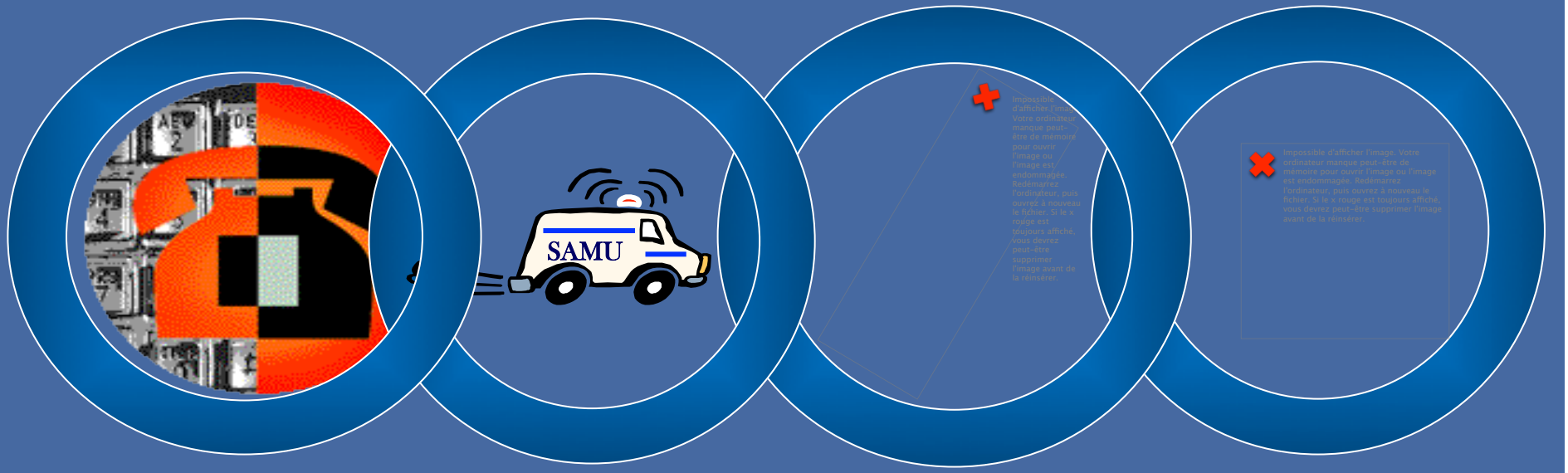
APPAC

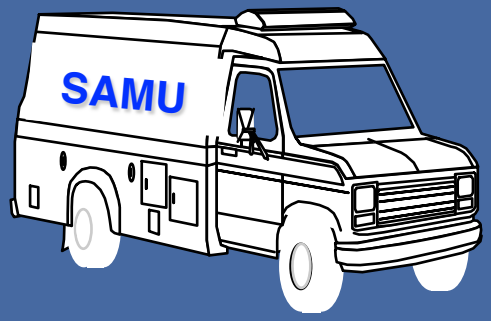
2012

Un pré-traitement dans le SCA : est-ce utile?



Patrick Ecollan
DAR-SMUR Pitié-Salpêtrière
SAMU de PARIS

Le traitement SAMU dans le SCA



THR 1985

Boersma

THR preH

Gusto IV

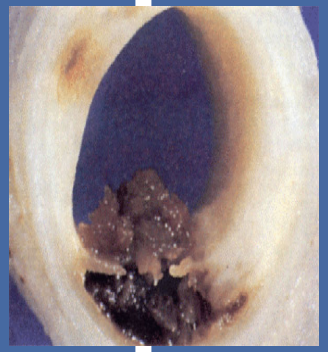
THR preH ou/et PCI

Captim

Si < 2h THR preH = PCI

Assent IV

THR preH ou PCI



2012

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

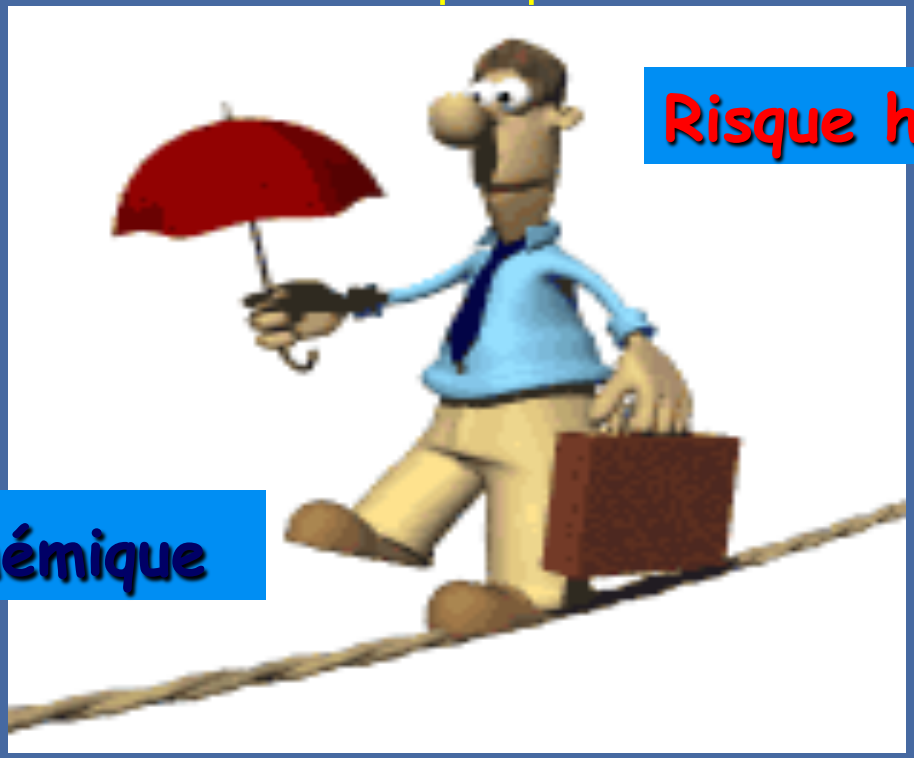
Isis 2
Delucas
Admiral
Create
Commit
Ex Timi 25
Finesse
On Time 2
Triton Timi 38
Atoll……..

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

pré-traitement dans le SCA non ST+

P2 Y12 ?

ESC Guidelines for the Management of NSTE-ACS

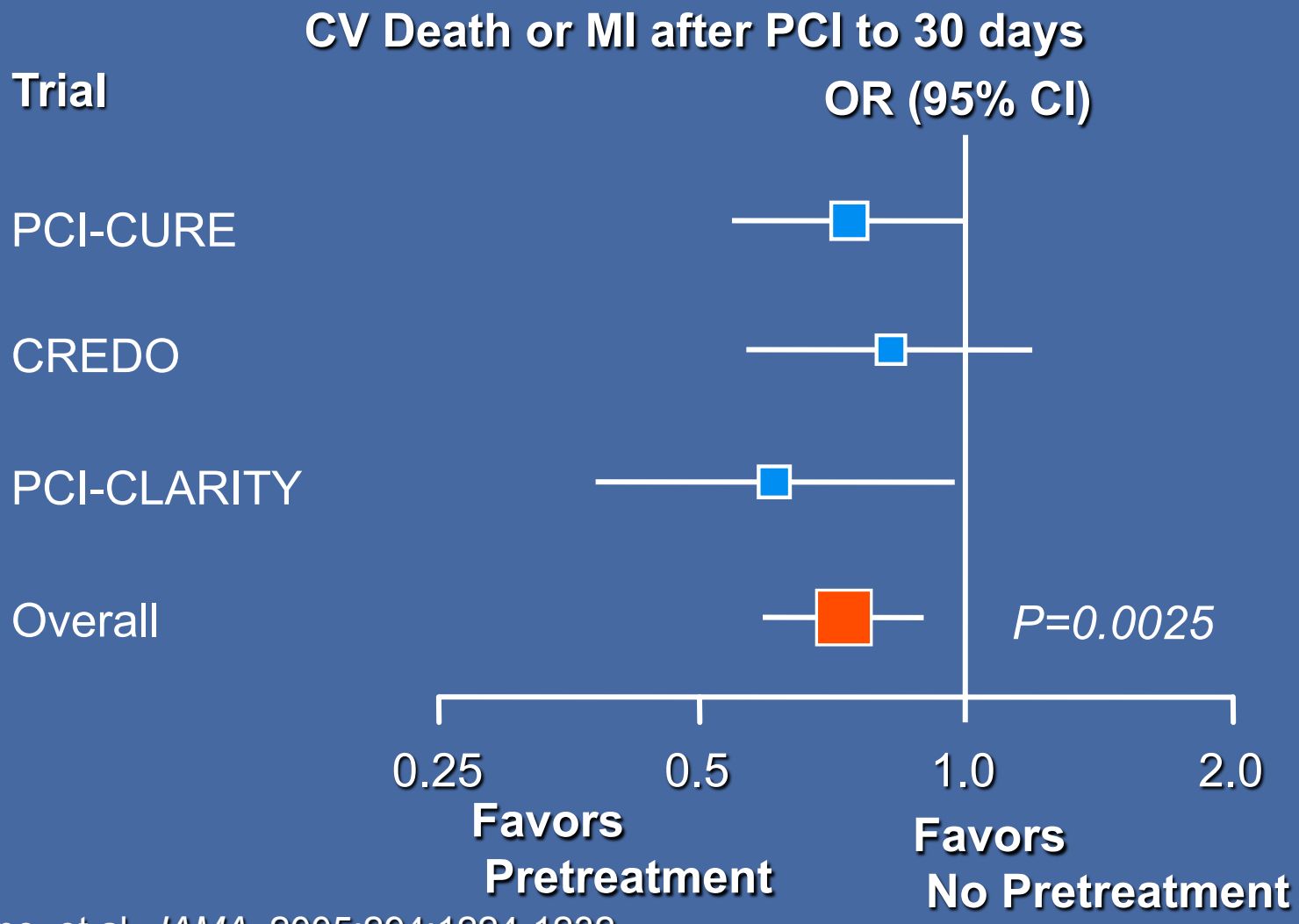
ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction

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

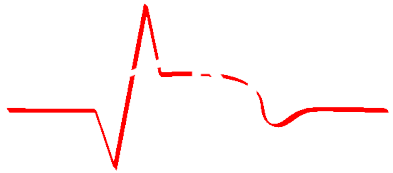
Eur Heart J. 2011 Dec;32(23):2999-3054

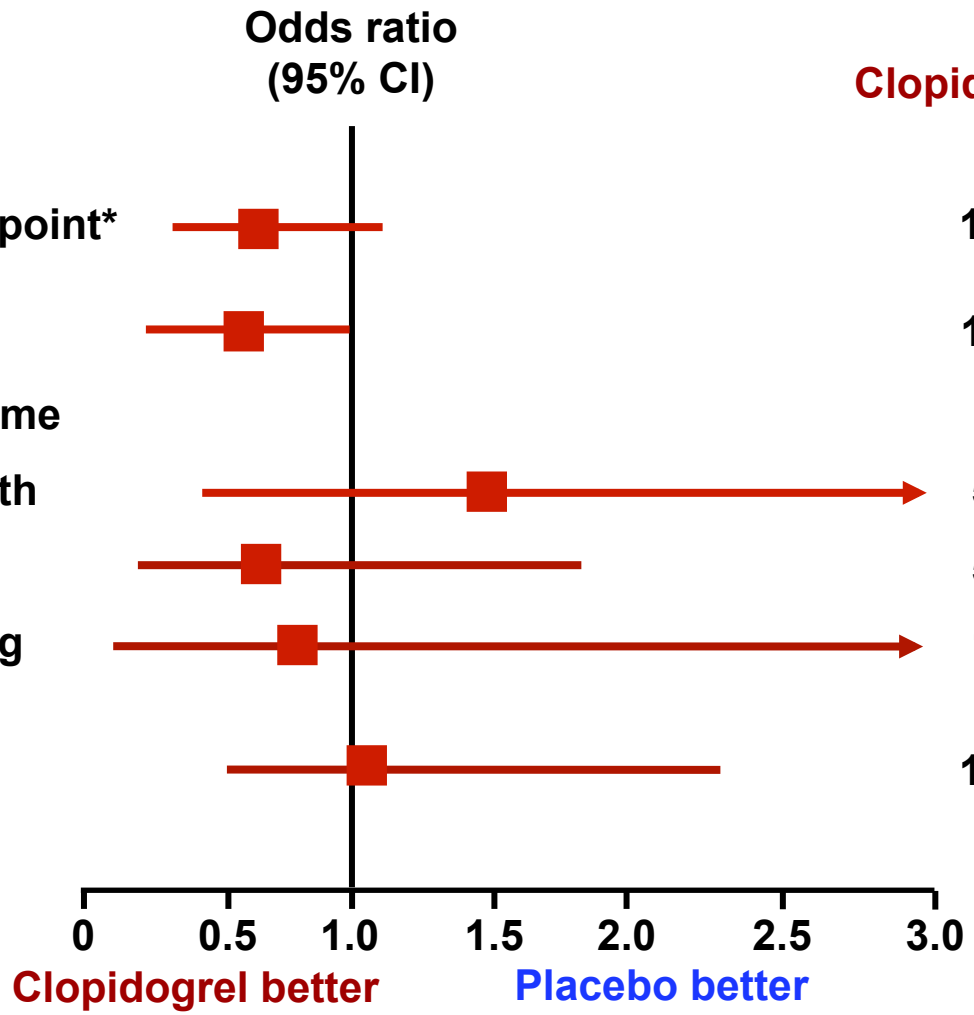
PCI Pre-Treatment (With 300mg load) → Events



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

Primary Outcome Parameters:
Ambulance Subgroup

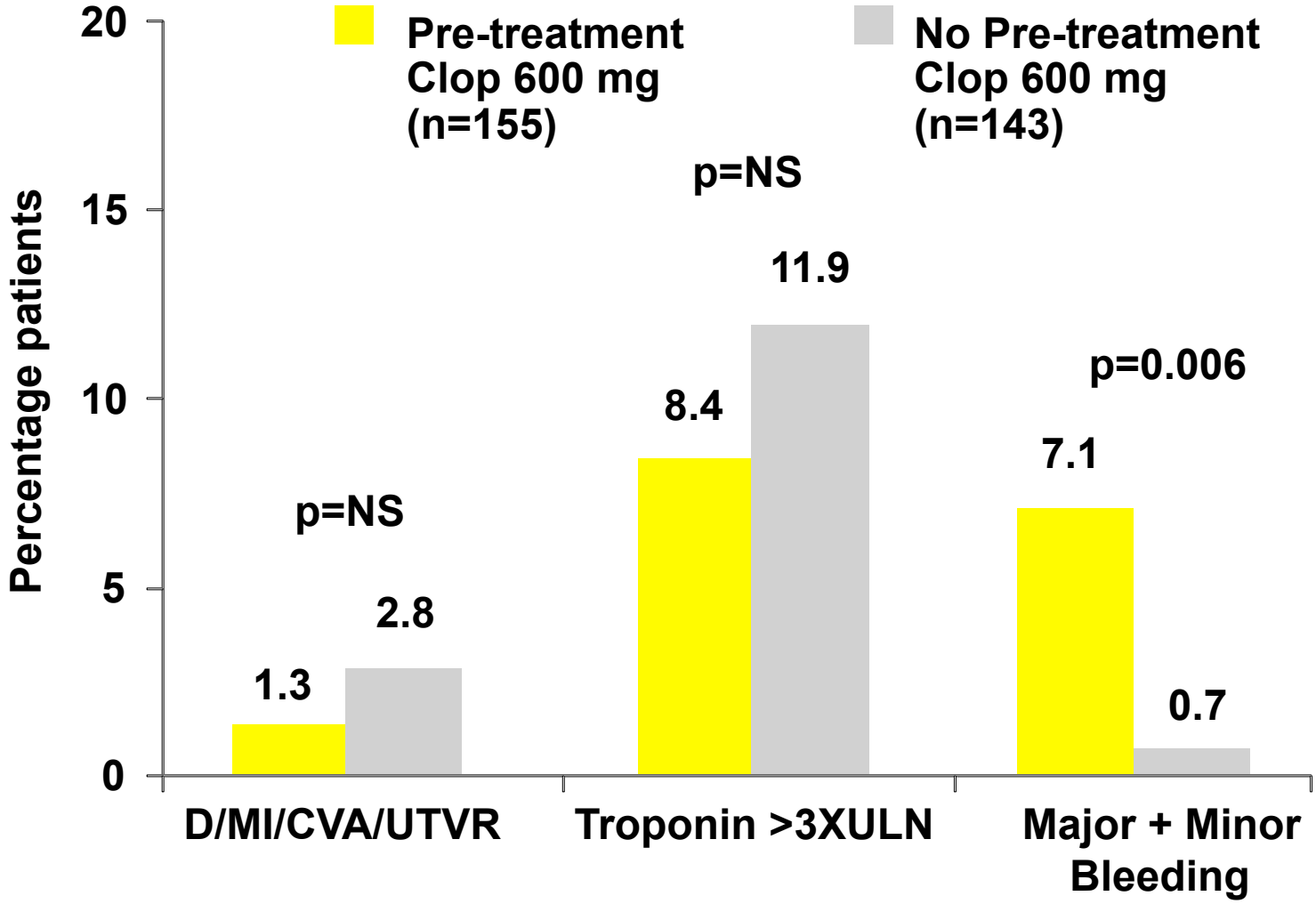




	Clopidogrel		p value
Primary efficacy endpoint*	16.5	27.1	0.06
TFG 0/1	11.8	22.3	0.05
30-day clinical outcome			
Cardiovascular death	5.5	3.7	NS
Re-MI	5.5	9.3	NS
Re-ischaemia urging revascularization	1.8	2.8	NS
Overall	12.8	14.0	NS

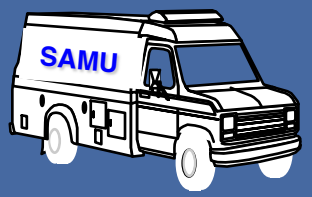
**Occluded infarct artery (TFG 0/1) + death + re-MI prior to angiography*

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

NSTEMI / Troponin +, n~4100+ (event driven)
clopidogrel naive or long-term 75 mg

Plan Angio/PCI >2 h and <24 h

Randomise

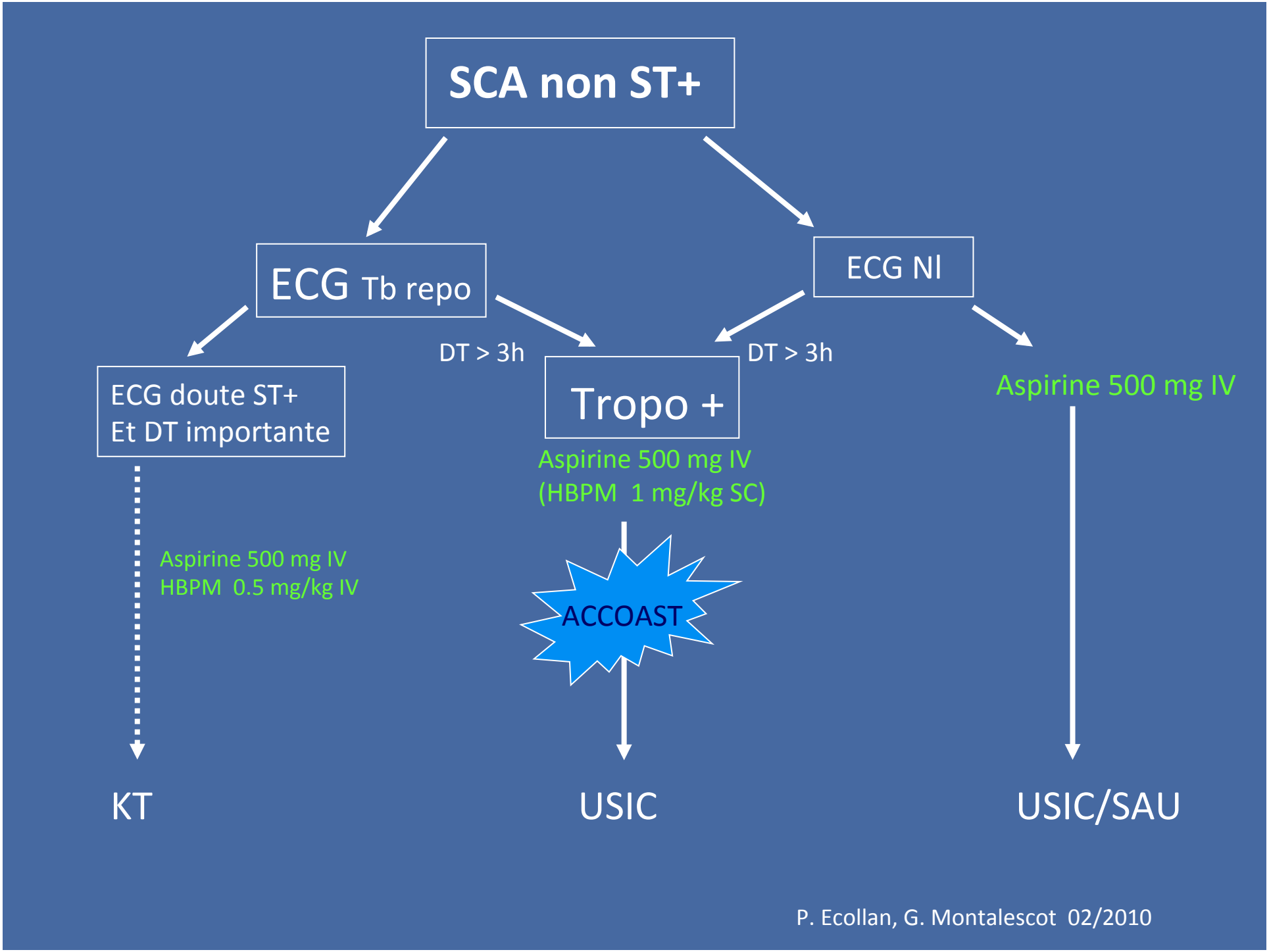
Pras 30 → **Angio** → **PCI** → **Pras 30**

Inactive → **Angio** → **PCI** → **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 500 mg IV
Aspirine 500 mg IV
(HBPM 1 mg/kg SC)
Aspirine 500 mg IV
HBPM 0.5 mg/kg IV
ACCOAST
KT
USIC
USIC/SAU
P. Ecollan, G. Montalescot 02/2010

Avec le partenariat méthodologique et le soutien financier de la Haute Autorité de santé

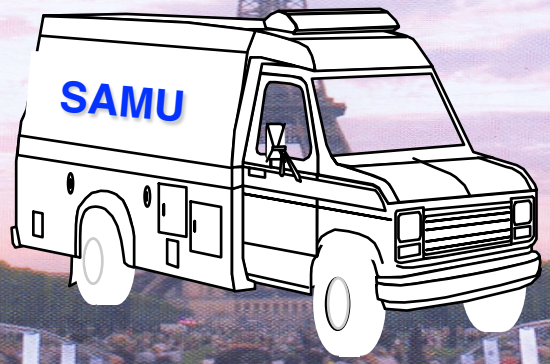
Conférence de consensus

Prise en charge de l'infarctus du myocarde à la phase aiguë en dehors des services de cardiologie

ORGANISÉE PAR
SAMU de France
Société Francophone de Médecine d'Urgence
Société Française de Cardiologie

23 Novembre
PARIS 2006

Amphithéâtre Farabeuf
Faculté de Médecine
15, rue de l'Ecole de Médecine - 75006 Paris



N° FMC 93 13 09 625 13

Société Française de Cardiologie
FMU
SAMU de France
HAS Haute Autorité de Santé

HAS SFC/ SDF/SFUM recommendations 2007

Traitement adjuvant pré hospitalier
SCA ST +

- Quelle que soit la stratégie choisie

  Aspirine 500 mg (160 mg à 500 mg)

- Avec la Thrombolyse pré hospitalière

  Clopidogrel 300 mg per-os

  HBPM bolus de 30 mg/kg IV+1mg/kg SC si < 75 ans

  HNF 60 UI / kg IV (<4000) si > 75 ans, Ins. Rén., risque Hém.

- Avant l'Angioplastie

  Clopidogrel 300 mg per-os (600 à 900 mg)per-os

  HNF ou HBPM IV fonction des habitudes des services

  (HNF 60 UI/kg ou HBPM 0,5 mg/kg)

  Abciximab bolus 0,25 mg/kg IV

  et perfusion continue de 0,125µ/kg/min

En 2012

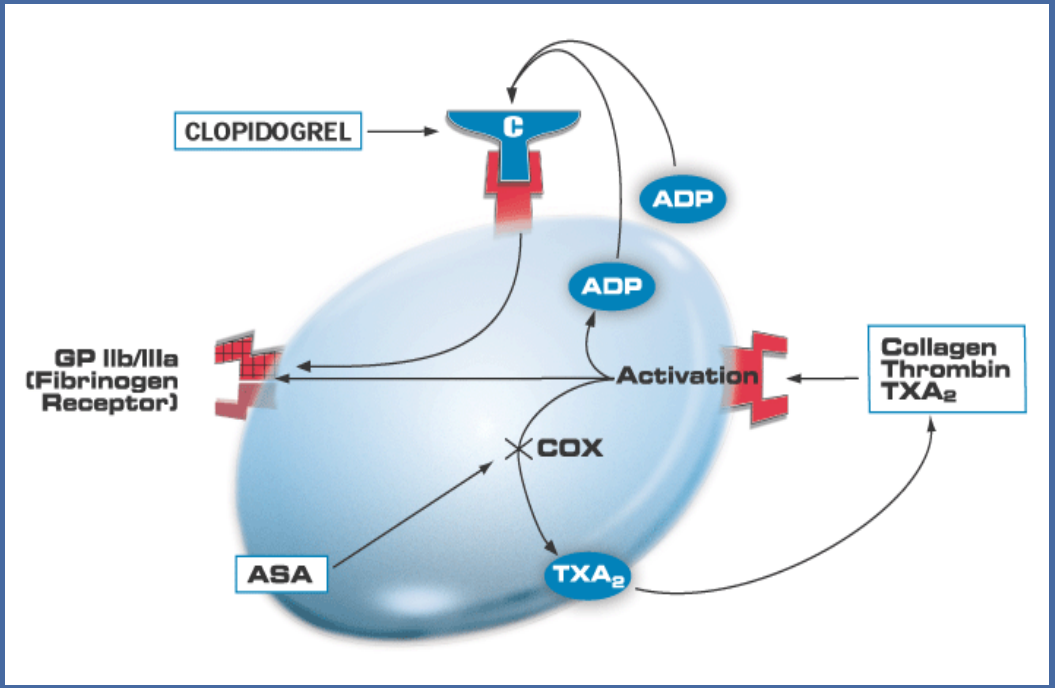
SCA ST+ dirigé vers salle de KT

Traitement préhospitalier ?

En France qui fait quoi ?

- Aspirine + Hép/HBPM+ Plavix (300/600/900) ?
- Aspirine + Hép/HBPM+ Plavix + Réopro ?
- Aspirine + Hép/HBPM+ Prasugrel 60 mg + Réopro?
- Aspirine + Hép/HBPM+ Prasugrel 60 mg + autre AGP 2b3a ?
- Aspirine + Hép/HBPM+ Prasugrel 60 mg seulement ?
- Aspirine + Hép/HBPM+ Réopro seulement ?

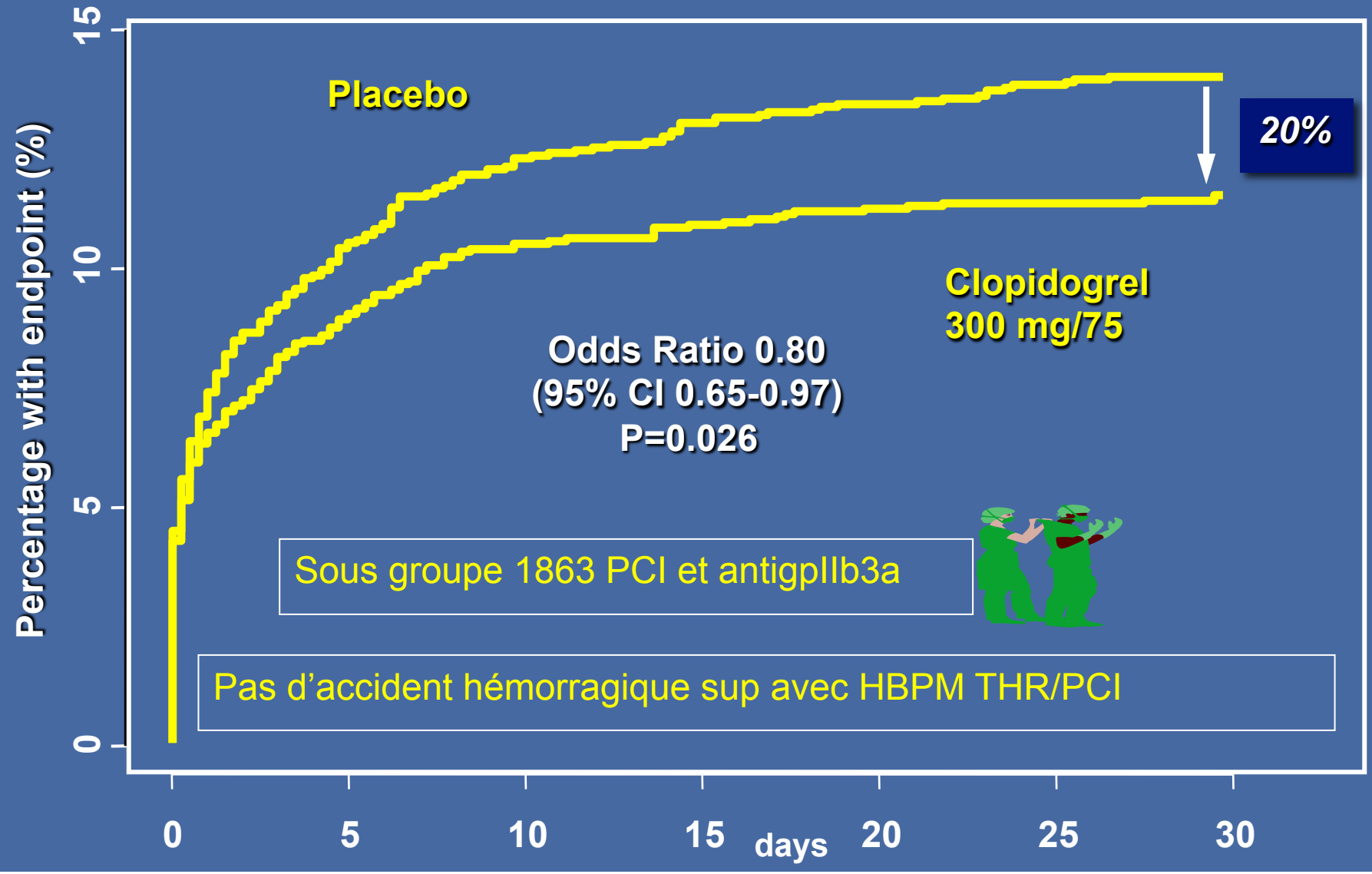
Les antiagrégants plaquettaires



CLARITY TIMI 28

Sabatine MS et al. *New Engl J Med* 2005;352:1179-89

3491 IDM/ TH (ASA+ UFH)
1 mois : CV Death, MI, RI → Urg Revasc



TRITON-TIMI 38 : Schéma de l'étude

SCA (STEMI ou AI/NSTEMI) avec angioplastie programmée

Aspirine **N = 13 608**

Double aveugle

CLOPIDOGREL
dose de charge **300 mg**
dose d'entretien **75 mg**

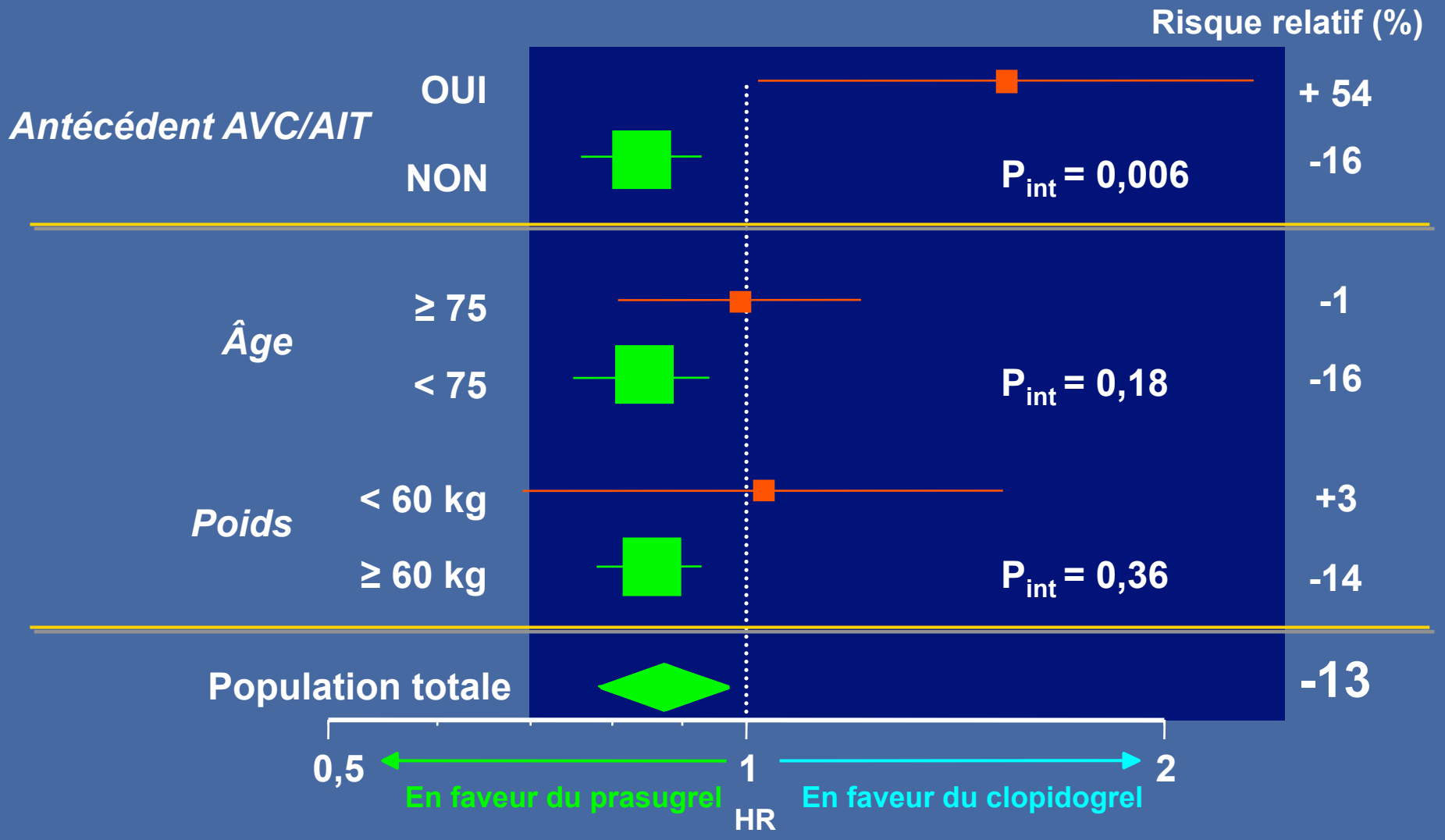
PRASUGREL
dose de charge **60 mg**
dose d'entretien **10 mg**

Durée moyenne du traitement : 12 mois (6-15 mois)
Durée médiane du traitement : 14,5 mois

Critère principal d'efficacité : Décès CV, IDM, AVC non fatals
Critère principal de tolérance : Saignements majeurs TIMI

Wiviott et al. *N Engl J Med* 2007;357:2001-2015

TRITON-TIMI 38 : Bénéfice clinique net
Sous-groupes à risque de saignements



Analyse post-hoc

Adapté d'après Wiviott et al. *N Engl J Med* 2007;357:2001-2015

Efient et STEMI: oui mais quand ?

En SMUR ? Pour QUI ?

- STEMI et Diabétique
- Groupe STEMI de TRITON: Prasugrel avant coro
- Rapidité action primordiale dans STEMI
- Délai action Prasugrel 30-40 min

  → le plus tôt possible

Montalescot et al, Lancet 2009

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

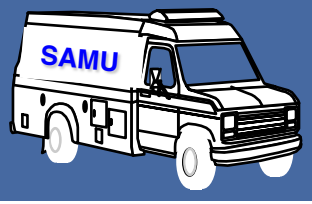
1. A loading dose of thienopyridine is recommended for STEMI patients for whom PCI is planned. Regimens should be 1 of the following:
   a. At least 300 to 600 mg of clopidogrel† should be given as early as possible before or at the time of primary or nonprimary PCI. (*Level of Evidence: C*)
   b. Prasugrel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

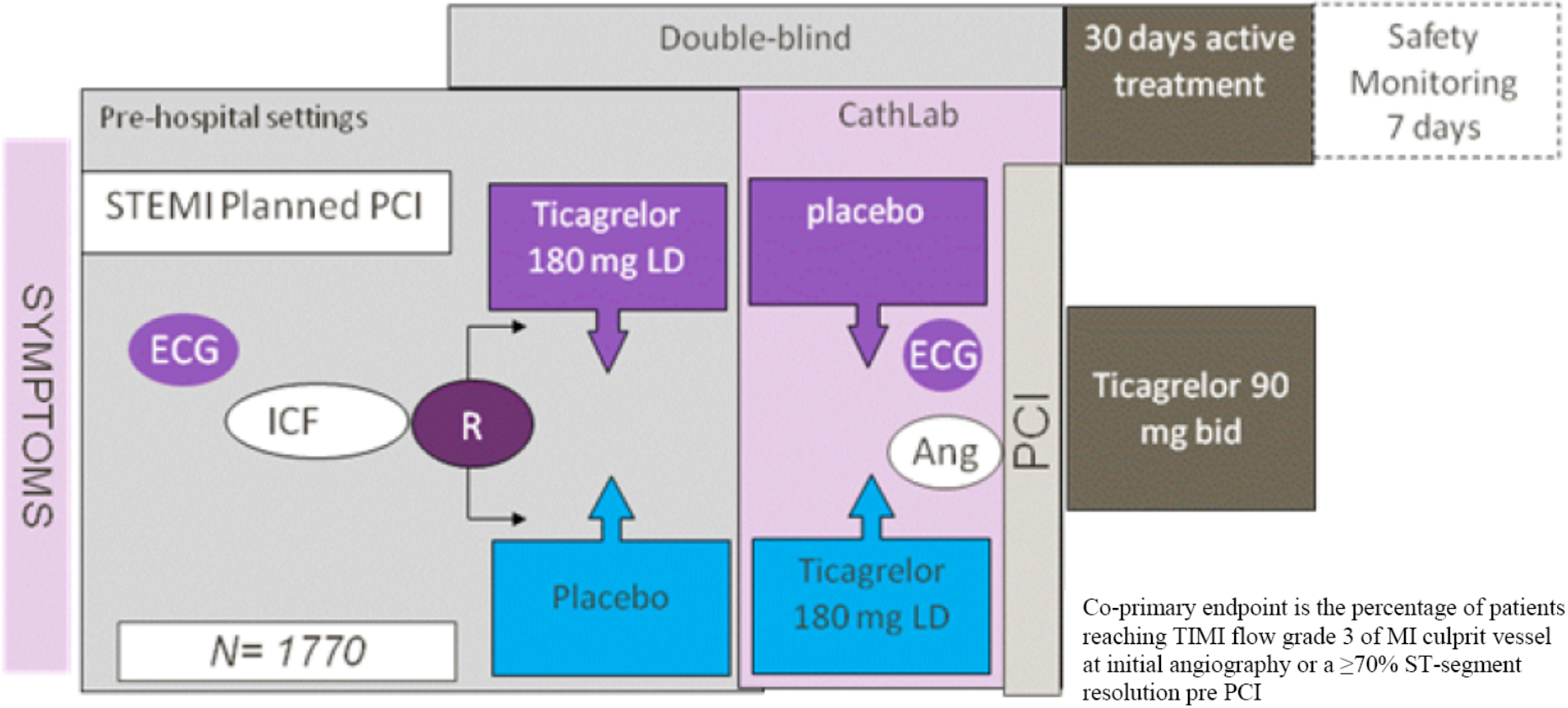
Class III

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

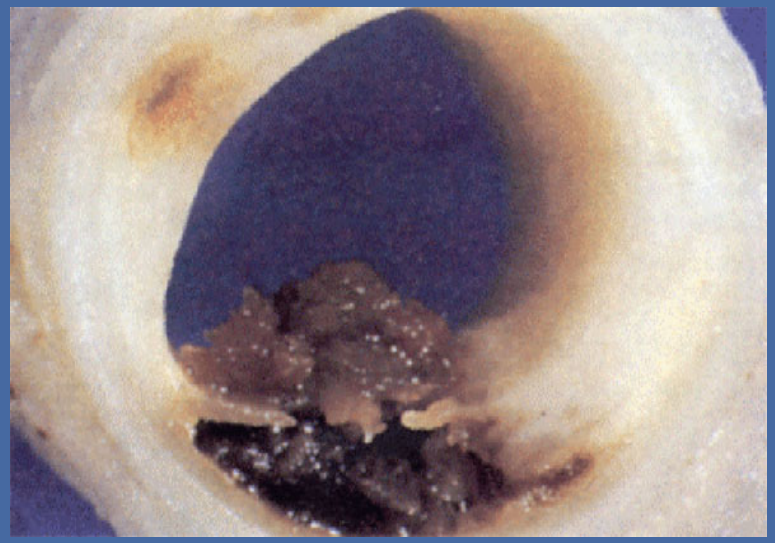
ATLANTIC: Pre-treatment in STEMI





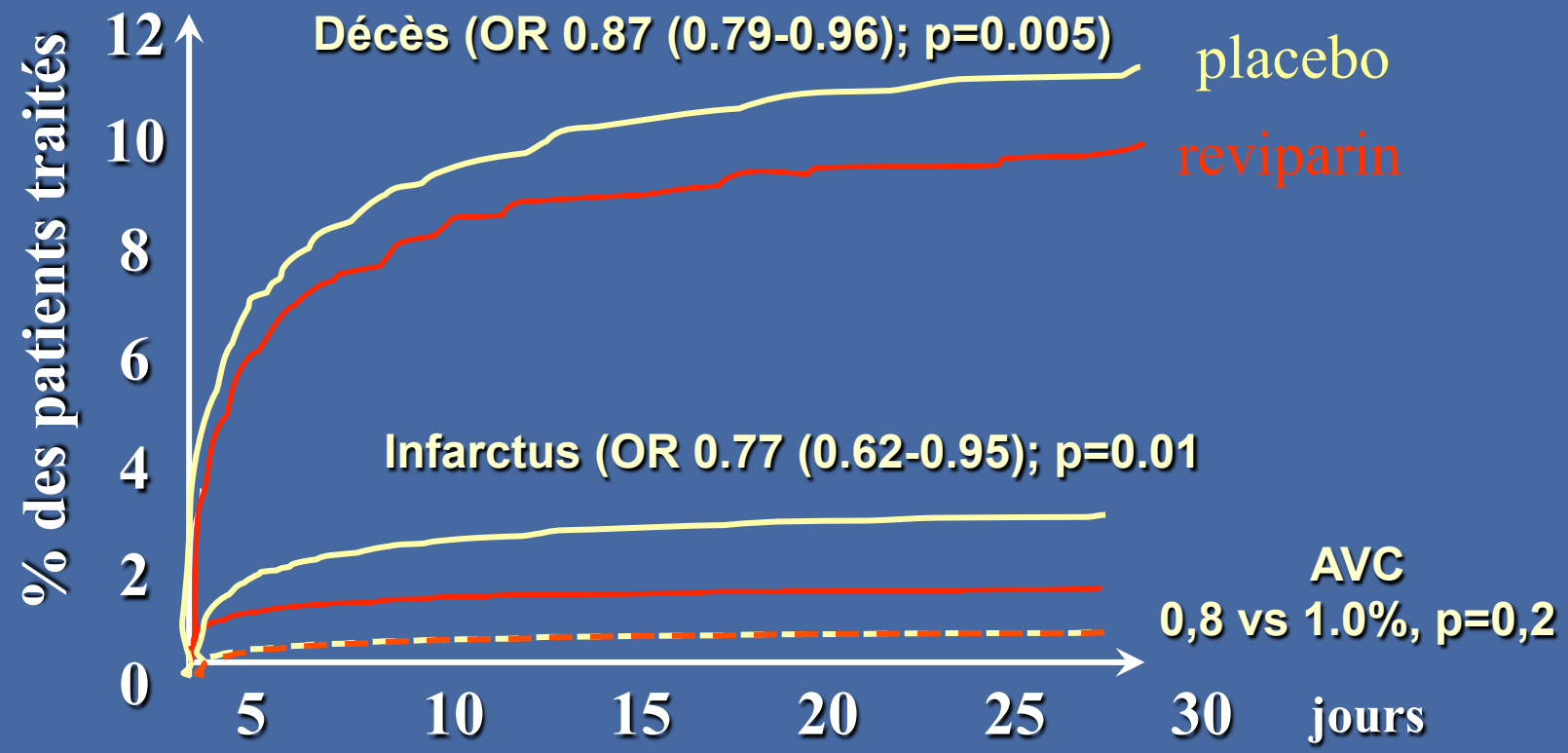
Co-primary endpoint is the percentage of patients reaching TIMI flow grade 3 of MI culprit vessel at initial angiography or a ≥70% ST-segment resolution pre PCI

Les Anticoagulants



Etude CREATE

15 570 patients admis pour STEMI (75% de thrombolyse 6%PCI) randomisés (ASA, clopi/2) pour recevoir du placebo ou l'HBPM reviparine à dose curative pendant 7 jours

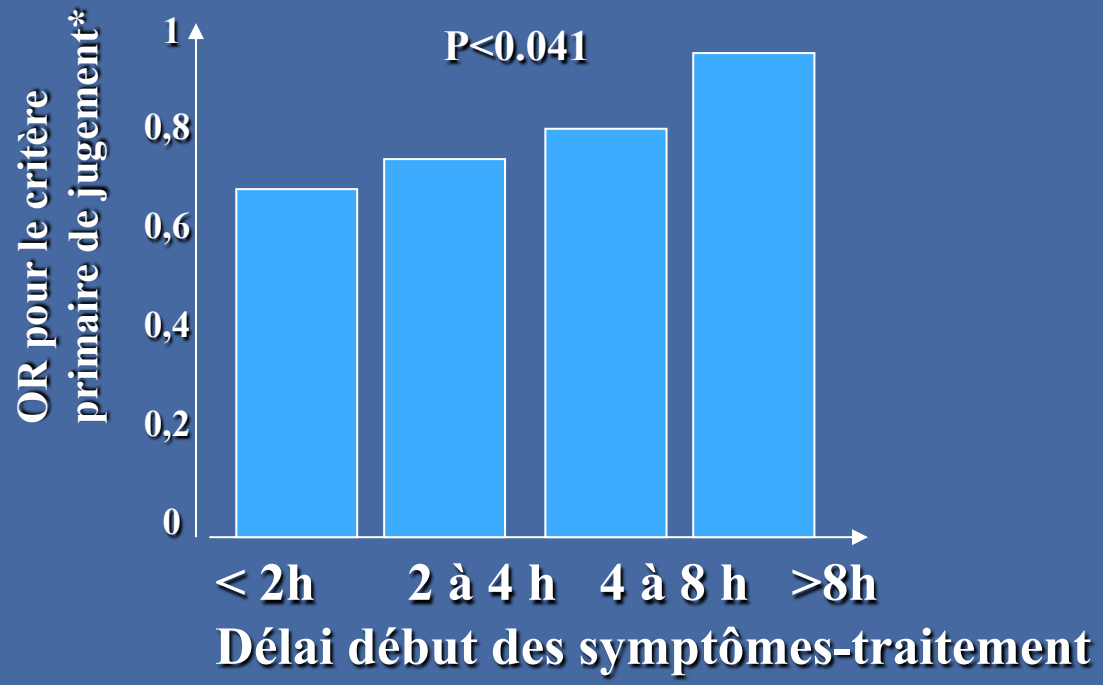


saignements mettant en jeu le pronostic vital (0.2% vs 0.1%, p=0.07)

JAMA. 2005;293:427-436

Étude CREATE

Un bénéfice temps dépendant

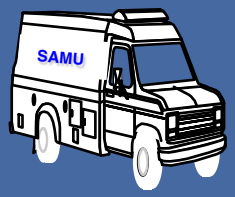


*critère primaired'évaluation (décès, IDM et AVC à J7)

6% des patients ont une PCI

JAMA. 2005;293:427-436

ATOLL Trial design



Randomization as *early* as possible (MICU +++)
Real life population (shock, cardiac arrest included)
No anticoagulation and no lytic **before** Rx
Similar antiplatelet therapy in both groups

STEMI → Primary PCI

ENOXAPARIN IV
0.5 mg/kg
with or without GPIIbIIIa

IVRS

UFH IV
50-70 IU with GP IIbIIIa
70-100IU without GP IIbIIIa
(Dose ACT-adjusted)

Primary PCI

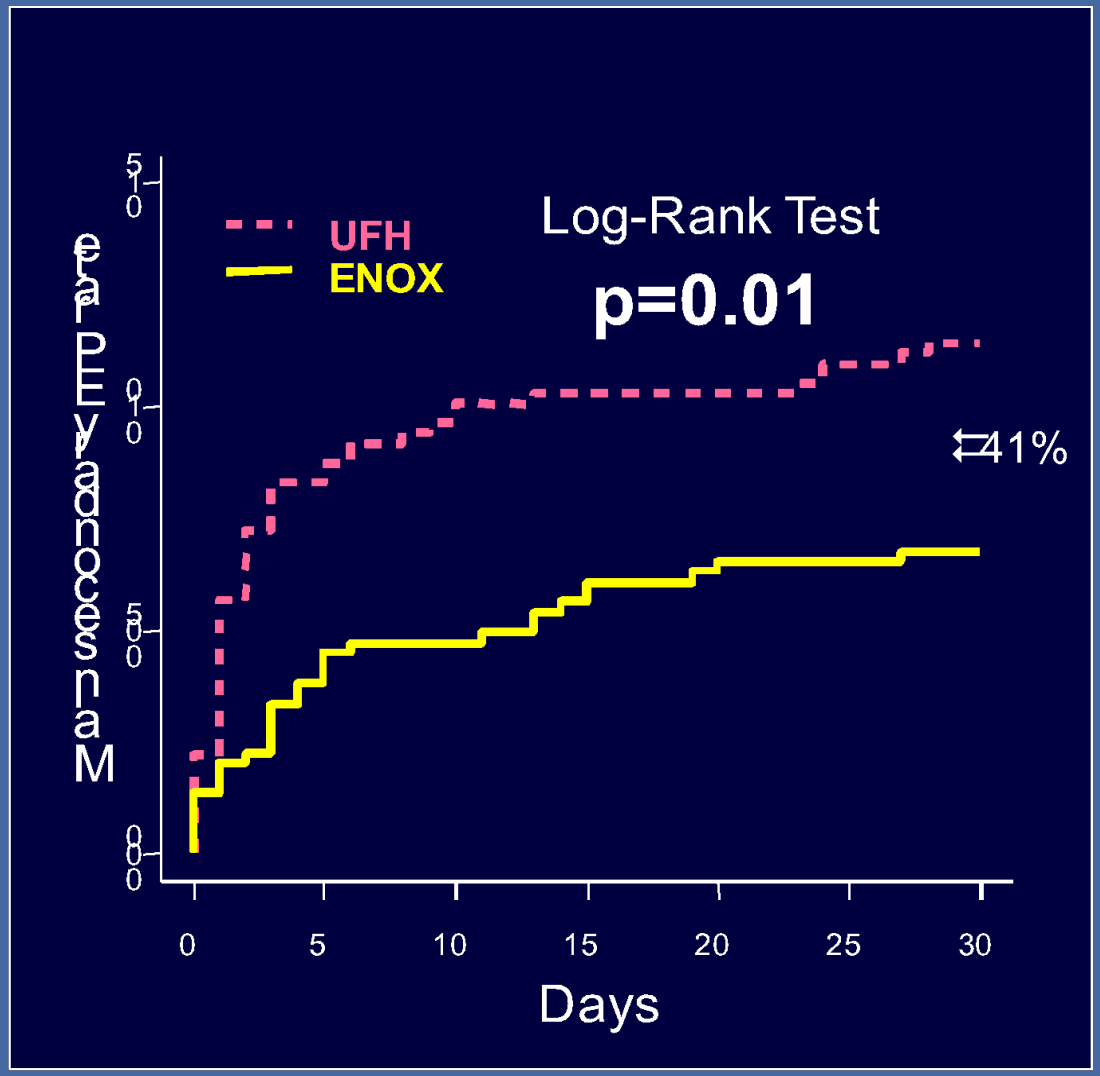
ENOXAPARIN SC

UFH IV or SC

30-day results

Ischemic Endpoint

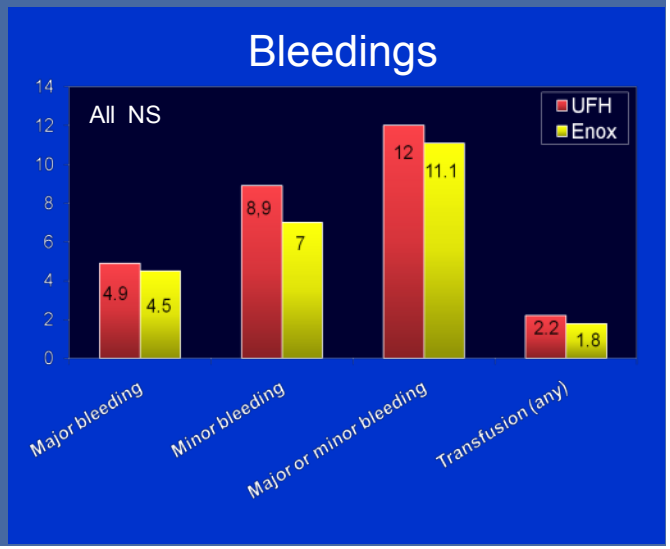
Death, Recurrent MI/ACS or Urgent Revasc



30d rate (%)

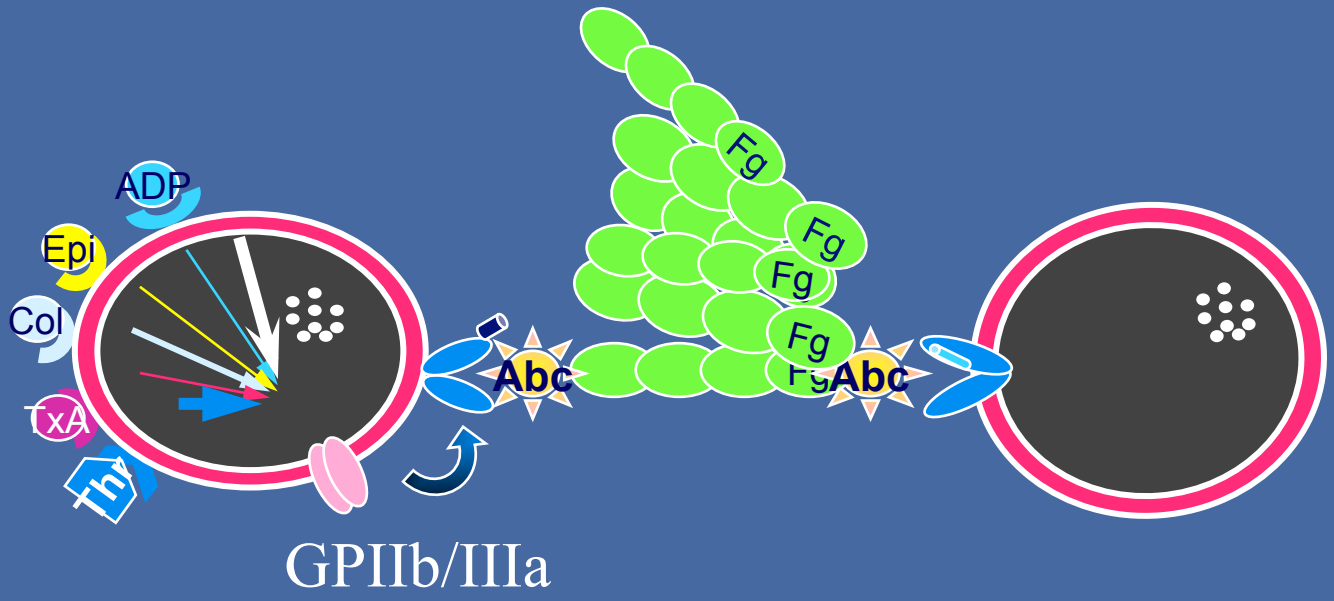
11.3%

6.7%



ATOLL Trial G. Montalescot et al Lancet 2011 aug20 378

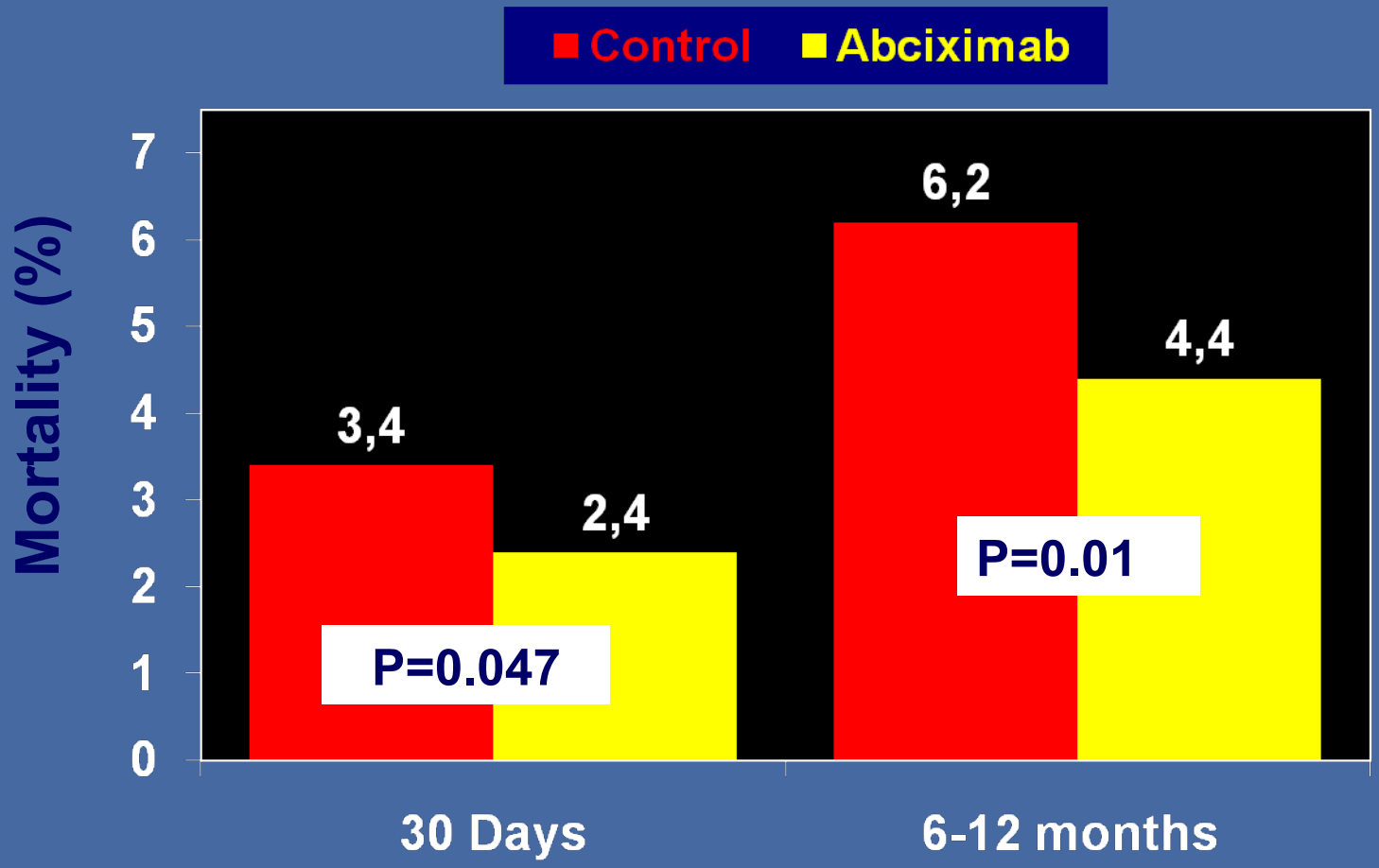
Les anti-GP IIb/IIIa



Meta-analysis de De Luca

Short and long term mortality

Meta-analysis primary angioplasty trials with abciximab (antiGP-IIb/IIIa)



Trials (N=3949)

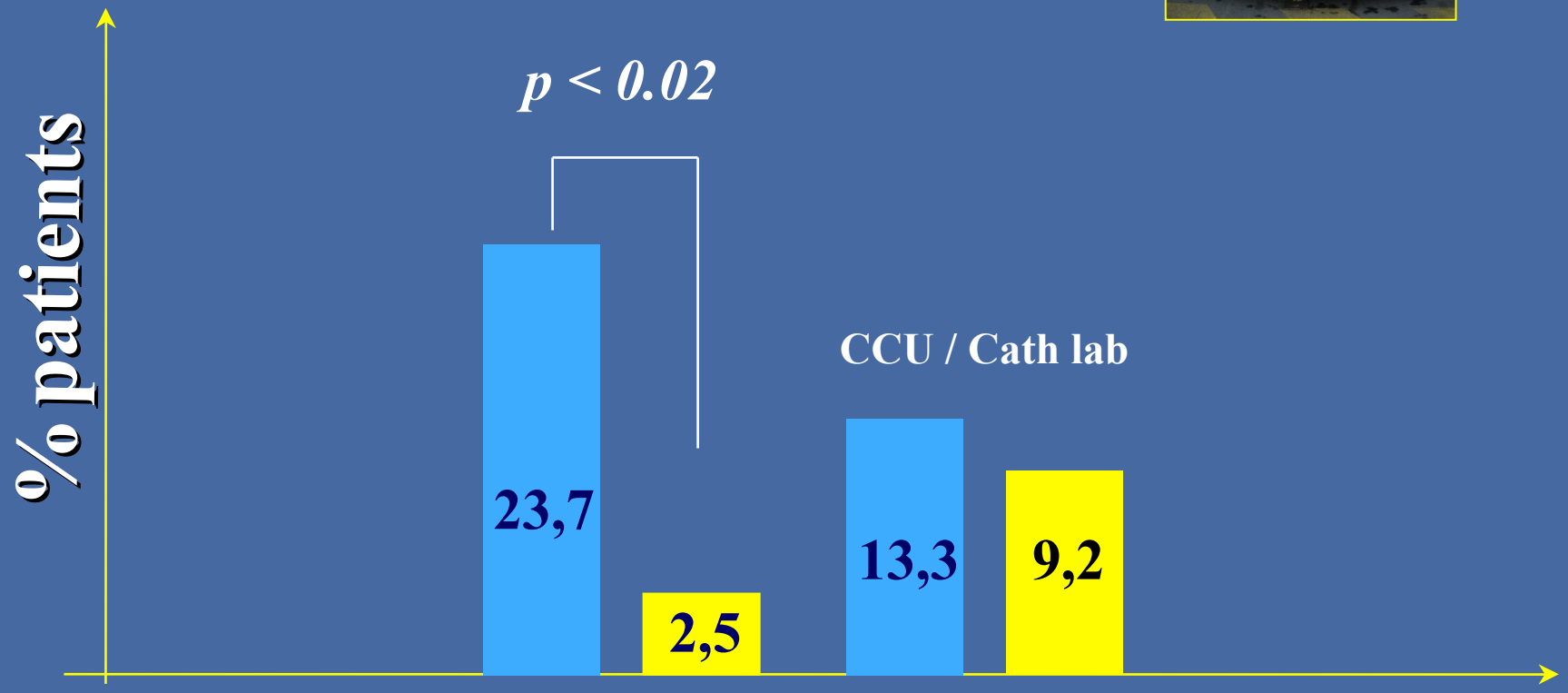
RAPPORT
ISAR-2
ADMIRAL
CADILLAC
Petronio et al (2002)
Zorman et al
ACE
Petronio et al (2003)

JAMA 2005; 293 (14): 1759-65.

ADMIRAL

PRIMARY ENDPOINT

Placebo
Abciximab

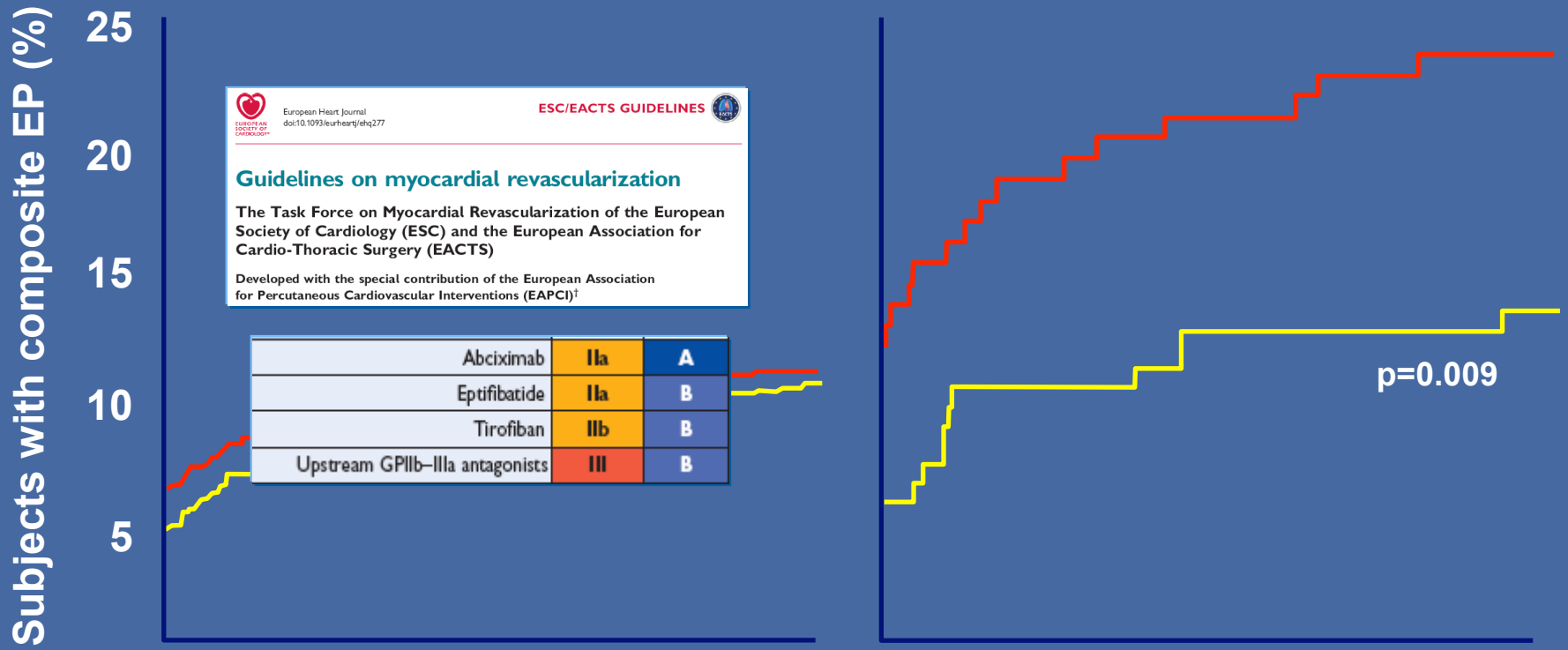


P Ecollan, G. Montalescot, JE De La Coussaye, J Vaque, PE Bollaert, P Barragan, P Pinton on behalf of the MICU Investigators of the ADMIRAL study NEJM 2001

FINESSE: Early vs. late → primary EP at 90d

All patients (N=2452)

Spoke site, TIMI score ≥3 and Sx to RAND ≤4h (N=397)



European Heart Journal doi:10.1093/eurheartj/ehq277

ESC/EACTS GUIDELINES

Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

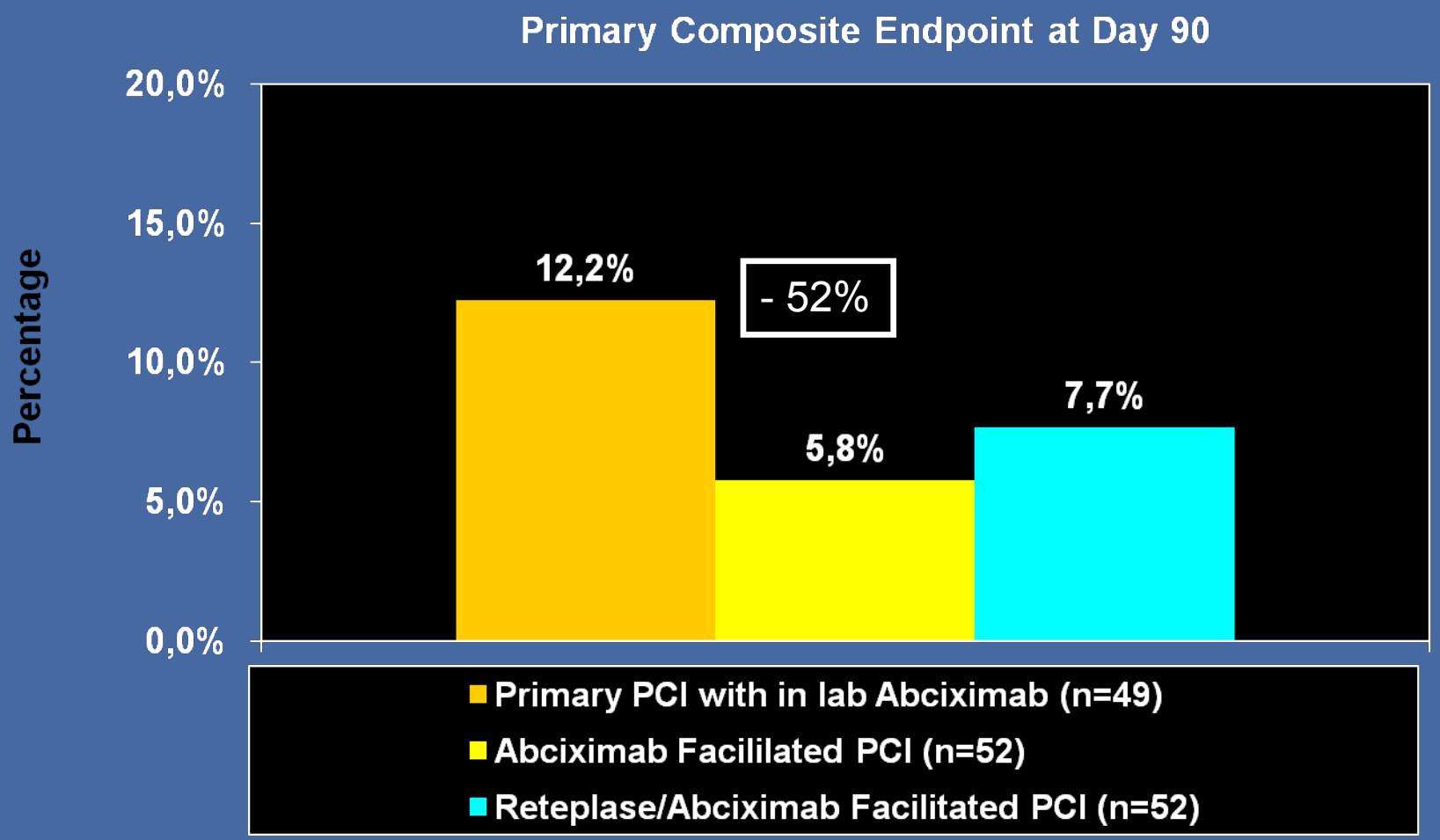
Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)†

Abciximab	IIa	A
Eptifibatide	IIa	B
Tirofiban	IIb	B
Upstream GPIIb–IIIa antagonists	III	B

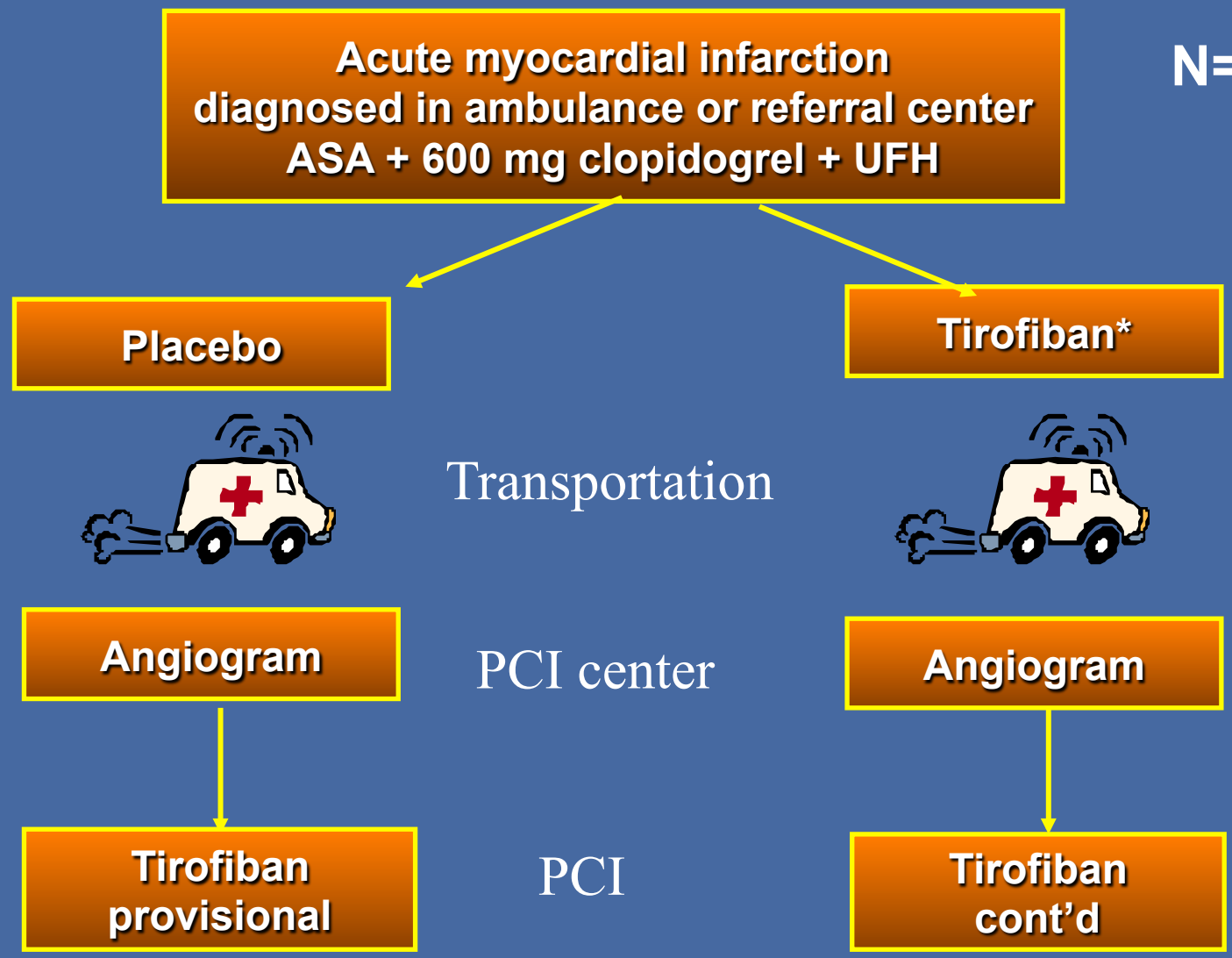
Ellis. *N Engl J Med* 2008;358:2205–17

Herrman H, et al. JACC CI 2009

France: Primary Endpoint



ON-TIME 2



**Bolus: 25 µg/kg and 0.15 µg/kg/min infusion*

Résultats à 30 jours

	Placebo (%)	Tirofiban (%)	p-value
DC/reIDM/rev Ur	8,6	5,8	0.043
DC	4,1	2,2	0.051
AVC	1,4	0,3	0,031
Événement clin.	11.6	8,0	0,024

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

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

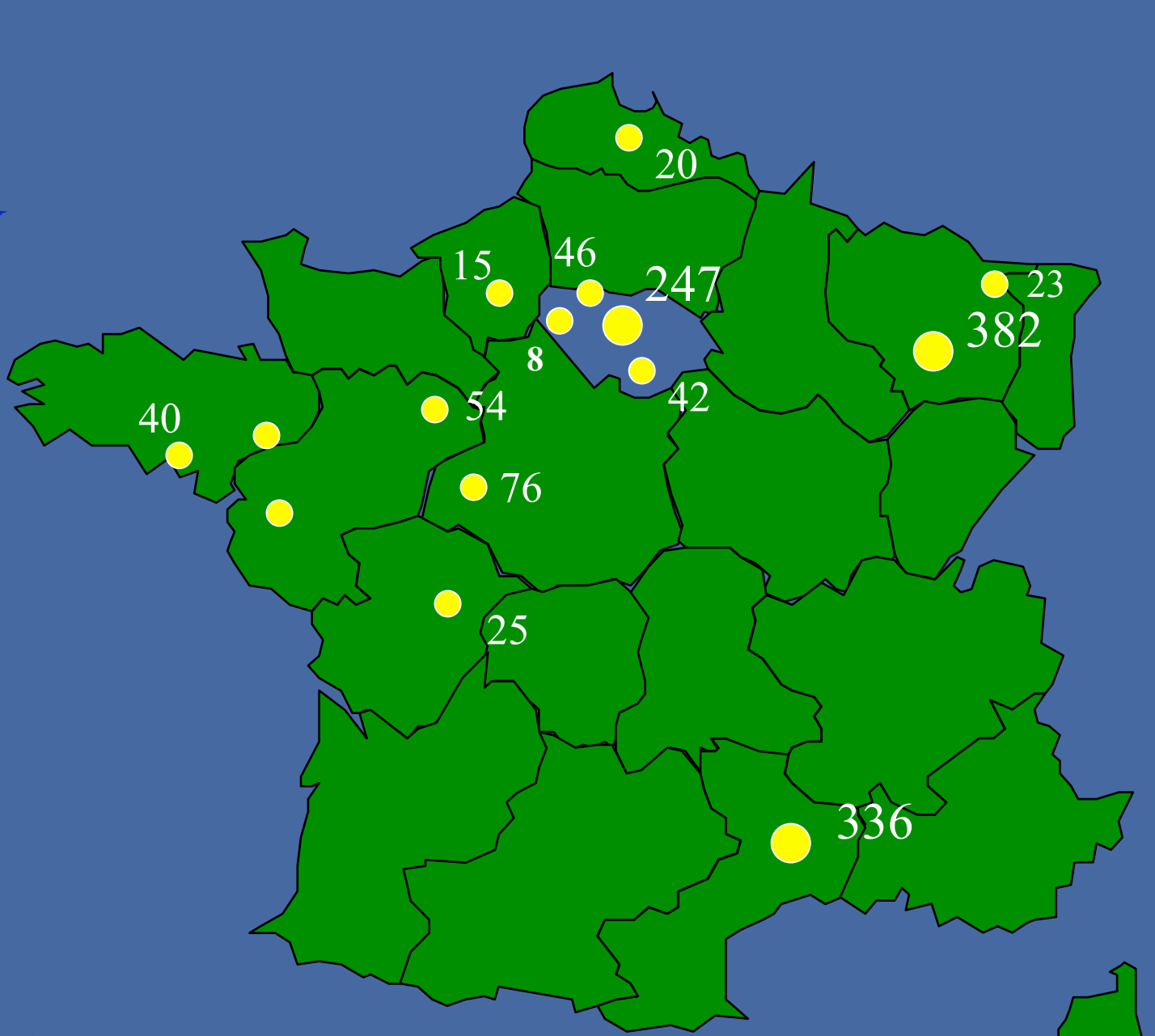
- NON → KT
- OUI → Réopro → KT

OUI

Plavix
(dose en fonction du risque)

→ KT

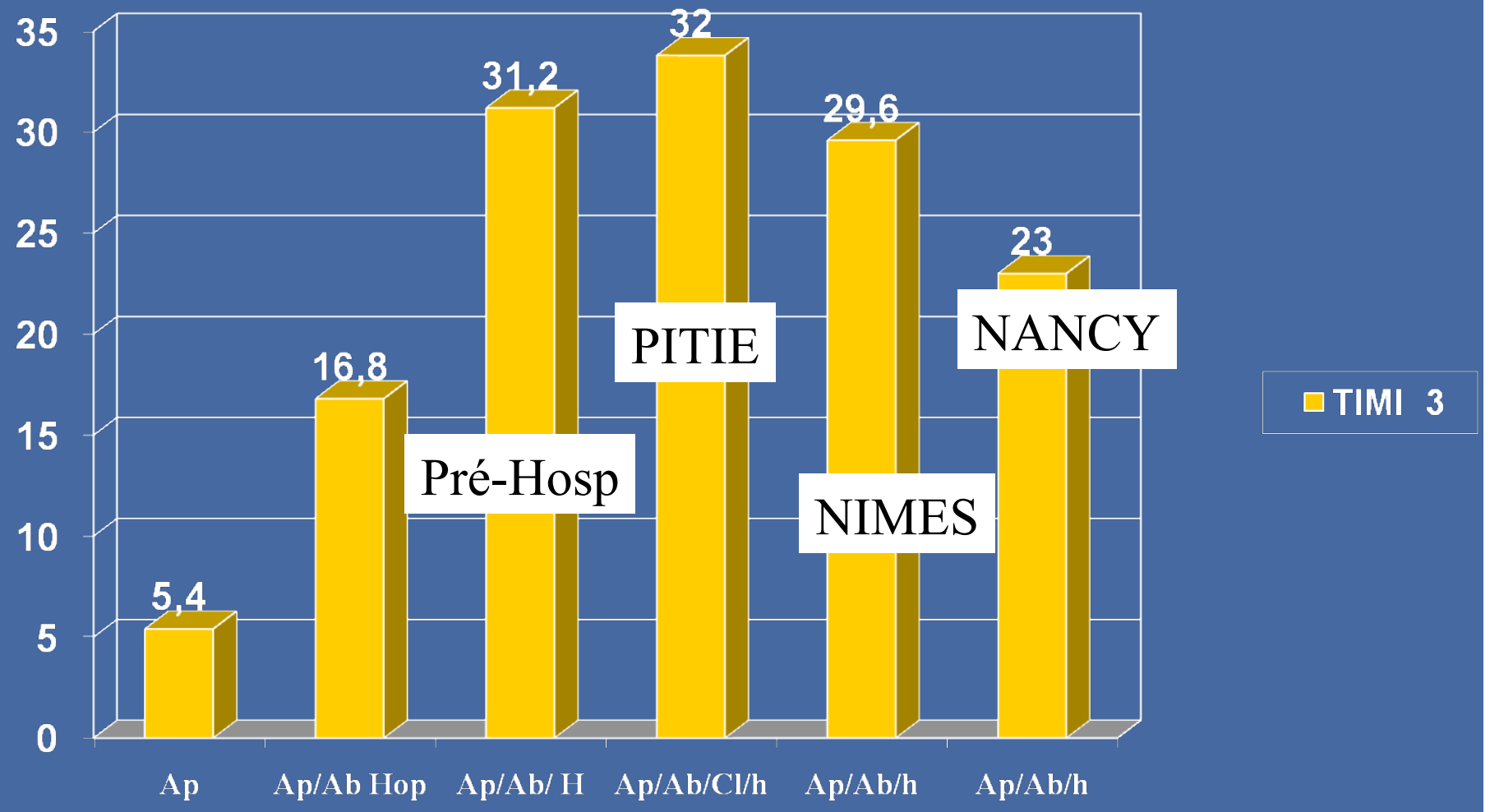
P. Ecollan, G. Montalescot 02/2010



Registre RIPOSTE n = 1244

Flux TIMI avant dilatation (%)

Ap = Aspirine Ab = Reopro Cl = Plavix



REGISTRE EFISMUR
SMUR PITIE

Douleur-PEC = 117 mn

- 95 SCA ST+ depuis mars 2010
- 55 ont reçu 60 mg de prasugrel en pré H (29% TIMI 3 av PCI)
- 31 ont reçu Prasugrel + reopro

  (48% TIMI 3 av PCI)
- 1 saignement digestif a 4 jours

Conclusion

- La meilleur stratégie pour le SCA ST+ en France en 2012 est, si le temps « Diagnostic/ponction » le permet, l'angioplastie.
- Pour être efficace cette stratégie impose un traitement de préparation qui doit être donné en pré hospitalier. Malheureusement peu d'étude nous permettent d'avoir des recommandations pour le pré hospitalier.
- Le meilleur traitement pré hospitalier nous parait depuis 2010 être, en tenant compte des contre indications, l'association :

ASPIRINE + HBPM + EFIENT + Ag P 2b3a