



Antiplatelet therapy: State of the **Art**

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Conflict of interest

Within the past 12 months, I have had a financial interest/arrangement or affiliation with the organization(s) listed below

Physician Name

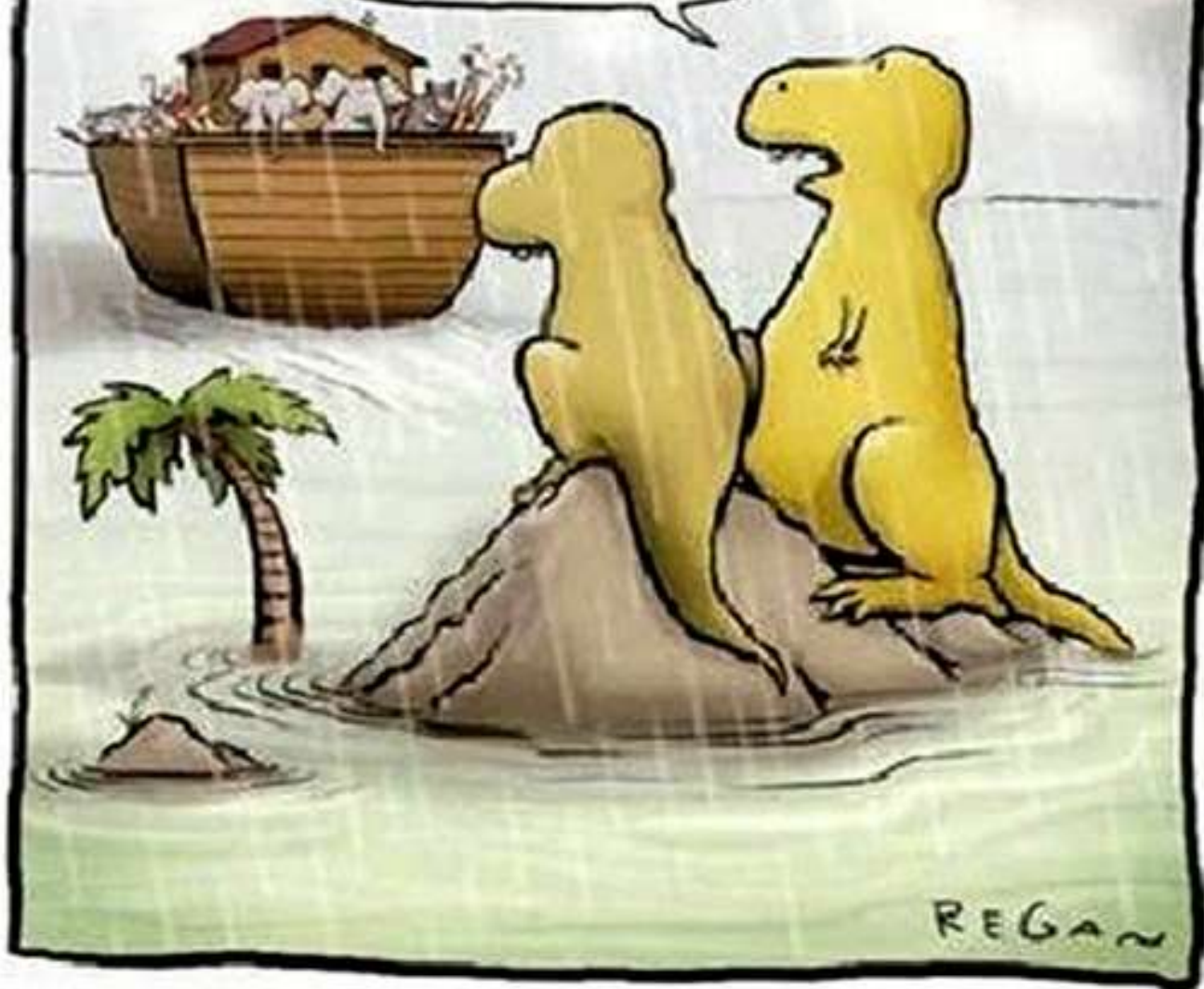
Dharam J. Kumbhani, MD

Company/Relationship

Honoraria/consulting: American College of Cardiology

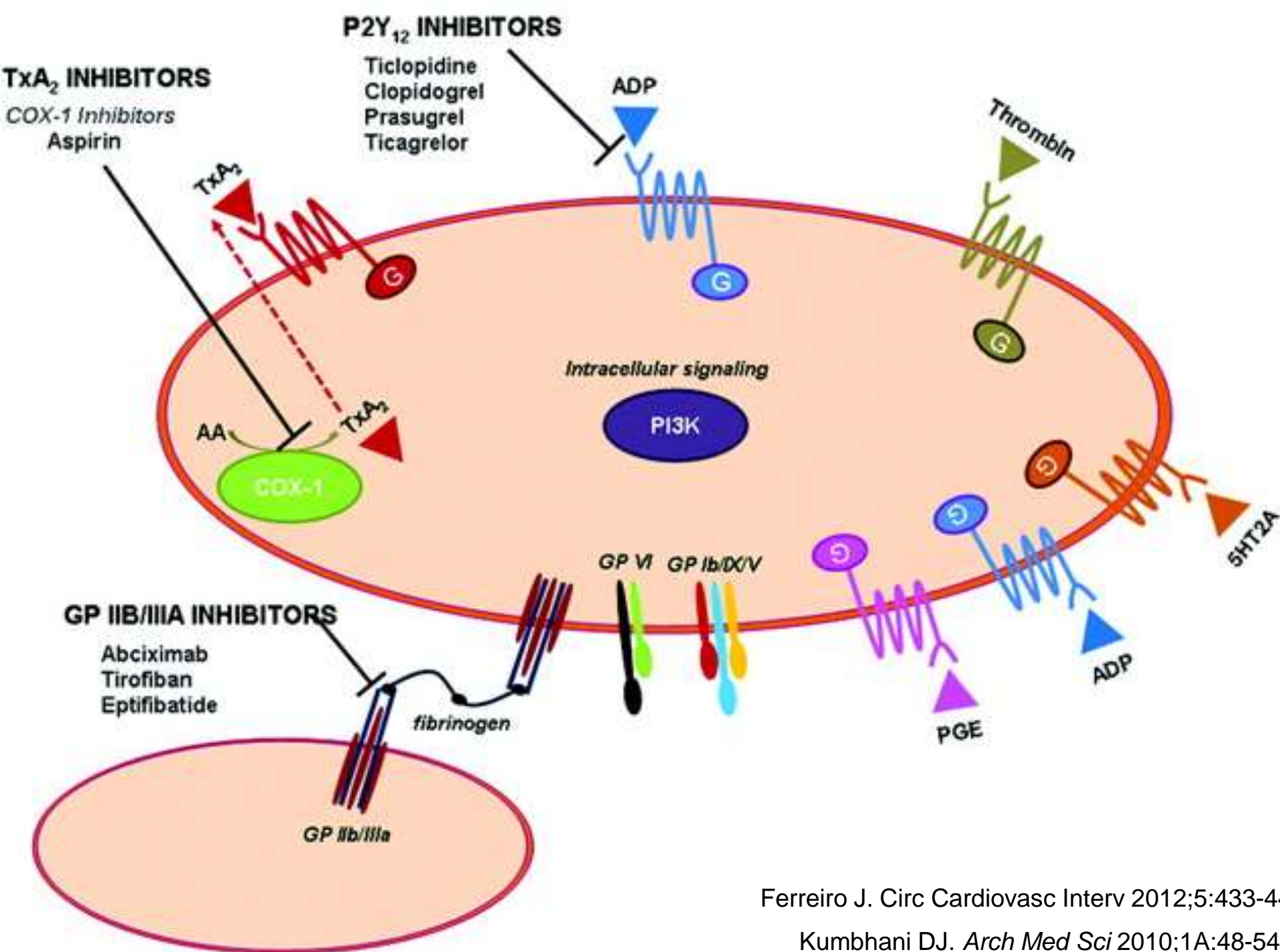
Disclaimer: I will be describing off-label use and investigational devices which are not currently approved by the US-FDA

Oh, crap!
Was that
TODAY?



Outline

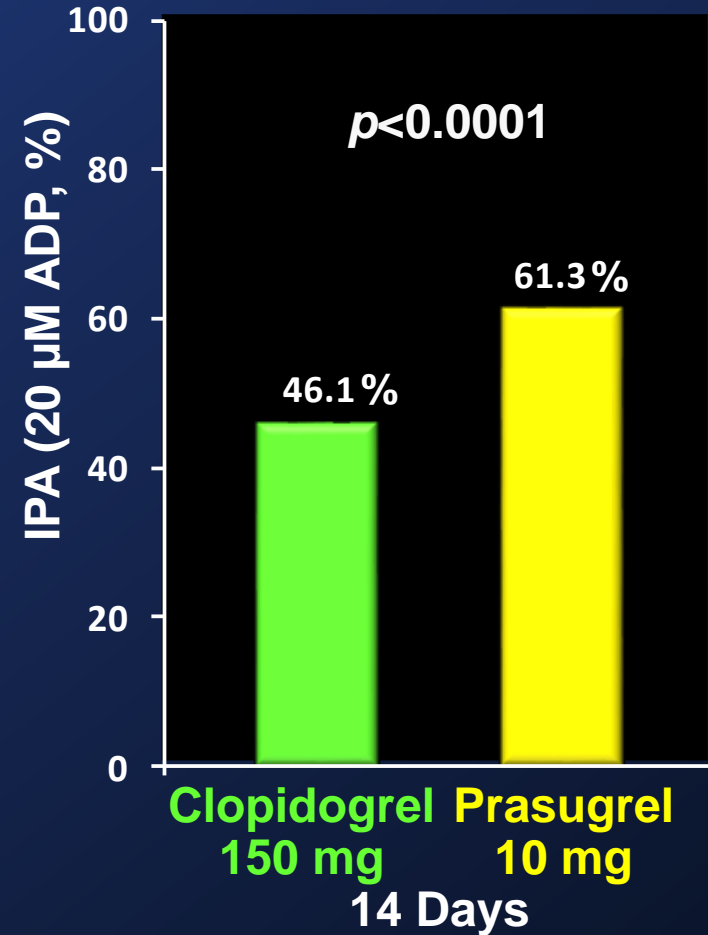
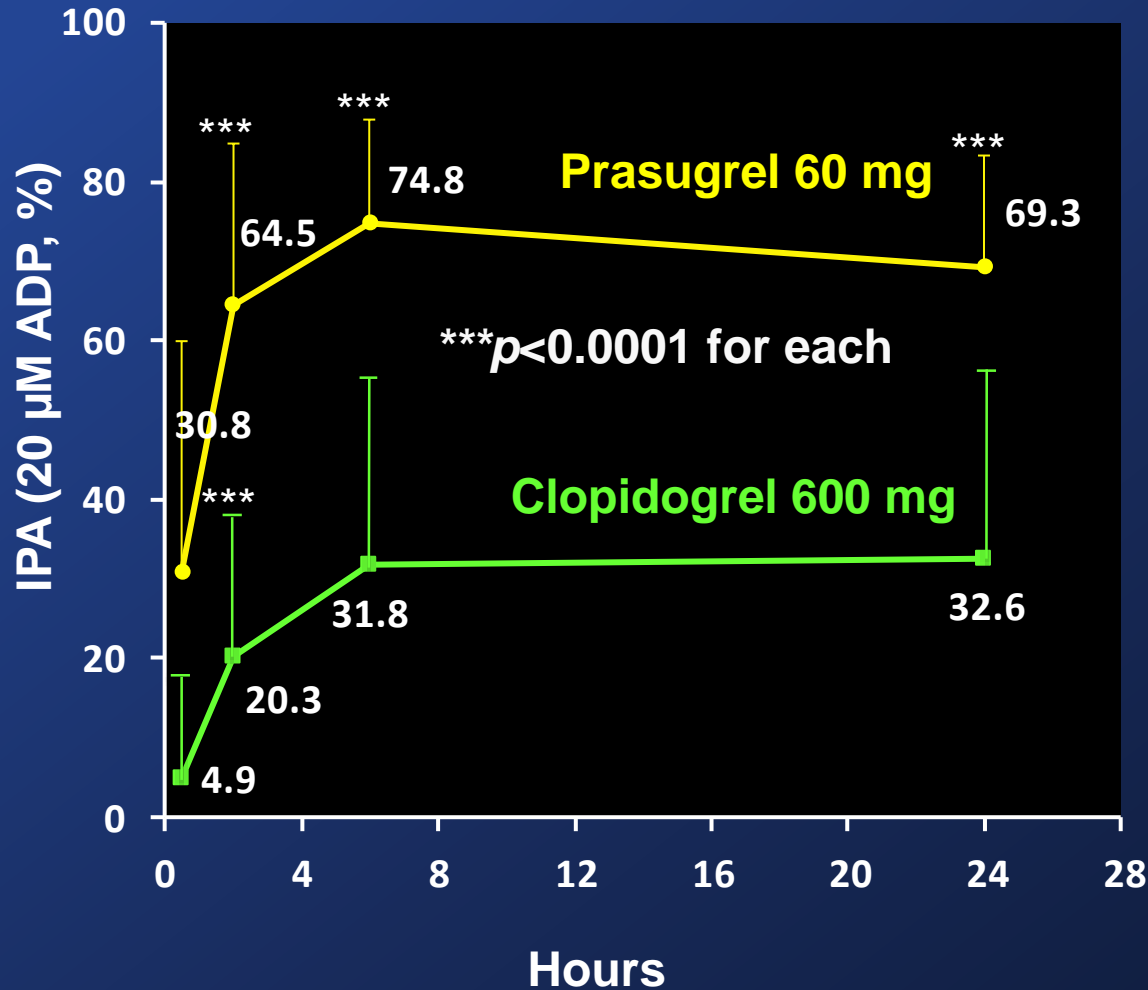
- Classes of antiplatelet agents
- PK/PD
- Landmark trials
- Antiplatelet testing
- Guidelines

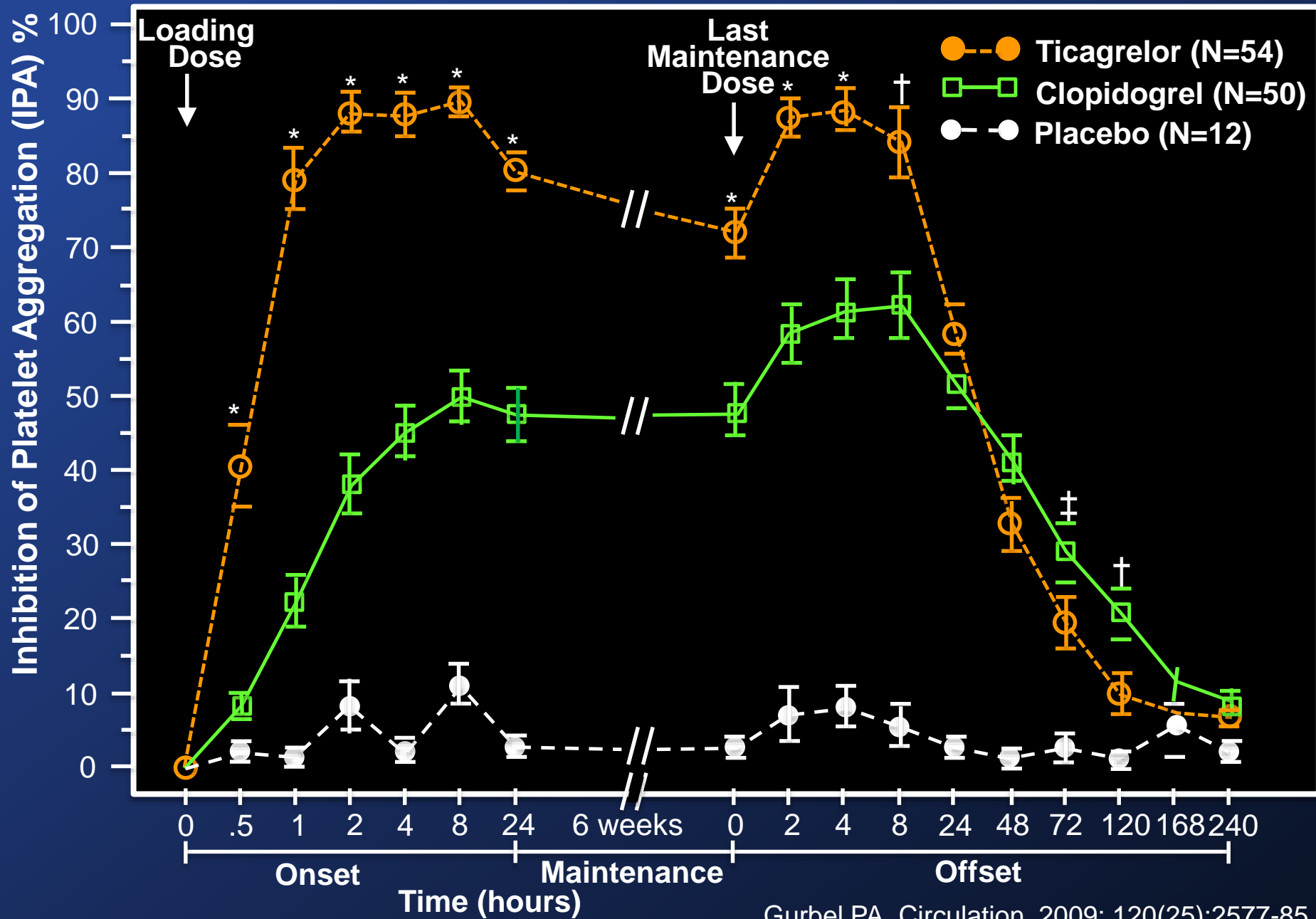


Ferreiro J. *Circ Cardiovasc Interv* 2012;5:433-4

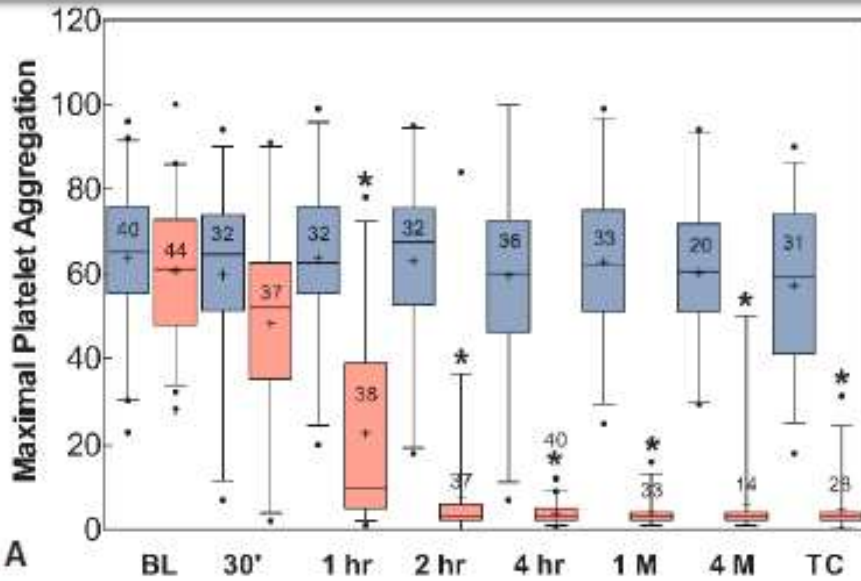
Kumbhani DJ. *Arch Med Sci* 2010;1A:48-54

PRINCIPLE-TIMI 44

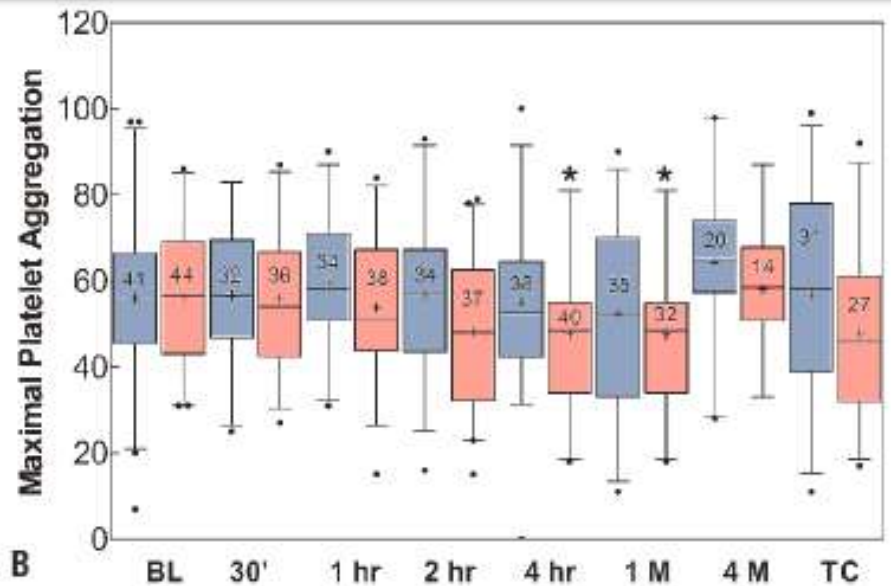


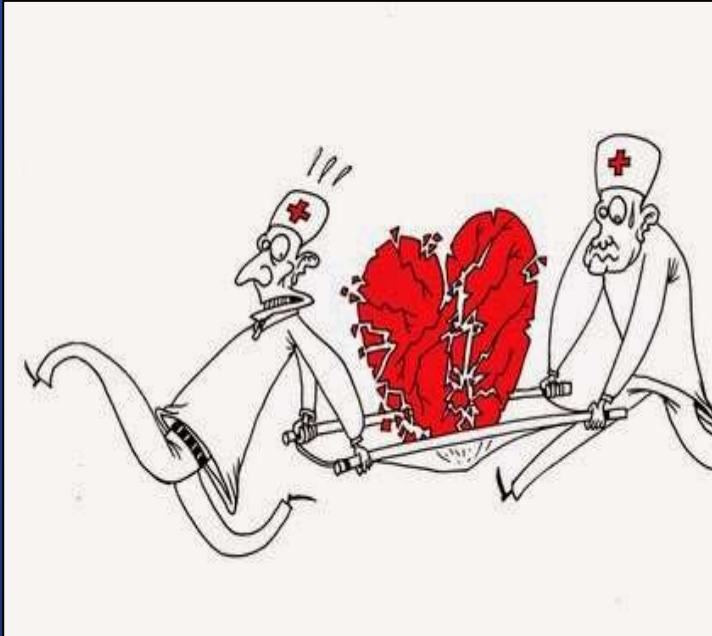


TRACER

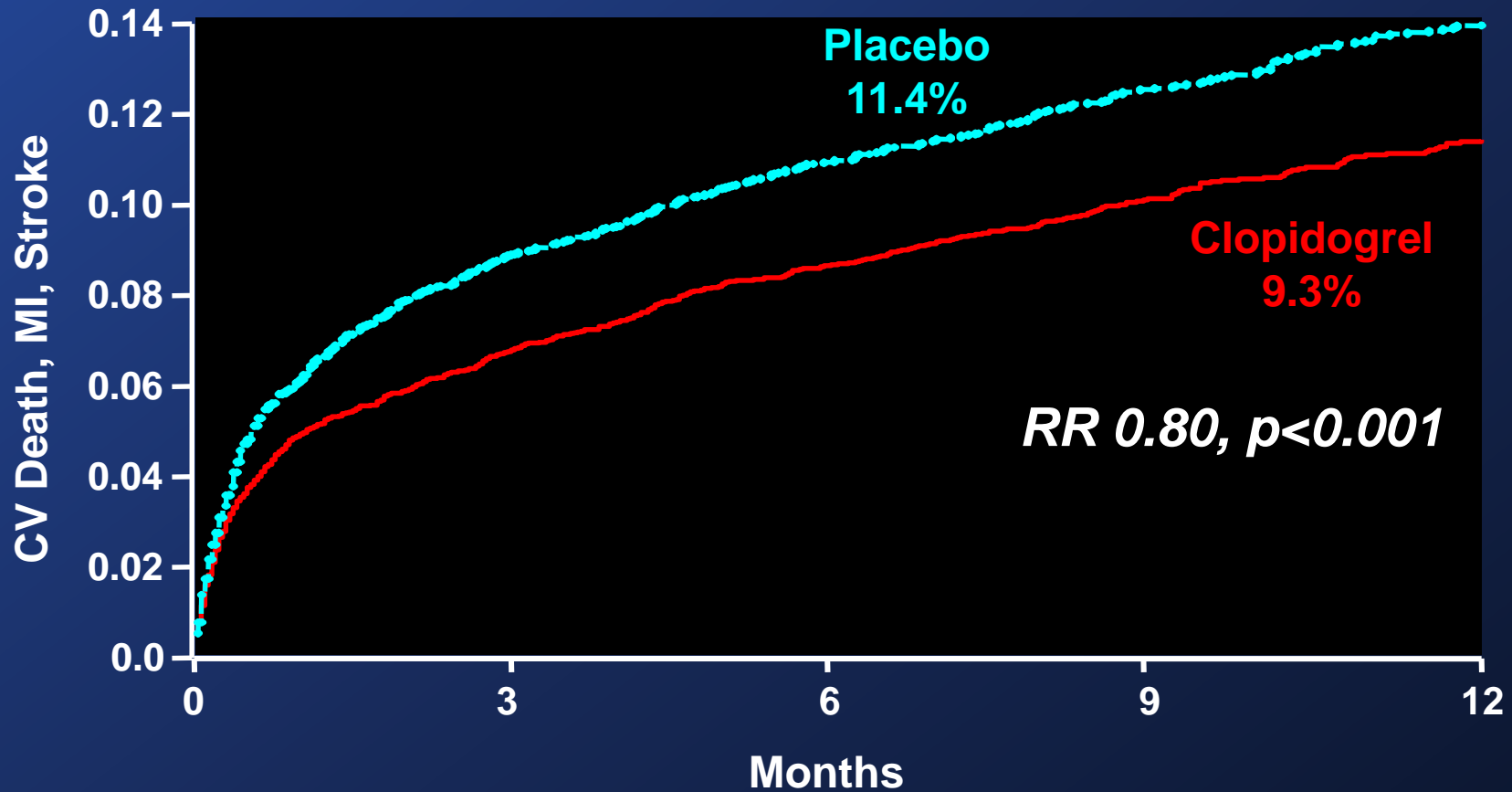


TRAP

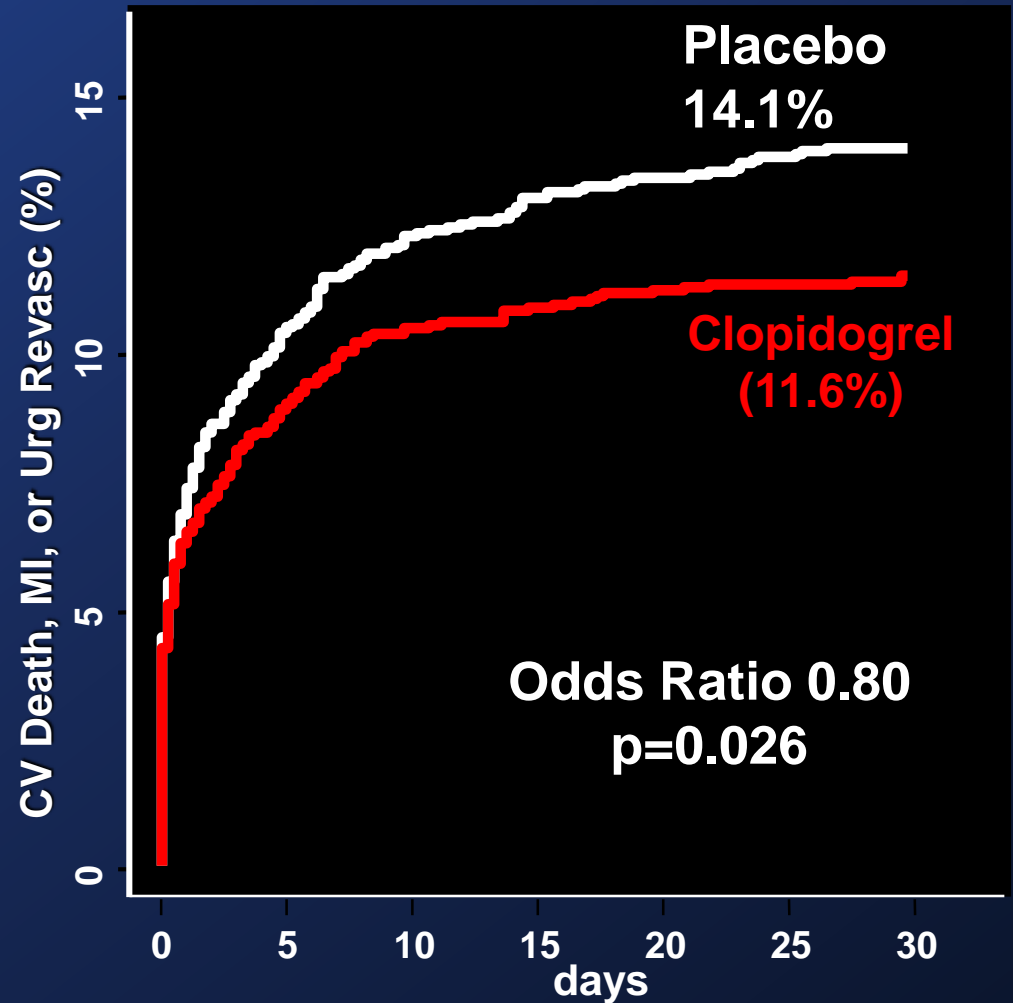
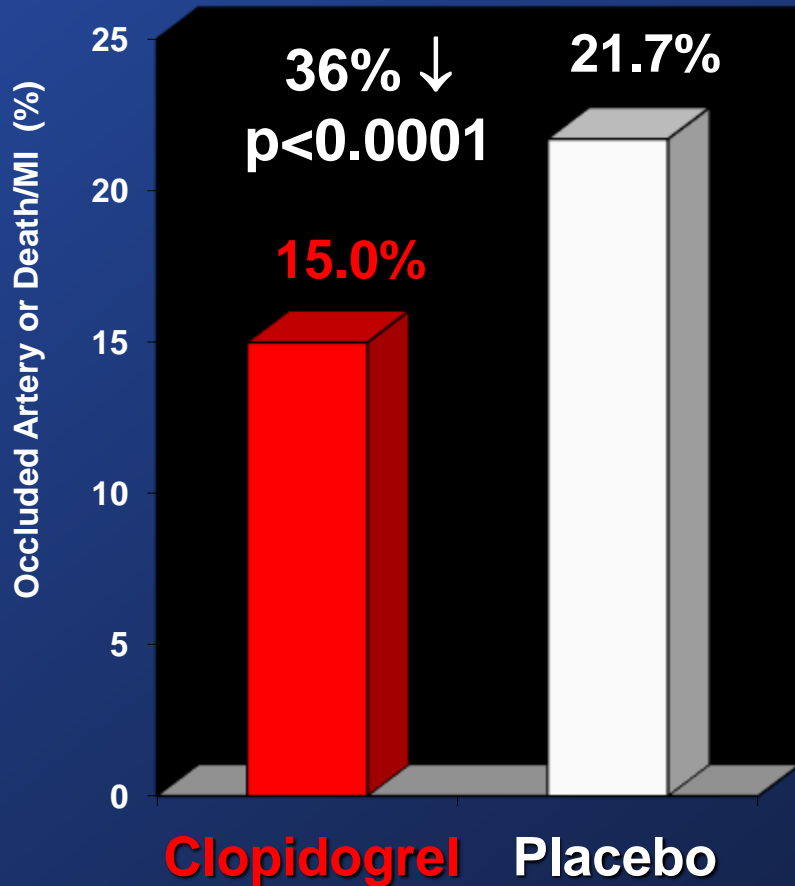




CURE

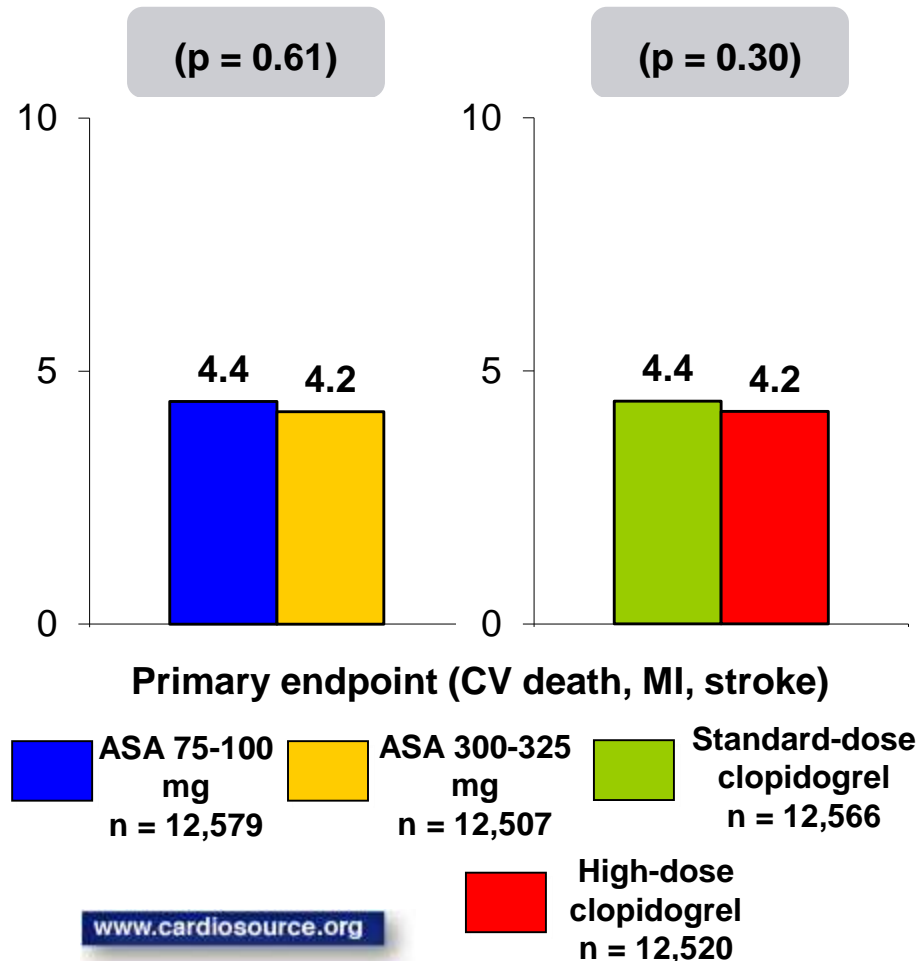


CLARITY-TIMI 28



CURRENT-OASIS 7

Patients presenting with ACS were randomized in a 2 x 2 factorial design to either low-dose or high-dose aspirin (ASA), and standard-dose or high-dose clopidogrel. Patients were followed for 30 days.



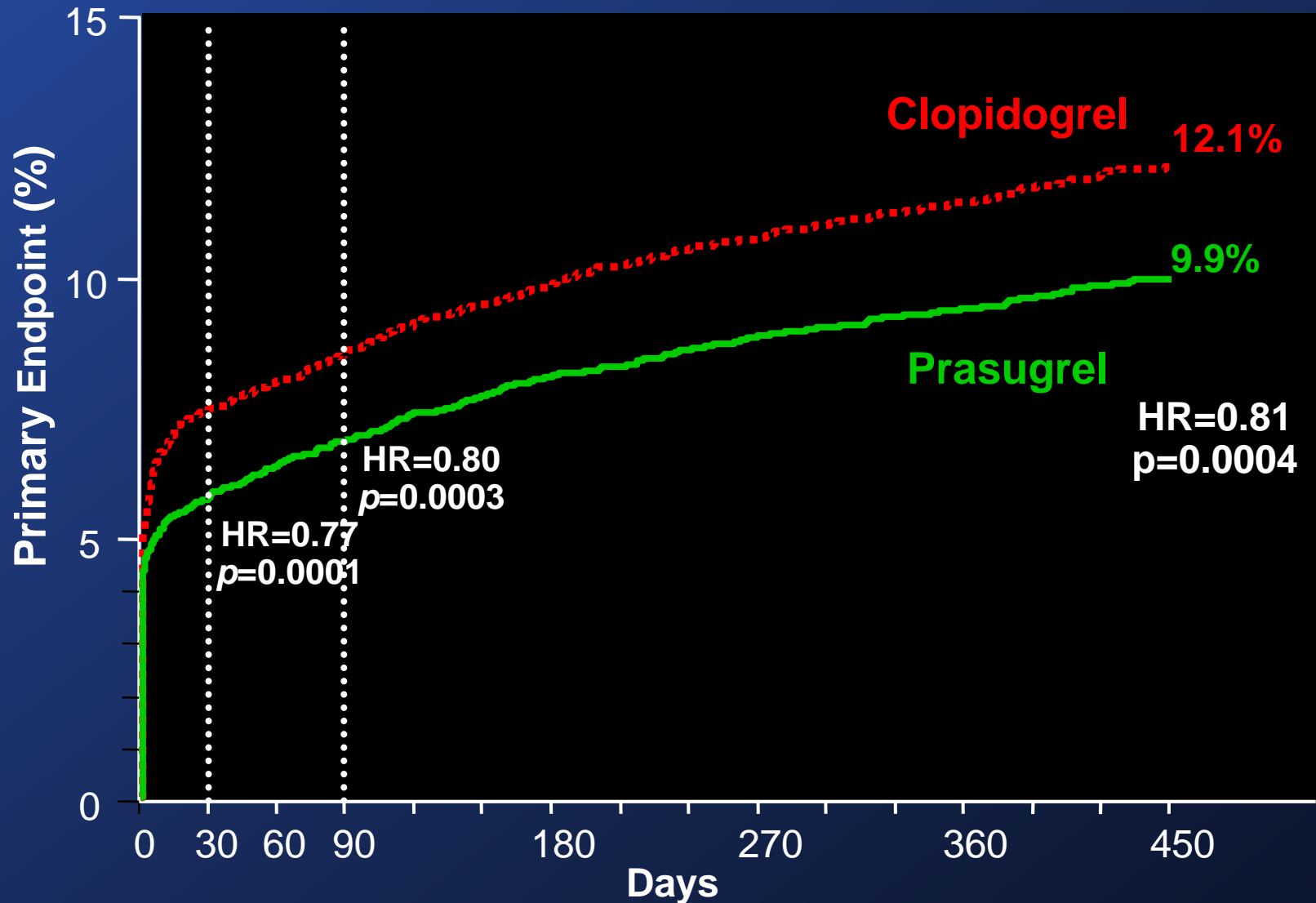
Results

- No difference between low- and high-dose ASA
- No difference in primary endpoint between standard & high-dose clopidogrel
- Benefit noted in high-dose arm undergoing PCI
- Major bleeding similar in both ASA arms, but higher in high-dose clopidogrel arm

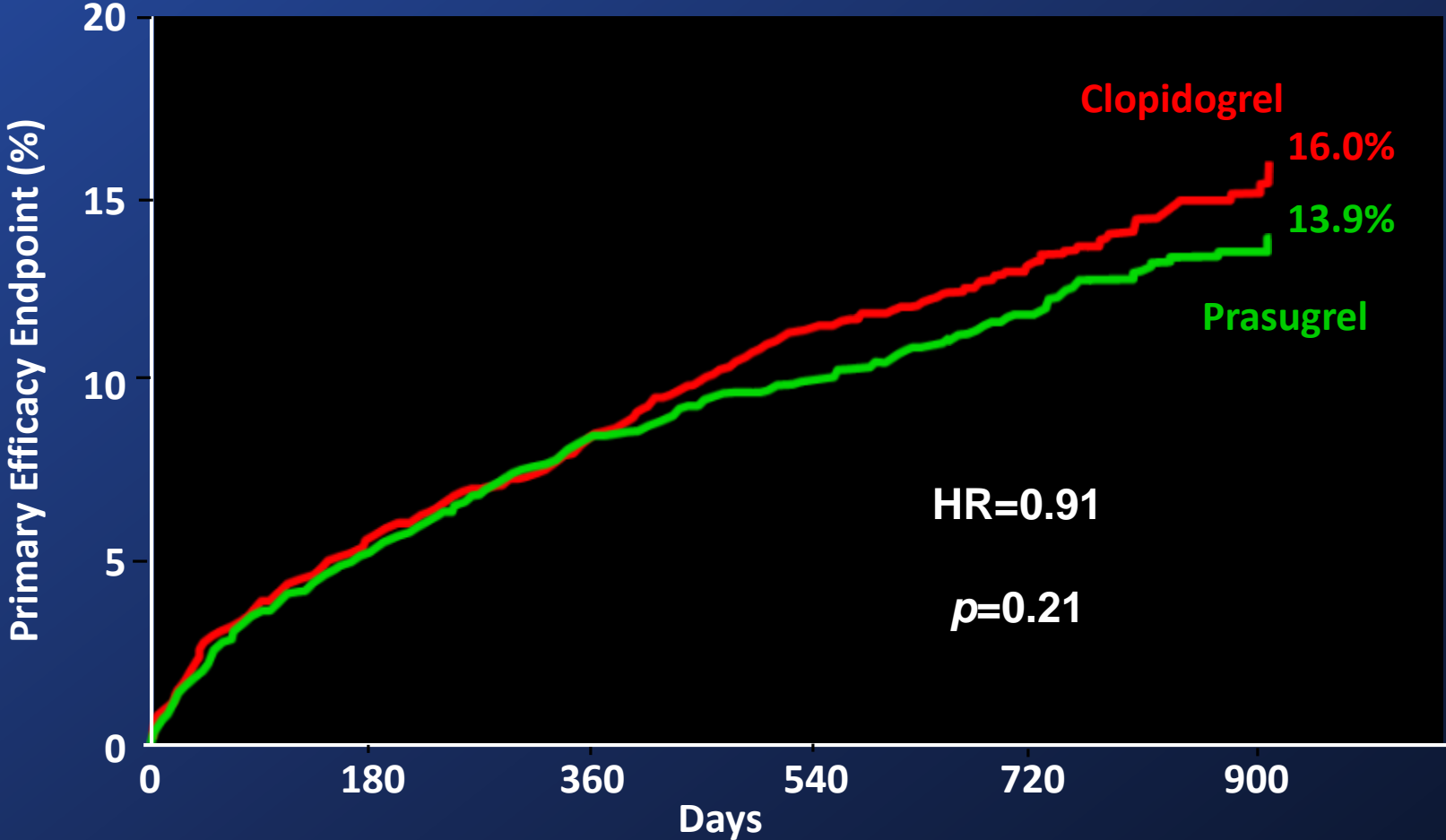
Conclusions

- Treatment with high-dose ASA and high-dose clopidogrel not associated with significant clinical benefit at 30 days in ACS patients
- Possible benefit in high-dose clopidogrel arm undergoing PCI, higher bleeding

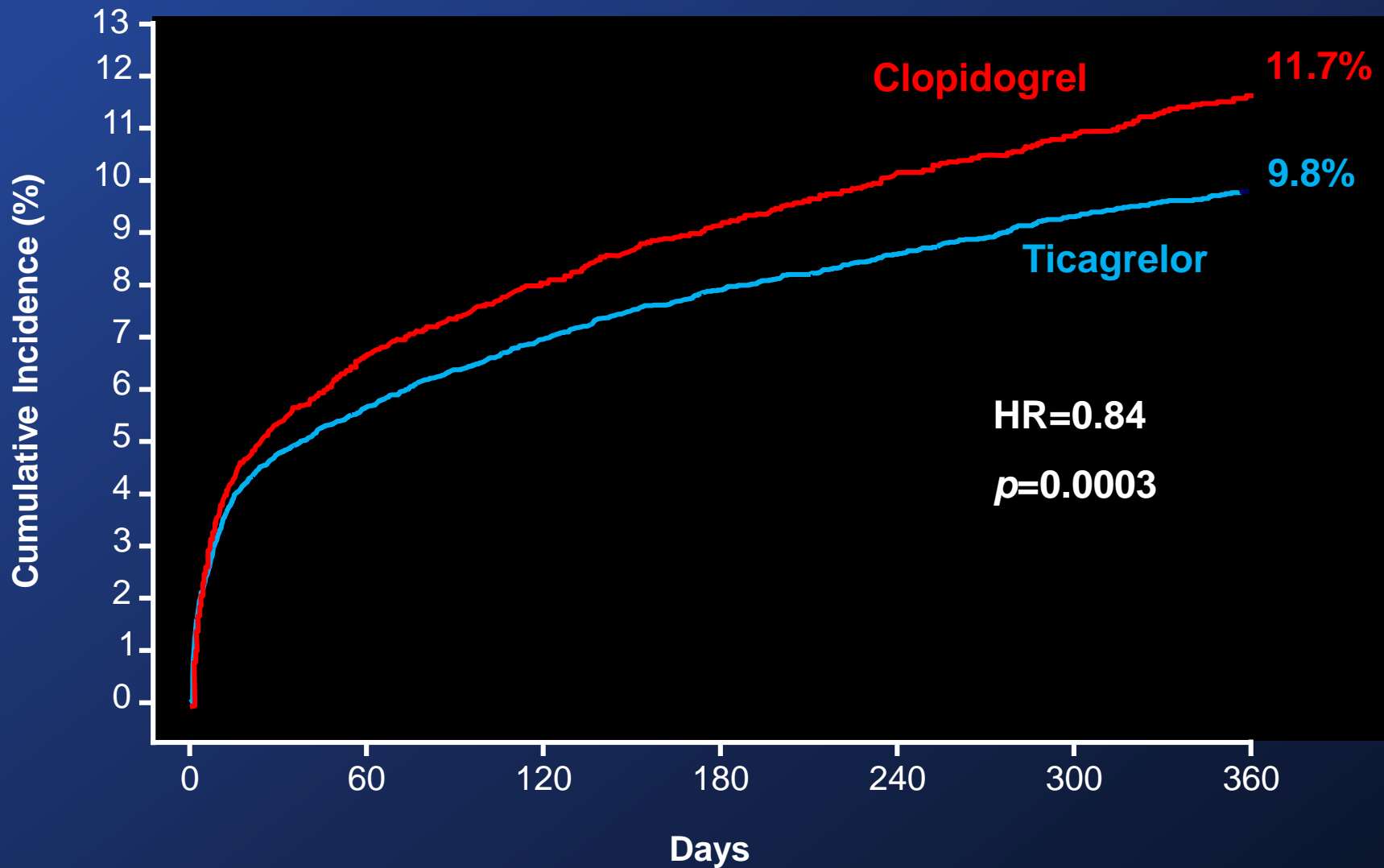
TRITON-TIMI 38



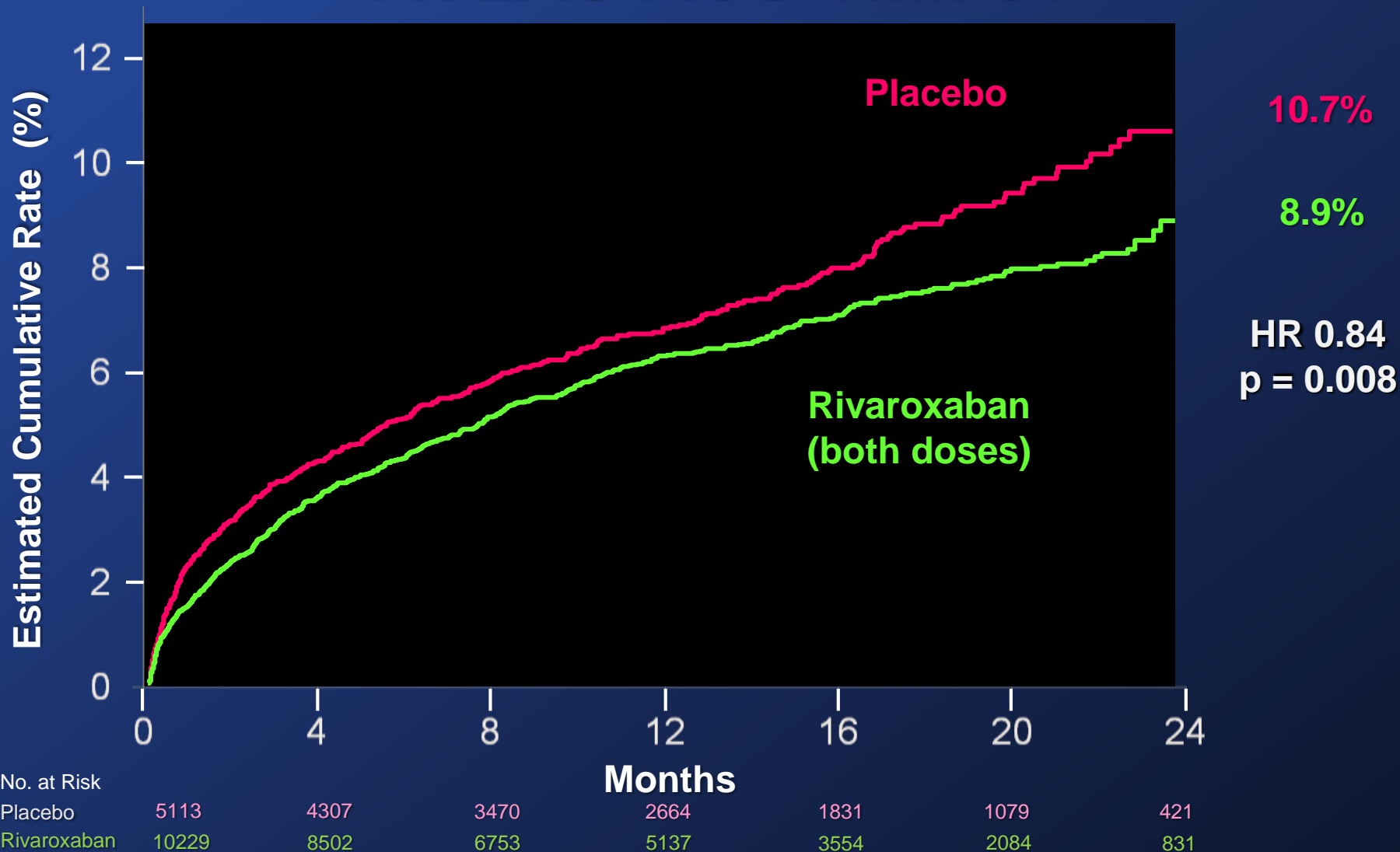
TRILOGY-ACS



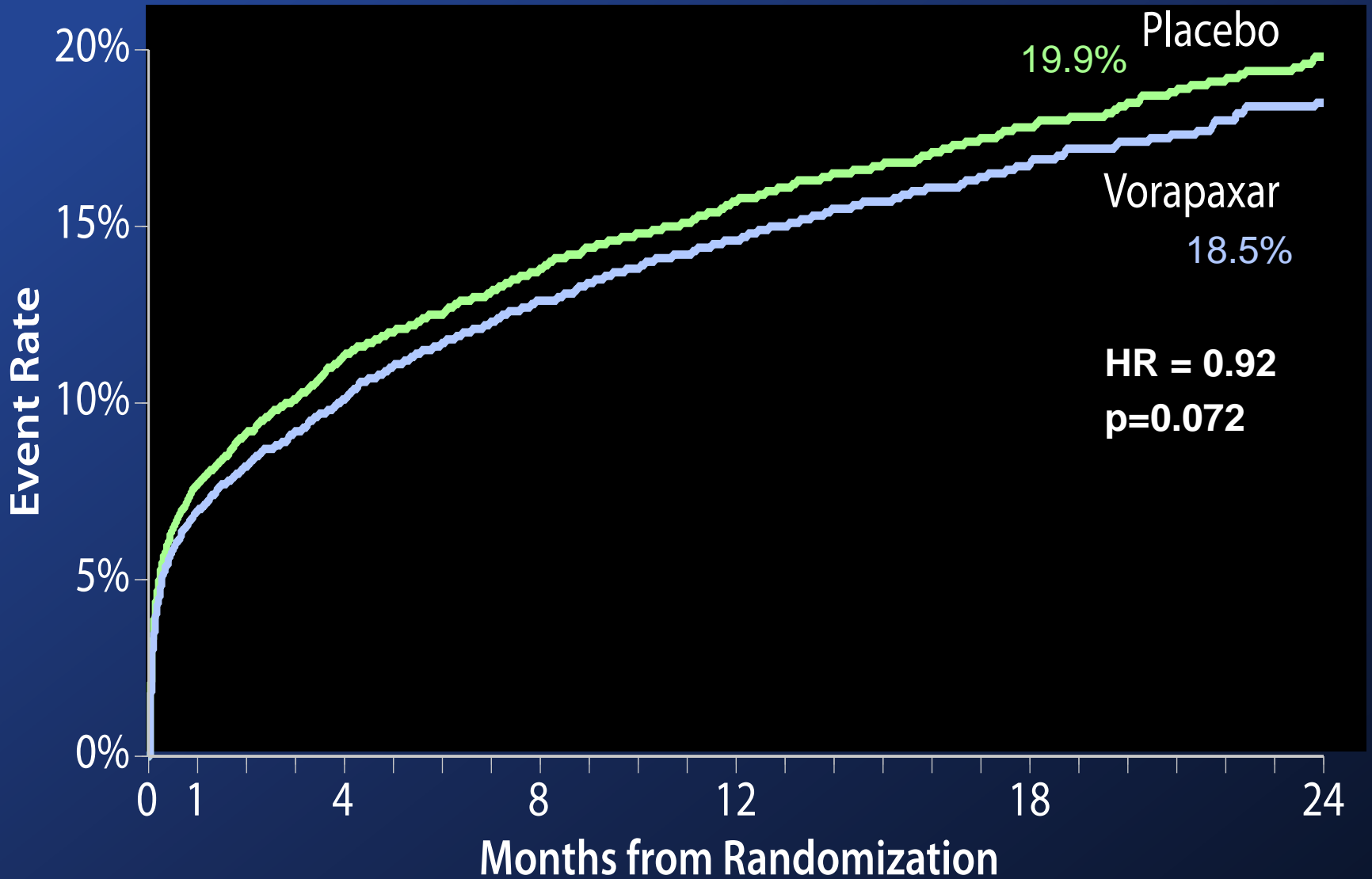
PLATO



ATLAS ACS TIMI 51



TRACER



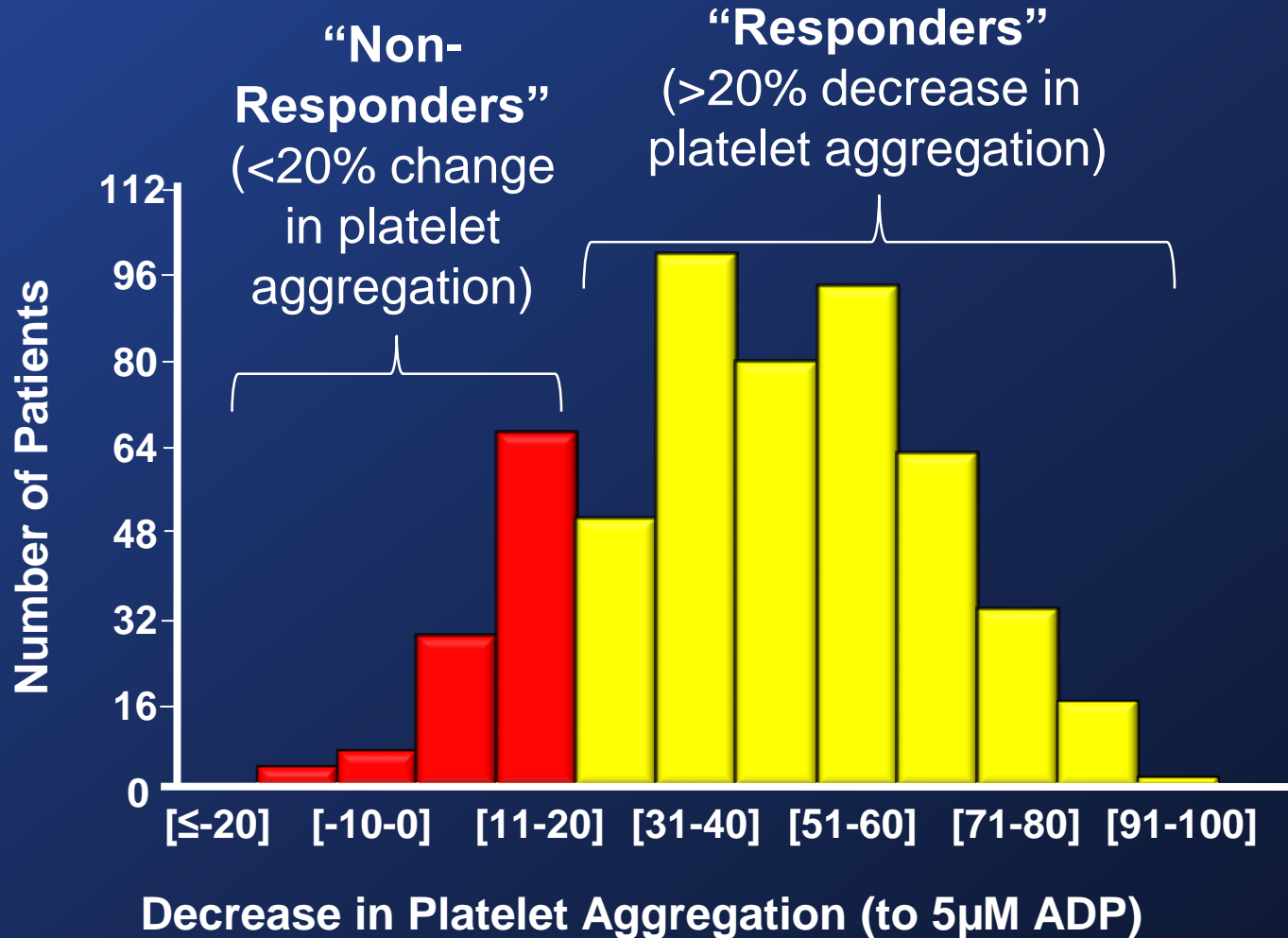


Major Bleeding

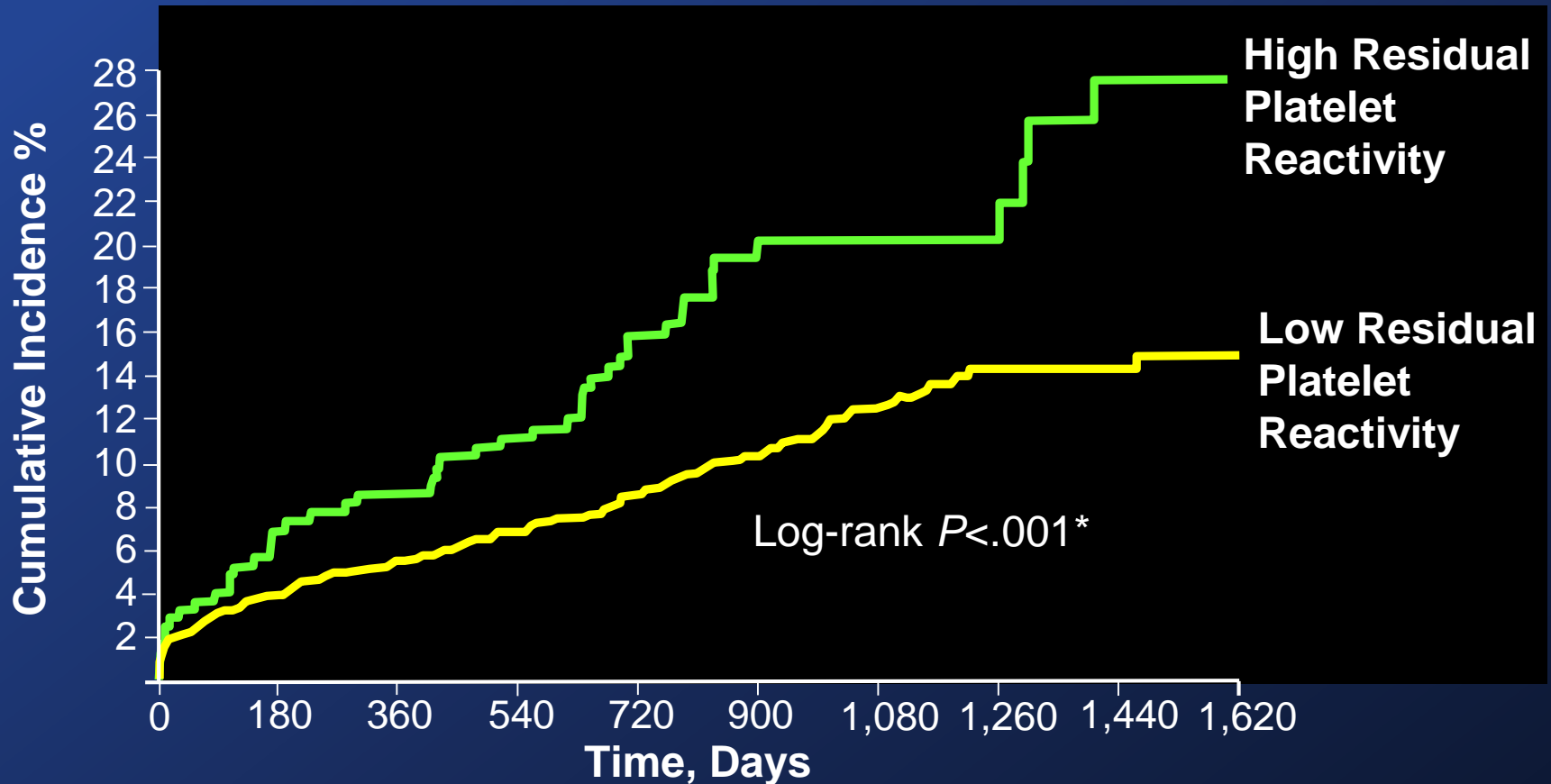


* Stopped early due to bleeding

Clopidogrel “resistance”

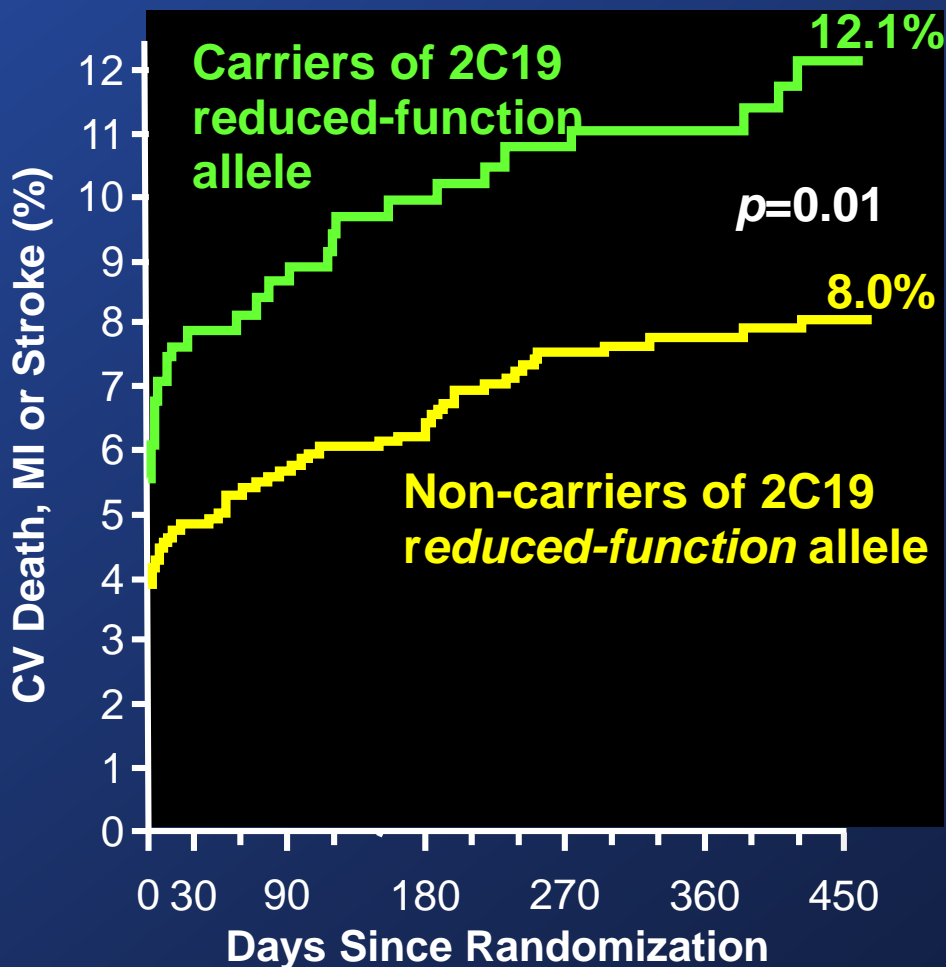


Residual platelet activity

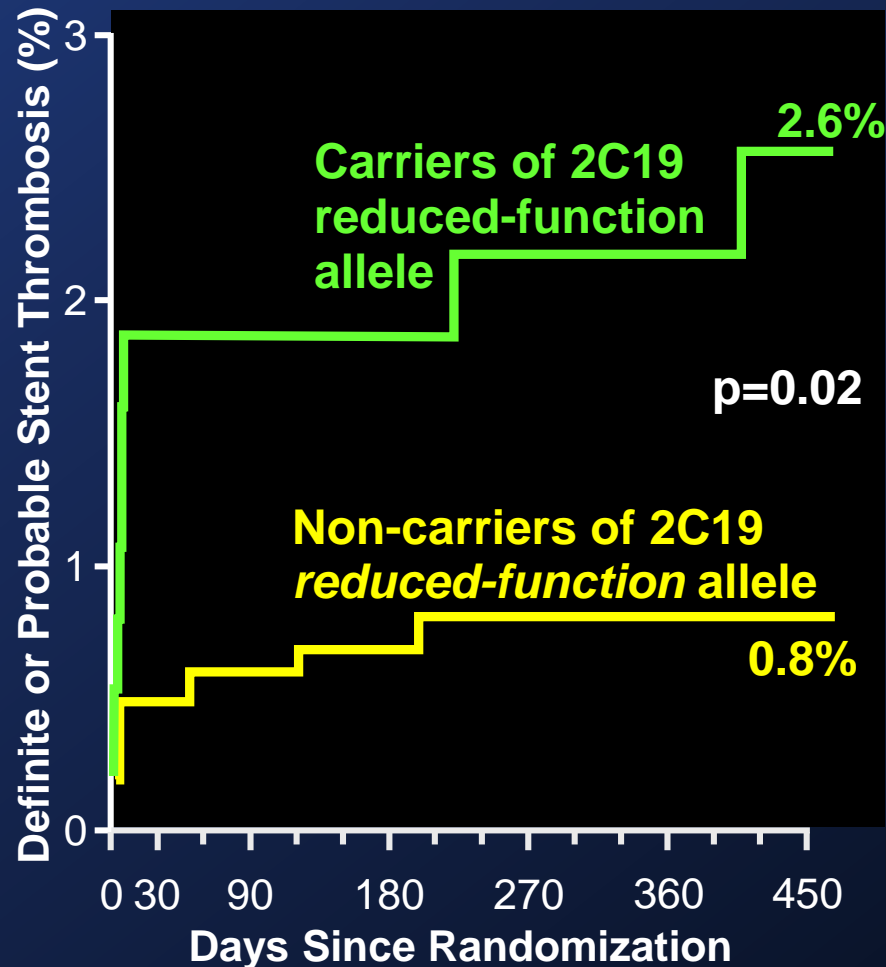


Genetic polymorphisms

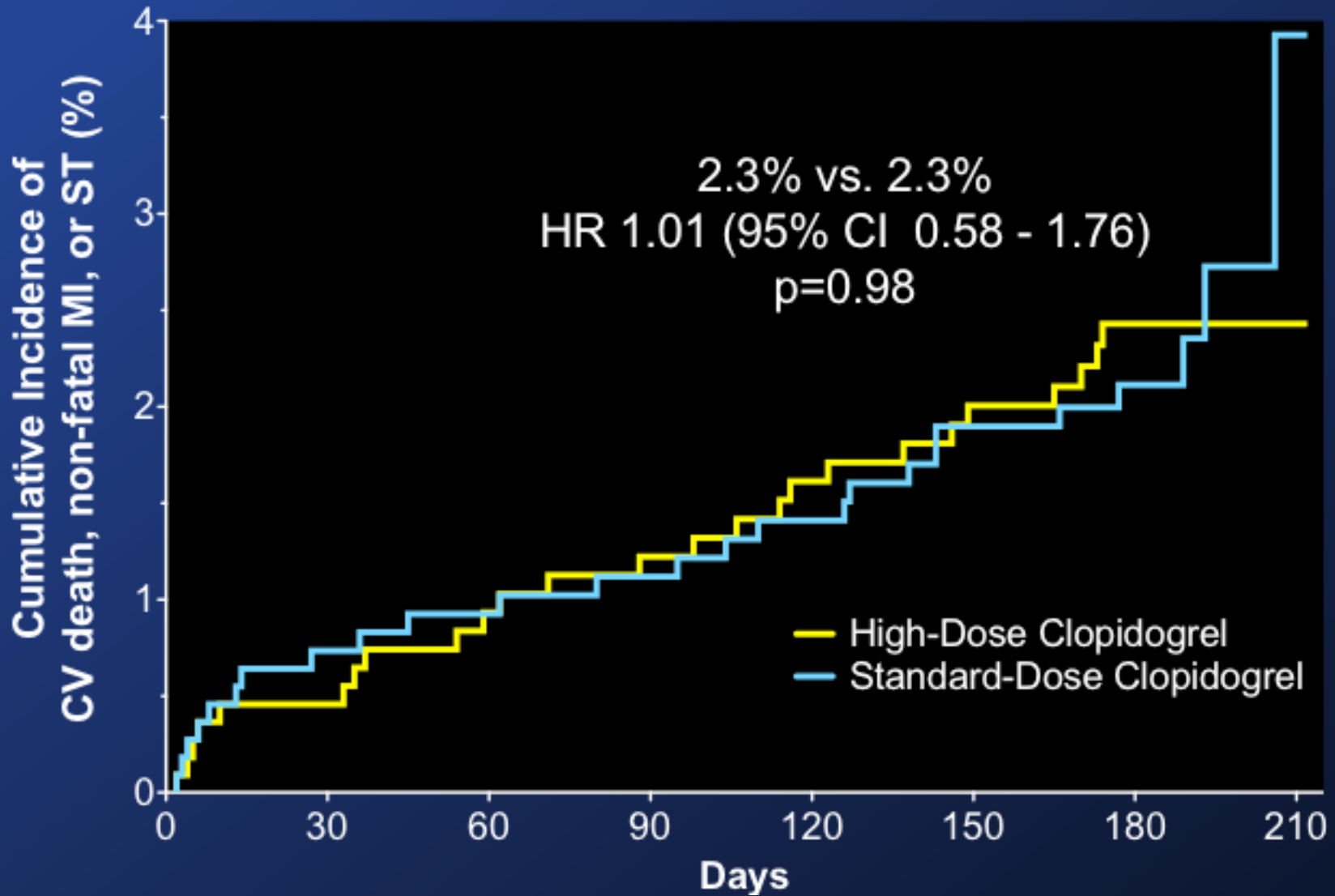
Primary Efficacy Outcome



Stent Thrombosis



GRAVITAS



2014 ACCF/AHA UA/NSTEMI guidelines

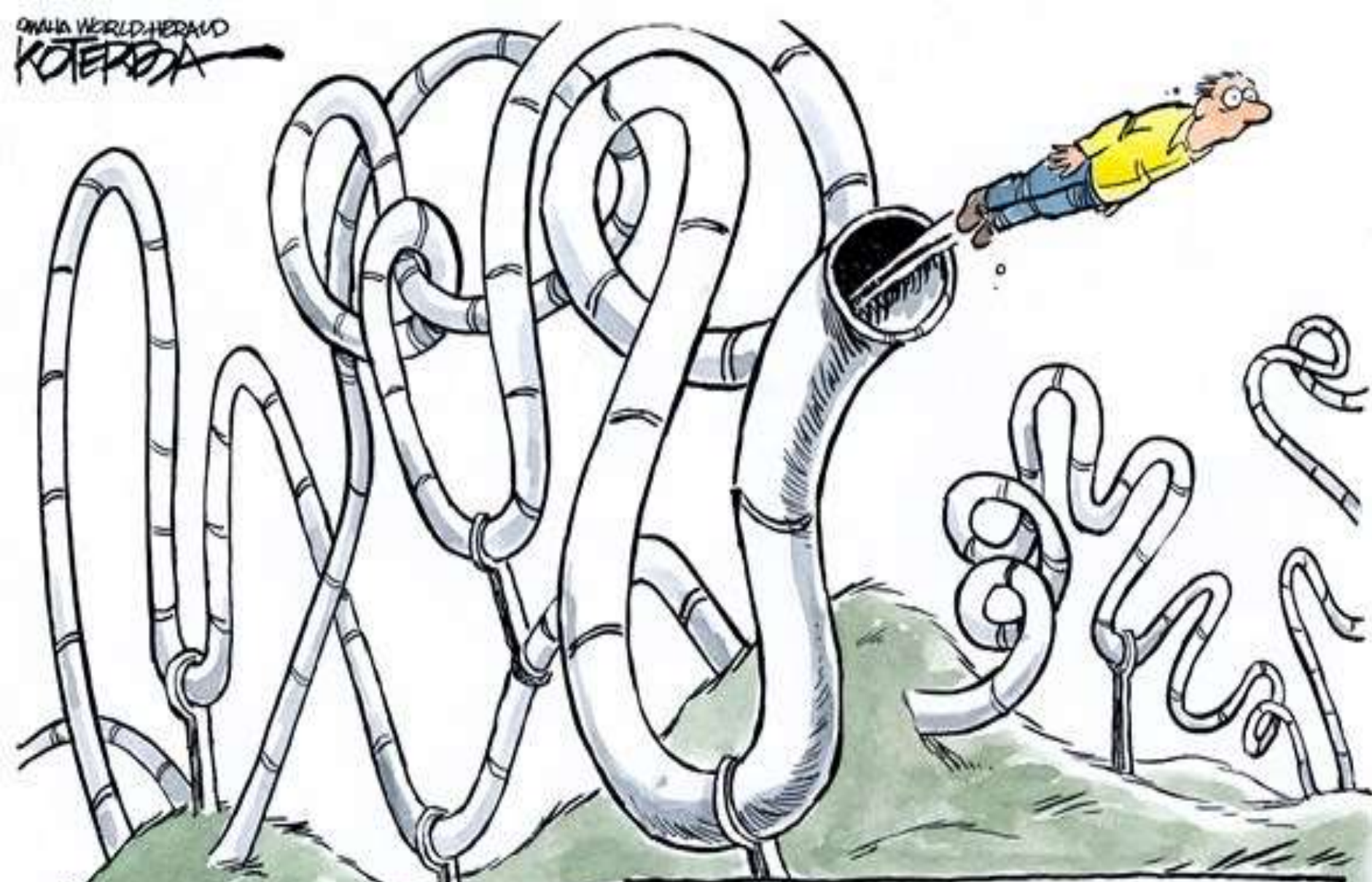
Recommendation	CO R	LOE
Clopidogrel loading dose followed by daily maintenance dose in patients unable to take aspirin	I	B
P2Y₁₂ inhibitor , in addition to aspirin, for up to 12 mo for patients treated initially with either an early invasive or initial ischemia-guided strategy: - Clopidogrel - Ticagrelor	I	B
P2Y₁₂ inhibitor therapy (clopidogrel, prasugrel or ticagrelor) <i>should be given</i> for at least 12 months in patients receiving a stent (BMS or DES) during PCI for ACS	I	B
Ticagrelor in preference to clopidogrel for patients treated with an early invasive or ischemia-guided strategy	IIa	B

2011 ACCF/AHA/SCAI PCI Recommendations: P2Y₁₂ Inhibitor Therapy with Coronary Stents

Recommendation	CO R	LOE
Clopidogrel <i>should be given</i> for a minimum of 1 month and ideally up to 12 months in patients receiving a BMS for a non-ACS indication (unless the patient is at increased risk of bleeding; then it should be given for a minimum of 2 weeks)	I	B
Clopidogrel <i>should be given</i> for at least 12 months in patients treated with a DES for a non-ACS indication , if patients are not at high risk of bleeding	I	B
P2Y ₁₂ inhibitor therapy (clopidogrel, prasugrel or ticagrelor) <i>should be given</i> for at least 12 months in patients receiving a stent (BMS or DES) during PCI for ACS	I	B
Earlier discontinuation (eg, <12 months) of P2Y ₁₂ inhibitor therapy after stent implantation <i>is reasonable</i> if the risk of morbidity from bleeding outweighs the anticipated benefit afforded by a recommended duration of P2Y ₁₂ inhibitor therapy	IIa	C
Continuation of DAPT beyond 12 months <i>may be considered</i> in patients undergoing DES implantation	IIb	C

2014 ESC P2Y₁₂ Recommendations in Patients Undergoing PCI

Recommendation	COR	LOE
Stable CAD		
Clopidogrel is recommended for elective stenting	I	A
Treatment with clopidogrel in patients with known anatomy, 600 mg preferably ≥2 hours before procedure	I	A
NSTE-ACS		
Prasugrel in patients in whom coronary anatomy is known and who are proceeding to PCI if no contraindication	I	B
Ticagrelor in patients at moderate-to-high risk of ischaemic events, regardless of treatment strategy including those pre-treated with clopidogrel if no contraindication	I	B
Clopidogrel (only when prasugrel or ticagrelor are not available or contraindicated)	I	B
STEMI		
Prasugrel if no contraindication	I	B
Ticagrelor if no contraindication	I	B
Clopidogrel (only when prasugrel or ticagrelor are not available or contraindicated)	I	B



INTRODUCING... THE KEYSTONE XL
ROLLER COASTER

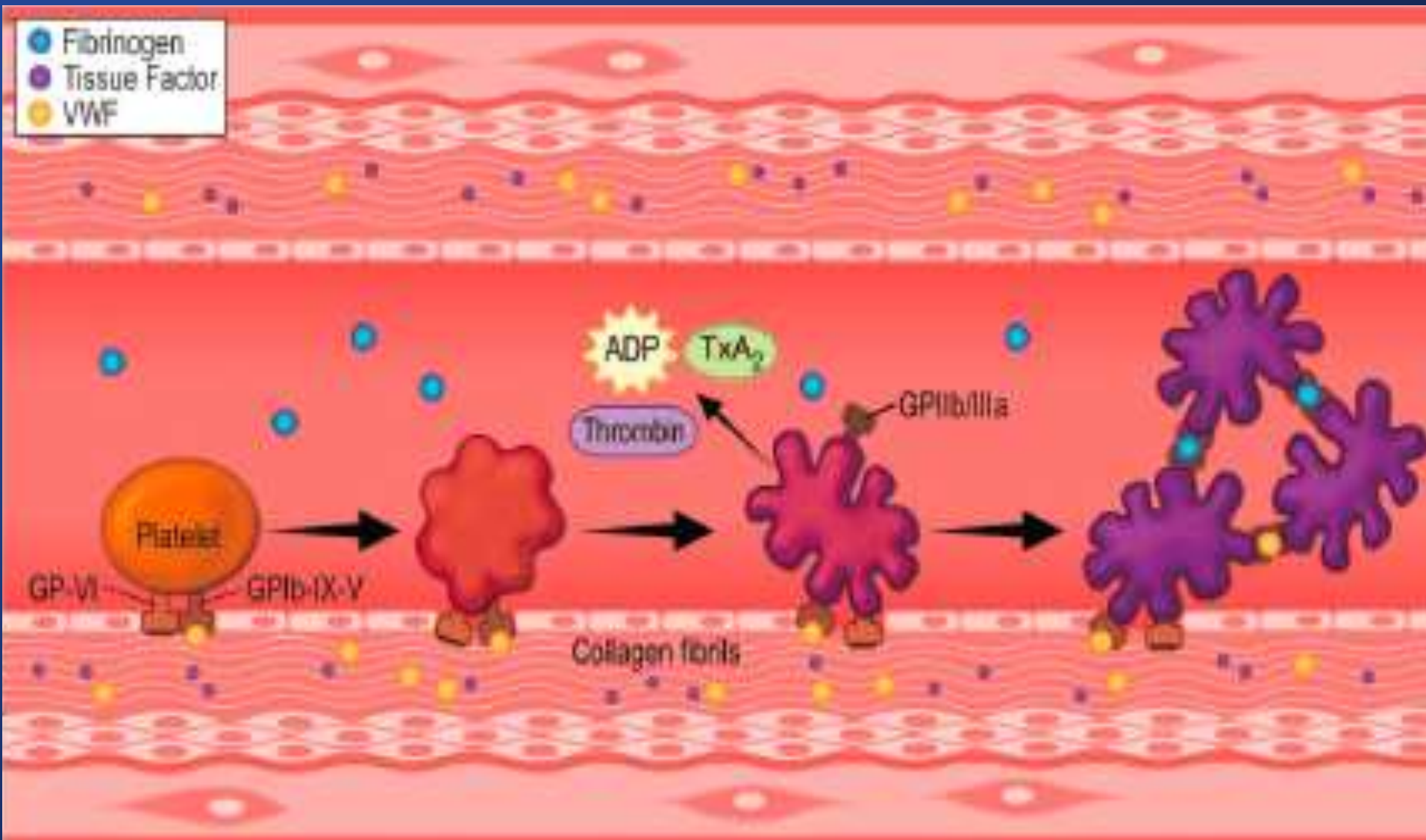


PEGASUS-TIMI 54 study of BRILINTA® meets primary endpoint in both 60mg and 90mg doses

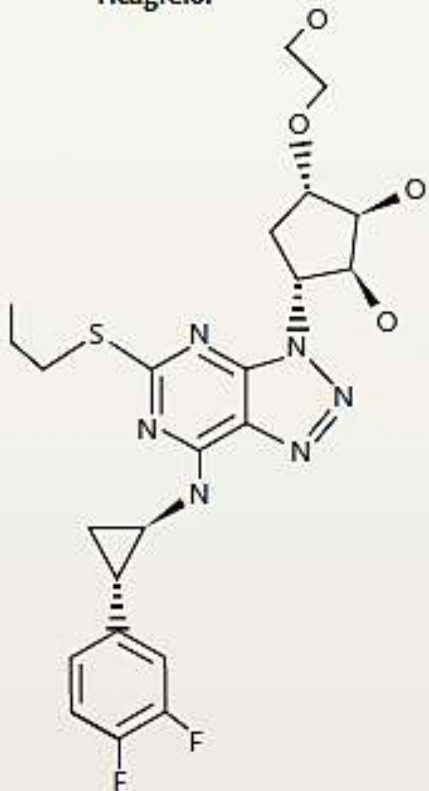
Classes of antiplatelet agents

- Thromboxane A₂ inhibitors
 - Aspirin
- P2Y₁₂ inhibitors
 - Clopidogrel
 - Ticlopidine
 - Prasugrel
 - Ticagrelor
- GPI
 - Sibrafiban
- Thrombin receptor antag
 - Vorapaxar
 - Atovapaxar
- PDE inhibitors
 - Cilostazol
 - Dipyridamole
- Miscellaneous
 - NCX-4016 (ASA + NO)
 - CTRP (collagen/platelet adhesion inhibitor)

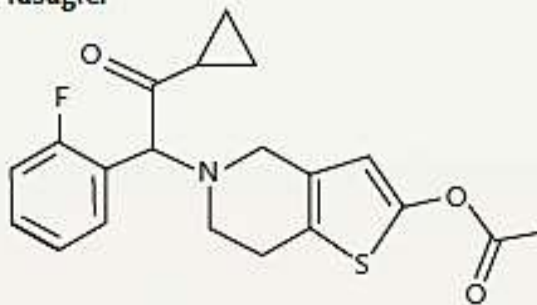
Platelet biology 101



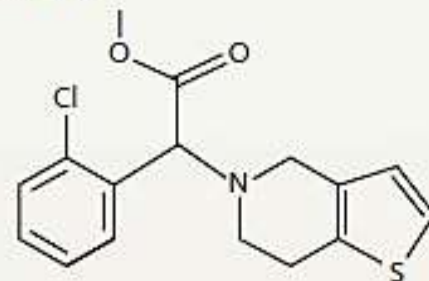
Ticagrelor



Prasugrel



Clopidogrel



No in vivo biotransformation

CYP-dependent oxidation
 CYP3A4/5
 CYP2B6
 CYP2C19
 CYP2C9
 CYP2D6

Hydrolysis by esterase

CYP-dependent oxidation
 CYP1A2
 CYP2B6
 CYP2C19

CYP-dependent oxidation
 CYP2C19
 CYP3A4/5
 CYP2B6

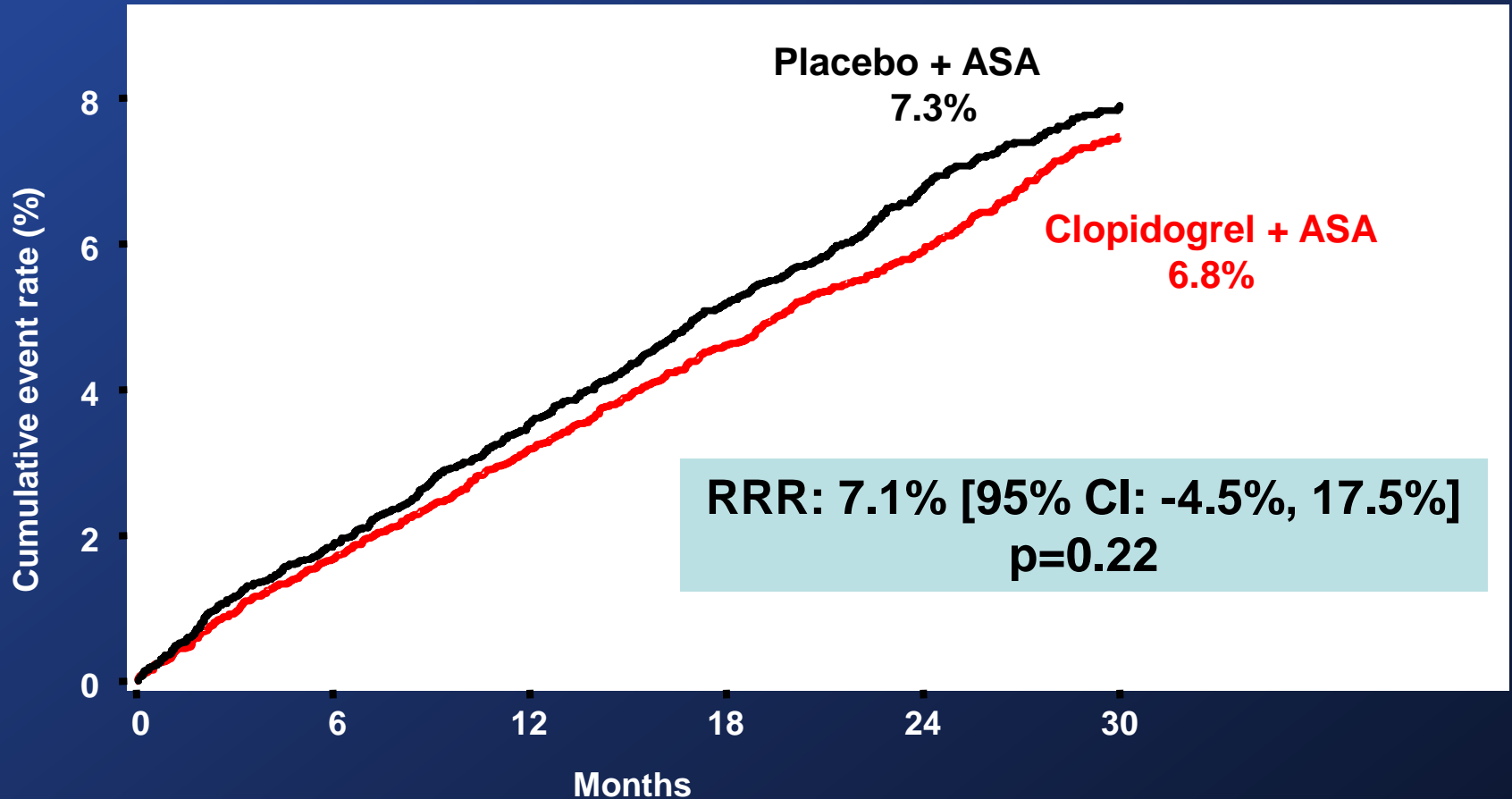
Binding

Platelet

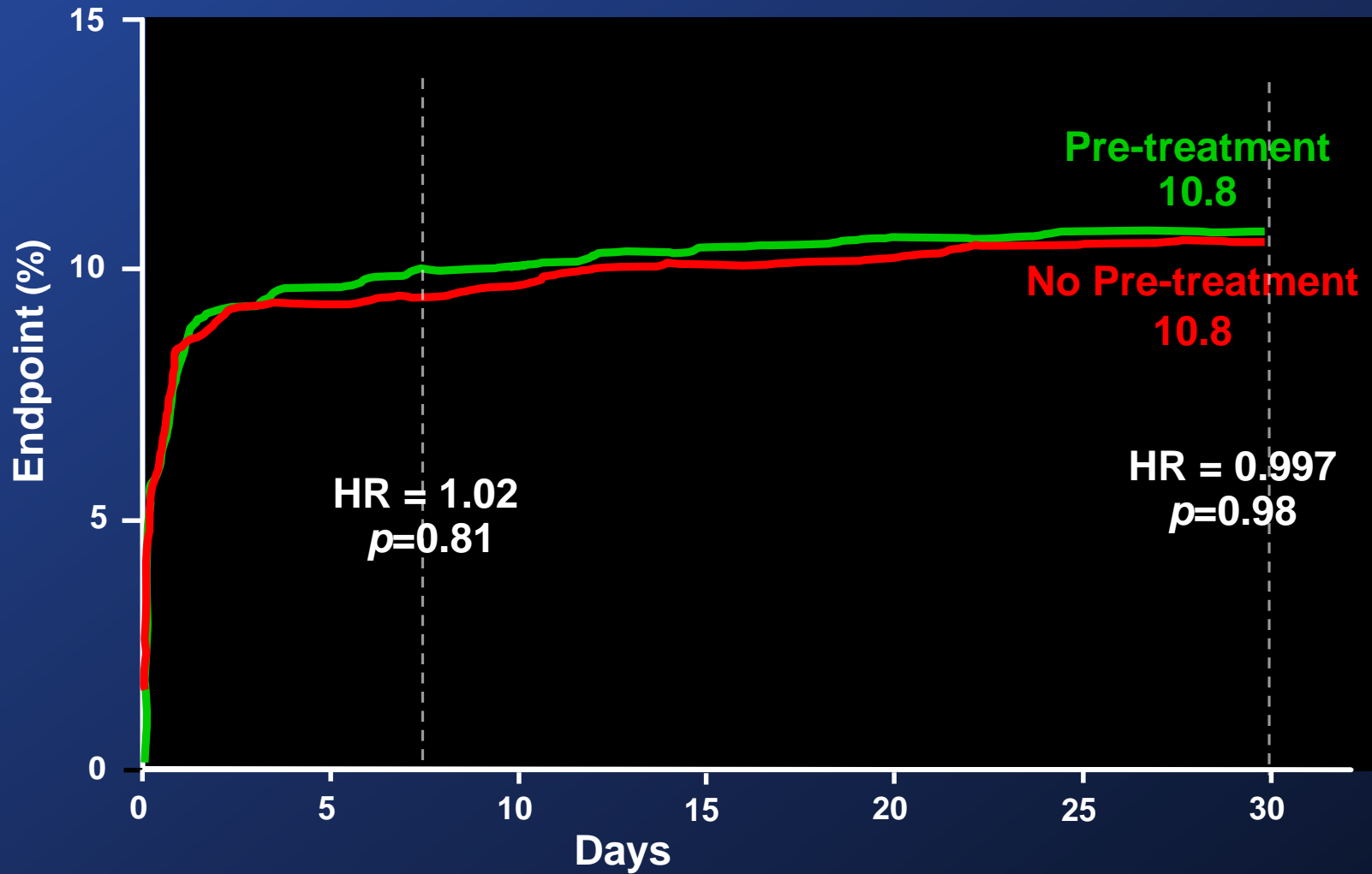
P2Y12

- Active compound
- Intermediate metabolite
- Prodrug

CHARISMA



ACCOAST





Distilled Water

H_2O



CAS No.: 7732-18-5

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