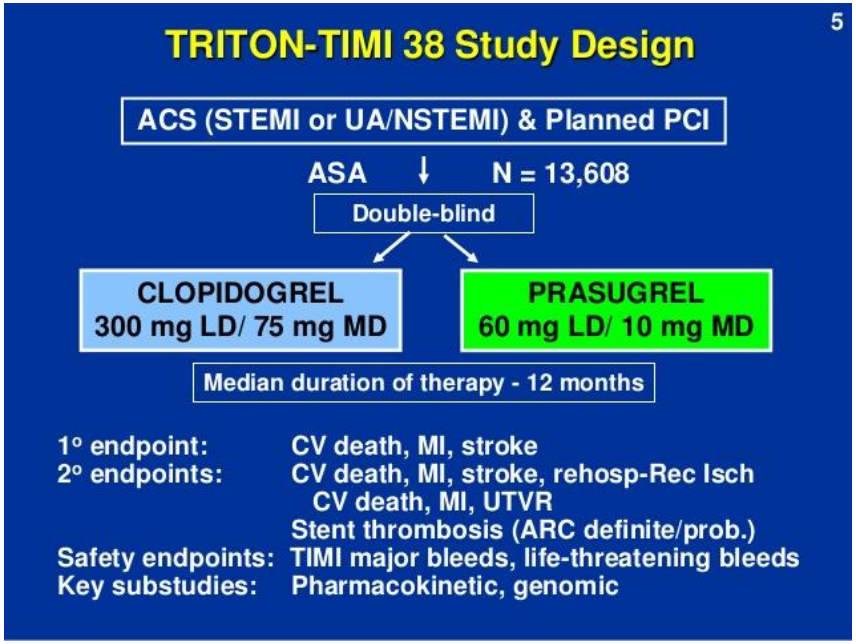
- **This suggests that switching from clopidogrel to ticagrelor without a reloading dose is feasible, and it does not delay platelet inhibition in patients with ACS**
- **Recommended:** clopidogrel to ticagrelor- 90 mg bd. Refrain from loading doses

Clopidogrel to novel inhibitors

- Incidence is 5-50%
- RESPOND TRIAL
  - Stable CAD patients based on HPR as responders and non-responders.
  - PR decreased significantly in those on ticagrelor
- Clopidogrel to ticagrelor
  - In acute phase: LD 18o mg irrespective of timing to be given followed by 90 mg bd
  - In chronic phase, 90 mg bd can be initiated without loading dose

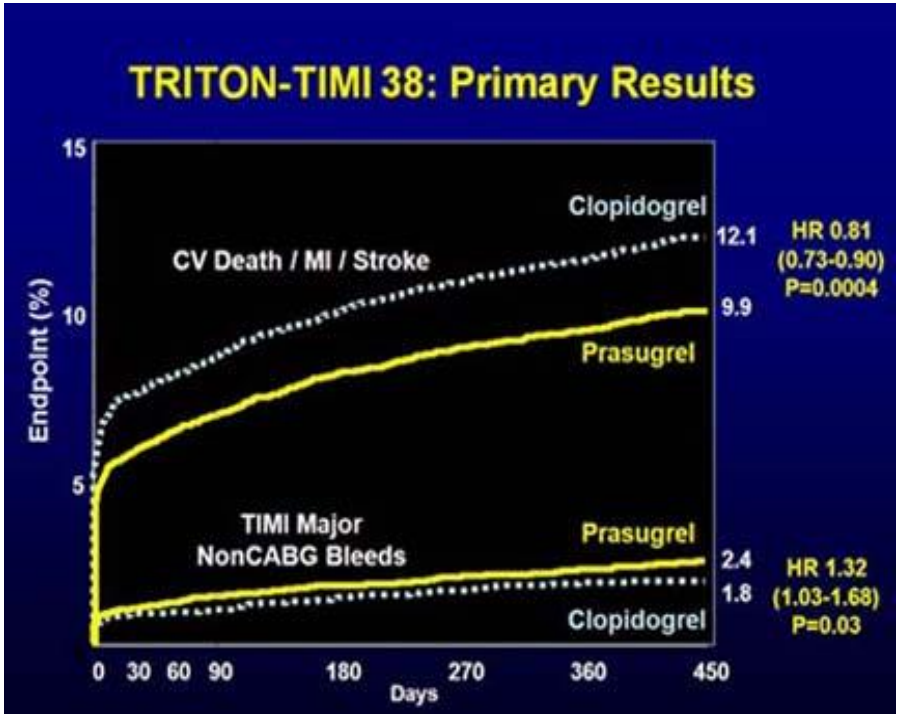
WHY NOT PRASUGREL?

- A third generation thienopyridine
- Orally administered prodrug that needs hepatic biotransformation into its active metabolite to irreversibly block the $P2Y_{12}$ receptor.
- Pharmacological advantages over clopidogrel:
  - It is more effectively converted into its active metabolite (oxidized in 1 step)
  - displays a faster onset of action (within 30 min)
  - greater degree of platelet inhibition (10 times potency)
  - less variability in response, even when compared with high dose clopidogrel.



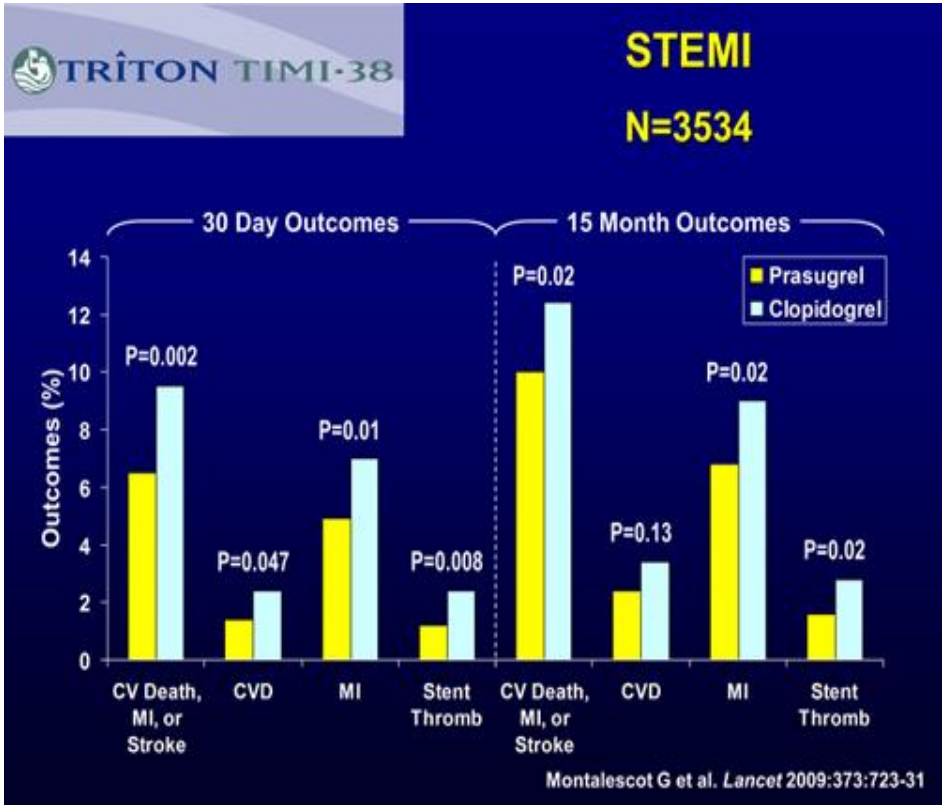
RESULTS

- **The primary efficacy end point**, over a follow-up period of 15 months, occurred in 9.9% of patients treated with prasugrel and in 12.1% of patients treated with clopidogrel, thus resulting in a **significant 19% relative reduction with prasugrel** (HR, 0.81 [0.73–0.90]; *P*<0.001).
- This benefit was hampered by an increased risk of TIMI major non-coronary artery bypass graft (CABG) related bleeding (2.4% versus 1.8%; *P*=0.03), including fatal bleeding (0.4% versus 0.1%; HR, 4.19 [1.58–11.11];*P*=0.002), which occurred mostly in the maintenance phase of prasugrel treatment.

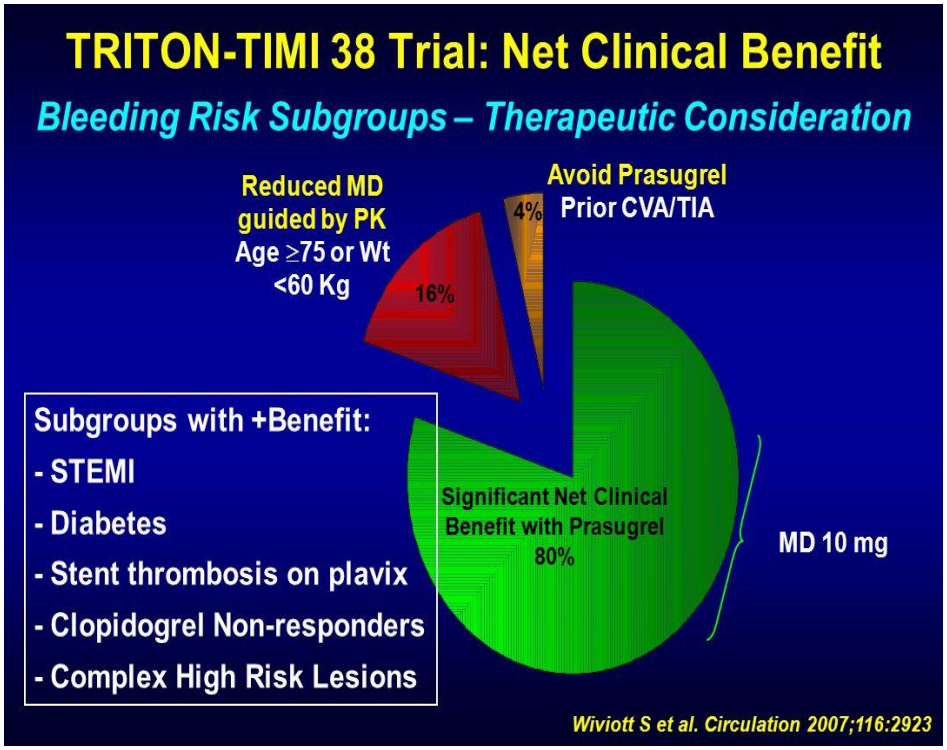


Risk vs. benefit

- A pre-specified net clinical benefit was performed and a significant net clinical benefit was associated with prasugrel therapy despite the excess in bleeding
  - marked reduction in nonfatal MI, approximately 40%
  - 52% reduction of the rates of definite or probable stent thrombosis
  - Such benefit was both early (<30 days) and late (up to 15 months)
  - both BMS and DES
  - The benefit was striking (30%) in diabetics

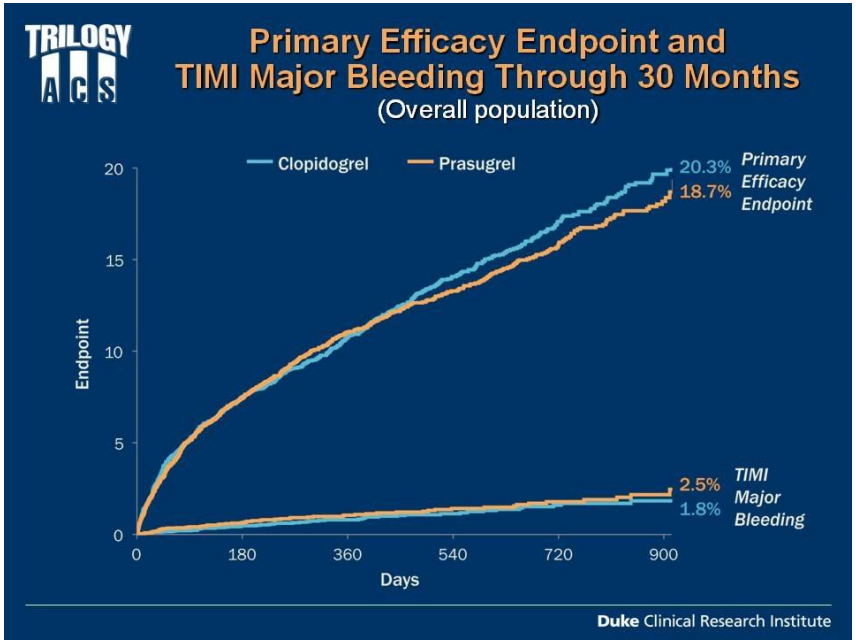


CONCLUSION



- Prasugrel proved superior over clopidogrel but at the cost of excess bleeding

Prasugrel-medical management of CAD
TRIOLOGY ACS TRIAL



Prasugrel 10 mg was compared with clopidogrel 75 mg in 7243 patients younger than 75 years being managed medically following NSTEMI.
No difference occurred in the primary composite endpoints of cardiovascular death, MI, or stroke nor in severe bleeding

Recommendations-prasugrel

- ACC/AHA guidelines
  - LD of 60 mg as early as possible or at time of PCI (class IB)
  - MD of 10 mg daily for 12 months (class IB)
    - CI in patients with previous TIA/CVA
    - Not recommended for patients >75 yrs (class IB)
    - Considered lower doses of patients <60 kg (class IB)
- ESC guidelines:

Pre-treatment with prasugrel

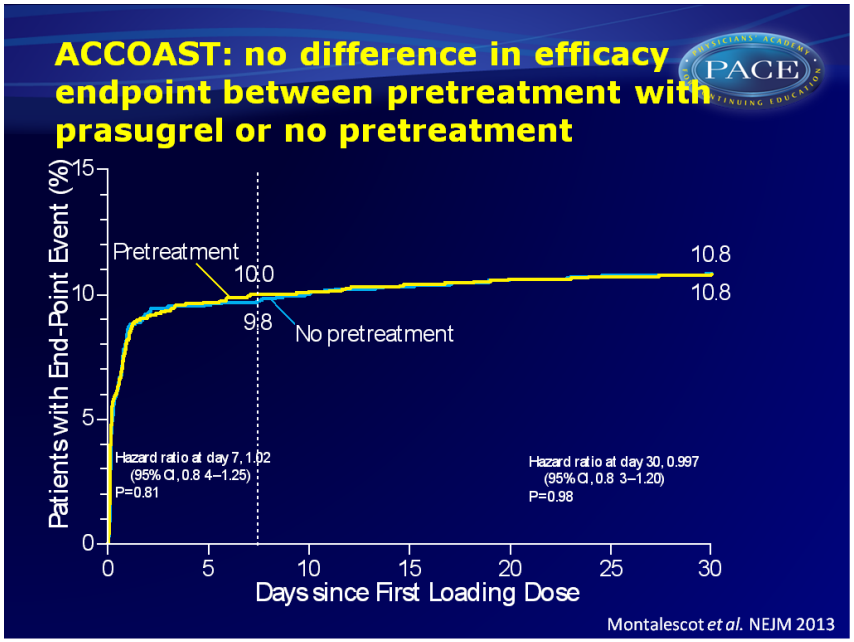
ACCOAST: Results

- Pretreating NSTE-ACS patients with prasugrel at the time of diagnosis, rather than after angioplasty, does not improve ischemic events but does drive up major bleeding complications.
- The trial's data and safety monitoring committee stopped enrollment at 4033 patients in November 2012 after noticing an increase in major and life-threatening bleeding and no reduction in CV events.
- The primary efficacy end point was not significantly different between the two treatment groups at seven or 30 days. TIMI major bleeding (either related to CABG or not) was significantly higher in the pretreatment group at both time points, as were rates of non-CABG TIMI major bleeding and life-threatening bleeding

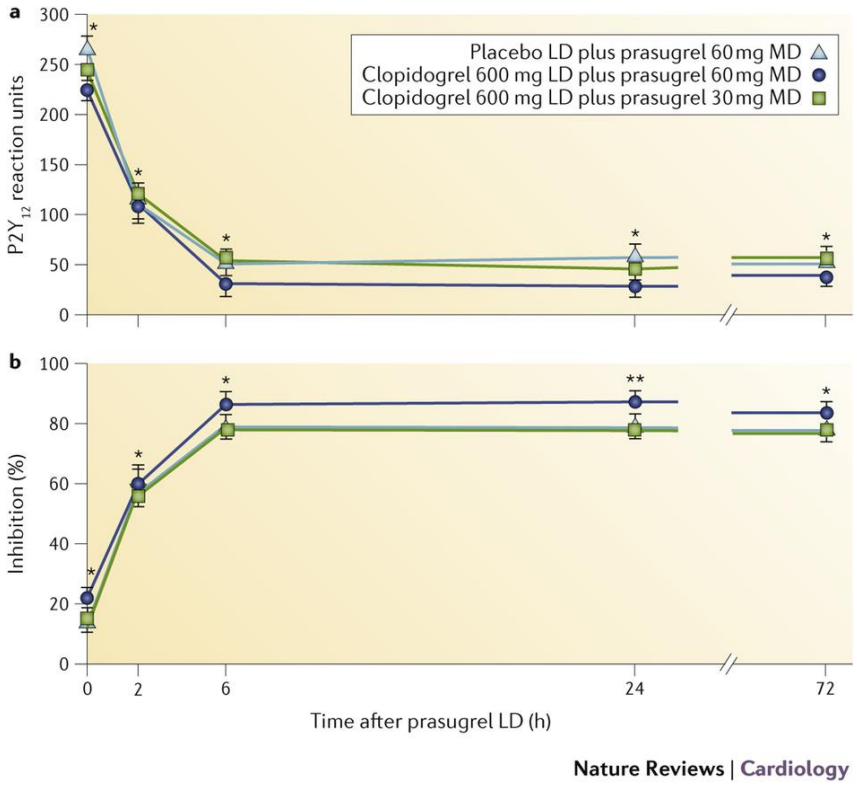
Differences Between Prasugrel Pretreatment and No Pretreatment

End point	Pretreatment, n (%)	No pretreatment, n (%)	Hazard ratio	p
Primary end point, 7 d	203 (10)	195 (9.8)	1.02	0.81
Primary end point, 30 d	219 (10.8)	216 (10.8)	0.997	0.98
All CABG or non-CABG TIMI major bleeding, 7 d	52 (2.6)	27 (1.4)	1.90	0.006
All CABG or non-CABG TIMI major bleeding, 30 d	58 (2.8)	29 (1.5)	1.97	0.002
Life-threatening bleeding	22 (1.1)	4 (0.2)	5.40	<0.001

theheart.org | Medscape CARDIOLOGY



SWITCH OVER IN ACS



- Clopidogrel To Prasugrel **TRIPLET STUDY**
- No statistically significant difference in platelet inhibition was observed at any time point across the 3 groups.
- The treatment-emergent adverse events, including those hemorrhagic, were low and evenly distributed across treatment groups

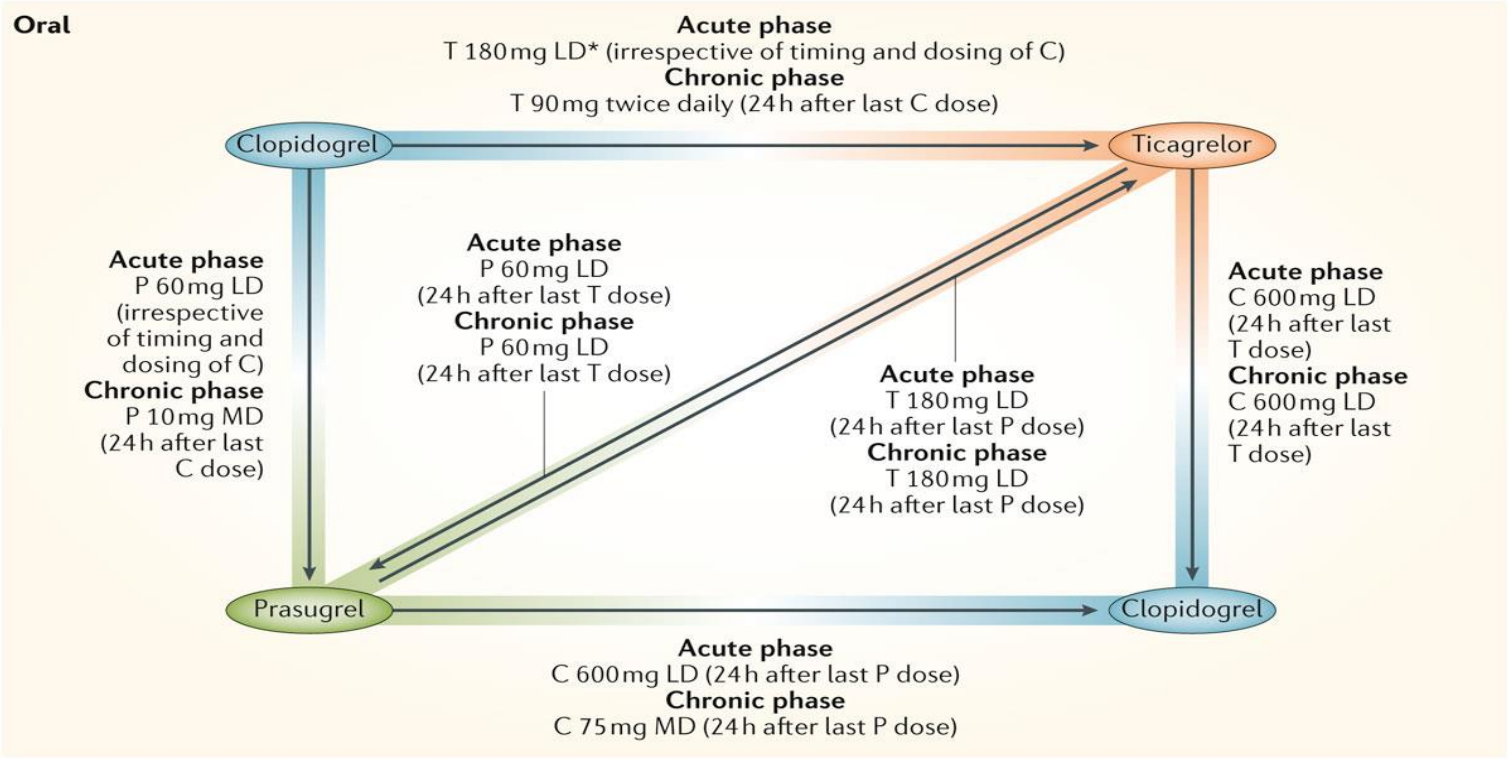
SWAP study

- The was a multicenter, randomized, double blind trial to assess the pharmacodynamic response after switching to prasugrel from clopidogrel MD therapy
  - Switching from clopidogrel to prasugrel 10-mg MD, with or without LD, resulted in significantly higher platelet inhibition at 7 days as assessed by multiple platelet function testing.
  - When switching was initiated with prasugrel 60-mg LD, a significant reduction in platelet aggregation was observed at 2 hours and continued for 24 hours after the first dose.
  - No TIMI major bleeding event occurred. Observed bleeding complications were all considered minimal according to the TIMI criteria and were similar between groups

Clopidogrel to Prasugrel

- In the acute phase: 60 mg LD irrespective of timing of clopidogrel dosing followed by MD of 10 mg daily
- Chronic phase: 10 mg to be give 24 hours after last dose of clopidogrel

SWITCHING OF ANTIPLATELETS DRUGS



Nature Reviews | Cardiology

Switching $P2Y_{12}$-receptor inhibitors in patients with coronary artery disease

Fabiana Rollini, Francesco Franchi & Dominick J. Angiolillo

Nature Reviews Cardiology 13, 11–27 (2016) doi:10.1038/nrcardio.2015.113

- This patient was taken up for Primary angioplasty under coverage of Ticagrelor And Aspirin. Successful PTCA To Proximal LAD was done and Promus stent was implanted.
  - Would u continue ticagrelor. For how long?
  - If he does not tolerate or cannot afford ticagrelor, how can we shift to other antiplatelets?
  - Any role for platelet inhibition studies?

What is the optimal duration of DAPT?

- Initially prescribed for 4 weeks after BMS implantation,
- increased to 3 months after SES in 2003,
- 6 months after PES in 2004.
- Soon , duration of clopidogrel therapy to 12 months, on the basis of findings in PCI-CURE, CREDO and observational studies
  - all stents were BMS

- In PLATO and TRITON-TIMI 38 , DES were used in 19% and 40% of cases, respectively, but all these stents were first-generation sirolimus-eluting stents and PES.

Stent type has emerged as an important risk factor for stent thrombosis

Newer-generation DES, are associated with a risk of stent thrombosis approximately one half that of the first generation DES

ACC/AHA Task Force on Clinical Practice Guidelines: writing committee

- **Q1**. When compared with 12 months, is 3 to 6 months of DAPT as effective in 1) preventing stent thrombosis, 2) preventing major adverse cardiac events (MACE), and/or 3) reducing bleeding complications?
- **Q2**. When compared to 12 months, does >12 (18 to 48) months of DAPT result in 1) differences in mortality rate, 2) decreased MACE, 3) decreased stent thrombosis, and/or 4) increased bleeding?
- **Q3**. In post-MI patients who are clinically stable and >12 months past their event, does continued DAPT, compared with aspirin monotherapy, result in differences in 1) mortality rate, 2) decreased nonfatal MI, 3) decreased MACE, and/or 4) increased bleeding?

Duration of DAPT After Implantation of Newer-Generation DES

- 11 RCT- 33,051 patients who underwent implantation of predominantly newer generation DES.
- All 11 RCTs were judged to be of moderate to high quality, with at least moderate relevance, fidelity, and freedom from bias

- Trials of DAPT Duration after Stenting (Months after PCI)
- DES Late (n=5045) – 12 to 36 months
- DAPT DES (n=9961) – 12 to 30 m
- DAPT BMS (n=1687) – 12 to 30 m
- ITALIC (n=1850) – 6 to 24 m
- PRODIGY (n=2014) – 6 to 24 m
- ARCTIC-Interruption (n=1259) – 6 to 24 m
- ISAR-SAFE (n=4000) – 6 to 12 m
- EXCELLENT (n=1443) – 6 to 12 m
- OPTIMIZE (n=3119) – 3 to 12
- RESET (n=2117) – 3 to 12 m

Prolonged DAPT trials

Study	Year	Trial Completion	Primary Study endpoint	Trial design and outcome	Expected event rate in control group (%)	Observed event rate in control group (%)	% of newer generation stents
DES LATE (12 vs. 36 mo)	2010	Extension of ZEST-LATE and REALLATE	Cardiac death, MI, or stroke <24h	Superiority not shown	2.7	2.6	30
ARCTIC (12 vs. 18 mo)	2014	Extension of ARCTIC	Death, MI, ST. Stroke or urgent TVR	Superiority not shown	6.0	4.0	63
SECURITY (6 vs. 12 mo)	2014	Stopped after 1,399 enrolled of 2,740	Cardiac death, MI, ST, or stroke	Non-inferiority confirmed	4.5	4.5	100
ITALIC (6 vs. 24 mo)	2015	Stopped after 2,031 enrolled of 2,475 planned	Death, MI, urgent TVR, stroke, or major bleeding	Non-inferiority confirmed	3.0	1.5	100
DAPT (12 vs. 30 mo)	2015	Enrollment completed	Co primary: ST and MACCE	Superiority shown	0.5/2.9	0.5/2.4	59
OPTIDUAL (12 vs. 48 mon	2015	(Stopped after 1,385 enrolled of 1,966 Planned	Death, MI, stroke, or major bleed	Superiority not shown	7.0	7.5	59

18 to 48 Months of DAPT Versus 6 to 12 Months of DAPT

- 6 RCTs- 20,973 patients
  - Prolonged DAPT, reduced the risk of MI (OR: 0.67; 95% CI: 0.47 to 0.95) and stent thrombosis (OR: 0.42; 95% CI: 0.24 to 0.74) and produced a borderline reduction in the prospectively defined primary endpoints (OR: 0.85; 95% CI: 0.72 to 1.00).
  - Prolonged DAPT was associated with no difference in all-cause death (OR: 1.14; 95% CI: 0.92 to 1.42***) but increased major hemorrhage*** (OR: 1.58; 95% CI: 1.20 to 2.09).

- The annual rate of major haemorrhage was
  - 1.26% (prolonged DAPT) vs. of 0.80% (shorter course)
  - 13 of 1,000 patients had major bleeding during each year of extended therapy, as compared with 8 receiving shorter courses of DAPT.
- A risk-benefit analysis found that extending DAPT to 18 to 48 months, as compared with stopping DAPT after 6 to 12 months, resulted in
  - 3 fewer stent thromboses (95% CI: 2 to 5)
  - 6 fewer MIs (95% CI: 2 to 11) but
  - 5 more major bleeds (95% CI: 3 to 9) and
  - a statistically non significant 2 more deaths (95% CI: -1 to 4) per 1,000 patients per year

NIPPON

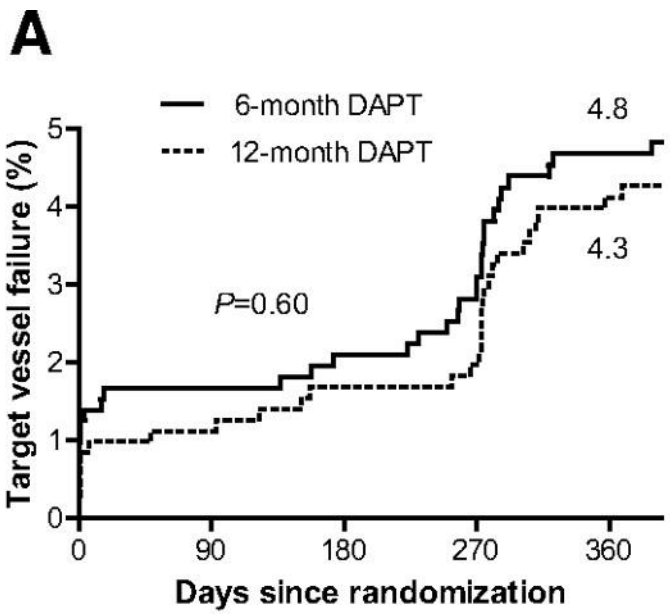
- NIPPON trial is a multi-center randomized study to test the non-inferiority of 6 months DAPT compared with 18 months DAPT following NOBORI stent
- NOBORI is a DES with bio absorbable polymer and abluminal coating

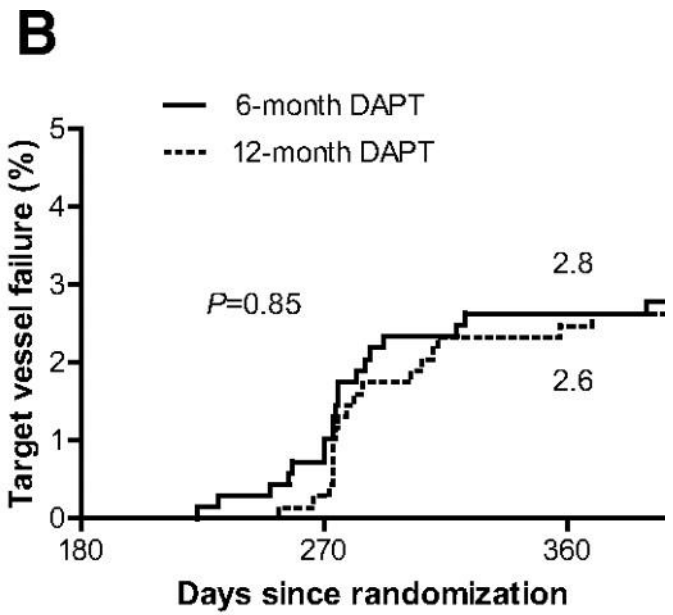
- 6 months of DAPT was statistically non-inferior to 18 months of DAPT in terms of net adverse clinical and cerebrovascular events, including all cause death, Q-wave or non-Q wave MI, cerebrovascular events, and major bleeding. However, the results need to be interpreted with caution given premature termination of enrollment, an open-label design with frequent crossover and a wide non-inferiority margin.

12 vs. 3-6 months of DAPT trials

Study	Year	Trial Completion	Primary Study endpoint	Trial design and outcome	Expected event rate in control group (%)	Observed event rate in control group (%)	% of newer generation stents
PRODIGY (6 vs. 24 mo)	2012	Enrolment completed	Death, MI or stroke	Superiority not shown	8.0	10.1	67
EXCELLENT (6 vs. 12 mo)	2012	Enrolment completed	Cardiac death, MI or ischemia drived TVR	Non-inferiority confirmed	10	4.5	75
RESET (3 vs. 12 mo)	2012	Enrolment completed	Cardiac death, MI, ST revas or bleeding	Non-inferiority confirmed	10.5	4.7	85
OPTIMIZE (3 vs. 12 mo)	2013	Enrolment completed	NACCE-death, MI, strike or bleed	Non-inferiority confirmed	9.0	6.0	100
ISAR-SAFE (6 vs. 12 mo)	2015	Stopped after 4,005 enrolled of 6,000 Planned	Death, MI, ST, stroke, or TIMI major bleed	Non-inferiority confirmed	10.0	1.5	72

Kaplan-Meier curves for the primary end point of target vessel failure. – EXCELLENT trail





6-month DAPT	722	692	686	680	663
12-month DAPT	721	697	692	687	668

6-month DAPT	686	680	663
12-month DAPT	692	687	668

Hyeon-Cheol Gwon et al. Circulation. 2012;125:505-513

American Heart Association.

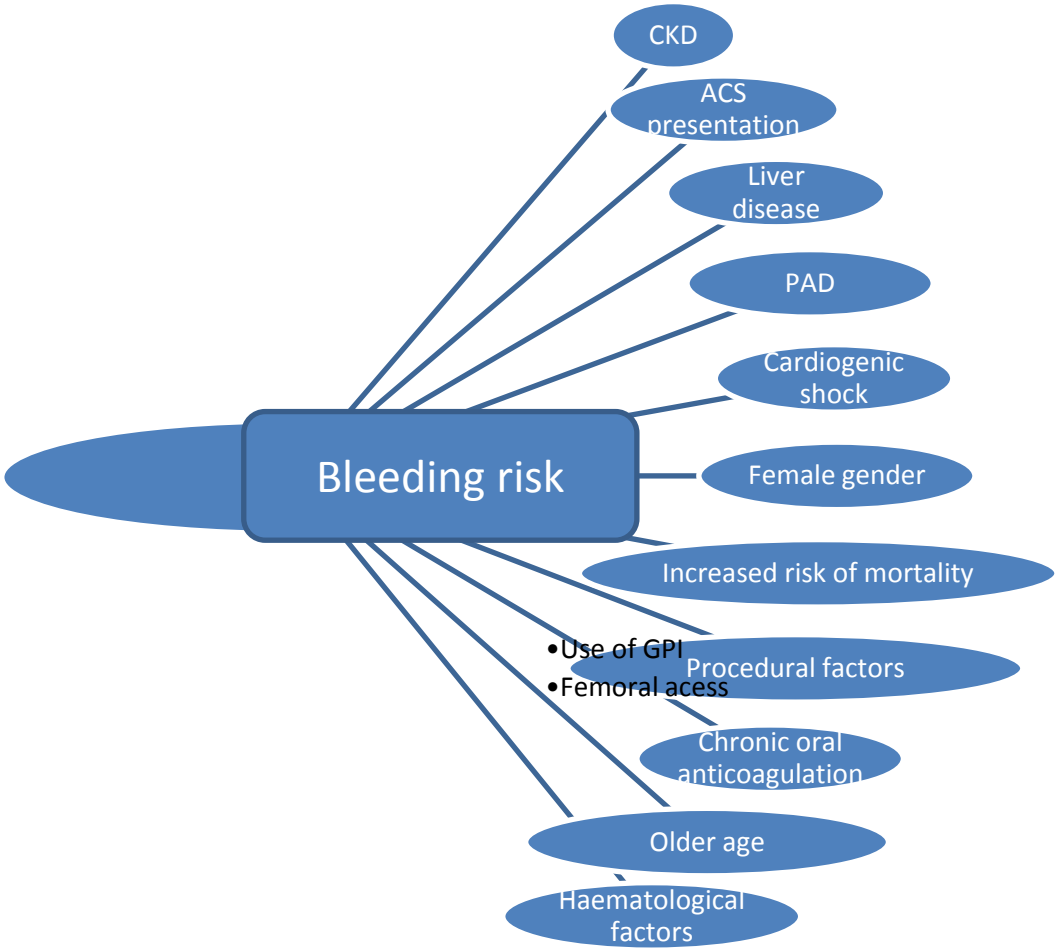
12 Months of DAPT Versus 3 to 6 Months of DAPT

- 5 RCTs-12,078 patients
- DAPT of 12 months' duration was associated with No differences in:
  - Death (odds ratio [OR]: 1.17; 95% CI: 0.85 to 1.63),
  - Major hemorrhage (OR: 1.65; 95% CI: 0.97 to 2.82)
  - MI (OR: 0.87; 95% CI: 0.65 to 1.18),
  - Stent thrombosis (OR: 0.87; 95% CI: 0.49 to 1.55), and
  - Primary endpoint for each study (OR: 0.96; 95% CI: 0.80 to 1.16).

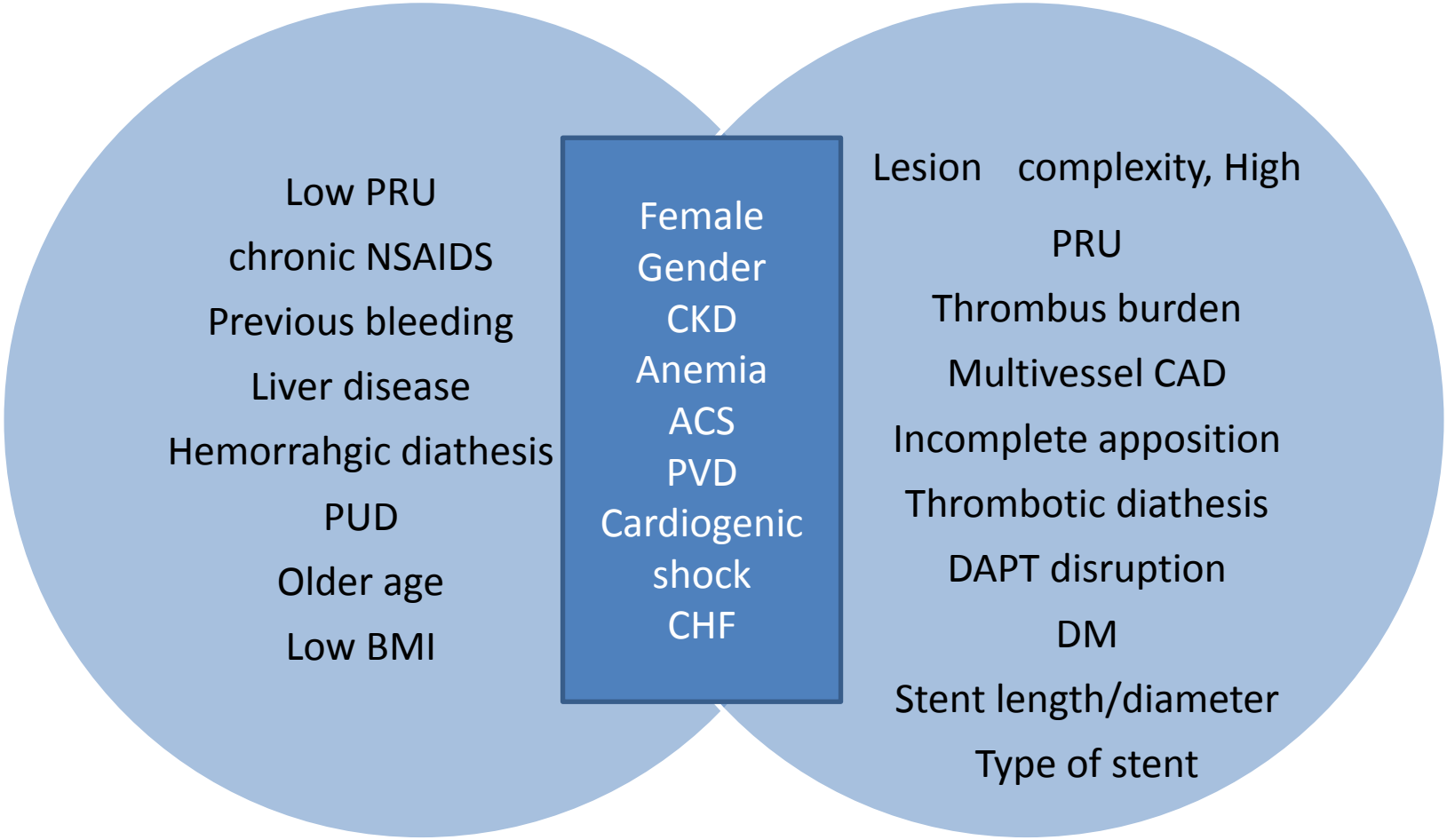
Duration of DAPT determinant

Ischemic events (MI, CPK raise, Stent thrombosis)

Bleeding


Bleeding risk
CKD
ACS presentation
Liver disease
PAD
Cardiogenic shock
Female gender
Increased risk of mortality
Procedural factors
•Use of GPI
•Femoral acess
Chronic oral anticoagulation
Older age
Haematological factors

Overlap Between Bleeding and Ischemic Risk Clinical Factors



Optimal duration of DAPT

- Safer, newer-generation DES may be treated with a minimum DAPT duration of 3 to 6 months to prevent early and largely stent-related thrombotic events.
  - EXCELLENT trial surmised that “DAPT may not be necessary beyond the initial 6 months, at least in low-risk patients
  - RESET trial : “With newer-generation DES, 6 months DAPT might be sufficient, and 3 months not completely off the wall in low-risk groups
  - SECURITY trial concluded, “Shorter DAPT duration seems very reasonable to consider and is increasingly used in the art of taking care of these patients

DAPT AFTER BVS

- BVS – PCI
- 2012 - 2014 BVS implantation strategy resulted in high acute and subacute scaffold thrombosis rate
- Low late ST rate while on continuous DAPT
- Minor effect of DAPT termination after 12 months on ST rate
- ST at planned DAPT termination might be result of suboptimal implantation
- Effect of DAPT termination for BVS similar to DES

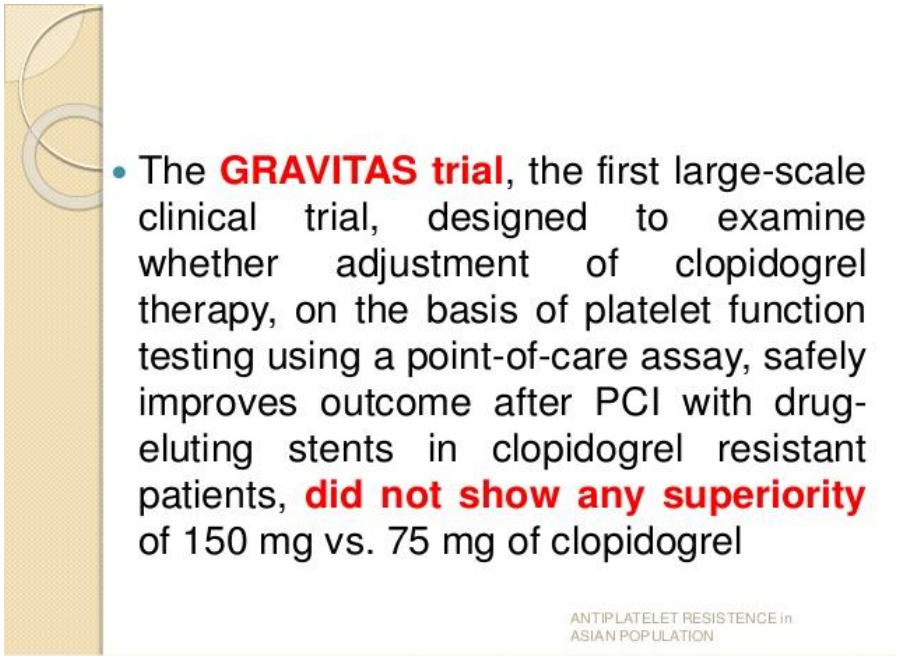
Platelet inhibition studies

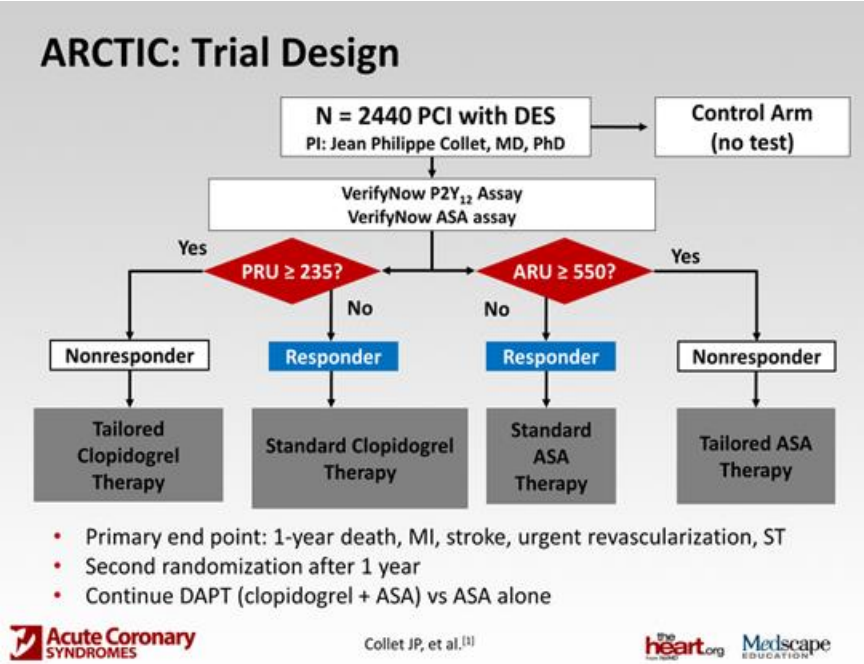
- RESPOND trial
- TRANSLATE-ACS TRIAL
- GRAVITAS study
- ARCTIC TRIAL
- Morphine increases platelet reactivity. Hence higher dose of antiplatelets required
- Gender differences
- Ongoing studies

- Guidelines recommendation:
  - Class III recommendation- routine use of platelet function testing is not advised
  - Class IIb in patients at high risk for poor clinical outcome

GRAVITAS STUDY

- The efficacy of high dose clopidogrel (600 mg initial dose and 150 mg daily thereafter for 6 months) versus standard dose clopidogrel (no additional loading dose and 75 mg daily) was compared in 2214 patients with high on-treatment reactivity, on the basis of Verify Now P2Y12 assay measurement, 12 to 24 hours after PCI with drug-eluting stents.
  - No differences in the rates of ischemic (2.3% versus 2.3%; HR, 1.01 [0.58–1.76]; *P*=0.97) or bleeding outcomes (1.4% versus 2.3%; HR, 0.59 [0.31–1.11]; *P*=0.10) were found.
  - Thus, a benefit of a tailored strategy with clopidogrel therapy was not observed in this trial





- It was a flat trial. For the primary composite end point, there was no difference;
- 34% of events in the group of patients that was monitored,
- 31% in the control group, no difference statistically speaking.
- It was the same for the main secondary end point,
- urgent revascularization and/or stent thrombosis

Gender difference in PI - NIMS

Parameter	Male	Female	p Value
Total No	112(78.9%)	30(21.1%)	-
Age	57.1± 9.6	56.2 ± 10.4	0.7
HTN	67 (59.8%)	22(73.3%)	0.15
DM	43(38.4%)	19(63.3%)	0.01
SM	45(39.3%)	1(3.3%)	0.000
PVD	2(1.8%)	0(0%)	0.15
CVA	2(1.8%)	0(0%)	0.15

Parameter	Female	Male	p Value
Hb	12.3± 1.4	13.5 ± 2.1	0.000
Chad Vas Score	2.7± 0.95	1.4± 1.3	0.000
ACS	60(53.6%)	16(53.3%)	0.98
LVD	49(43.8%)	8(26.7%)	0.067
GPI	9(8.04%)	4(13.3%)	0.43

Gender difference in PI

- There are 9(30%) females with high on-treatment platelet reactivity in whom there are nil events in them
- There are 24 (21.43%) males with high on-treatment platelet reactivity in whom there are 3 non cardiac events (AV fistula, CSA+CIN, CCF) in them
- Even total event rate(MACCE) is higher in females(10%) than in males (8.04%), Which is not statistically significant (Chi square test person = 1.238, p=0.266, and fisher exact test p= 0.545, OR = 0.00, 95% CI 0.00 to 6.649, RR = 0.00, 95% CI 0.00 TO 5.389) .

Conclusion:

- Though there is a tendency of high on-treatment platelet reactivity in females, this is not translated into the clinical events at one year.

ONGOING STUDIES

- TROPICAL-ACS study:
  - To assess the use of novel P2Y12 inhibitors therapies on the basis of pharmacodynamic studies.
  - Prasugrel to clopidogrel if PR is below threshold
- HEIGHTEN study:
  - Effect of switching patients with HPR from prasugrel to ticagrelor

- This patient presented 5 months later with acute abdomen-intestinal obstruction requiring emergency surgery.
- What advice would you give-DISCONTINUE ANTIPLATELETS?

DURATION DEPENDING ON TYPE OF STENT

- Zotarolimus-3 months
- RESET trail
- 2,117 patients with coronary artery stenosis into 2 groups according to DAPT duration and stent type: 3-month DAPT following Endeavor zotarolimus-eluting stent (E-ZES) implantation (E-ZES+3-month DAPT, n=1,059) versus 12-month DAPT following the other DES implantation (standard therapy, n=1,058).
- E-ZES+3-month DAPT was non-inferior to the standard therapy with respect to the occurrence of the primary endpoint.
- OPTIMIZE trail
- Results of the OPTIMIZE trial showed the non-inferiority of 3-month DAPT to standard 12-month therapy after implantation of a zotarolimus-eluting stent (ZES; Endeavor, Medtronic). Importantly, abbreviated DAPT did not increase the risk of stent thrombosis.

- Antiplatelet Therapy and Outcomes in Patients Undergoing Surgery After Stenting
- **SAS registry** tracks the feasibility and outcomes of patients treated according to 2014 Italian consensus recommendations
- Aspirin should be continued perioperatively in most surgeries, as should DAPT in surgeries with low-surgical risk
- 85% of the 1,082 patients
- In-hospital rate of net adverse clinical events (death, MI, ST, and bleeding) was 12.7%, while 30-day MACE and ST rates were 3.5% and 0.2%, respectively
- Implications: Adherence to Italian consensus recommendations is feasible, with event rates within the “acceptable range,” say researchers.
- Rossini R, et al. Catheter Cardiovasc Intv. 2016;Epub ahead of print.

- LEADERS trail
- The aim of this pre specified sub study was to evaluate the safety and efficacy of the Bio Freedom™ BA9 DCS followed by 1 month DAPT in patients presenting with an ACS
- In ACS patients with high bleeding risk a polymer-free BA9- DCS combined with 1-month DAPT displays significantly better efficacy and safety than a BMS, the latter driven by significantly lower cardiac mortality and MI.
- Current guidelines should be reconsidered for high bleeding risk patients presenting with ACS: → BMS can no longer be recommended → Data on DES with shortened DAPT are scarce → Bio Freedom™ BA9-DCS has strongest evidence in these patients.

Continuation of DAPT after 1 year

- The CHARISMA sub study and the PEGASUS trial evaluated initiation of DAPT beyond 1 year among patients with prior MI, regardless of whether PCI had been undertaken at the time of the MI.
- In the setting of PCI, the DAPT trial alone evaluated the impact of extended-duration DAPT in the subgroup of patients presenting with MI as the clinical indication for PCI and showed that
  - Continued DAPT beyond 1 year reduced the rate of MACCE by a larger amount in patients presenting with MI (3.9% versus 6.8%, $p<0.001$) than in patients without MI at presentation (4.4% versus 5.3%; p for interaction=0.03
- These findings highlighted the potential benefit of DAPT among patients with high athero-thrombotic risk.

- Treatment with DAPT beyond 1 year after DES implantation reduces MI and stent thromboses, it is associated with increased mortality because of an increased risk of non cardiovascular mortality not offset by a reduction in cardiac mortality
  - 21% increase in mortality rate with prolonged DAPT was seem in RCTs and supported by several other published reports

DAPT trial

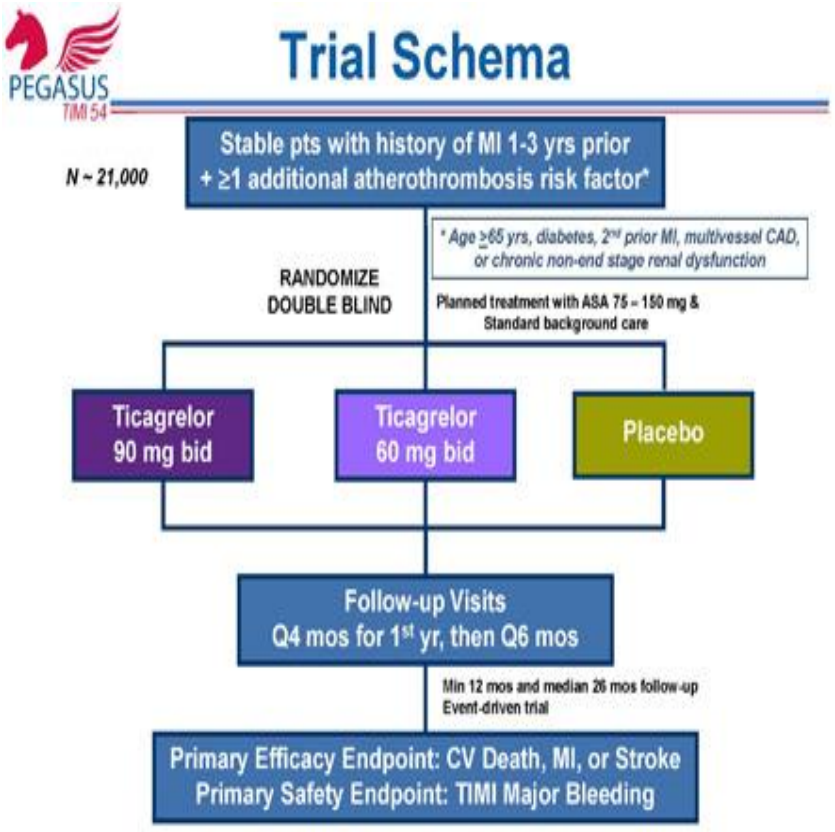
- The DAPT trial met its primary endpoints and thus stood apart from the remaining 10 RCTs, which either refuted a superiority hypothesis or met a non-inferiority hypothesis.
  - The DAPT trial reported that prolonged therapy was associated with a borderline increase in mortality rate. Although the mortality outcome in the trial has been attributed to non cardiovascular causes
  - The DAPT investigators (68) reported that the 4,703 patients who underwent EES implantation had higher mortality rates after 30 months of DAPT than after 12 months of therapy (2.1% versus 1.1%, p=0.02)
  - In a subgroup analysis of the DAPT trial, investigators (44) found that the reduction in MACCE seen with prolonged DAPT was greater for patients with MI at presentation (3.9% versus 6.8%; HR: 0.56; p<0.001) than for those without MI at presentation for PCI (4.4% versus 5.3%; HR: 0.83; p=0.08; interaction p=0.03).

DAPT SCORE

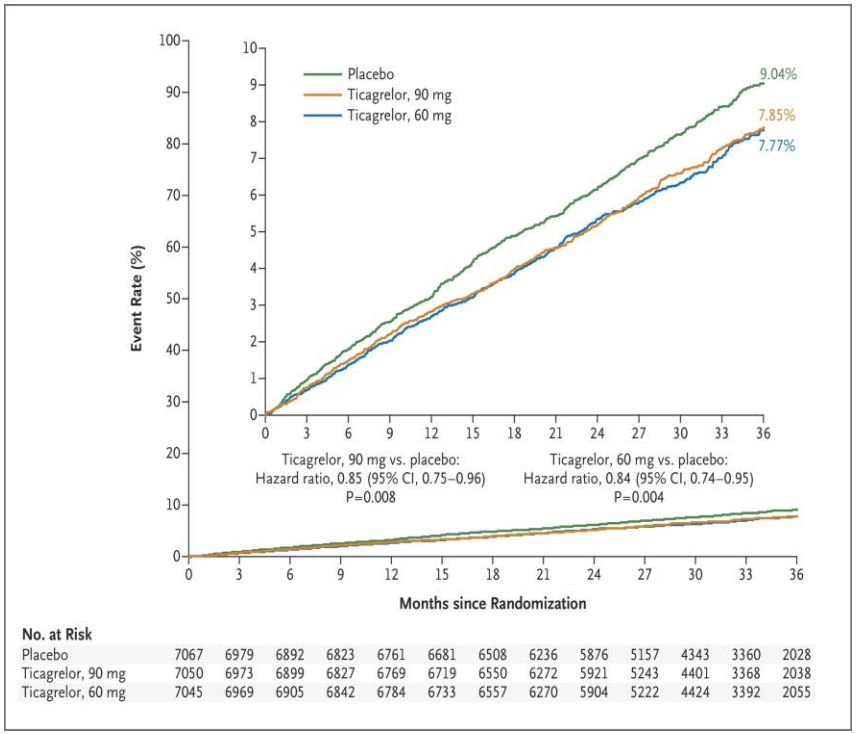
- Factors Used to Calculate a “DAPT Score”
- Variable Points
- Age ≥75 y -2
- Age 65 to <75 y -1
- Age <65 y 0
- Current cigarette smoker 1
- Diabetes mellitus 1
- MI at presentation 1
- Prior PCI or prior MI 1
- Stent diameter <3 mm 1
- Paclitaxel-eluting stent 1
- CHF or LVEF <30% 2

Saphenous vein graft PCI 2 A score of ≥2 is associated with a favourable benefit/risk ratio for prolonged DAPT while a score of <2 is associated with an unfavourable benefit/risk ratio. CHF indicates congestive heart failure; DAPT, dual antiplatelet therapy; LVEF, left ventricular ejection fraction; MI, myocardial infarction; and PCI, percutaneous coronary intervention. Adapted with permission from Yeh et al.

Ticagrelor for secondary prevention PEGASUS-TIMI 54



- Patients with myocardial infarction 1 to 3 years previously were assigned to ticagrelor, 90 or 60 mg twice daily, or to placebo, in addition to low-dose aspirin.
- At 3 years, ticagrelor reduced the risk of cardiovascular death, MI, or stroke but increased the risk of major bleeding.
- In patients with a myocardial infarction more than 1 year previously, treatment with ticagrelor significantly reduced the risk of cardiovascular death, myocardial infarction, or stroke and increased the risk of major bleeding



- The addition of ticagrelor, at a dose of 90 mg twice daily or 60 mg twice daily, to low-dose aspirin reduced the risk of cardiovascular death, myocardial infarction, or stroke and increased in the risk of TIMI major bleeding among patients who had had a myocardial infarction 1 to 3 years earlier.

Long-Term Use of DAPT After MI

- Activation of platelets, with resultant thrombosis, occurs not only in response to implantation of DES, but also as part of the process of atherosclerosis. Patients with a recent athero thrombotic coronary event are at high risk of recurrent events. Several trials have demonstrated the ability of DAPT to inhibit platelet activation and reduce the risk of recurrent MI in the year after an acute MI

- Current guidelines recommend that DAPT should be continued for up to 12 months after MI

NIMS STUDY- DAPT

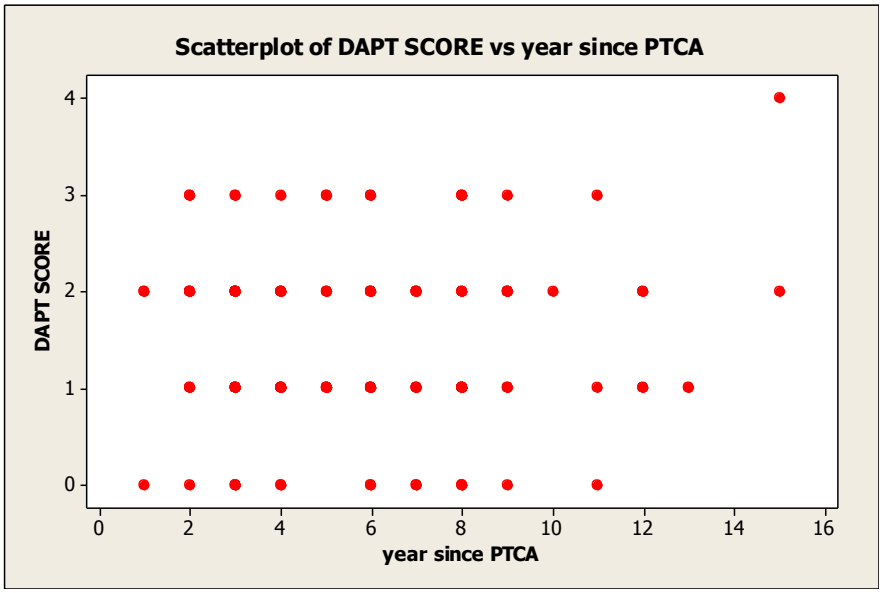
Parameter	**No (%)**
Total no.	127
Male	100 (78.74%)
Female	27(21.26%)
DM	95(74.8%)
HTN	98(77.17%)
SM	20(15.74%)
Prior MI or PCI	10 (7.87%)
MI as presentation at procedure time	12(9.44%)

VARIABLE	MEAN	SD	Median	Min-Max
AGE	60.82	9.2	62	35 – 80
DAPT SCORE	1.48	0.8	1	1 – 4
YEAR SINCE PTCA	5.92	3.0	6	1 - 15

Complication	No of Cases	Mean Age	DAPT Score	Average Years of follow up	Sex
CSA	3	51	1.67	7.33	2 (M),1 (F)
CVA	1	66	1	4	1 (F)

A. Ashok Kumar et al IJCD 2016 vol 1 issue 3

DAPT study cont…



DAPT score	No of patients	Complication
Zero	16 (12.6%)	Nil
One	52(40.9%)	Two (one CVA, one CSA) (1.6%)
Two	45(35.4%)	Two (CSA) (1.6%)
Three	14(11%)	Nil
Four	01(0.8%)	Nil

DAPT Study cont…

Conclusion

DAPT beyond one year has benefits in terms of low associated complications and low incidence of coronary events

GENDER SPECIFIC

- At 2 years there was no difference in death, MI, or stroke (primary endpoint) for women compared with men (adjusted HR 0.91; 95% CI 0.65-1.26)
- There was no sex difference for the primary endpoint when DAPT durations were compared
- Men had an increased risk of bleeding compared with women that was driven by BARC 2 events
- Gargiulo G, et al. J Am Coll Cardiol Intv.2016;Epub ahead of print.

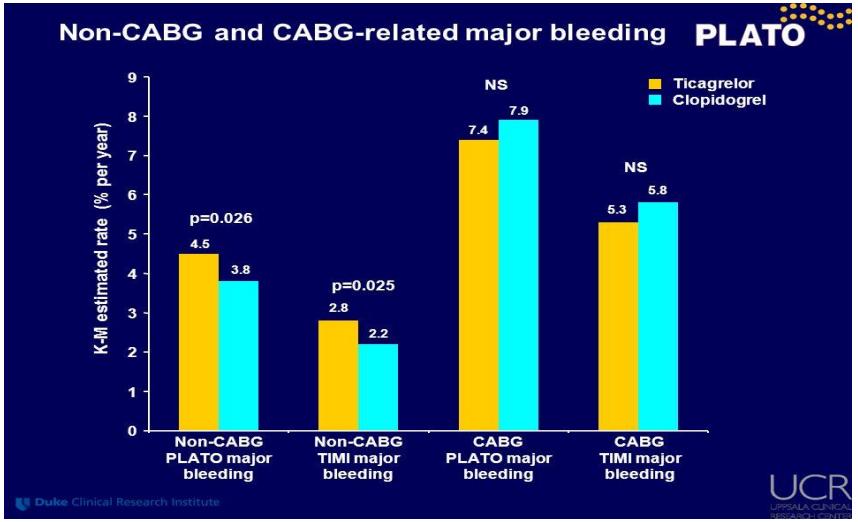
- Impact Of Gender on 2-Year Clinical Outcomes in Patients Treated With 6- or 24-Month DAPT
- Pre specified sex-based analysis from the **PRODIGY trial** of patients with ACS or stable CAD.
- **Implications:** After PCI, men and women have similar bleeding and ischemic risk, suggesting gender is not an important consideration in selection of DAPT duration.

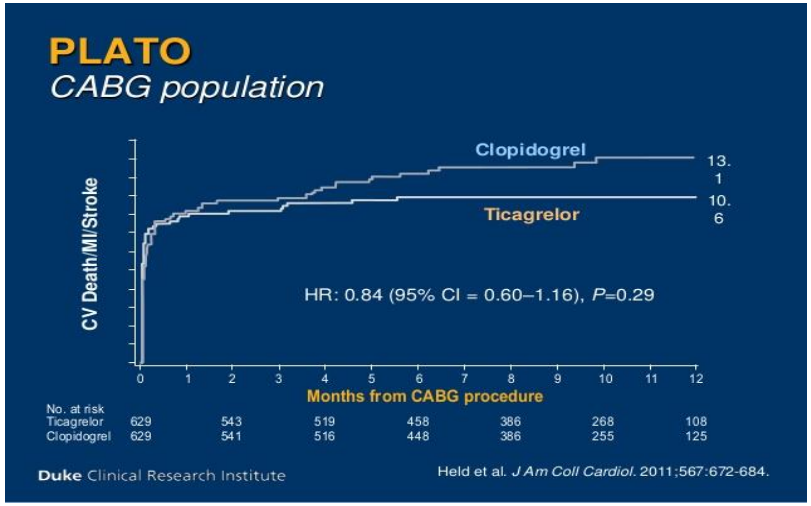
Case scenario-2

- 64 year old male, diabetic and hypertensive presented with typical chest pain. ECG suggestive of significant ST depression in chest leads. Diagnosed as ACS-NSTEMI. Patient was taken up for angiogram which showed TVD requiring surgery.
- Which antiplatelet agent would you have preferred?

PLATO-CABG

- 1,899 patients underwent CABG post-randomization. The protocol recommended ticagrelor/placebo to be withheld for 24 to 72 h and clopidogrel/placebo for 5 days preoperatively
- In the subgroup of patients undergoing CABG within 7 days after the last study drug intake, ticagrelor compared with clopidogrel was associated with a substantial reduction in total and CV mortality without excess risk of CABG-related bleeding

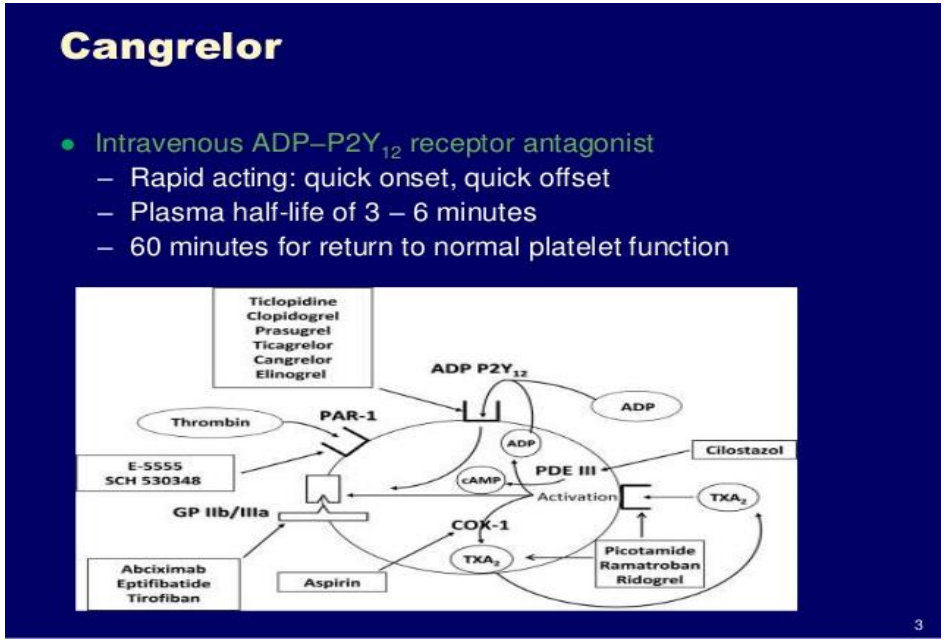




Cangrelor

- Analogue of ATP and the first reversible intravenous P2Y12 inhibitor.
- Does not undergo metabolic transformation
- Binds to P2Y12 receptor in a dose dependent fashion
- Potent, >90% platelet inhibition
- High levels of receptor occupancy, preventing ADP signalling
- Very short half life: 3-6 min
- Recovery of platelet function is very rapid : 30-60 min

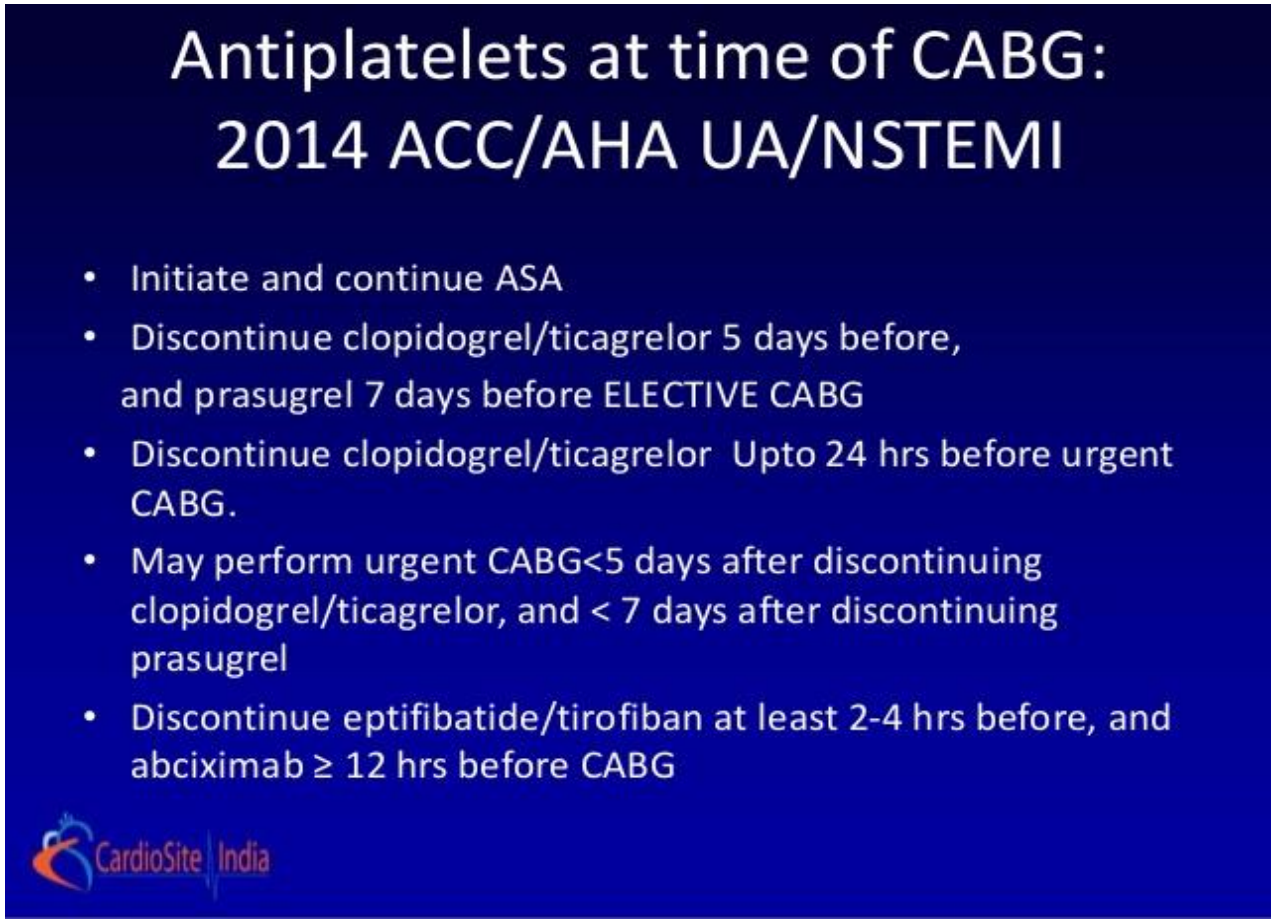
- FDA approval for use in PCI who did not receive oral P2Y12 inhibitor
- Adjunct to PCI to prevent peri procedural MI



Switch over

- **Cangrelor to oral inhibitors**
  - Interaction exists between clopidogrel, prasugrel and Cangrelor
  - Clopidogrel or prasugrel should not be started before cangrelor infusion as their effect is nullified
  - In the acute setting, bolus and infusion of cangrelor should be started before PCI and continued for the duration of procedure(<4 hours)
- Clopidogrel or prasugrel loading dose should be given immediately after discontinuation of infusion
- Ticagrelor can be given before. After or during cangrelor infusion without interaction
- **Oral inhibitors to cangrelor**
  - Infusion can be started at any time

Recommendations for antiplatelet discontinuation before Surgery.



Recommendations for DAPT after CABG

- COR LOE Recommendations
- I C-EO -In patients treated with DAPT after coronary stent implantation who subsequently undergo CABG, P2Y12 inhibitor therapy should be resumed postoperatively so that DAPT continues until the recommended duration of therapy is completed.
- I C-LD - In patients with ACS (NSTE-ACS or STEMI) being treated with DAPT who undergo CABG, P2Y12 inhibitor therapy should be resumed after CABG to complete 12 months of DAPT therapy after ACS (52-54,118-120).
- I B-NR - In patients treated with DAPT, a daily aspirin dose of 81 mg (range, 75 mg to 100 mg) is recommended (56-60,75-78).
- IIb B-NR - In patients with SIHD, DAPT (with clopidogrel initiated early postoperatively) for 12 months after CABG may be reasonable to improve vein graft patency (121125).

Aspirin-optimal dose

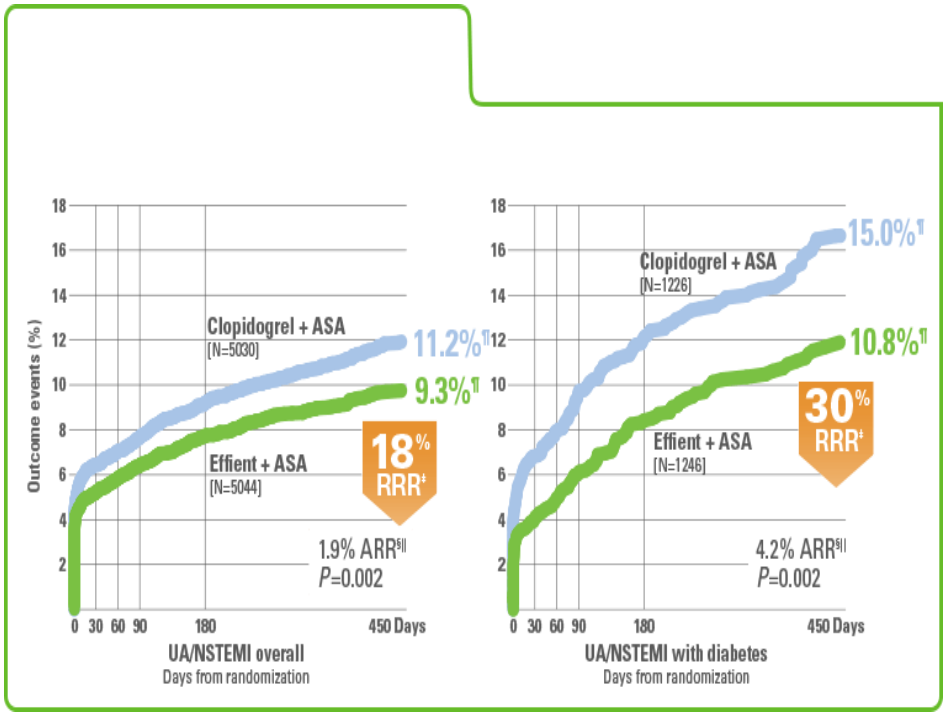
- NSTEMI
  - The Antithrombotic Trialists' Collaboration : greatest risk reduction was found with doses from 75 to 150 mg
  - Meta analysis showed doses 100 mg/d were associated with a significantly lower rate of major bleeding events than doses 200 mg/d
  - CURRENT-OASIS 7 Trial: Compared with low-dose aspirin, aspirin doses of 300 to 325 mg did not result in any significant differences in the primary outcome and in major bleeding
  - ACC/AHA 2012 guidelines for UA/NSTEMI:
    - 162-325 mg LD
    - 75-100 mg/d MD indefinitely
  - PCI guidelines:
    - 81-325 mg LD for those taking ASA before PCI (class IB)
    - Non-enteric ASA 325 mg LD for those not on chronic ASA (class IB) before PCI
    - ASA to be continued indefinitely (class IA), 81 mg/day is preferred (class IIaB)
  - ESC guidelines:

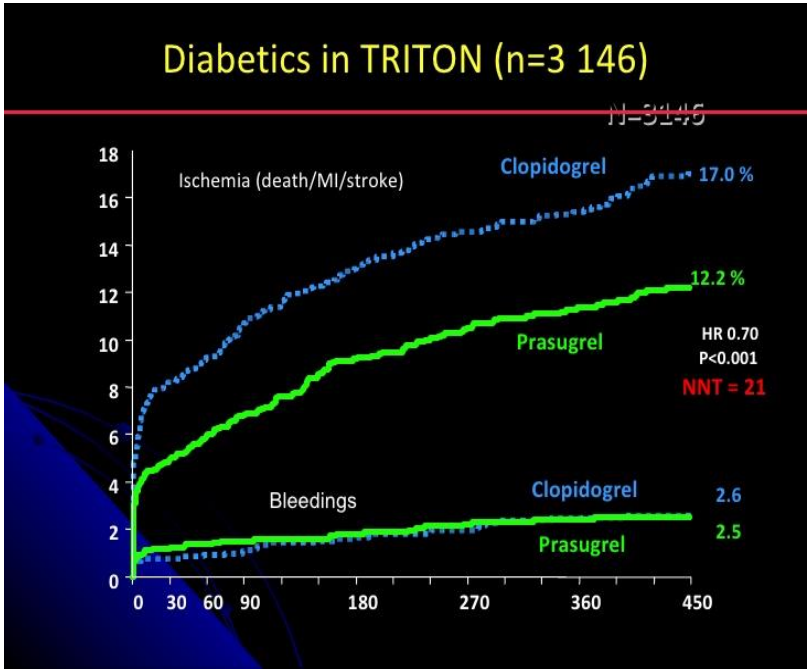
STEMI

- ACC/AHA guidelines for STEMI 2013 in PCI:
  - 162-325 mg LD before procedure (class IA)
  - 81-325 mg daily MD indefinitely (class IA)
  - 81 mg is the preferred maintenance dose (class IIaB)
- ACC/AHA guidelines in adjunct to TLT:
  - 162-325 mg LD (class IA)
  - 81-325 mg MD daily indefinitely (class IA)
  - 81 mg is the preferred MD (class IIaB)
- ESC guidelines:
- Trials/evidence

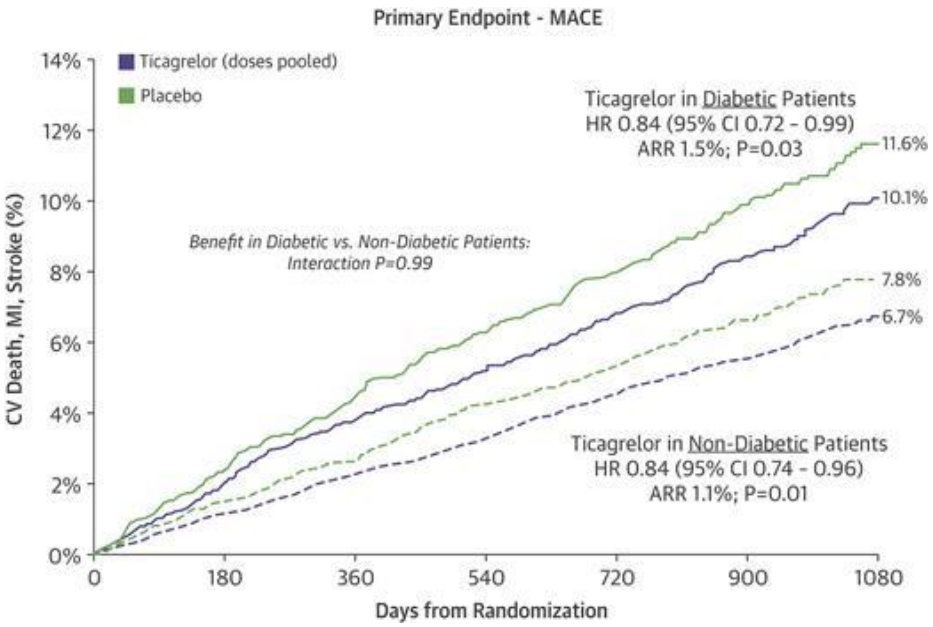
Antiplatelet superior in diabetics

TRITON-TIMI-38

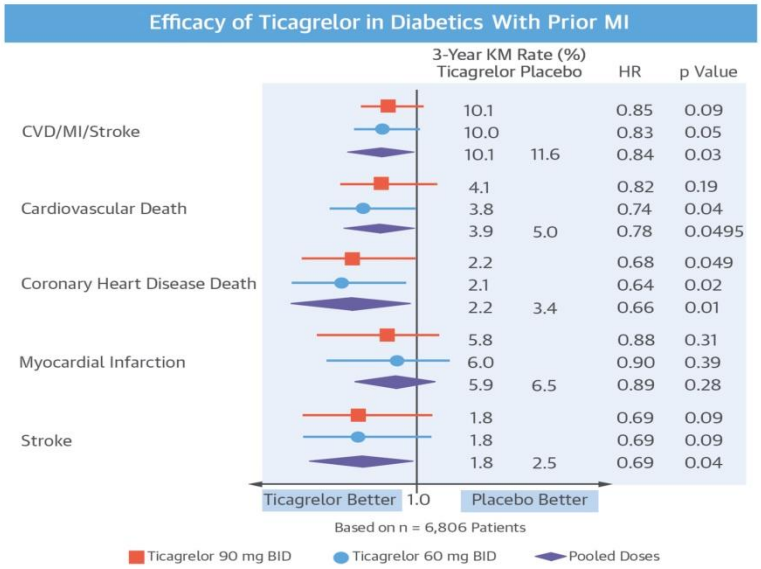




PLATO TRIAL



CENTRAL ILLUSTRATION: Ticagrelor in Patients With Diabetes: Consistent Reduction in Ischemic Endpoints



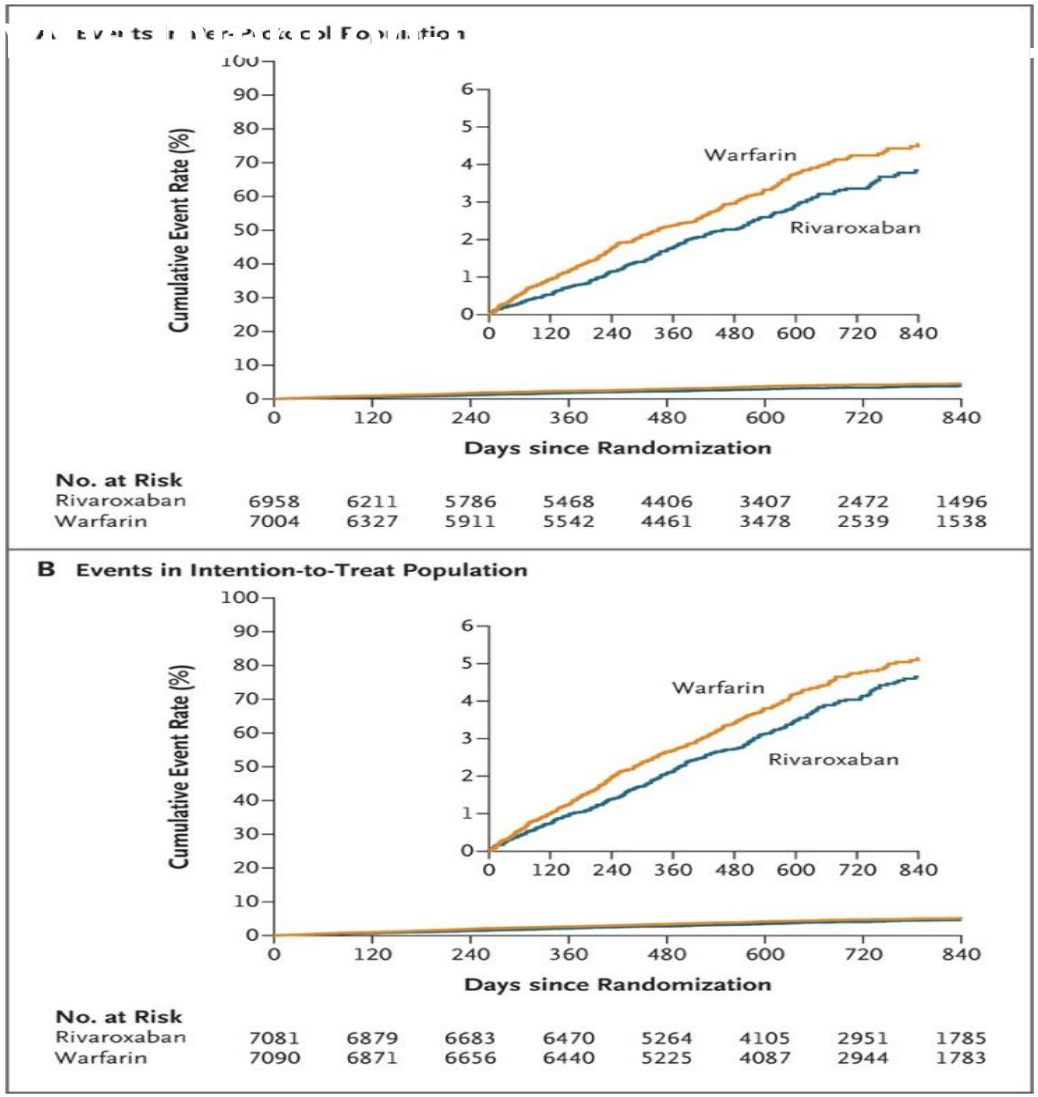
Bhatt, D.L. et al. J Am Coll Cardiol. 2016;67(23):2732-40.

PCI in AF

- 75 year old male diabetic, hypertensive known CAD with severe LV dysfunction, post CABG status presented with unstable angina. ECG showed AF which was not there previously Angio showed LIMA patent, PCI done to LMCA to LCX.
- What is the antiplatelet regimen to be given for him?

ROCKET AF

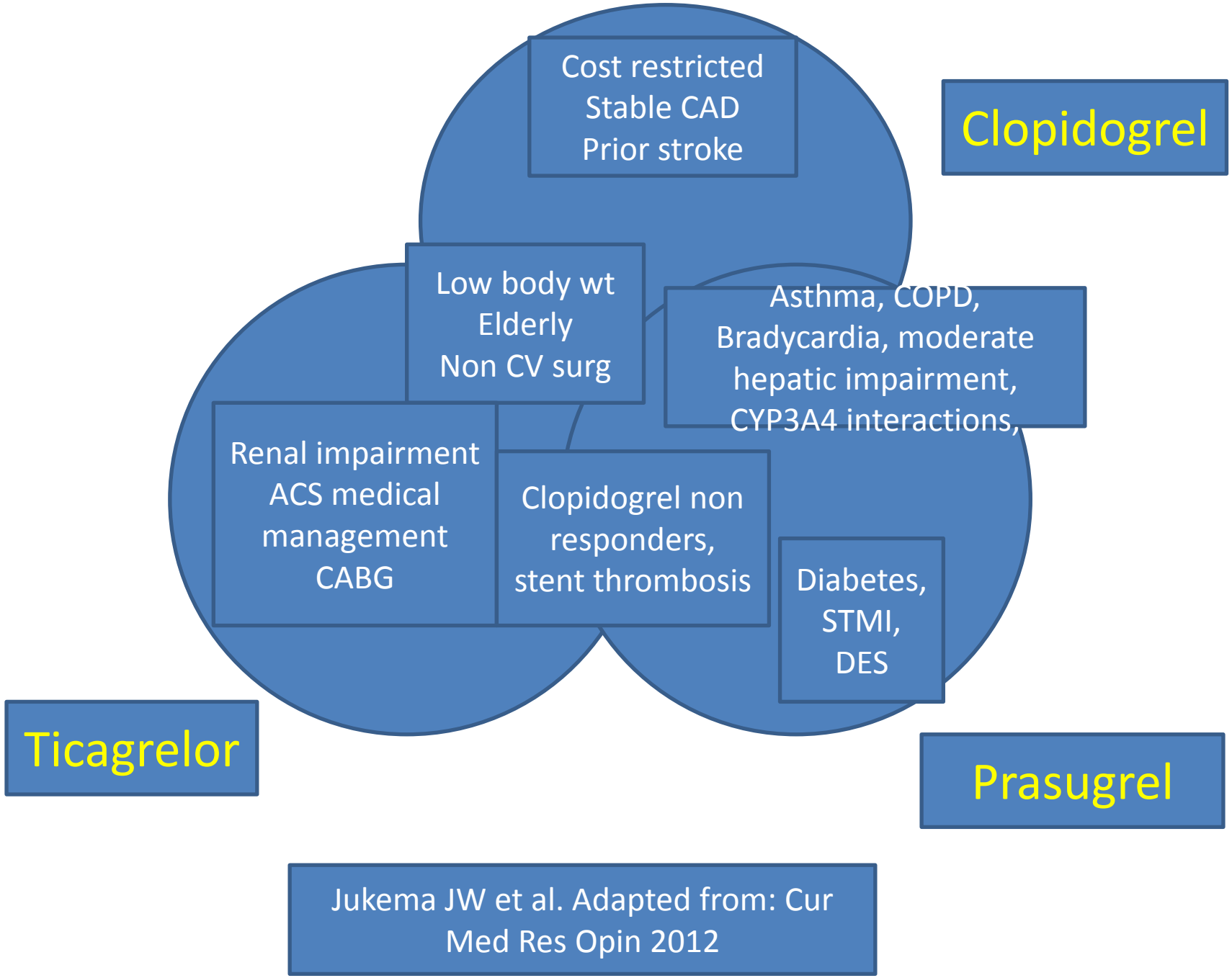
- Use of DAPT and Patient Outcomes in Those Undergoing PCI: The **ROCKET AF Trial**
- Analysis of the 151 patients (~1%) who underwent PCI after being randomized to rivaroxaban or warfarin.
- More than 80% remained on the anticoagulant they were randomized to in ROCKET AF
- Oral antiplatelet therapy given after PCI was highly varied and included clopidogrel plus aspirin, aspirin alone, clopidogrel alone, or no antiplatelet therapy in some cases
- Compared with patients in the trial who did not have PCI, those who did had more thrombotic events and bleeding
- Implications: Optimal treatment strategies remain unclear, leaving knowledge gaps for physicians faced with these vulnerable patients.
- Sherwood MW, et al. J Am Coll Cardiol Intv. 2016;9:1694-1702.



Patel MR et al. N Engl J Med 2011;365:883-891.

REDUAL –PCI

- Ongoing study
- The main objective of this study is to compare a Dual Antithrombotic Therapy (DAT) regimen of 110mg dabigatran etexilate b.i.d. plus clopidogrel or ticagrelor (110mg DE DAT) and 150mg dabigatran etexilate b.i.d. plus clopidogrel or ticagrelor (150mg DE-DAT) with a Triple Antithrombotic Therapy (TAT) combination of warfarin plus clopidogrel or ticagrelor plus ASA <= 100mg once daily (warfarin-TAT) in patients with Atrial Fibrillation that undergo a PCI with stenting (elective or due to an Acute Coronary Syndrome).


Cost restricted
Stable CAD
Prior stroke
Clopidogrel
Low body wt
Elderly
Non CV surg
Asthma, COPD,
Bradycardia, moderate
hepatic impairment,
CYP3A4 interactions,
Renal impairment
ACS medical
management
CABG
Clopidogrel non
responders,
stent thrombosis
Diabetes,
STMI,
DES
Ticagrelor
Prasugrel
Jukema JW et al. Adapted from: Cur
Med Res Opin 2012

The proposed algorithm for the decisions concerning the use and duration of dual antiplatelet therapy in acute coronary syndrome patients, irrespective of the use of stents

> 12 m DAPT

Documented CAD, No excess bleeding risk, no bleeding event

6 m DAPT

Documented obs. CAD, Bleeding risk factors (age, gender….

3 m DAPT

Documented obs. CAD, Recent /prior bleeding, Scheduled surgery, oral anticoagulation needed

SAPT only

No Q wave ,No prior stent,
No prior CABG, No CAG
No CT scan, Negative troponin
High bleeding risk

Gilles Montalescot, and Marc S. Sabatine
Eur Heart J 2016;37:344-352

Take home message

- DAPT is the crux of treatment in patients with ACS

and

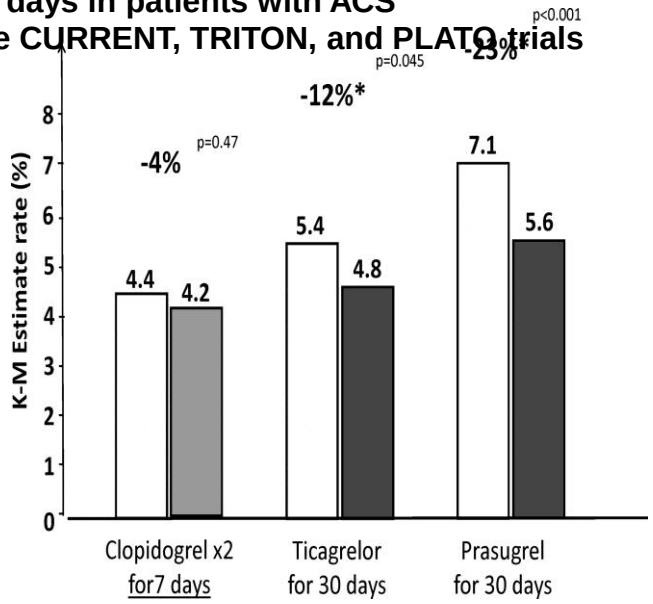
those undergoing PCI

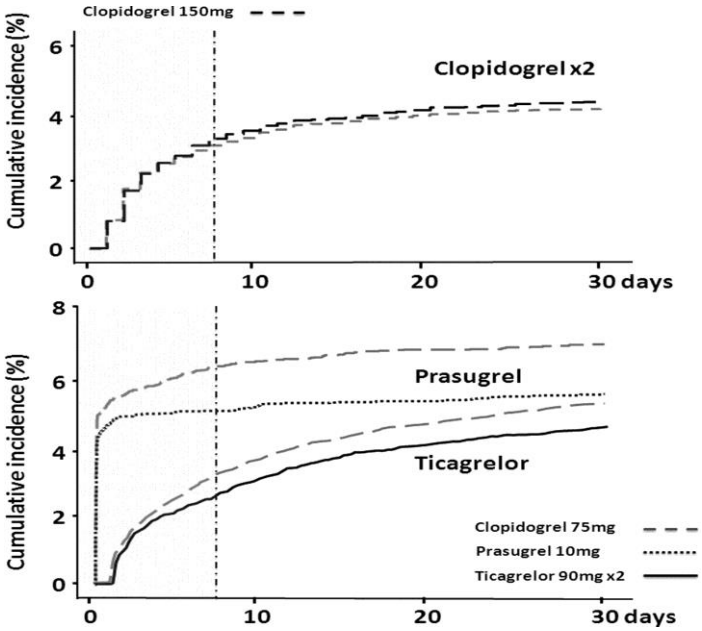
- Ticagrelor and Prasugrel are far more superior

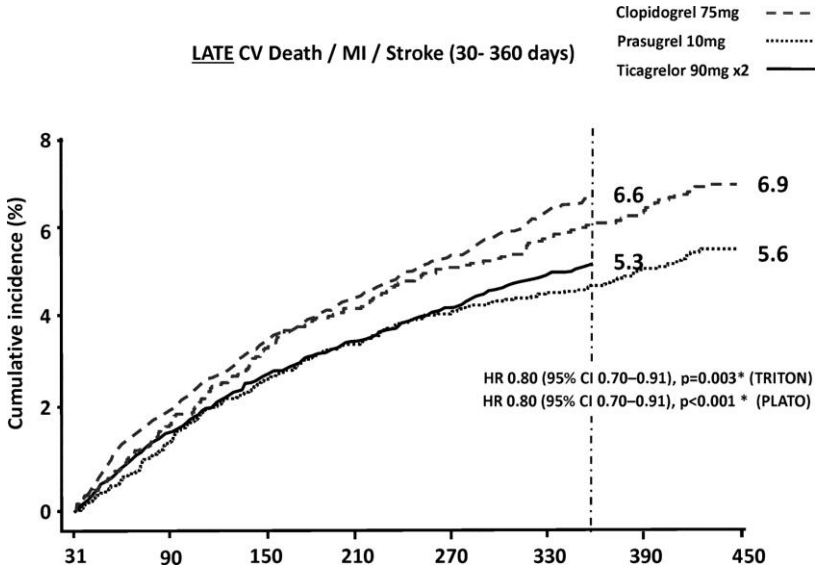
to Clopidogrel,

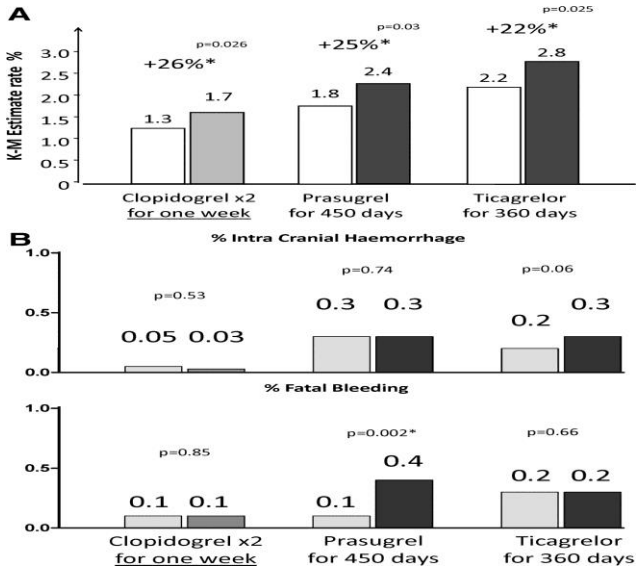
but clopidogrel is more frequently used

Rate of ischemic events (CV death, MI, stroke) at 30 days in patients with ACS in the CURRENT, TRITON, and PLATO trials









- Safer, newer-generation DES may be treated with a minimum DAPT duration of 3 to 6 months
- Extension of DAPT beyond 12 months entails a risk-benefit assessment.
  - Extension of DAPT beyond 12 months to prevent MI may be optimal in patients at relatively low bleeding risk of <2% over 2 years
  - DAPT SCORE
- In Patients with prior MI prolonged DAPT is adviced at a cost of increased bleeding events.
- Switch over of P2Y12 inhibitors is safe though further trials on clinical outcome are warranted

THANK YOU…