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Speaker's name: Thomas Cuisset, MD, PhD

X **I have the following potential conflicts of interest to report:**

x Consulting: Daiichi Sankyo, Eli Lilly

❒ Employment in industry

❒ Stockholder of a healthcare company

❒ Owner of a healthcare company

x Others: Lecture Fee

Abbott Vascular, Astra Zeneca, Biotronik, Boston Scientific, Cordis, Daichi Sankyo, Edwards, Eli Lilly, Iroko Cardio, Medtronic, Servier

❒ **I do not have any potential conflict of interest**

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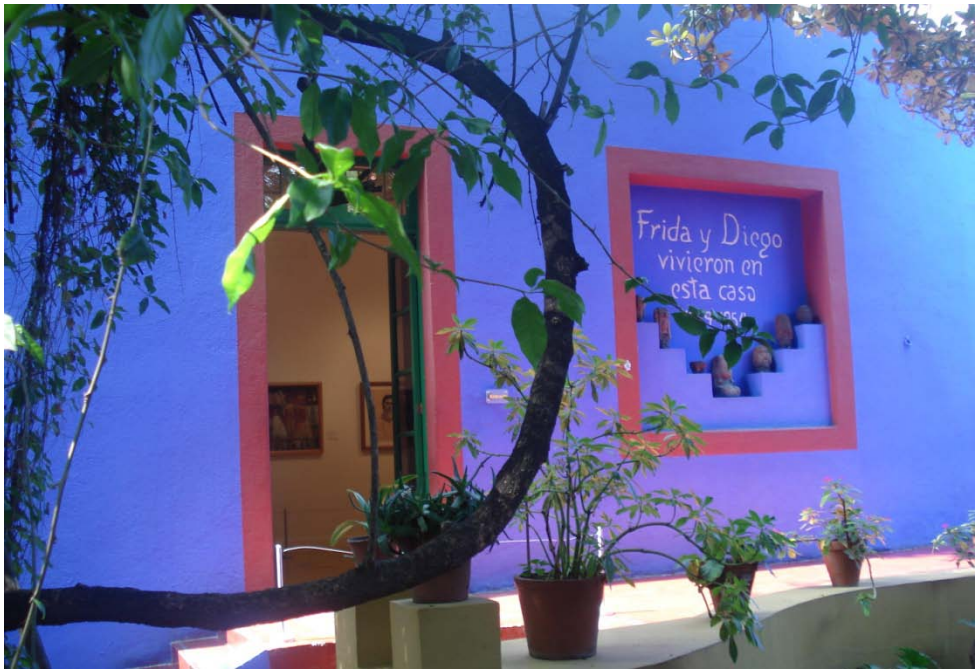
EAPCI-EuroPCR/ESC at SOLACI 2012
Current Management of NSTEMI-ACS

Which antiplatelet therapy for which patient ?



Thomas Cuisset, Marseille (Fr)

SOLACI 2012, Mexico City

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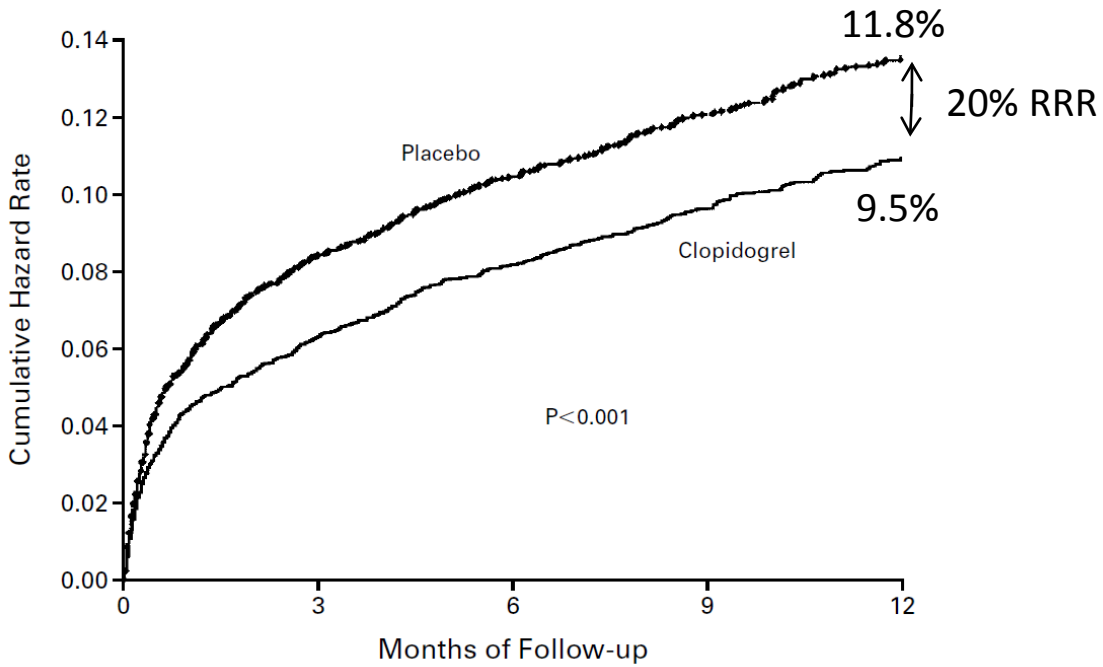
Dual antiplatelet therapy in ACS= Gold Standard



CURE trial, N Engl J Med 2001

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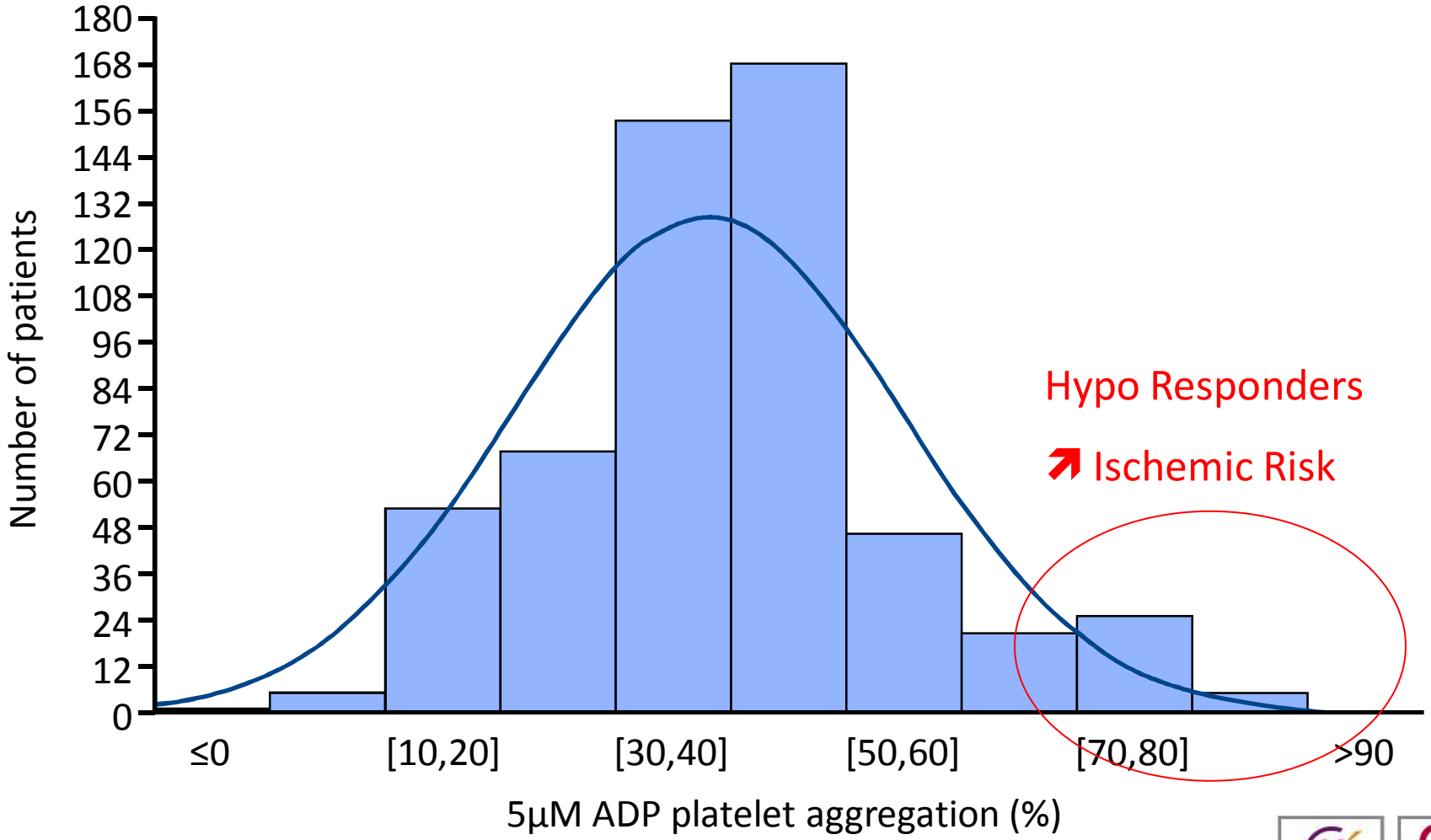
Clopidogrel : An unreliable platelet inhibition !



Serebruany et al. JACC 2005

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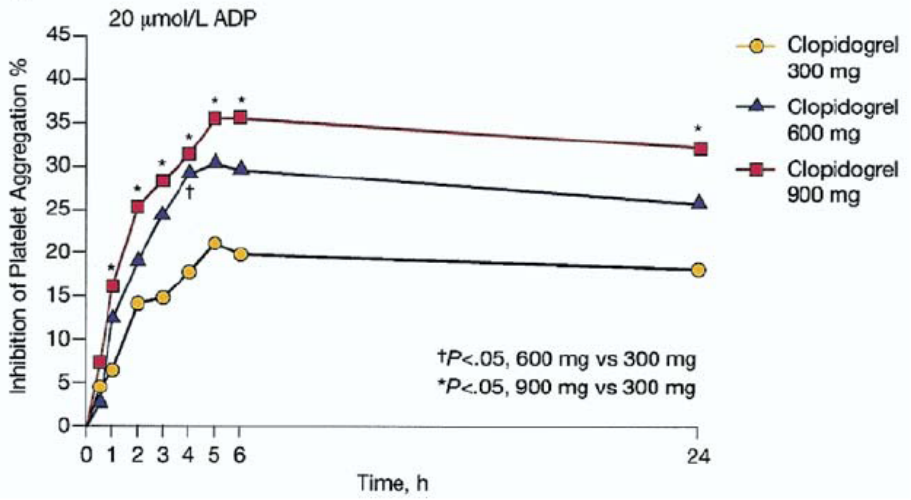
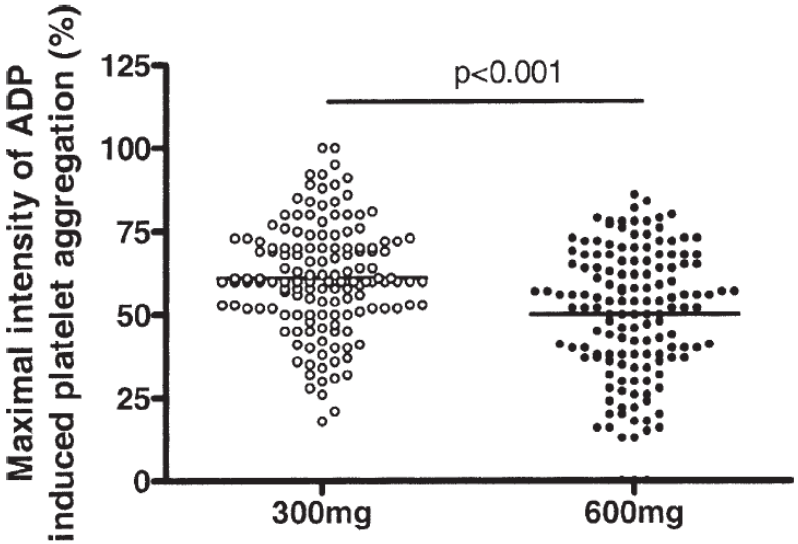
Higher doses of clopidogrel ?



Montalescot et al. JACC 2006



Cuisset et al. JACC 2006

Higher Dose → Higher Platelet Inhibition / Lower Incidence of 'Resistance'

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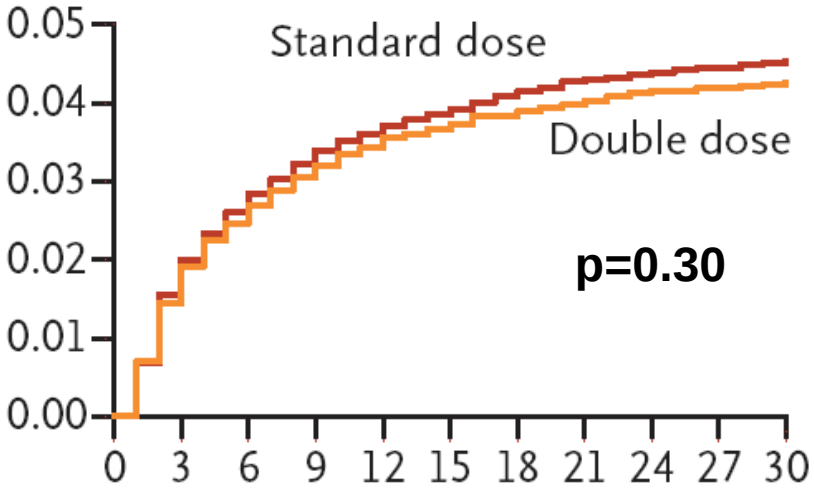
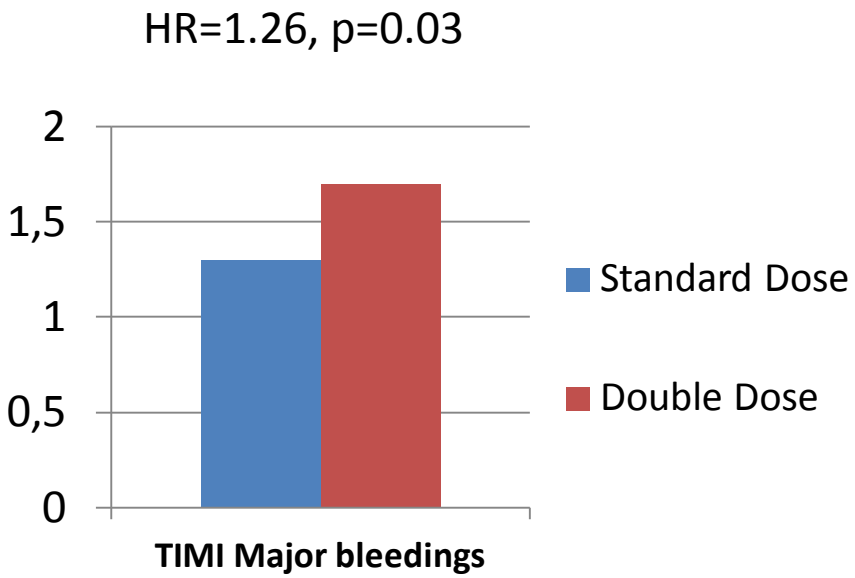
Higher doses of clopidogrel ?

Dose Comparisons of Clopidogrel
and Aspirin in Acute Coronary Syndromes

The CURRENT–OASIS 7 Investigators*





No ischemic benefit, Higher rate of bleeding complications

CURRENT OASIS 7 study, Mehta et al, NEJM 2010

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Higher doses of clopidogrel ?

Dose Comparisons of Clopidogrel and Aspirin in Acute Coronary Syndromes

The CURRENT–OASIS 7 Investigators*

Overall	25,086	4.2	4.4	0.94	0.31	
PCI after randomization						0.03
Yes	17,263	3.9	4.5	0.85	0.04	
No	7823	4.9	4.3	1.14	0.22	

Benefit of High doses of Clopidogrel in 'PCI subgroup'

CURRENT OASIS 7 study, Mehta et al, NEJM 2010

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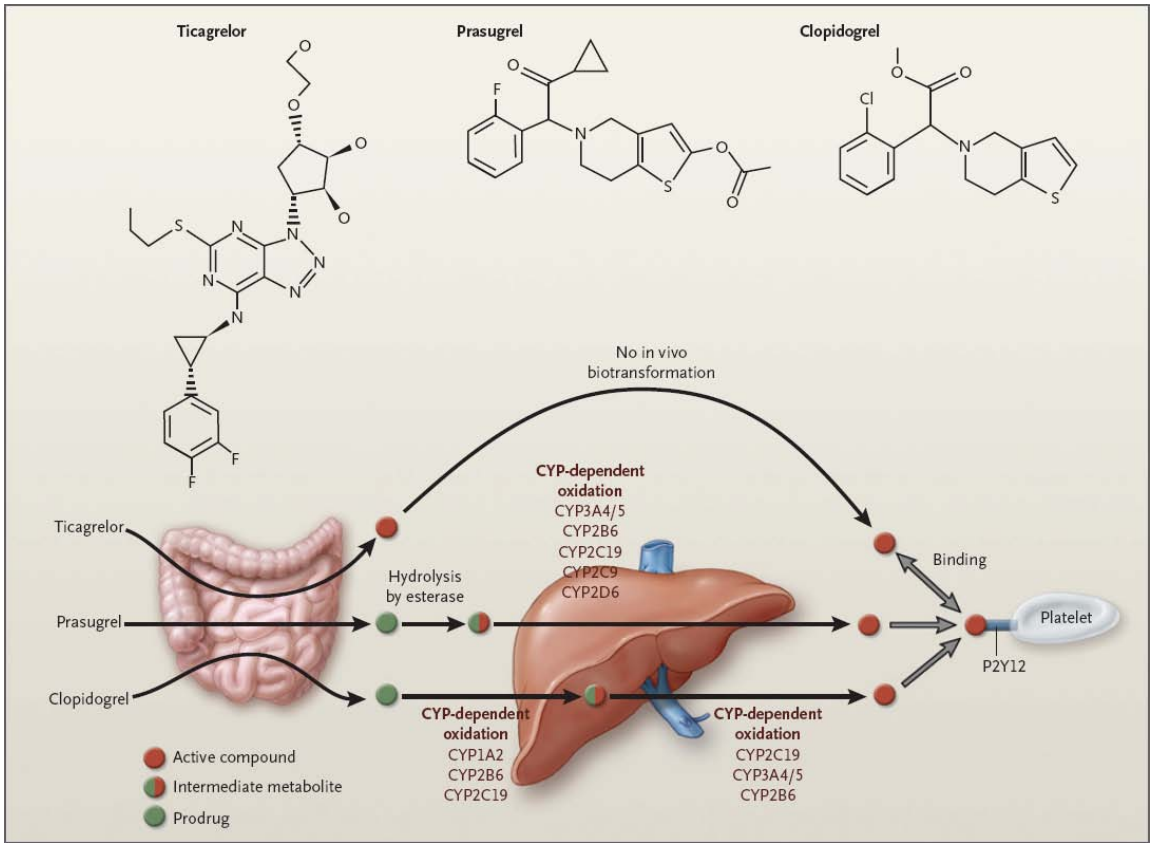
Prasugrel and Ticagrelor



New P2Y12 blockers provide higher, faster and predictable degree of platelet inhibition

Prasugrel: TRITON study

ACS (STEMI or UA/NSTEMI) & planned PCI

ASA

N= 13,600

Double-blind

CLOPIDOGREL
300 mg LD/ 75 mg MD

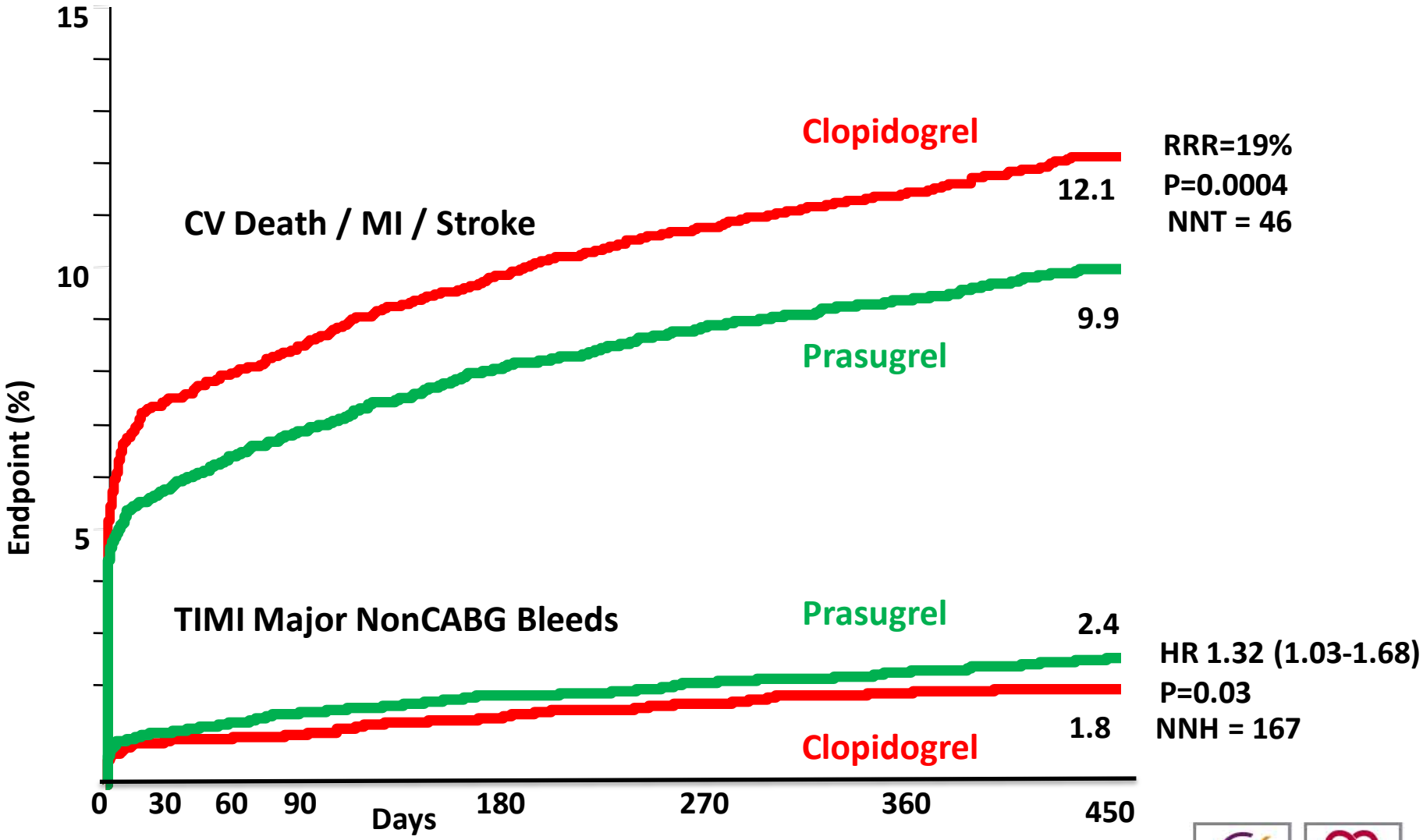
PRASUGREL
60 mg LD/ 10 mg MD

Median duration of therapy – 12 months

1º endpoint:	CV death, MI, stroke
2º endpoints:	CV death, MI, stroke, rehosp-rec isch
	CV death, MI, UTVR
	Stent thrombosis (ARC definite/prob.)
Safety endpoints:	TIMI major bleeds, Life-threatening bleeds

Wiviott SD et al. N Engl J Med 2007

TRITON: Balance of Efficacy and Safety



Wiviott SD et al. N Engl J Med 2007

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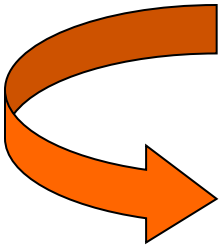
Choice of P2Y12 inhibitors

Ischemic Risk

Bleeding Risk



Selection of patients +++

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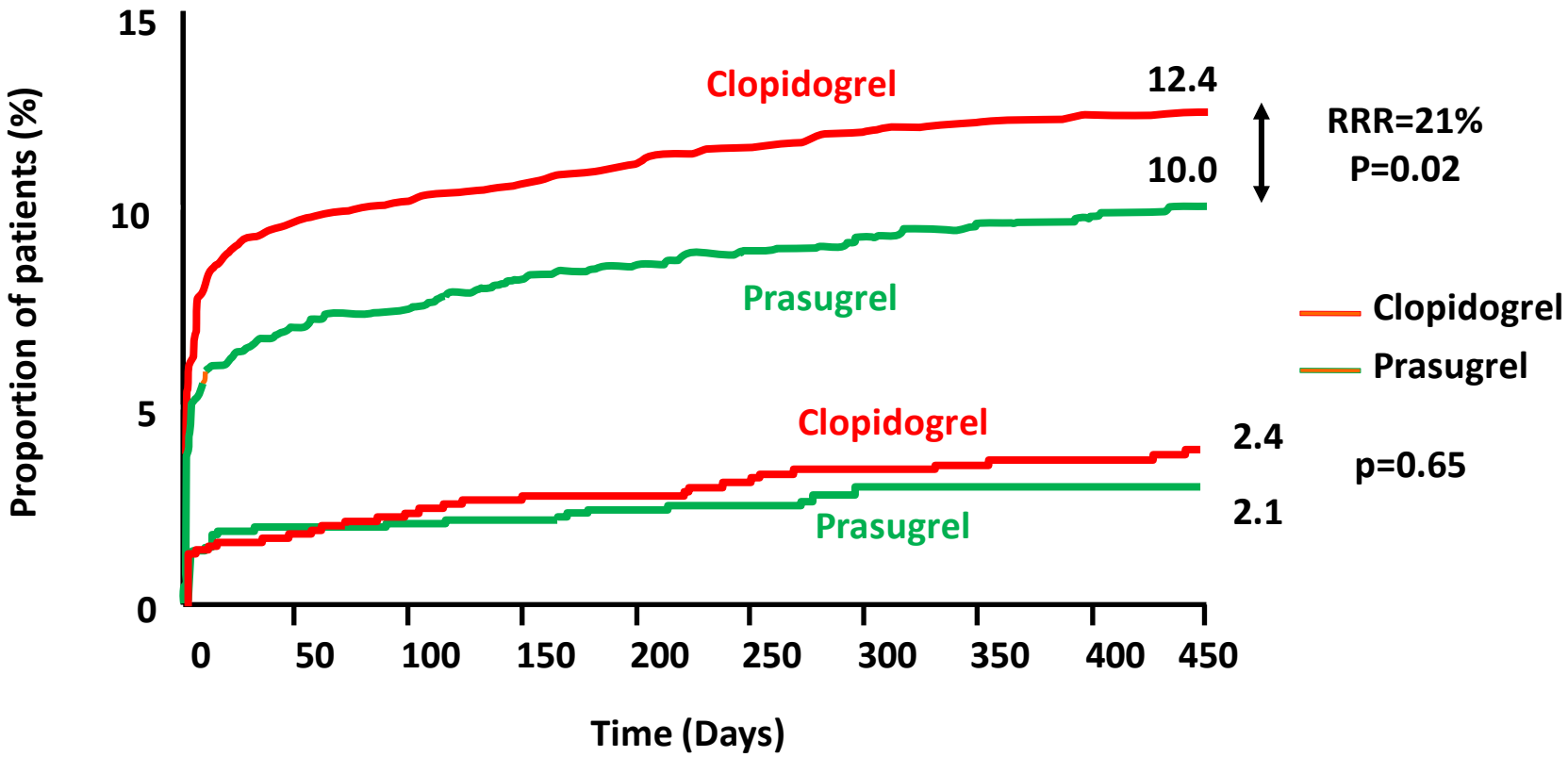
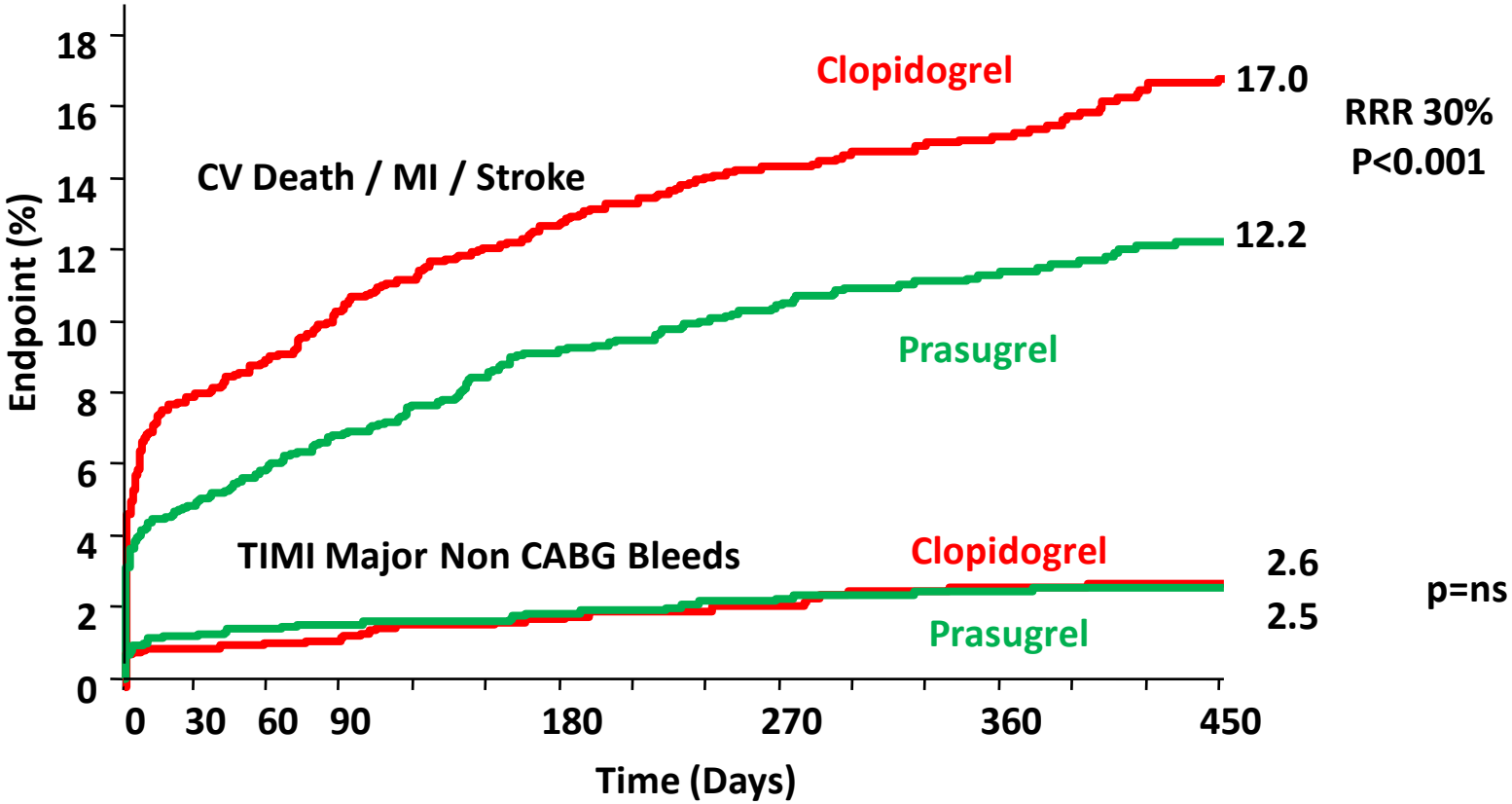
Prasugrel in STEMI



N=3534

Montalescot et al. Lancet 2009

Prasugrel in Diabetic Patients



N=3146

Wiviott et al, Circulation 2007

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In TRITON, for STEMI and diabetics:

- higher ischemic benefit

- same bleeding risk

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Safety Concern in subgroups ?

Higher rate of bleeding if > 75 y.o or < 60 kg

deleterious and CI if prior Stroke / TIA

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Ticagrelor: PLATO study

NSTE-ACS (moderate-to-high risk) STEMI (if primary PCI)
Clopidogrel-treated or -naive;
randomised within 24 hours of index event
(N=18,624)

Clopidogrel
If pre-treated, no additional loading dose;
if naive, standard 300 mg loading dose,
then 75 mg qd maintenance;
(additional 300 mg allowed pre PCI)

Ticagrelor
180 mg loading dose, then
90 mg bid maintenance;
(additional 90 mg pre-PCI)

6–12-month exposure

Primary endpoint: CV death + MI + Stroke
Primary safety endpoint: Total major bleeding

Wallentin et al, N Engl J Med 2010

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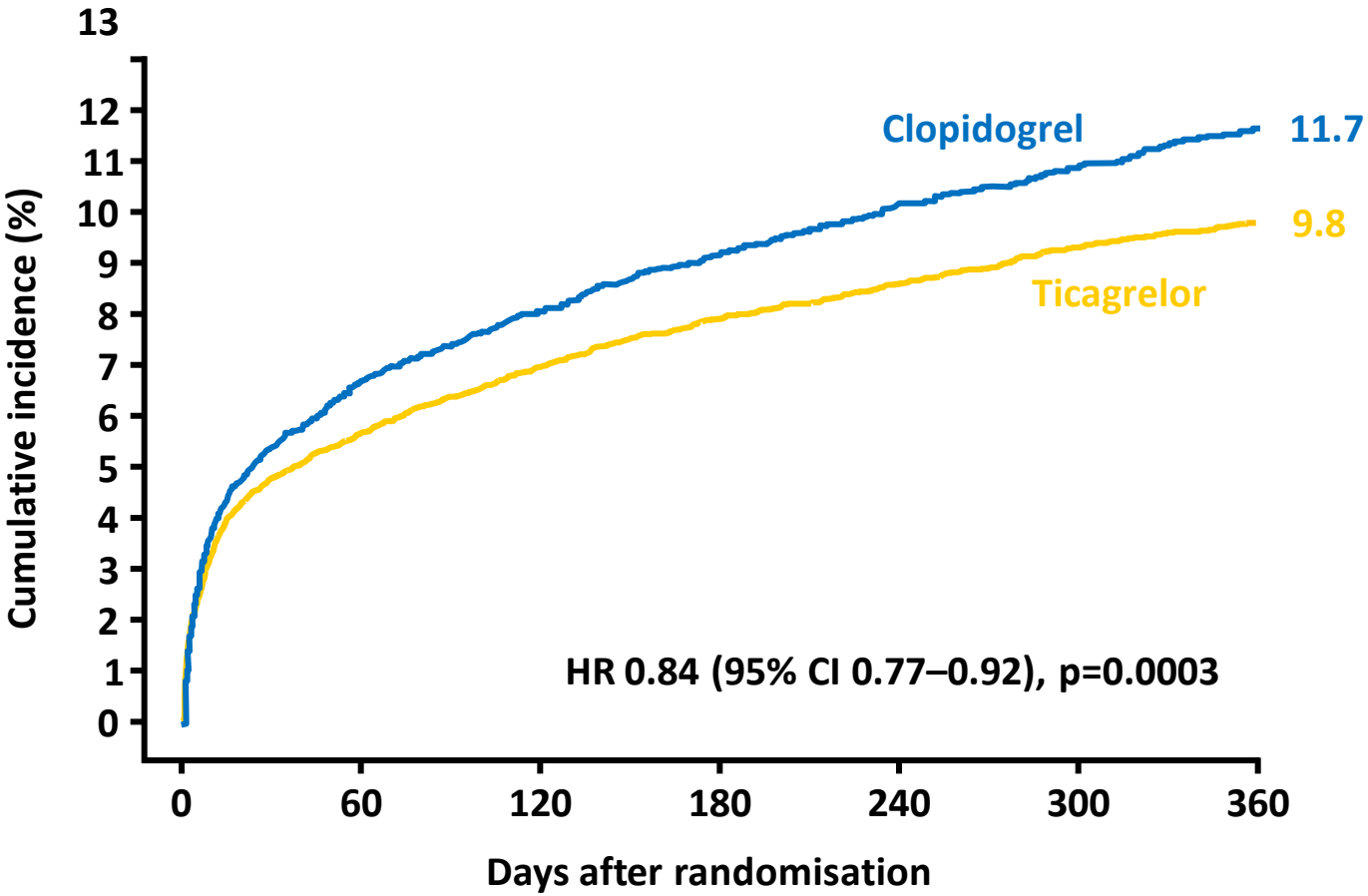
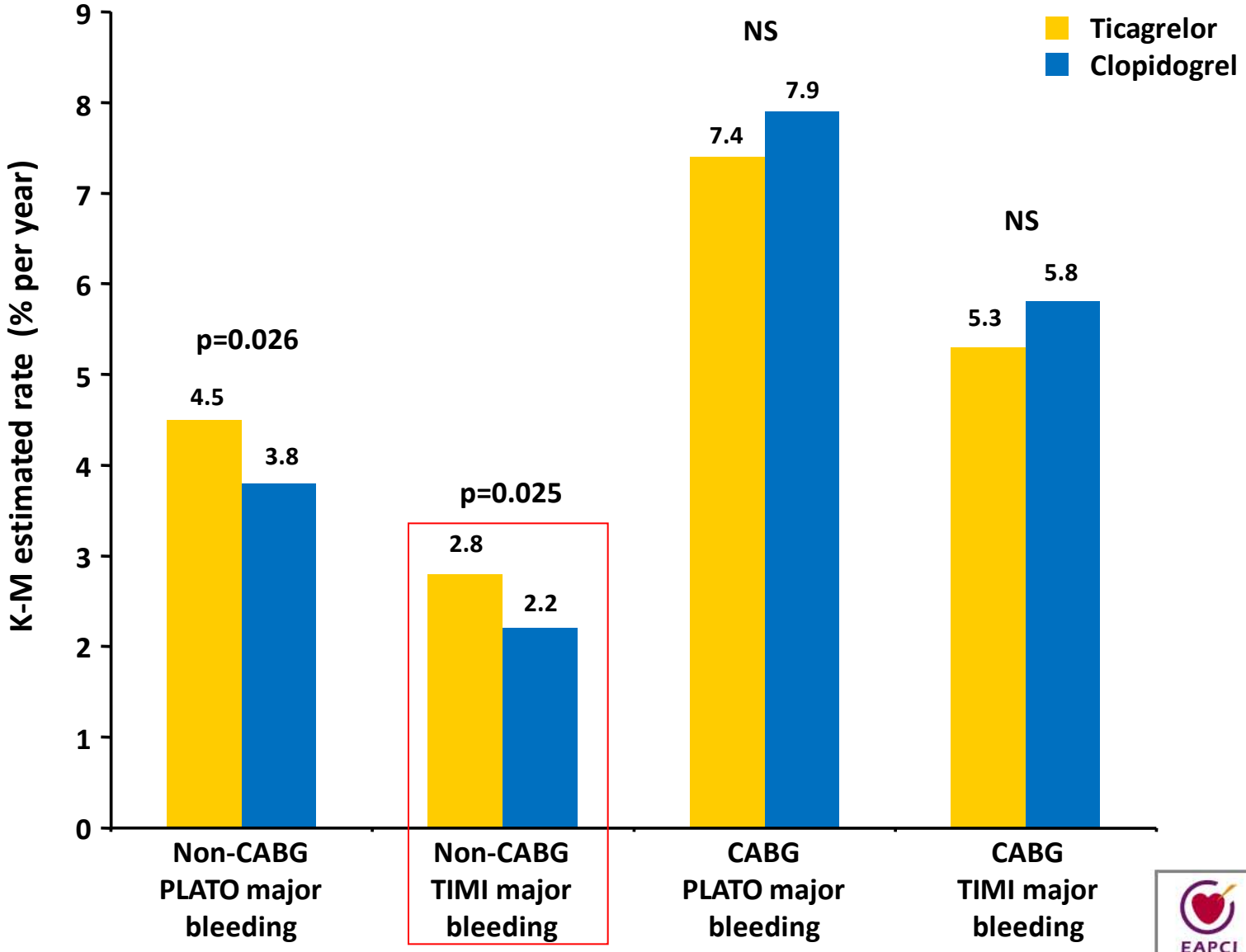
Primary EP (CV death, MI or stroke)

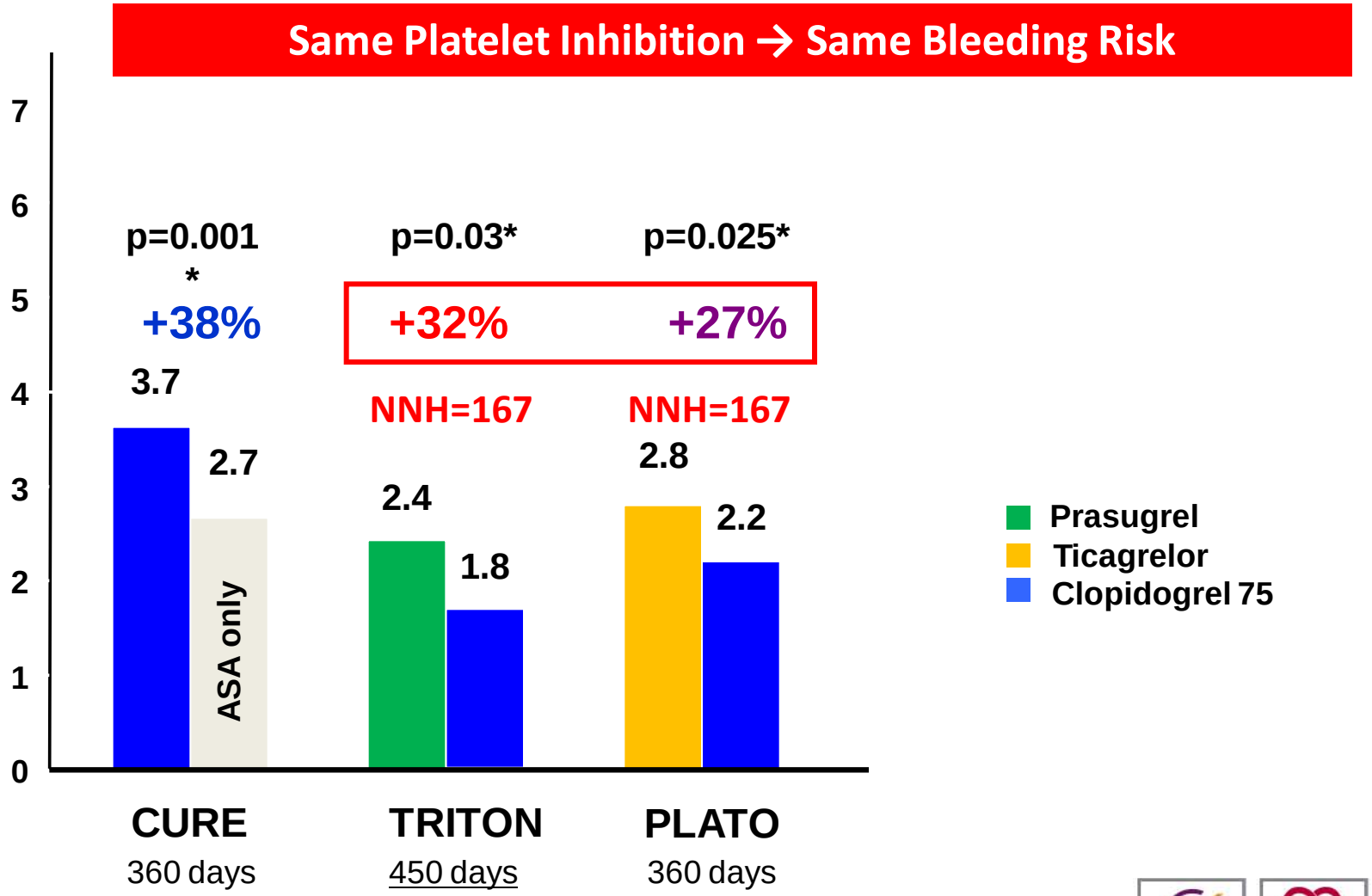


Wallentin et al, N Engl J Med 2010

Non-CABG and CABG-related major bleeding



Safety = Non-CABG related TIMI major bleedings



Wiviott et al, NEJM 2007, Wallentin et al, NEJM 2010

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Subgroup analysis ?
Same Than TRITON ?
Others ?

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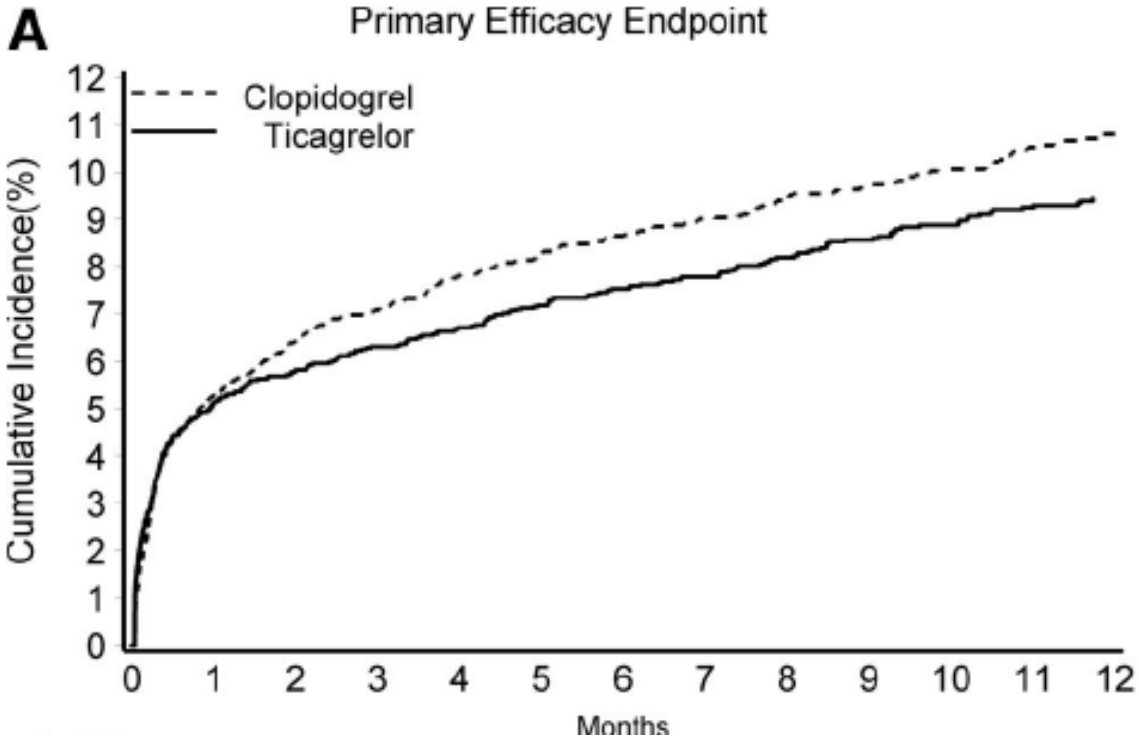
PLATO: STEMI Subgroup



10.8 %

9.4 %

Δ=1.4 %

p=0.07

STEMI, N=7544

TRITON: N=3534, Δ=2.4 % for primary EP, p=0.02

Steg et al, Circulation 2010

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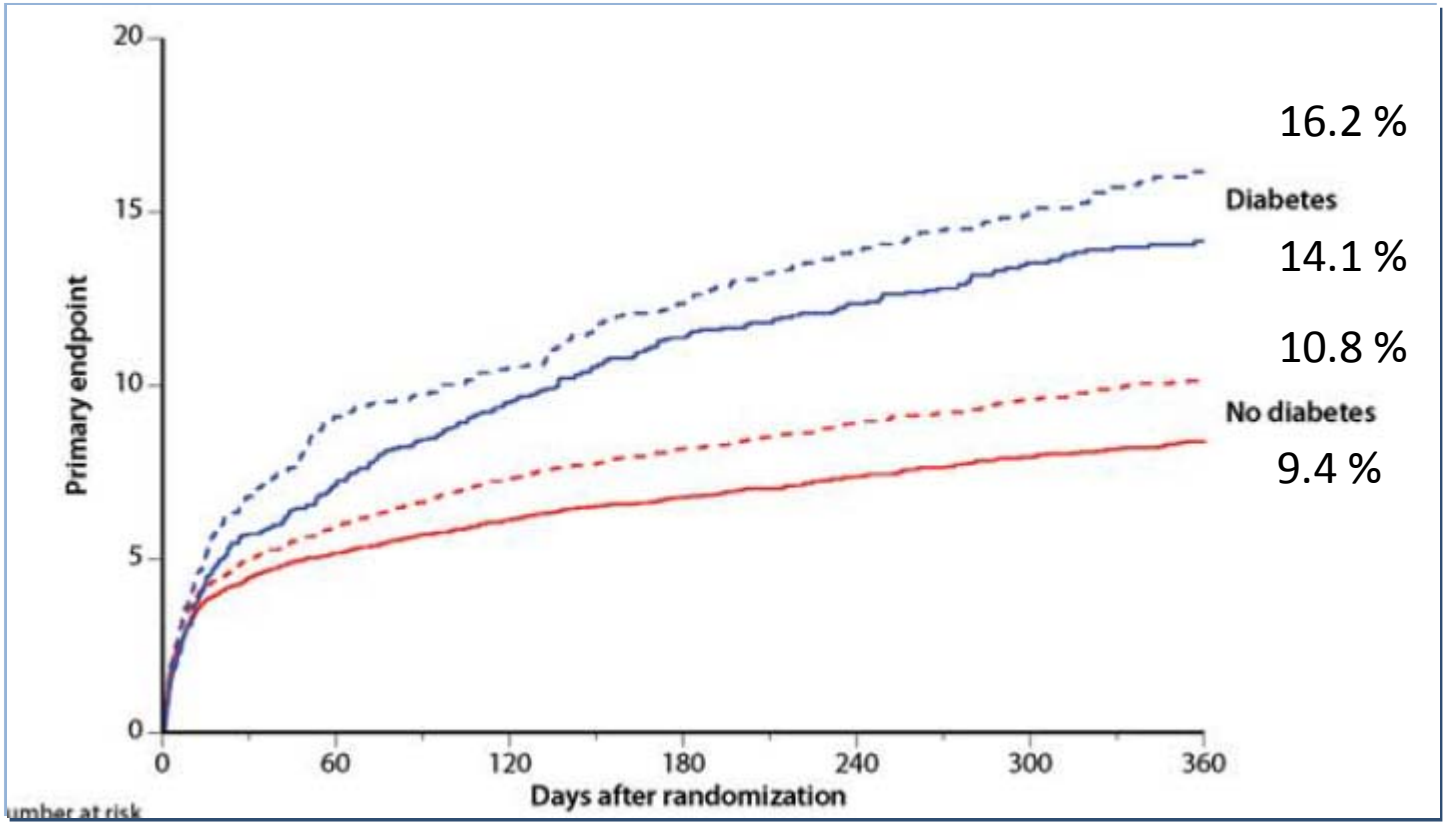
PLATO: Diabetic Subgroup



Δ=2.1 %

p=0.07

Δ=1.4 %

p<0.01

Diabetes, N=4662

TRITON: N=3146, Δ=5.2 % for primary EP, p<0.001

James et al, Eur Heart J 2010

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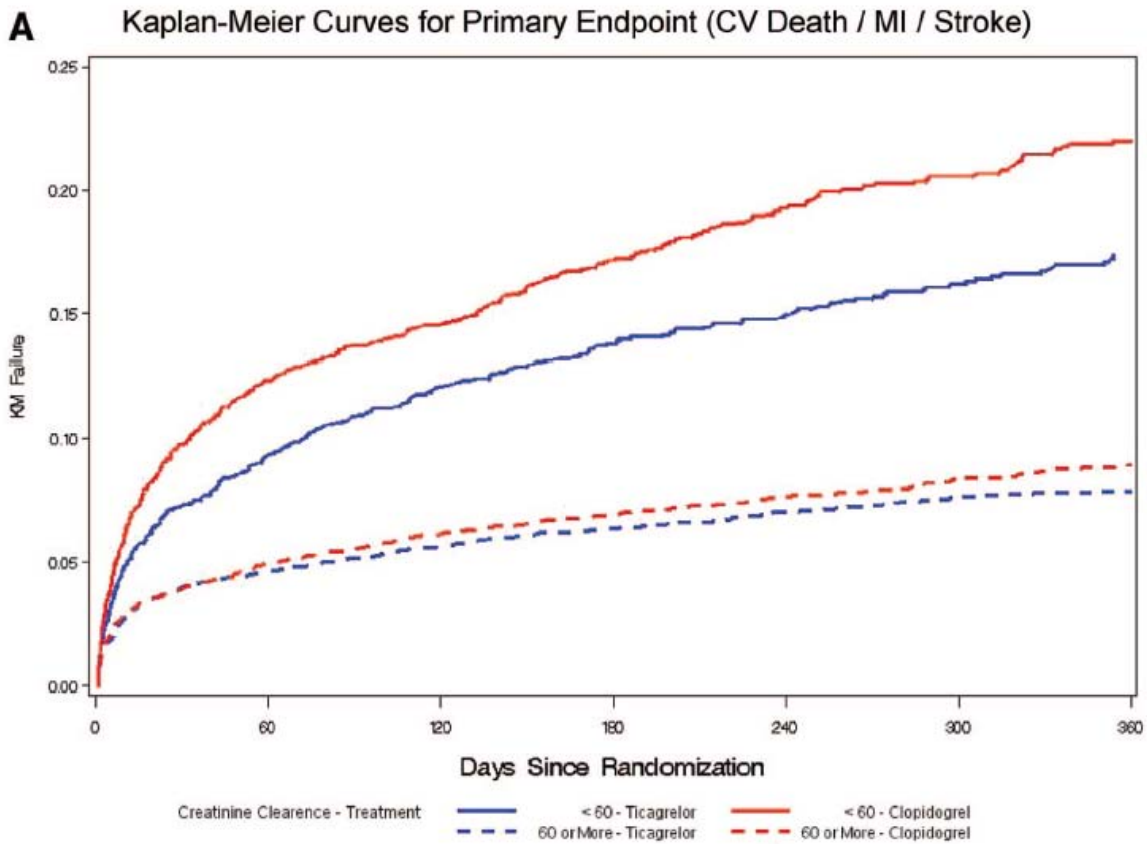
PLATO: Impact of CKD



22 %

17.3 %

8.9 %

7.9 %

Δ=4.7 %

p<0.01

N=3237 with CC < 60ml/min

James et al, Circulation 2010

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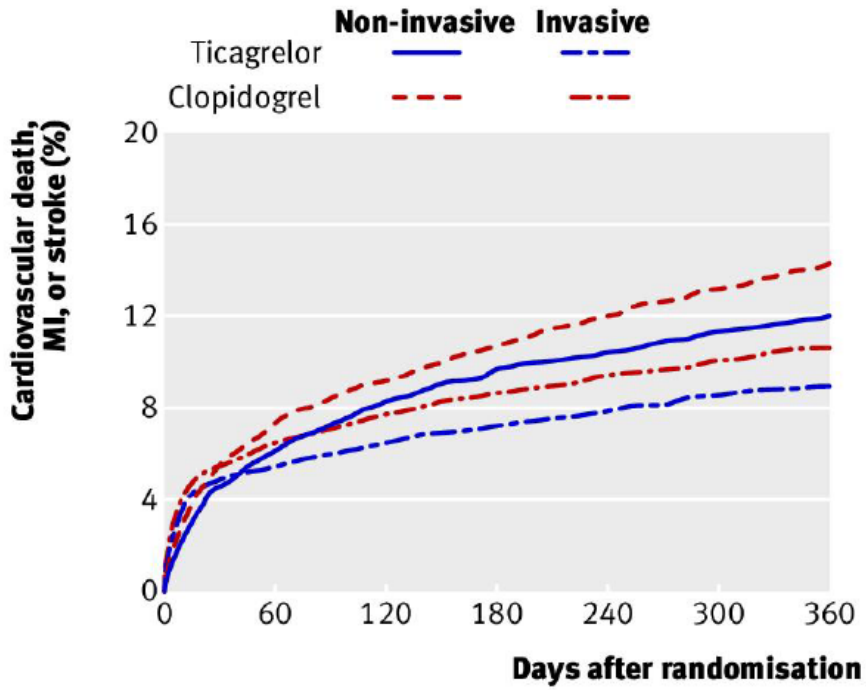
PLATO: ACS patients medically managed



Planned non-invasive strategy

Primary endpoint
12 % vs. 14.3%, p=0.04

Patients not included in TRITON

James et al, BMJ 2011

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New P2Y12 blockers for each patients ?
Prasugrel or Ticagrelor ?

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First Question

New P2Y12 blockers or Not ?

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Ischemic Risk **ACS patients** *Bleeding Risk*	**High risk** **STEMI** **Diabetes mellitus, CKD** **High-risk NSTE ACS** **(Tn + and/or ST changes)** **Recurrent event on clopidogrel** **Stent Thrombosis**	**Low risk** **No ST changes** **No Troponin elevation** ***(Patients not in Triton / Plato)***
High risk: **Prior stroke/TIA*** **Chronic OAC**** **Age > 75 y.o** **Weight < 60 kg** **Prior Bleeding**	Individual Decision Prasugrel 5 mg ?	Clopidogrel 600/150
Low risk **No prior stroke/TIA/Bleeding** **Age < 75 y.o** **Weight > 60 kg** **No Chronic OAC**	New P2Y12 Blockers	Clopidogrel 600/150

*** CI prasugrel** **** CI prasugrel and ticagrelor**

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First Question
New P2Y12 blockers or Not: YES

Second Question
Which One ?

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Prasugrel in ACS

PROS

- Benefit on primary EP
- Benefit on stent thrombosis
- Benefit ++ in STEMI / DM
- 3rd generation Thienopyridine *(Known Active MB)*

CONS

- Increased non CABG bleeds
- Increased CABG bleeds
- CI if prior stroke/TIA
- Less benefit: >75, <60 kg
- Only ACS patients with PCI

Ticagrelor in ACS

PROS

- Benefit on primary EP
- Benefit on Mortality (+++)
- Benefit in all ACS patients *(PCI/Med/CABG)*
- Benefit ++: CKD
- Reversibility

CONS

- Increased non CABG bleeds
- Intake twice daily (Compliance !)
- Less Benefit: STEMI, Diabetes
- New drug with side effects

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Selection of P2Y12 blockers in ACS Patients

Prasugrel and Ticagrelor

'Good Candidates'

High Risk NSTEMI (Both)

Recurrent event/Clopidogrel (Both)

STEMI (Both, Prasugrel ?)

Diabetic patients (Prasugrel)

Patient with CKD (Ticagrelor)

High Risk ACS medically treated (Ticagrelor)

High ACS treated by CABG (Ticagrelor)

General Warning

Patients > 75 years old (Both)

Low Body Weight (< 60 kg) (Both)

Prior Bleeding (Both)

COPD, AV block (Ticagrelor)

Contraindications

Chronic OAC (Both)

Prior Stroke / TIA (Prasugrel)

Active Bleeding Disease (Both)

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Conclusion

Which Antiplatelet Therapy for which patient ?

- ***No systematic prescription***

- ***Tailored oral antiplatelet therapy*** according to:
- patient's characteristics / clinical presentation
- risk profile (efficacy/safety balance)
- local contraints

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Gracias por su atención

Marseille, FR