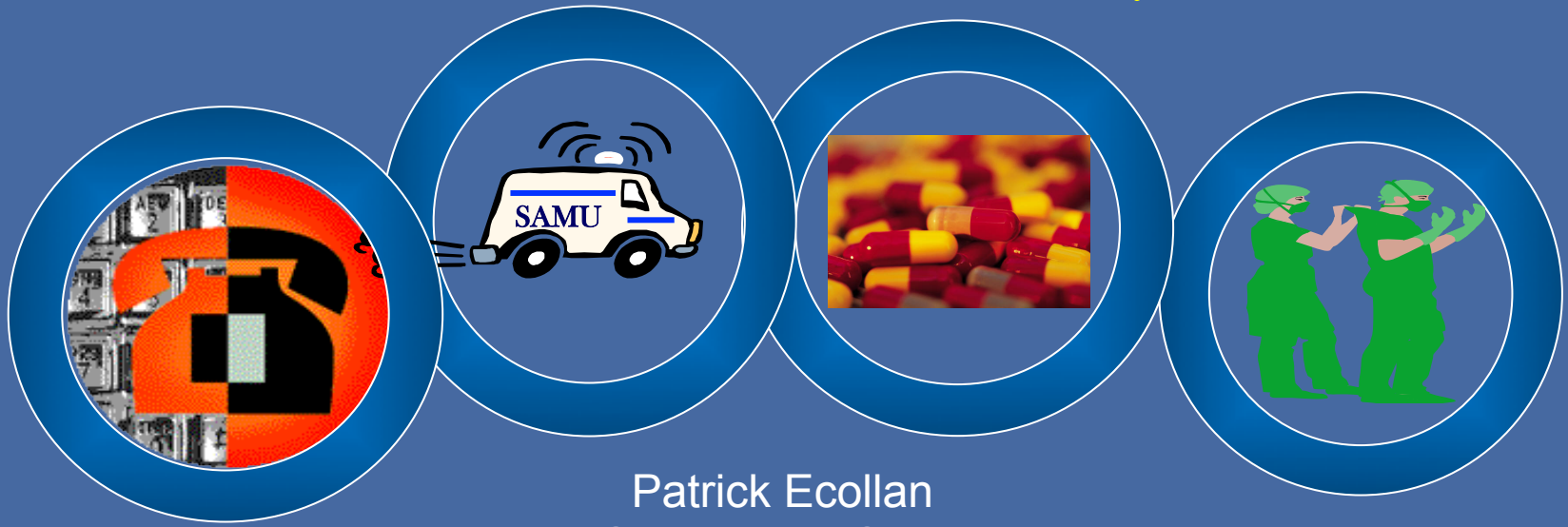
APPAC

2013

SCA :

Doit on encore donner des anti agrégeant plaquettaires per os avant l'hôpital ?

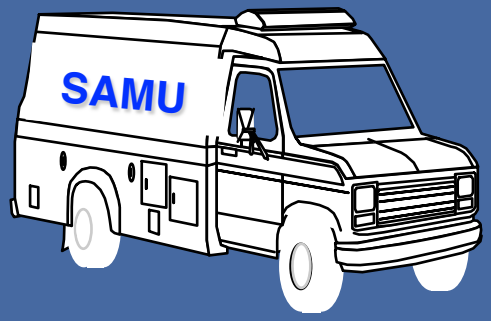


Patrick Ecollan
DAR-SMUR Pitié-Salpêtrière
SAMU de PARIS

Research Grants to the Institution or Consulting/Lecture/CME Fees from Astra-Zeneca, Abbott, Boehringer-Ingelheim, Daiichi-Sankyo, Iroko, Sanofi-Aventis, Radiometer, Biomérieux, SFMU, ADRMU, CFRCP, Société Française de Cardiologie, ma mère!.

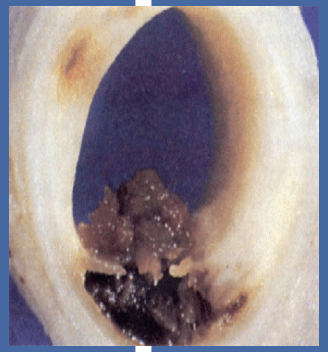
On n’aime pas en SMUR !

Le traitement SAMU dans le SCA



THR

1985



THR preH

Gusto IV

THR preH ou/et PCI

Captim

Si < 2h THR preH = PCI

Assent IV

THR preH ou PCI

- Isis 2
- Delucas
- Admiral
- Create
- Commit
- Ex Timi 25
- Finesse
- On Time 2
- Triton Timi 38
- Atoll
- Accoast
- Atlantic……

2012

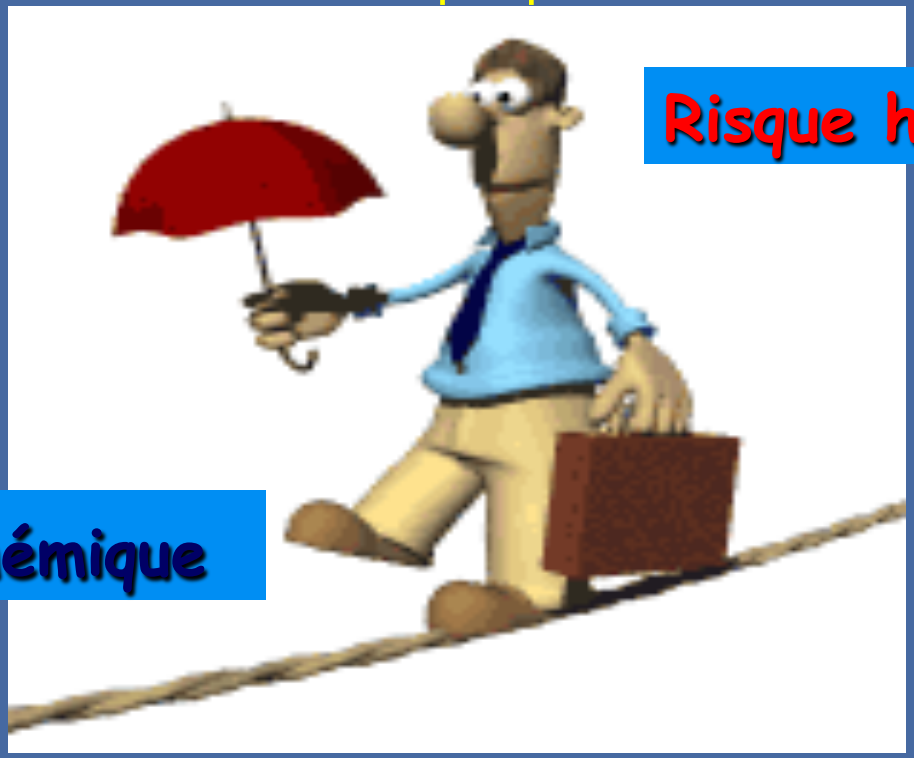
PCI facilité préH = 3 injections + 1 perfusion continue - de 1 à 6 cp

Traitement adjuvant pré hospitalier

Quel médicament utiliser?
Quand le donner?

Dépend du couple cardiologue /urgentiste

Inhibition plaquettaire



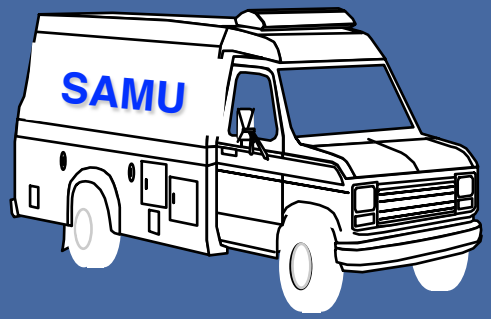
Risque hémorragique

Risque ischémique

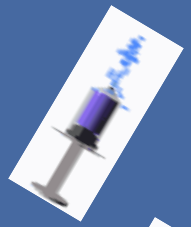
Bénéficier de l'efficacité supérieure en limitant les risques

Identifier les patients plus ou moins bon candidats

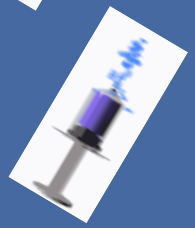
Traitement adjuvant pré hospitalier



- Aspirine

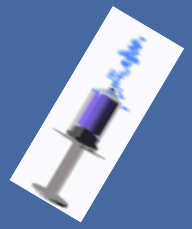


- Héparine



- Inhibiteur P2Y12

- Sous certaines conditions AGp2b3a (SCA ST+ <3h)



New $P2Y_{12}$ inhibitors

Recommendations	Class [a]	Level [b]
Aspirin should be given to all patients without contraindications at an initial loading dose of 150–300 mg, and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A
A $P2Y_{12}$ inhibitor should be added to aspirin as soon as possible and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding.	I	A
Prolonged or permanent withdrawal of $P2Y_{12}$ inhibitors within 12 months after the index event is discouraged unless clinically indicated.	I	C
Ticagrelor (180-mg loading dose, 90 mg twice daily) is recommended for all patients at moderate-to-high risk of ischaemic events (e.g. elevated troponins) , regardless of initial treatment strategy and including those pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced).	I	B
Prasugrel (60-mg loading dose, 10-mg daily dose) is recommended for $P2Y_{12}$-inhibitor-naïve patients (especially diabetics) in whom coronary anatomy is known and who are proceeding to PCI unless there is a high risk of life-threatening bleeding or other contraindications.[d]	I	B
Clopidogrel (300-mg loading dose, 75-mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel.	I	A
A 600-mg loading dose of clopidogrel (or a supplementary 300-mg dose at PCI following an initial 300-mg loading dose) is recommended for patients scheduled for an invasive strategy when ticagrelor or prasugrel is not an option.	I	B

Eur Heart J. 2011 Dec;32(23):2999-3054

pré-traitement dans le SCA non ST+

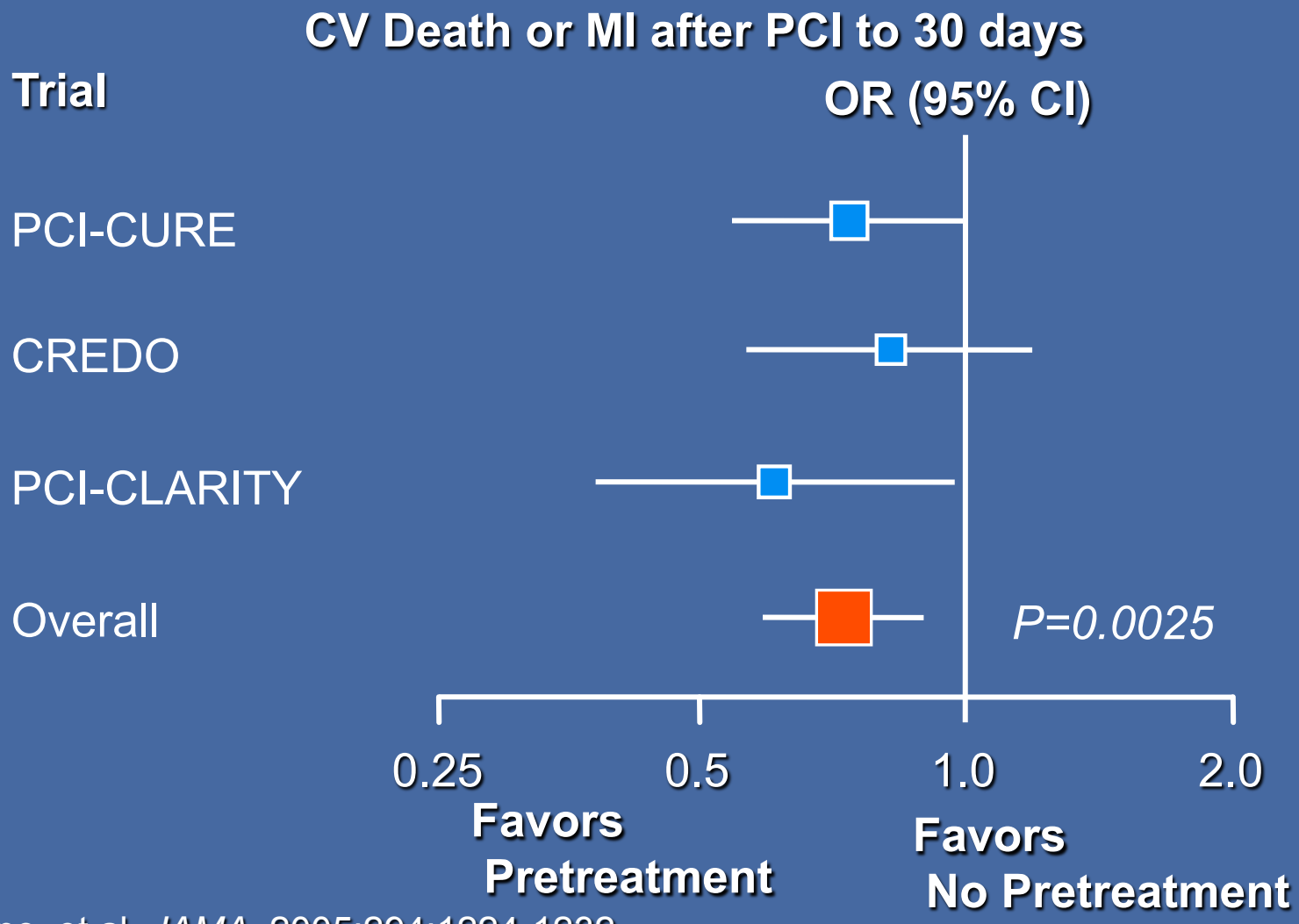
P2 Y12

I C ?

ESC Guidelines for the Management of NSTE-ACS

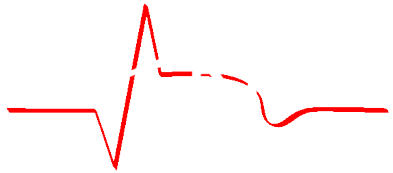
ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction

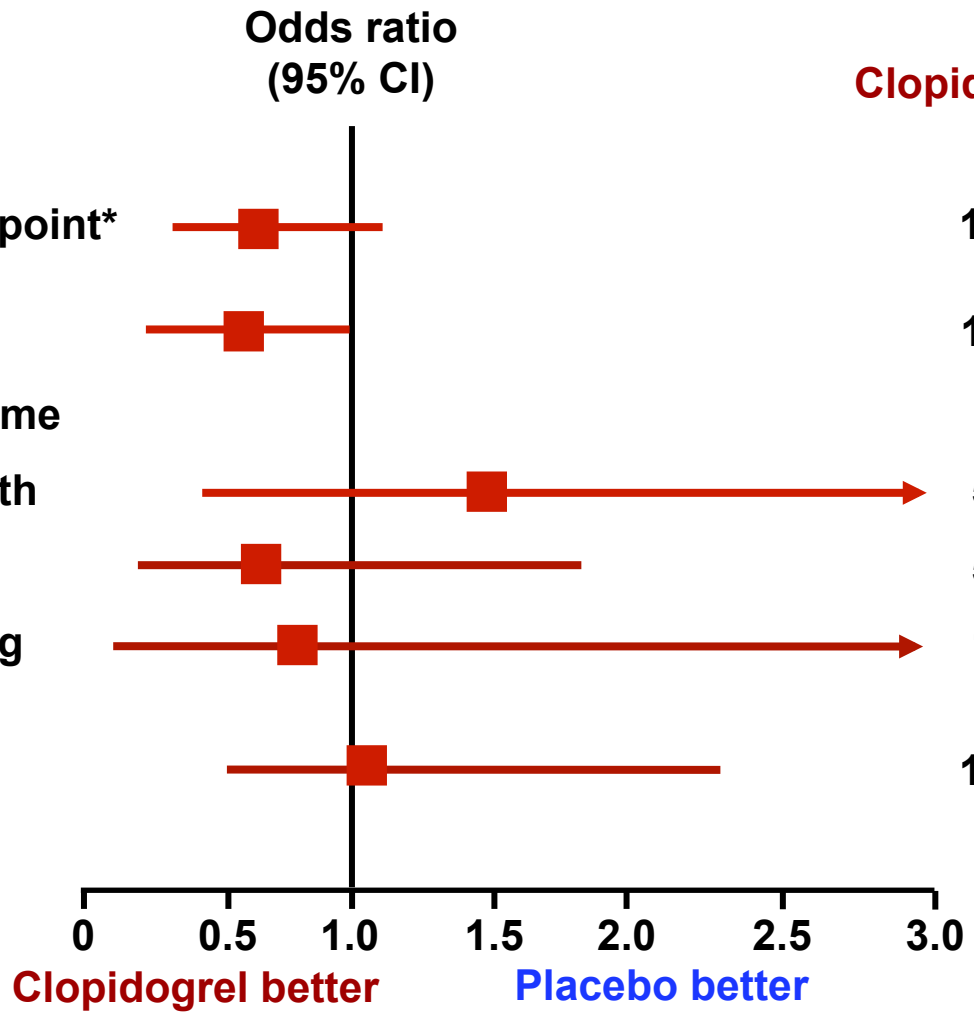
PCI Pre-Treatment (With 300mg load) → Events



Sabatine. et al. *JAMA*. 2005;294:1224-1232.

Primary Outcome Parameters:
Ambulance Subgroup

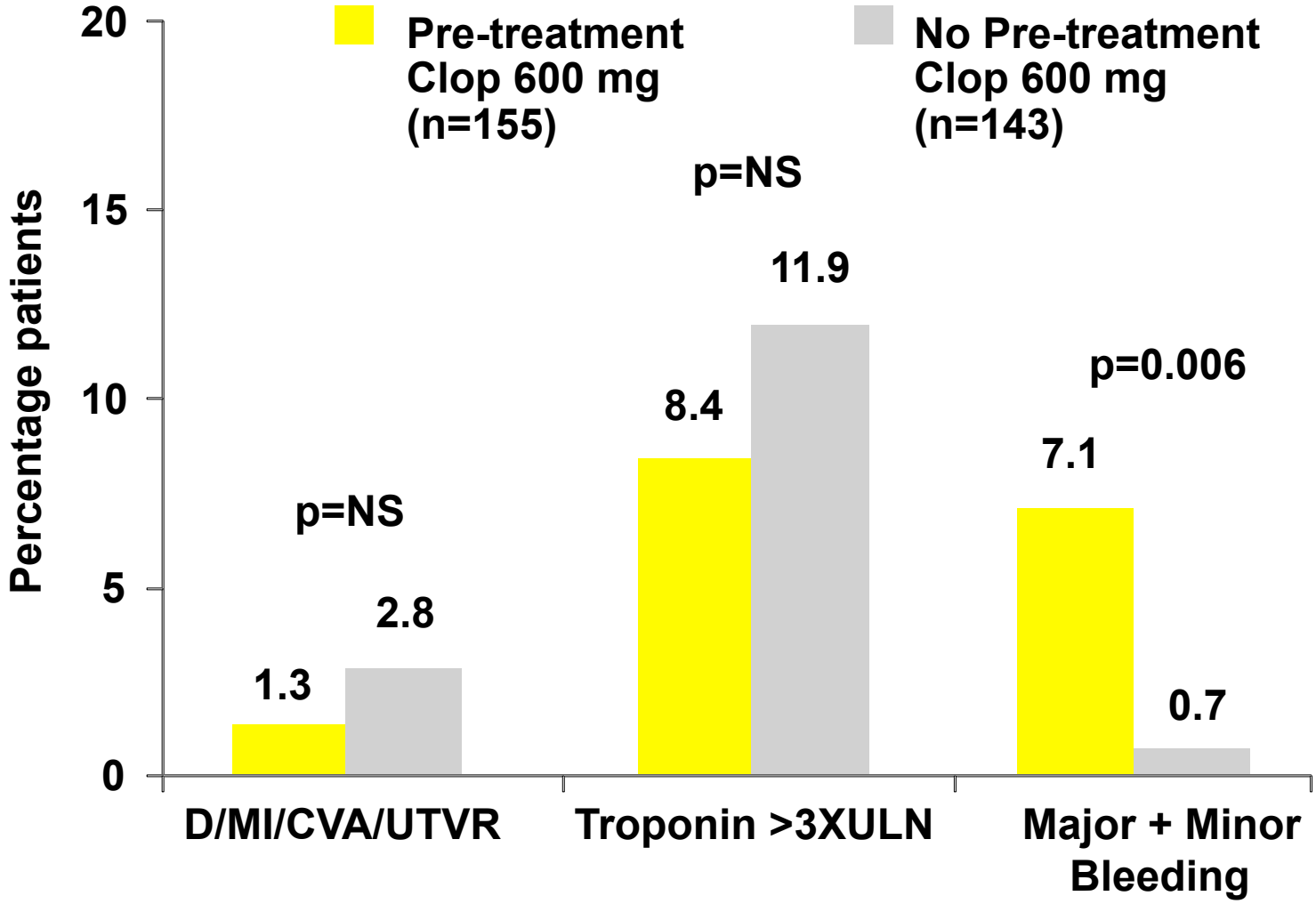




	Clopidogrel		p value
Primary efficacy endpoint*	16.5	27.1	0.06
TFG 0/1	11.8	22.3	0.05
30-day clinical outcome			
Cardiovascular death	5.5	3.7	NS
Re-MI	5.5	9.3	NS
Re-ischaemia urging revascularization	1.8	2.8	NS
Overall	12.8	14.0	NS

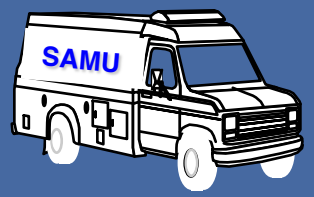
**Occluded infarct artery (TFG 0/1) + death + re-MI prior to angiography*

PRAGUE-8 (with 600 mg load): Patients undergoing elective PCI



Widimsky P et al. Eur Heart J 2008;29:1495-1503

ACCOAST



Diagnosis + Transfer to cath lab >2 h to <24 h

Cath lab

30 d FU

NSTEM / Tropor 100+ (event driven)
c pidogrel n ng-term 75 mg

Plan Ang <24 h

Ran

Pras 30

Inactive

Angio

Ang

PCI

P 30

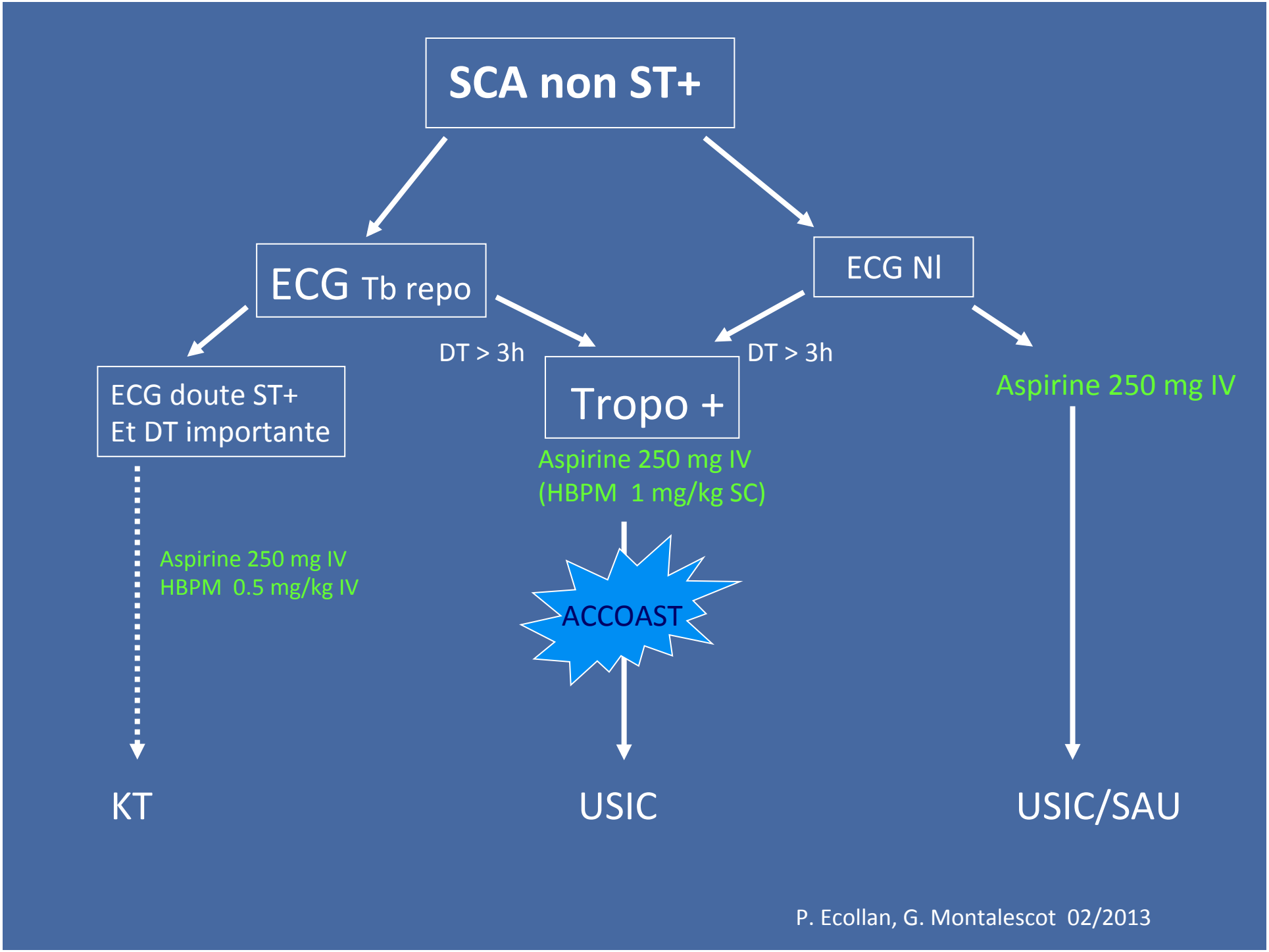
P

Pras 60

PE: CV-D, MI, stroke, urgent revasc., GPI bailout @ 7d
SEs: All TIMI major bleeding @ 7d; NetClinBenefit @ 7d

Pras 10(5) for 30d

Montalescot G, et al. *Am Heart J.* 2011;161:650-6


SCA non ST+
ECG Tb repo
ECG Nl
DT > 3h
DT > 3h
ECG doute ST+
Et DT importante
Tropo +
Aspirine 250 mg IV
Aspirine 250 mg IV
(HBPM 1 mg/kg SC)
Aspirine 250 mg IV
HBPM 0.5 mg/kg IV
ACCOAST
KT
USIC
USIC/SAU
P. Ecollan, G. Montalescot 02/2013

AHA Scientific Statement

2009 Focused Updates: ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (Updating the 2005 Guideline and 2007 Focused Update)

Class I

1. A loading dose of thienopyridine is recommended for STEMI patients for whom PCI is planned. Regimens should be 1 of the following:
   a. At least 300 to 600 mg of clopidogrel† should be given as early as possible before or at the time of primary or nonprimary PCI. (*Level of Evidence: C*)
   b. Prasugrel 60 mg should be given as soon as possible for primary PCI.[26,27] (*Level of Evidence: B*)

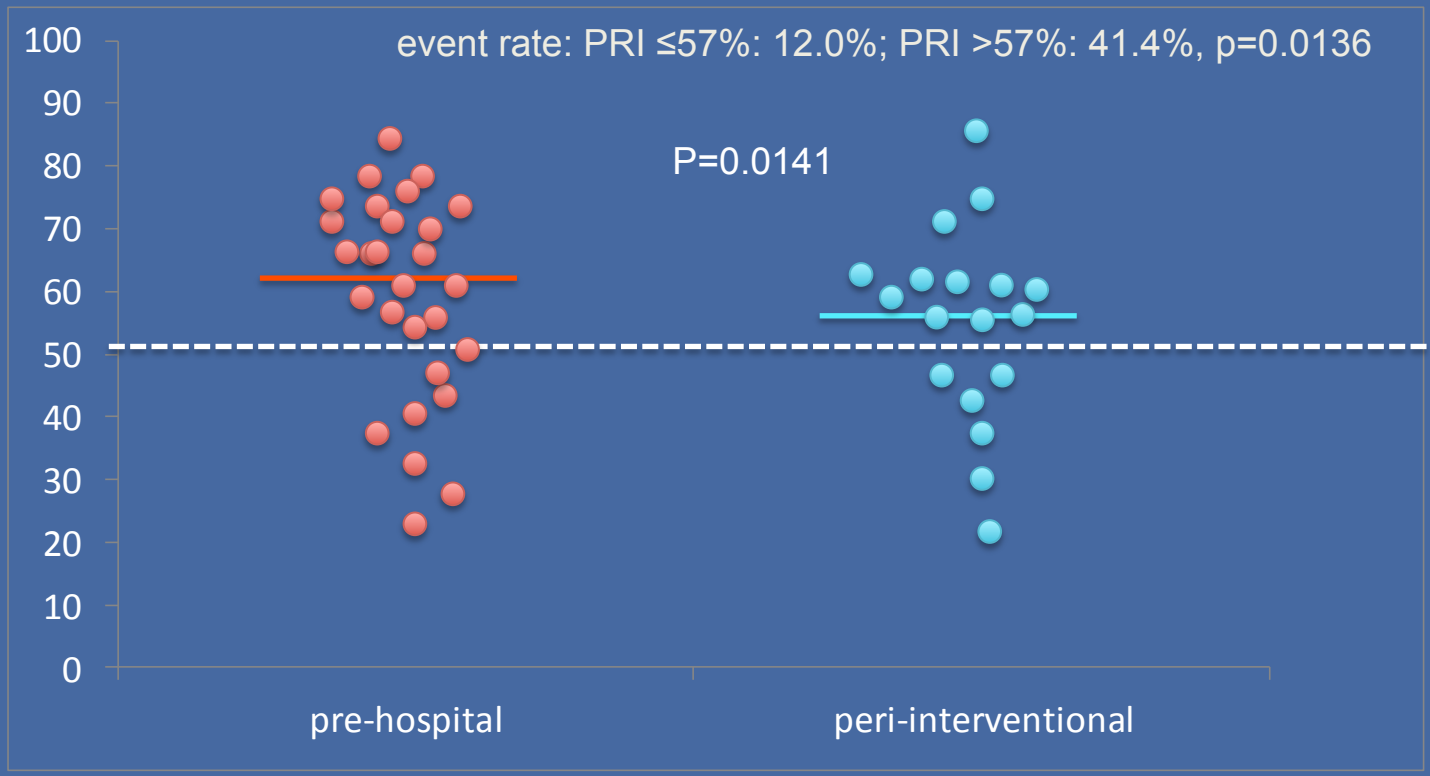
Class III

1. In STEMI patients with a prior history of stroke and transient ischemic attack for whom primary PCI is planned, prasugrel is not recommended as part of a dual-antiplatelet therapy regimen. (*Level of Evidence: C*)

ACC/AHA STEMI and PCI Guidelines update, Kushner et al. Circulation 2009

Pre-hospital clopidogrel loading

54 STEMI patients

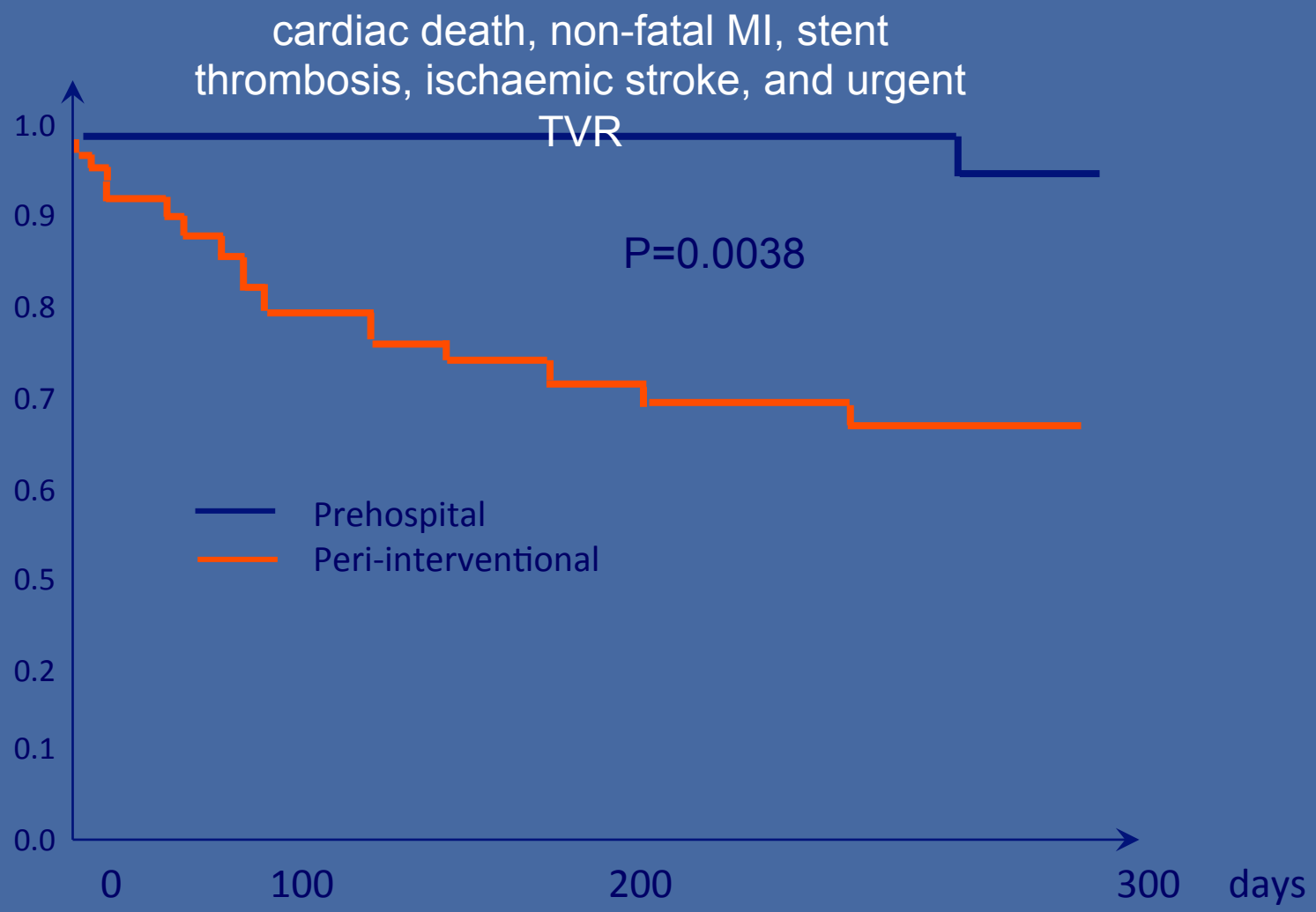


Diabetes, low high-density lipoprotein and pre-hospital clopidogrel loading were associated with impaired clopidogrel responsiveness

Thromb Haemost. 2011 Jul 4;106(1):141-8.

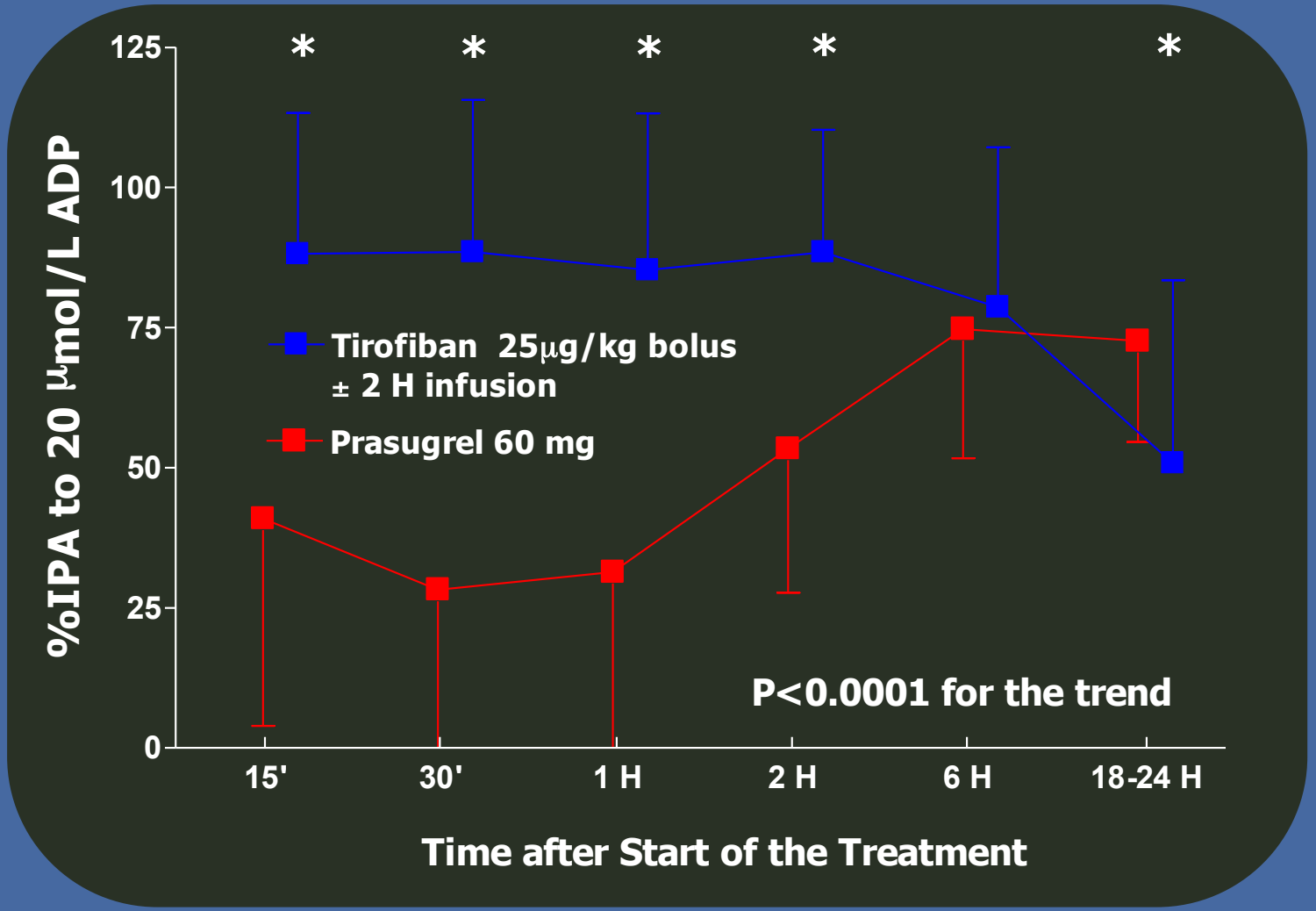
Pre-hospital clopidogrel loading

54 STEMI patients



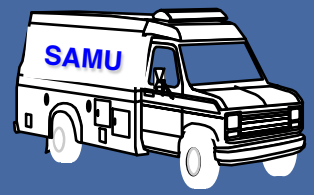
Thromb Haemost. 2011 Jul 4;106(1):141-8.

Late onset of action of Prasugrel in STEMI



Valgimigli M et al, J Am Coll Cardiol Intv 2012;5:268–77

ATLANTIC Design



N ~ 1770

STE –ACS planned for PCI

- Written informed consent in mobile care unit^
- Symptoms of acute MI of more than 30 min but less than 6 hours
- New persistent ST-segment elevation ≥ 1 mm in two or more contiguous ECG leads

RANDOMIZE
DOUBLE BLIND

Ticagrelor 180mg loading dose	Pre-Hospital	Loading dose placebo
Loading dose placebo	In-Hospital	Ticagrelor 180mg loading dose

Primary Objective:

- TIMI flow grade 3 of MI culprit vessel at initial angiography or
- ≥70% ST-segment elevation resolution pre-PCI

Ticagrelor 90mg/bid – 30d

NCT01347580 – G. Montalescot et al.

Triple thérapie avec antiGPIIbIIIa ?

Intérêt Prasugrel si antiGPIIbIIIa ?

- STEMI: Prasugrel > Clopidogrel (2/3 antiGPIIbIIIa)

- Prespecified subgroup STEMI + IIbIIIa (n=2226):
  Primary endpoint: Prasugrel 10.4% vs. Clopidogrel 13.5%, p=0.02

Montalescot et al, Lancet 2009

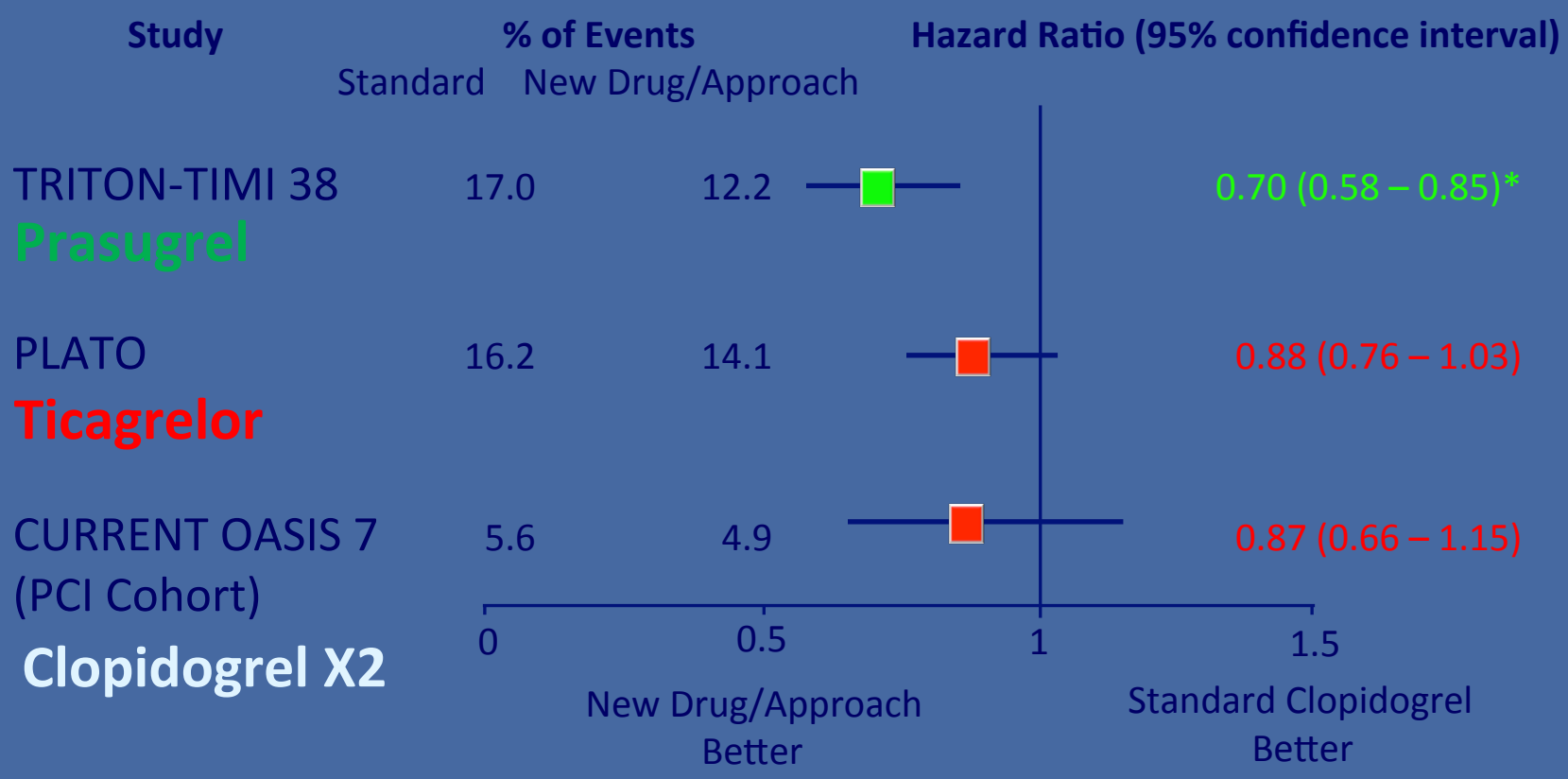
- Pas de sur risque hémorragique

Intérêt antiGPIIbIIIa si Prasugrel ?

- Délai action Prasugrel: Nécessité action rapide antiGPIIbIIIa dans STEMI

KEY SUBGROUPS

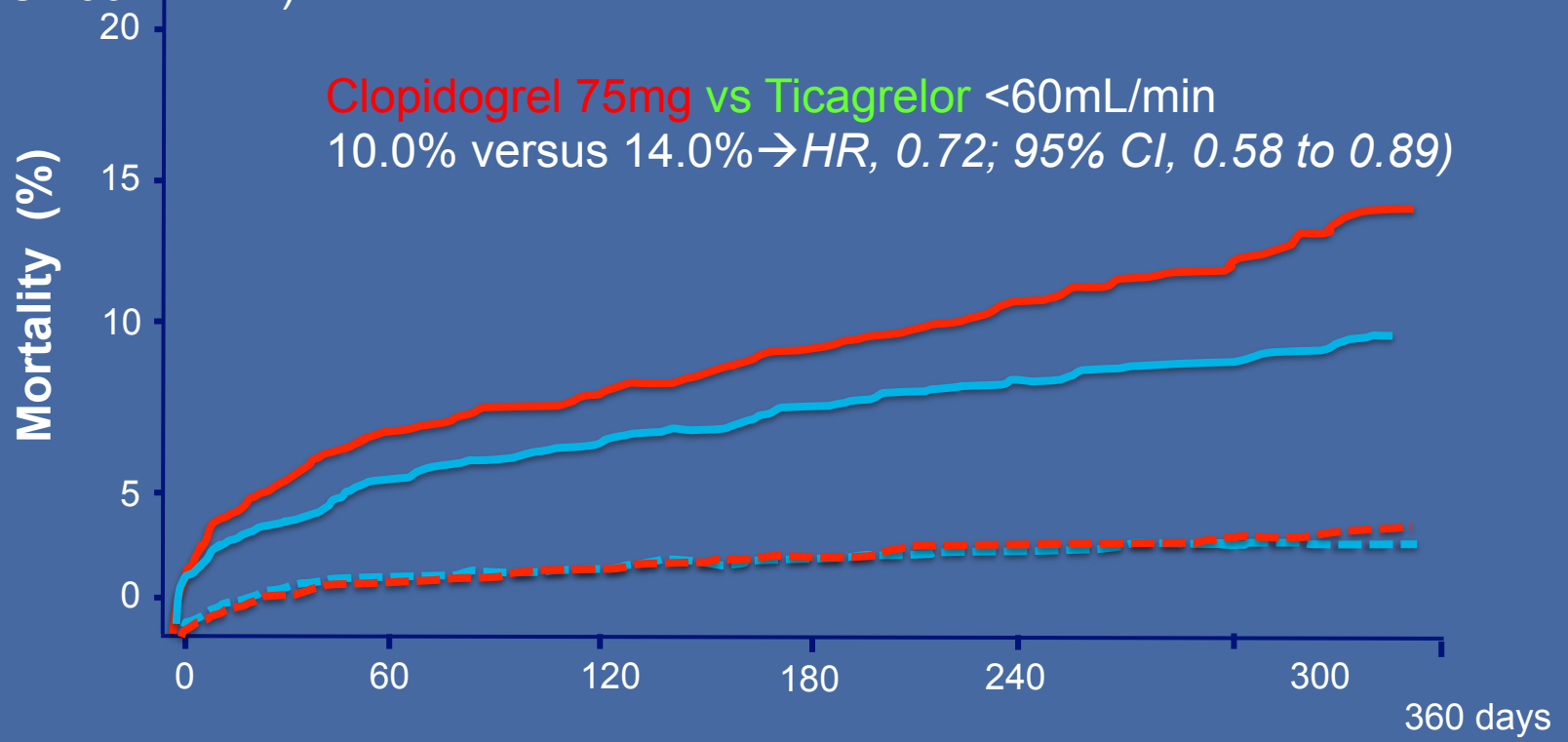
New Approaches in Diabetics



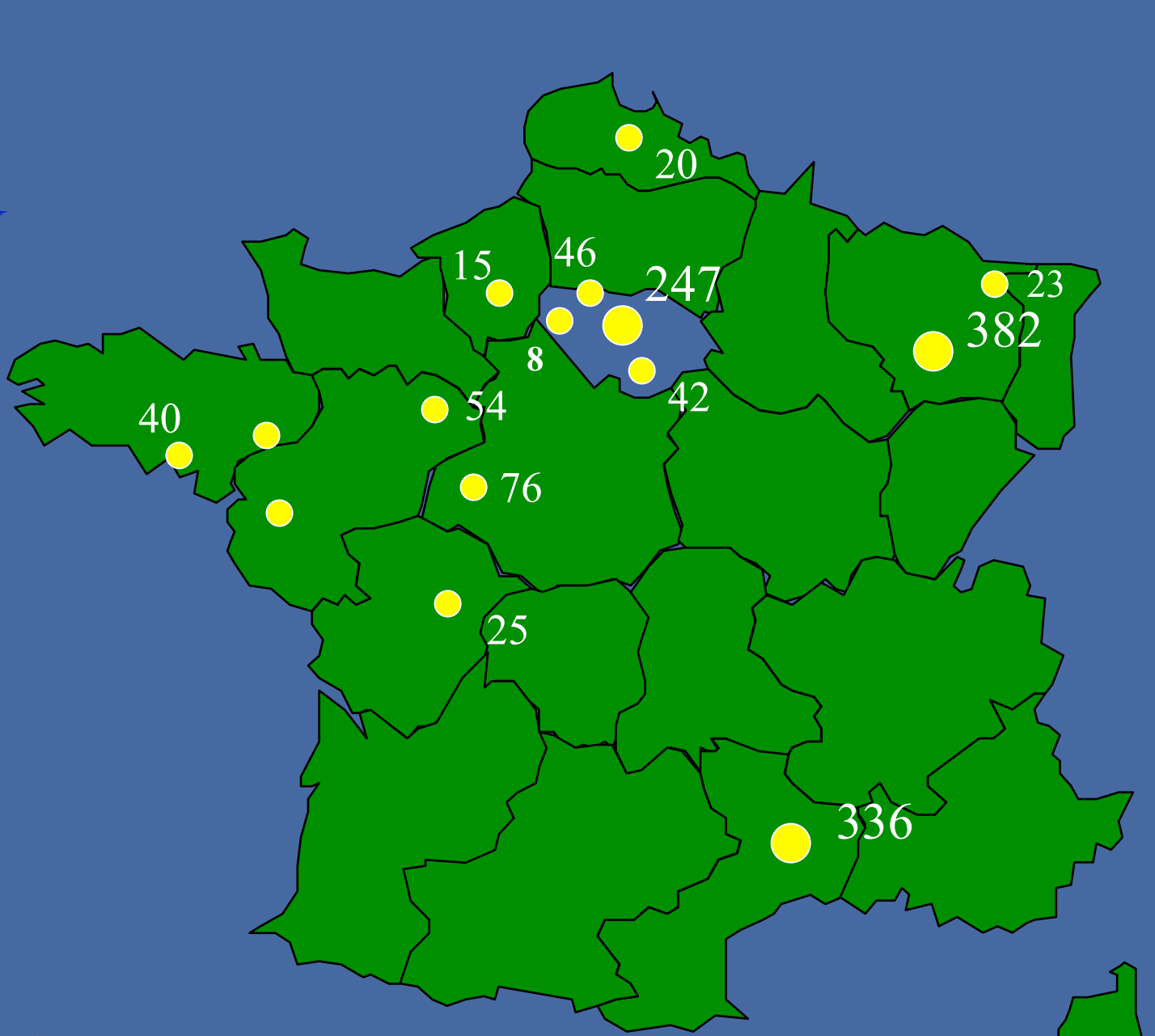
Ferreiro JL, Angiolillo DJ. *Circulation.* 2010. In press.

Renal failure patients

– From 17.3% to 22.0% [HR], 0.77; 95% [CI], 0.65 to 0.90 (n= 3237) (Cr Cl >60mL/min)
– From 7.9% to 8.9% (HR, 0.90; 95% CI, 0.79 to 1.02) (n=11 965) (Cr Cl≥60mL/min)



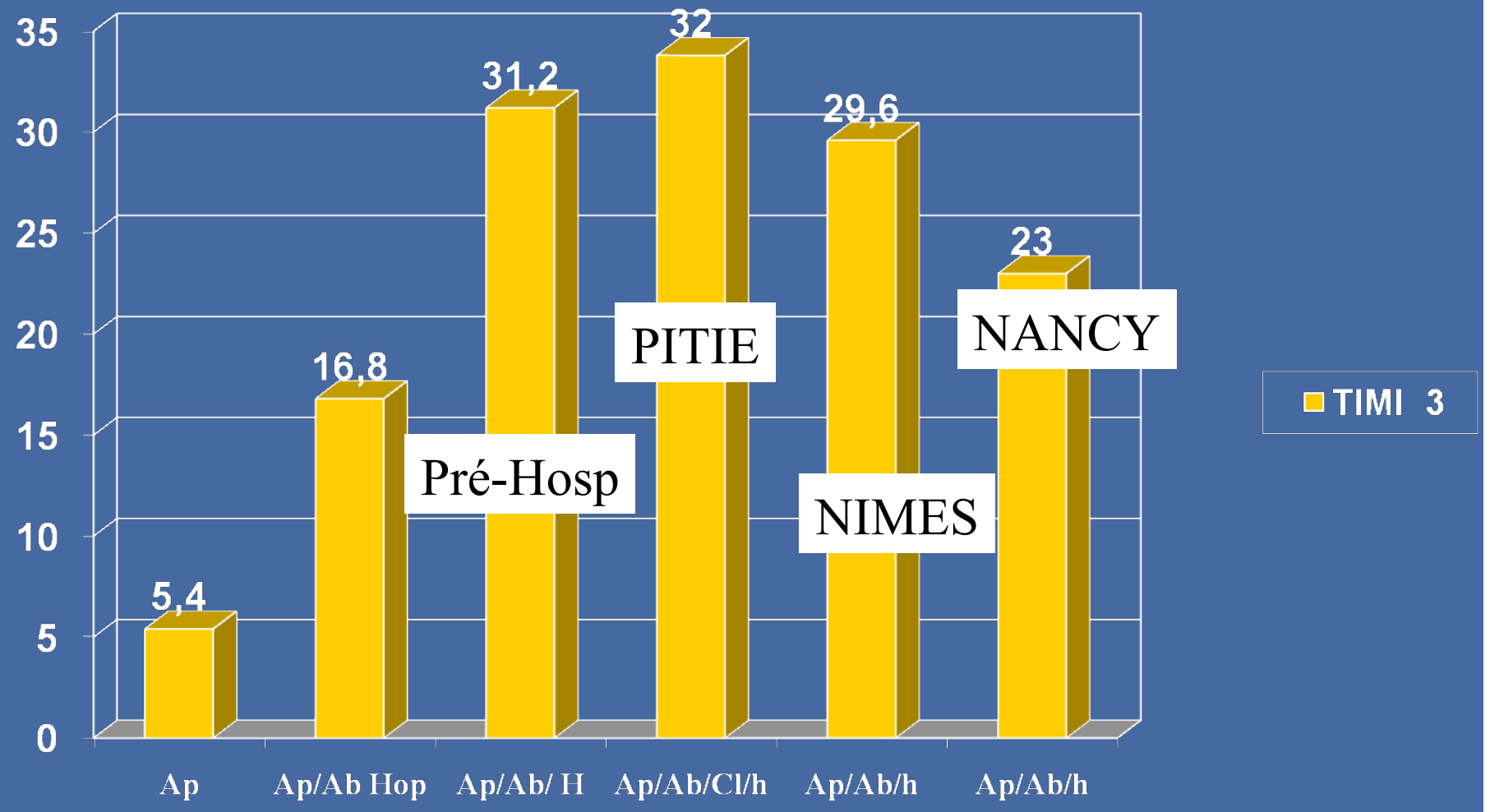
Circulation. 2010;122:1056-1067



Registre RIPOSTE n = 1244

Flux TIMI avant dilatation (%)

Ap = Aspirine Ab = Reopro Cl = Plavix



REGISTRE EFISMUR SMUR PITIE

Douleur-PEC = 122 mn

- 182 SCA ST+ depuis mars 2010
- 103 ont reçu 60 mg de Prasugrel en pré H
- 70 n'ont reçu que Prasugrel (TIMI 3 ap = 31,4%)
- 33 ont reçu Prasugrel + reopro (TIMI 3 ap = 48,4%)
- 4 ré infarctus, 2 revasc.
- 1 saignement digestif à 4 jours

SCA ST+ (prévu ATL) < 24 h

Aspirine 500 mg IV
HBPM 0.5 mg / kg IV

Risque hémorragique

ATCD AVC/AIT, Saignement, Chir dans le mois
TT AVK, Thrombopénie (< 50 000)

NON

Prasugrel 60 mg per os
(quelque soit le poids et l'âge et même si plavix)

Si < 3h et < 75 ans

- NON → KT
- OUI → Réopro → KT

OUI

Plavix
(dose en fonction du risque)

→ KT

P. Ecollan, G. Montalescot 02/2010

Conclusion

le pré traitement SCA SMUR

- Malheureusement peu d'étude nous permettent d'avoir des recommandations pour le pré hospitalier.
- Pour le SCA non ST le pré traitement de préparation

ASPIRINE IV + HBPM SC PAS de P2Y12 per os

- Pour le SCA ST+ le pré traitement de préparation

ASPIRINE IV + HBPM IV + P2Y12 +/- AgP2b3a

Importance des registres

CHAMPION PHOENIX – A Global Trial

12 Countries | 153 Sites

The NEW ENGLAND JOURNAL of MEDICINE

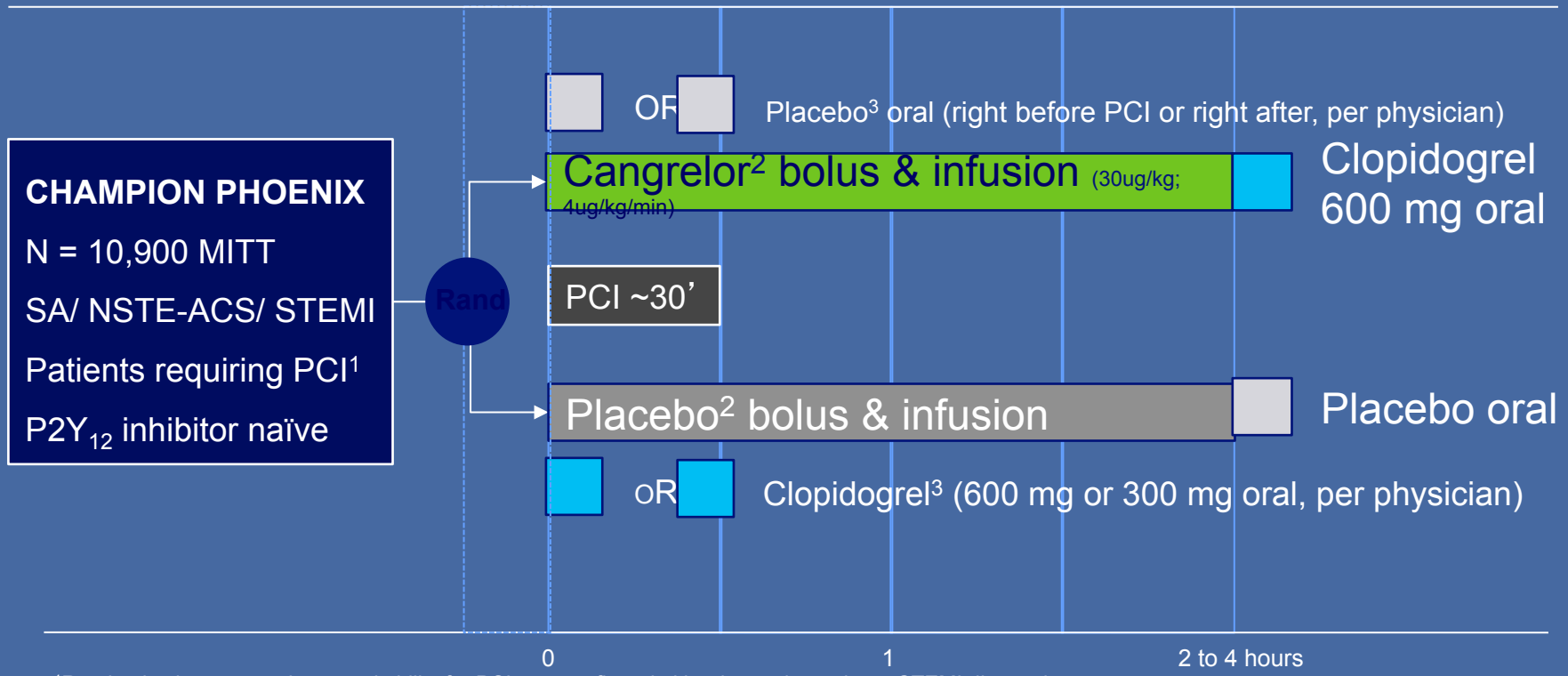
ORIGINAL ARTICLE

Effect of Platelet Inhibition with Cangrelor during PCI on Ischemic Events

Deepak L. Bhatt, M.D., M.P.H., Gregg W. Stone, M.D., Kenneth W. Mahaffey, M.D., C. Michael Gibson, M.D., P. Gabriel Steg, M.D., Christian W. Hamm, M.D., Matthew J. Price, M.D., Sergio Leonardi, M.D., Dianne Gallup, M.S., Ezio Bramucci, M.D., Peter W. Radke, M.D., Petr Widimský, M.D., D.Sc., Frantisek Tousek, M.D., Jeffrey Tauth, M.D., Douglas Spriggs, M.D., Brent T. McLaurin, M.D., Dominick J. Angiolillo, M.D., Ph.D., Philippe Généreux, M.D., Tiepu Liu, M.D., Ph.D., Jayne Prats, Ph.D., Meredith Todd, B.Sc., Simona Skerjanec, Pharm.D., Harvey D. White, D.Sc., and Robert A. Harrington, M.D., for the CHAMPION PHOENIX Investigators*

Bhatt DL, Stone GW, Mahaffey KW, et al…. Harrington RA. NEJM 2013 at www.nejm.org

CHAMPION PHOENIX Study Design



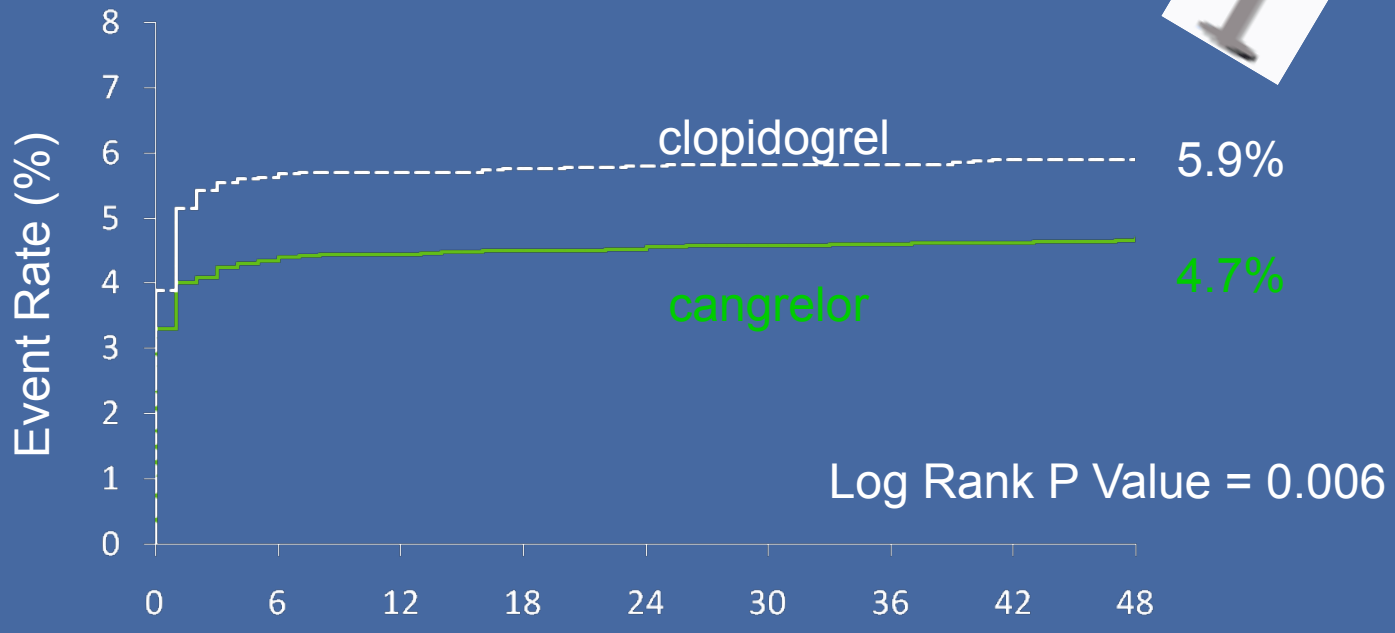
[1]Randomization occurred once suitability for PCI was confirmed either by angiography or STEMI diagnosis. Double blind study medication was administered as soon as possible following randomization.

[2]Study drug Infusion (cangrelor or matching placebo) was continued for 2-4 hours at the discretion of the treating physician. At the end of the infusion patients received a loading dose of clopidogrel or matching placebo and were transitioned to maintenance clopidogrel therapy.

[3]Clopidogrel loading dose (or matching placebo) was administered as directed by the investigator. At the time of patient randomization, a clopidogrel loading dose of 600 mg or 300 mg was specified by the investigator.

MITT=modified intent-to-treat; NSTE-ACS=non-ST-elevation acute coronary syndrome; PCI=percutaneous coronary intervention; SA=stable angina; STEMI=ST-elevation MI.

Death/ MI/ IDR/ Stent Thrombosis within 48 Hours



Patient at Risk									
Cangrelor:	5472	5233	5229	5225	5223	5221	5220	5217	5213
Clopidogrel:	5470	5162	5159	5155	5152	5151	5151	5147	5147

Bhatt DL, Stone GW, Mahaffey KW, et al…. Harrington RA. NEJM 2013 at www.nejm.org