La durée de la double antiagrégation plaquettaire après mise en place d'un DES de 3ème génération

Le SCA

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Hôpitaux de Toulouse

Pôle Cardiovasculaire et Métabolique

Faut-il implanter un DES après lors d'un SCA ?

Recommandation des sociétés savantes

If the patient has no contraindications to prolonged DAPT (indication for oral anticoagulation, or estimated high long-term bleeding risk) and is likely to be compliant, DES should be preferred over BMS.	IIa	A

BMS = bare-metal stent; DAPT = dual antiplatelet therapy; DES = drug-eluting stent;

HAS

HAUTE AUTORITÉ DE SANTÉ

- Les **patients à haut risque de resténose** représentent les indications privilégiées des stents actifs. Le risque de resténose est particulièrement élevé :
  - si la longueur des lésions dépasse 15 mm ;
  - si le diamètre du vaisseau atteint est inférieur à 3 mm ;
  - ou si le patient est diabétique.

Angioplastie coronarienne : intérêt et limites des « stents actifs »

- Double AA après un SCA : Le rationnel
- Les nouveaux AAP
- Le risque hémorragique
- Les modalités d'interruption
- Facteurs d'hétérogénéité
- Les DES de dernière génération

Les origines

Stent-Related Cardiac Events Beyond Three Years After Implantation of the Sirolimus-Eluting Stent (from the EVASTENT Patients)

Gilles Barone-Rochette, MD[a], Alison Foote, PhD[b], Pascal Motreff, MD[c], Gerald Vanzetto, MD, PhD[a], Jean-Louis Quesada, MSc[b], Nicolas Danchin, MD[d], and Jacques Machecourt, MD[a,*], for the EVASTENT Investigators

The frequency of very late stent thrombosis (VLST) up to 3 years after sirolimus-eluting stent implantation is 0.5% to 0.6%/year but incertitude remains about the frequency of VLAST after 3 years. Diabetic (db+) and nondiabetic (db−) patients with or without multiple diseased vessels included in the EVASTENT matched-cohort registry were followed up to 6 years after stent implantation. Long-term follow-up was obtained for 1,564 of the 1,731 included patients. All-cause deaths (including cancer and complications of diabetes) occurred at steady rates of 2.5%/year up to 3 years and 1.2%/year after 3 years (difference not significant). In contrast, VLST (any Academic Research Consortium defi-

db− patients. However, after 3 years compared to before 3 years, no differences between db+ and db− patients were observed for target lesion revascularization and ST rates. It is noteworthy that 51% of patients continued to be on clopidogrel therapy nearly 6 years after receiving ≥1 sirolimus-eluting stent. In conclusion, all-cause deaths continued at a steady

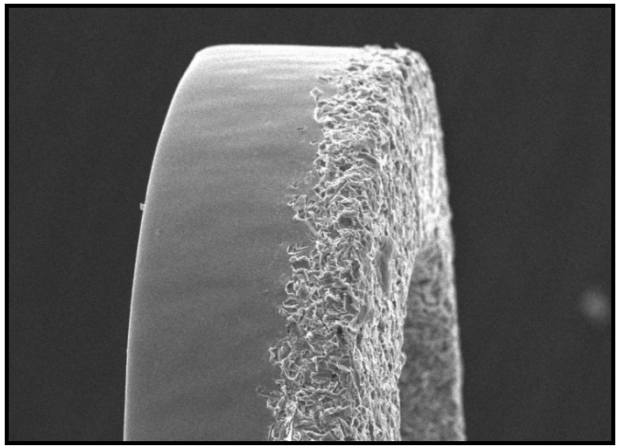
db+ and db− patients were observed for target lesion revascularization and ST rates. It is noteworthy that 51% of patients continued to be on clopidogrel therapy nearly 6 years after receiving ≥1 sirolimus-eluting stent. In conclusion, all-cause deaths continued at a steady rate over 6 years. However, cardiac deaths and "very" VLST leveled out beyond 3 years. (Am J Cardiol 2011;108:1401–1407)

Barone-Rochette Am J cardiol 2011

BioFreedom™

Les études en cours **LEADERS FREE PROTOCOL**

Selectively micro-structured surface holds drug in abluminal surface structures



Proprietary Highly Lipophilic Limus drug

Polymer-free DES

Avantages potentiels

- Absence d'effet proinflammatoire / prothrombogène du polymère
- Durée courte de DAP ?

A PROSPECTIVE RANDOMIZED COMPARISON OF THE BIOFREEDOM™ BIOLIMUS A9™ DRUG COATED STENT VERSUS THE GAZELLE™ BARE METAL STENT IN PATIENTS AT HIGH RISK FOR BLEEDING

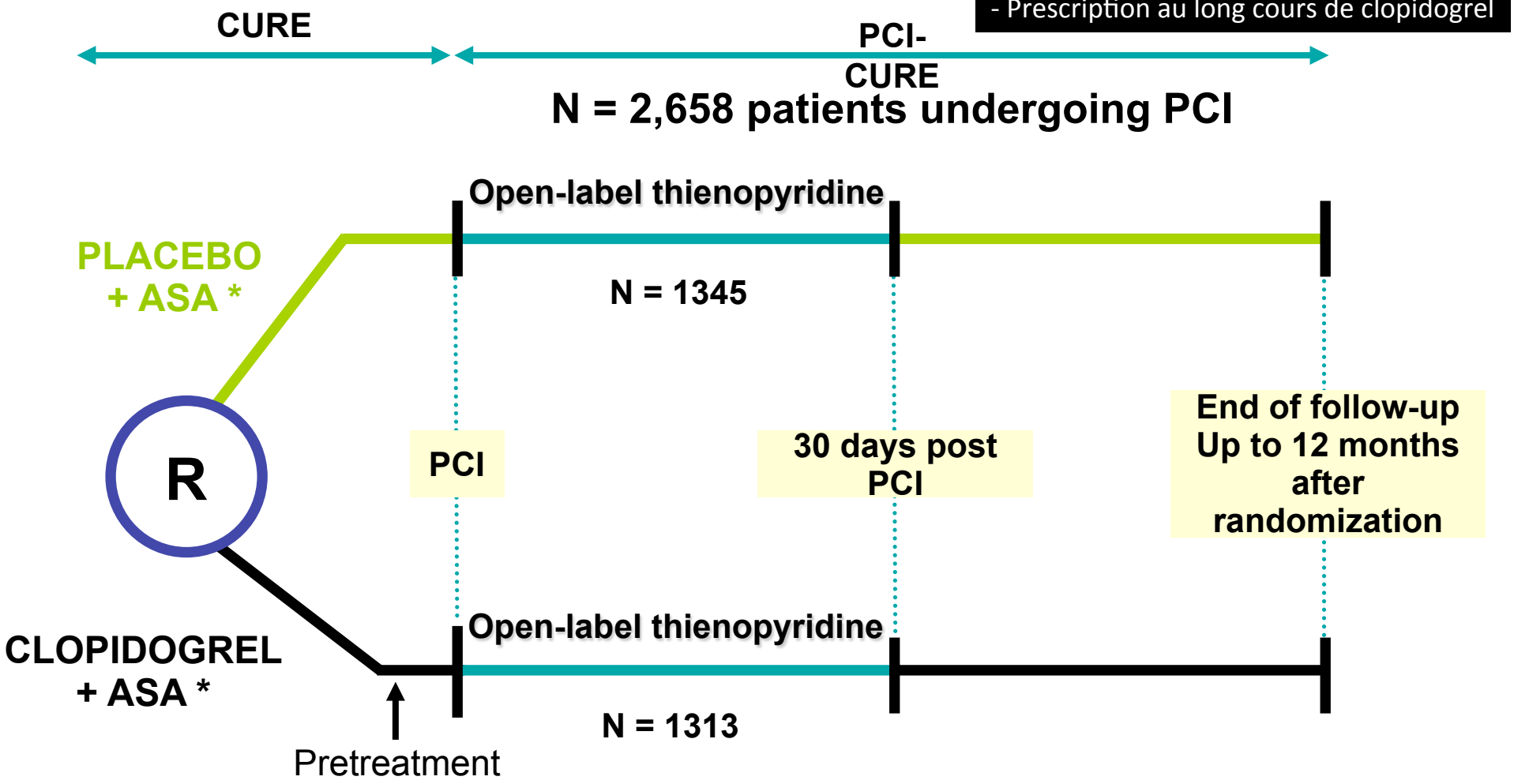
Aspirine : à vie
Clopidogrel (ou autre inhibiteur du récepteur P2Y12) : 1 mois

Le rationnel

PCI-CURE

Durée de 1 an : le rationnel

2 questions dans CURE :
- Prétraitement en clopidogrel
- Prescription au long cours de clopidogrel



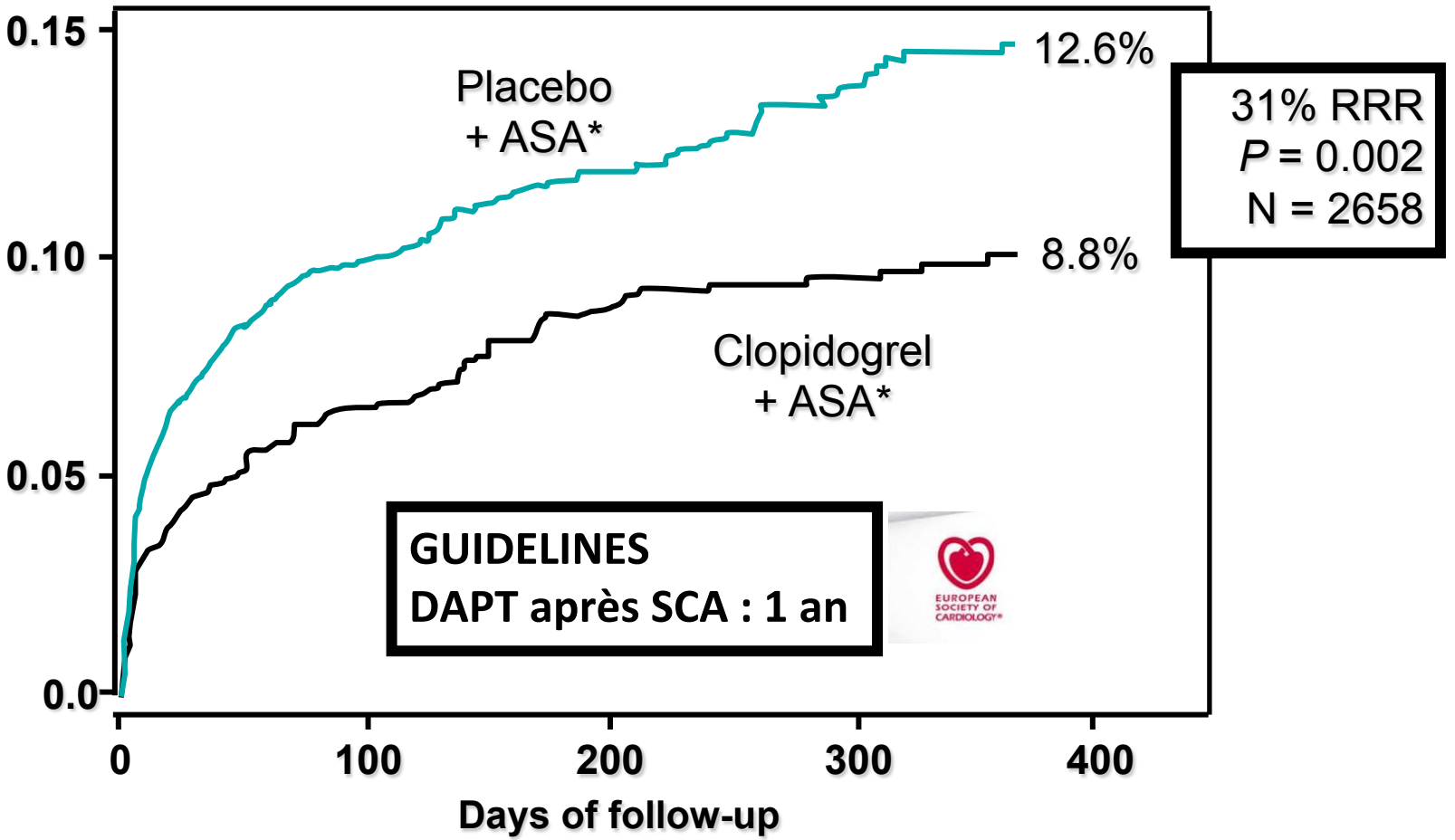
* In combination with standard therapy

Mehta, SR. et al for the CURE Trial Investigators. N Engl J Med. 2001;345:494-502.

PCI-CURE

Résultats à 1 an

Composite of cardiovascular death or MI from randomization to end of follow-up



* In combination with standard therapy

Mehta, SR. et al for the CURE Trial Investigators. *Lancet.* August 2001.

PCI-CURE

Interventional Characteristics

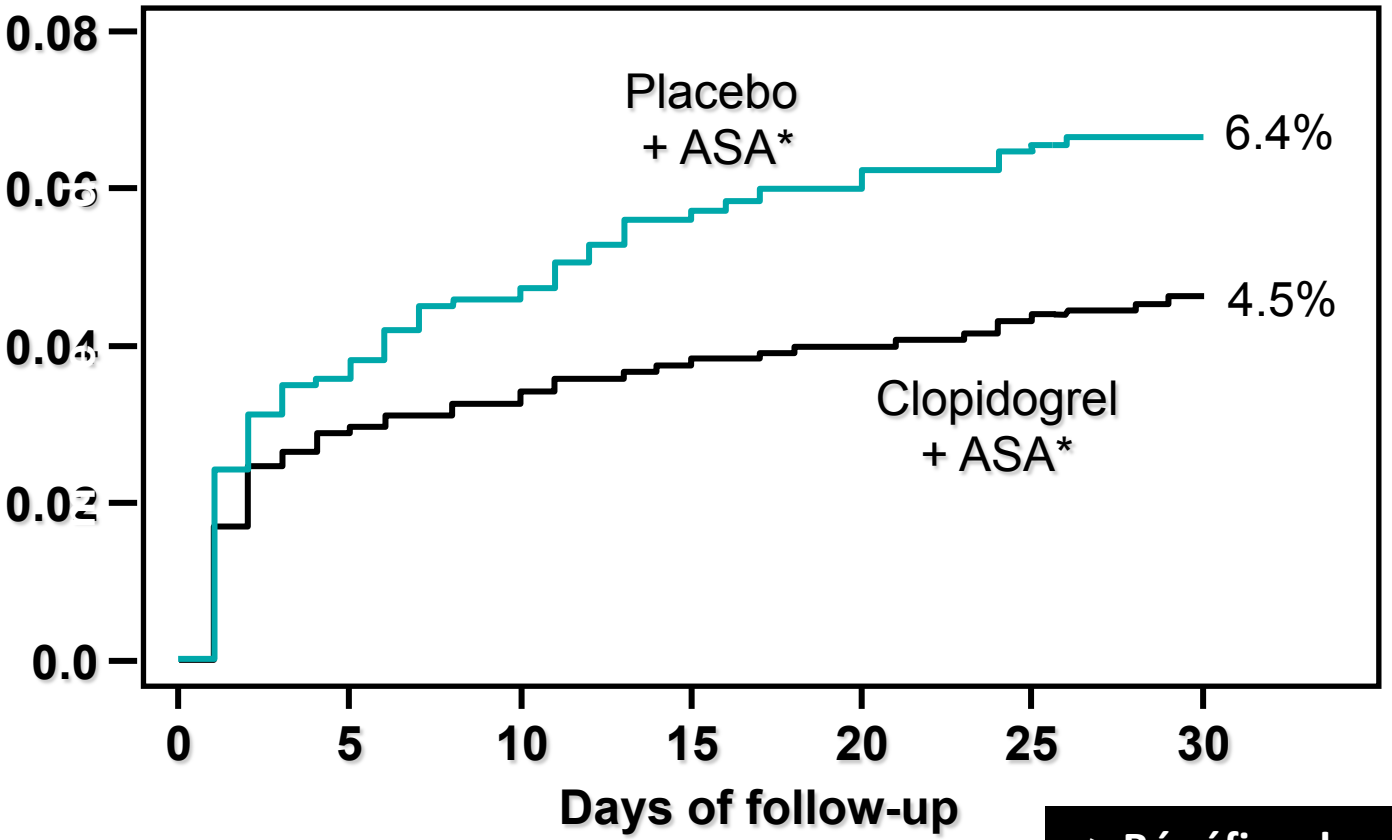
	Clopidogrel + ASA* (N = 1345)	Placebo + ASA* (N = 1313)
Overall median days after randomization on which PCI was done	**10**	**10**
PCI during initial hospitalization	6	6
PCI after initial hospitalization	49	49
•Stent use (%)	**81.3**	**82.4**
•Use of open-label thienopyridine		
Before PCI (%)	24.7	26.4
Overall (%)	84.1	82.9

Mehta, SR. et al for the CURE Trial Investigators. *Lancet.* August 2001

PCI-CURE

Résultats à 30 j

Composite of cardiovascular death, MI, or urgent revascularization



30% RRR
P = 0.03
N = 2658

=> Bénéfice du prétraitement

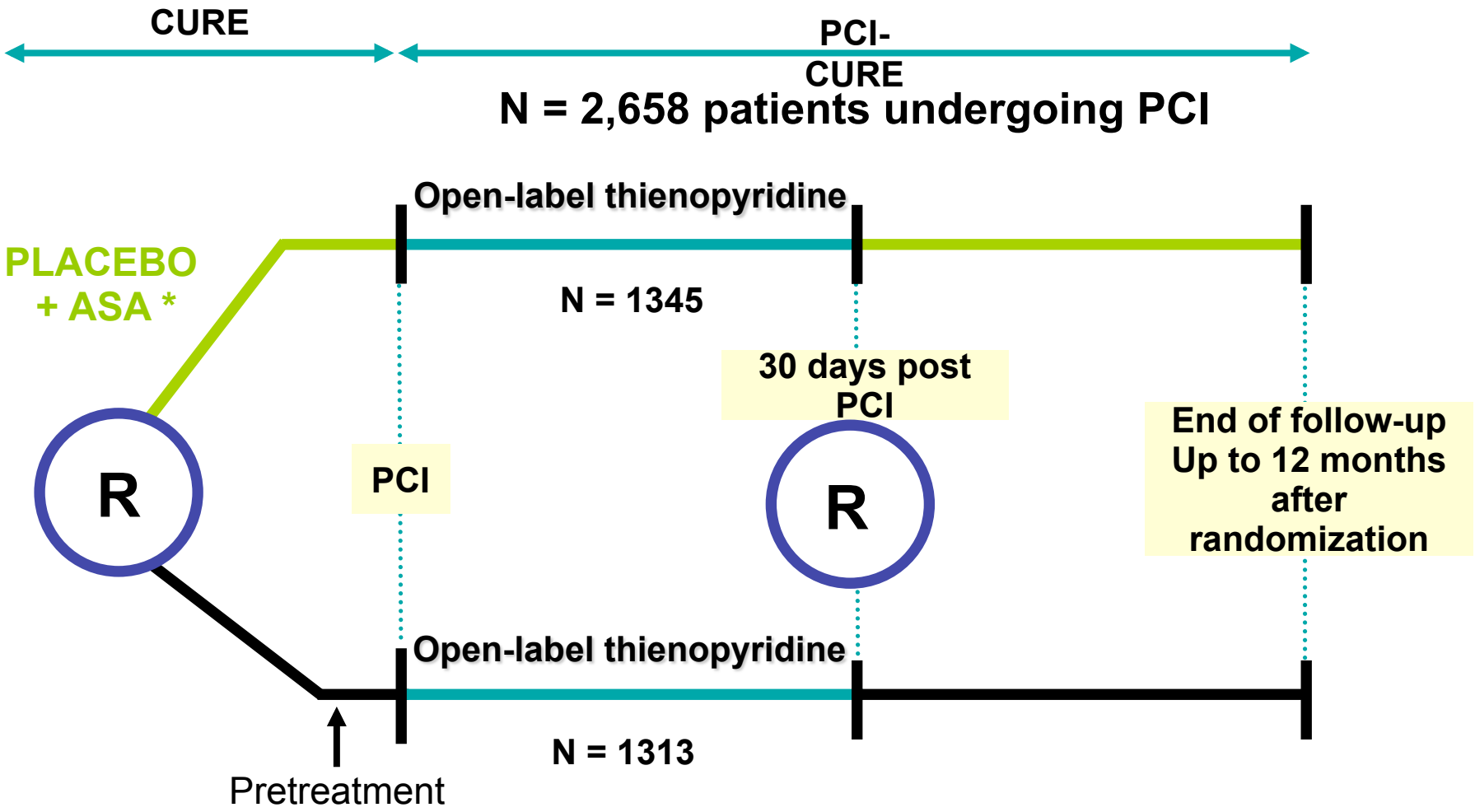
* In combination with standard therapy

Mehta, SR. et al for the CURE Trial Investigators. *Lancet.* August 2001;21:2033-41.

Problème méthodologique majeur :

L'impact de la durée prolongée de la double antiagrégation, indépendamment de l'effet du prétraitement est impossible à déterminer.

Seuls les patients ayant du clopidogrel avant la procédure continuaient à en recevoir à long terme.



PCI-CURE

Bleeding Outcomes

	Placebo + ASA*	Clopidogrel + ASA*	
From PCI to 30 days			
Major	**1.4%**	**1.6% †**	
Life threatening	**0.7%**	**0.7% †**	
Minor	**0.7%**	**1.0% †**	
From PCI to end of follow-up			
Major	**2.5%**	**2.7% †**	NS
Life threatening	**1.3%**	**1.2% †**	NS
Minor	**2.1%**	**3.5% ‡**	

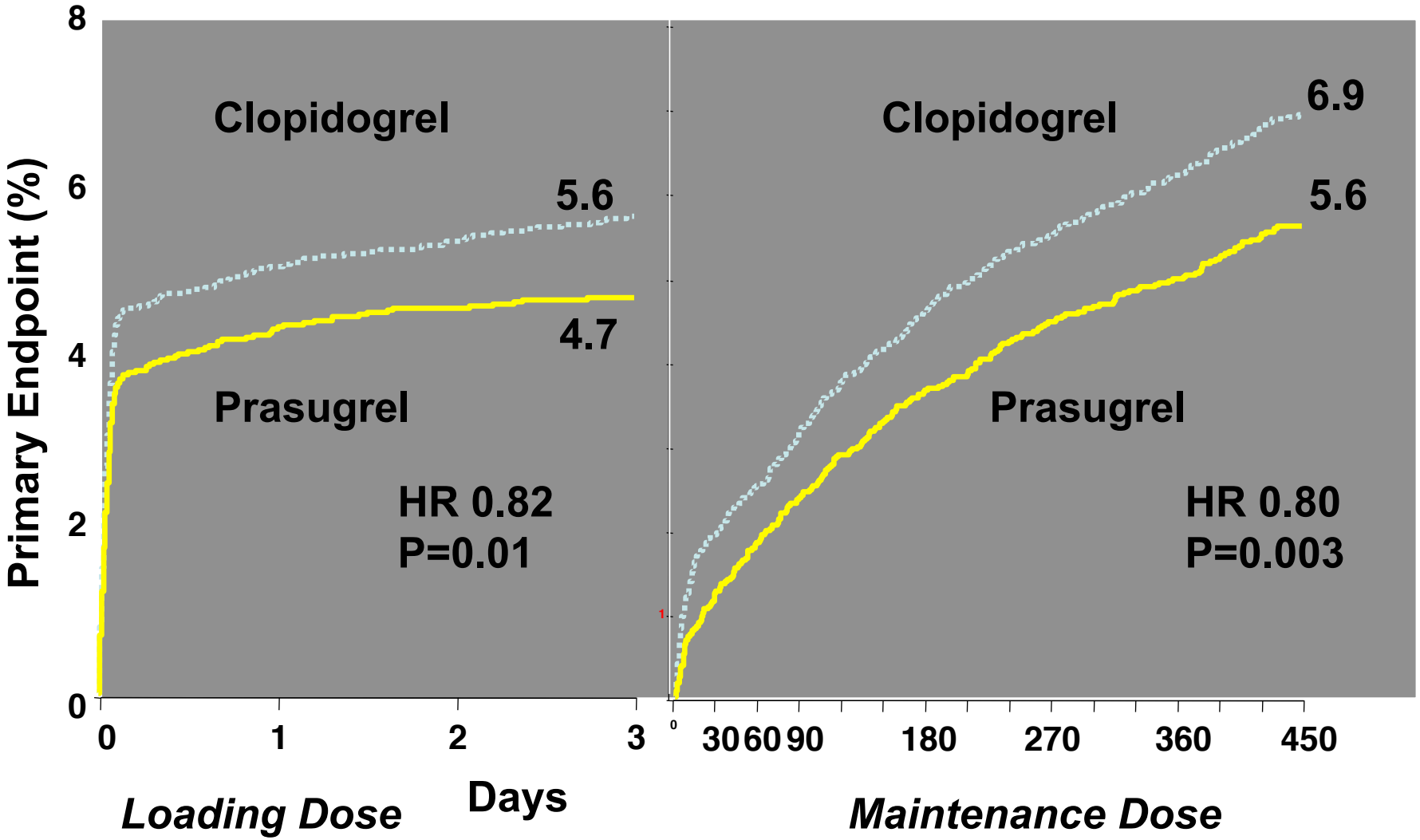
* In combination with standard therapy

† *P* = NS, ‡ *P* = 0.03

Mehta, SR. et al for the CURE Trial Investigators. Lancet. 2001

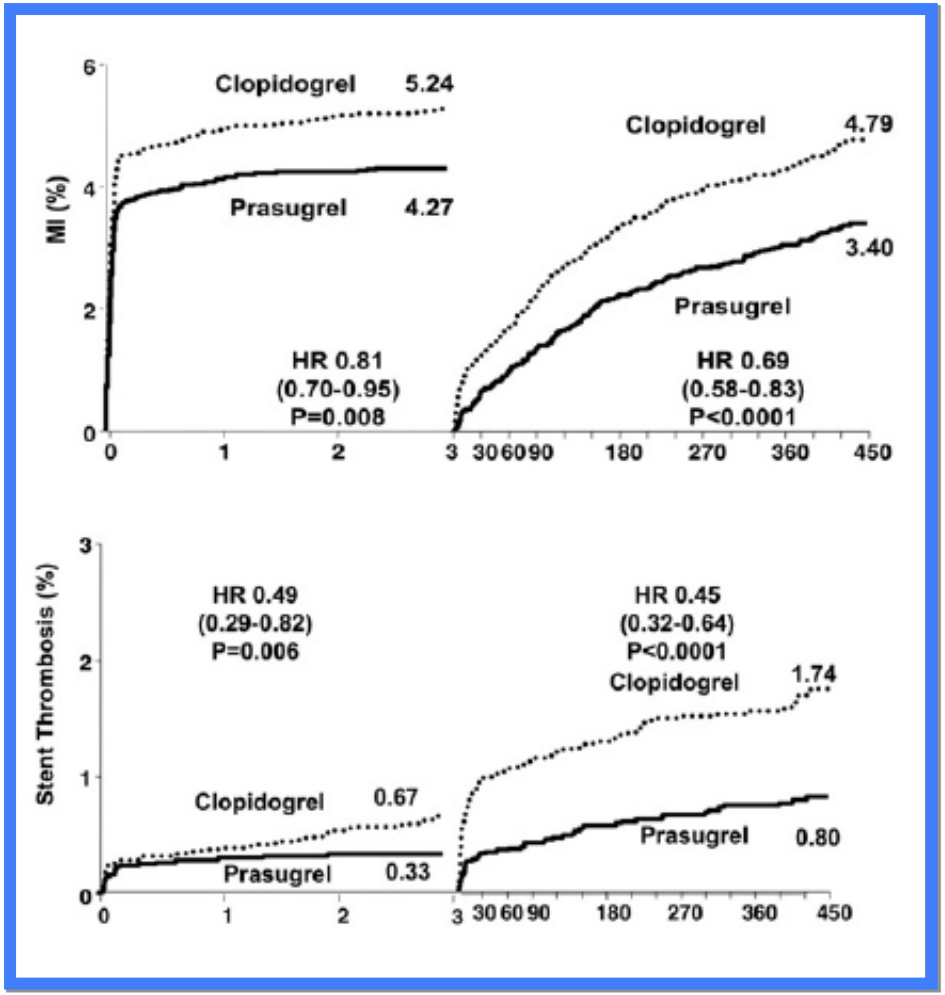
Les nouveaux AAP

Timing of Benefit

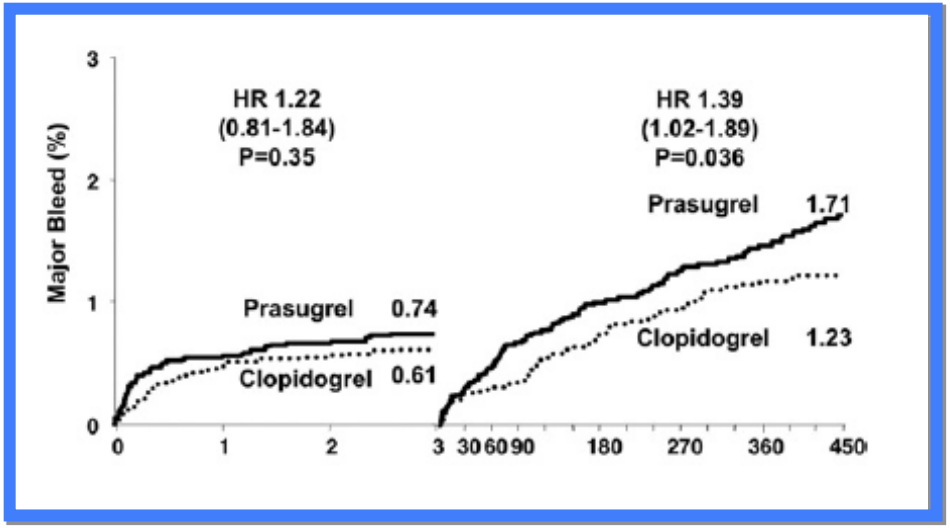


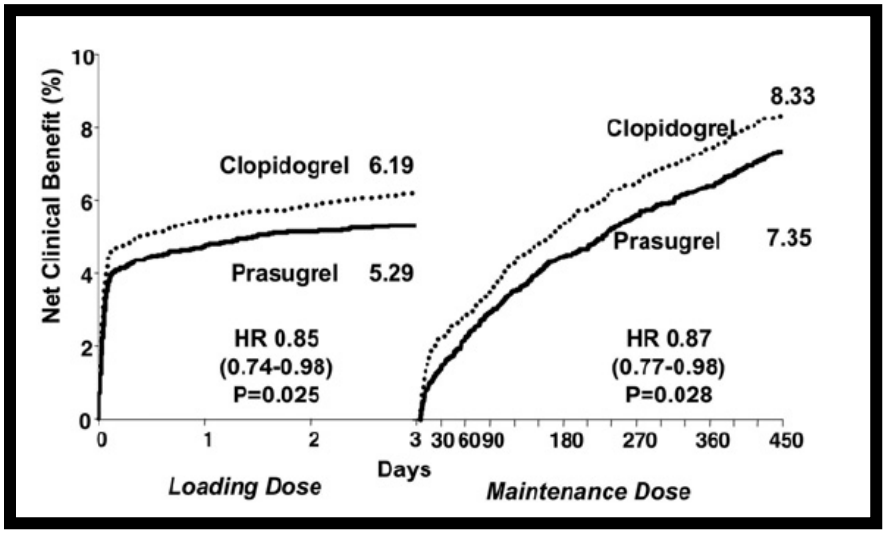
TRITON TIMI 38

MACE



Major bleeding

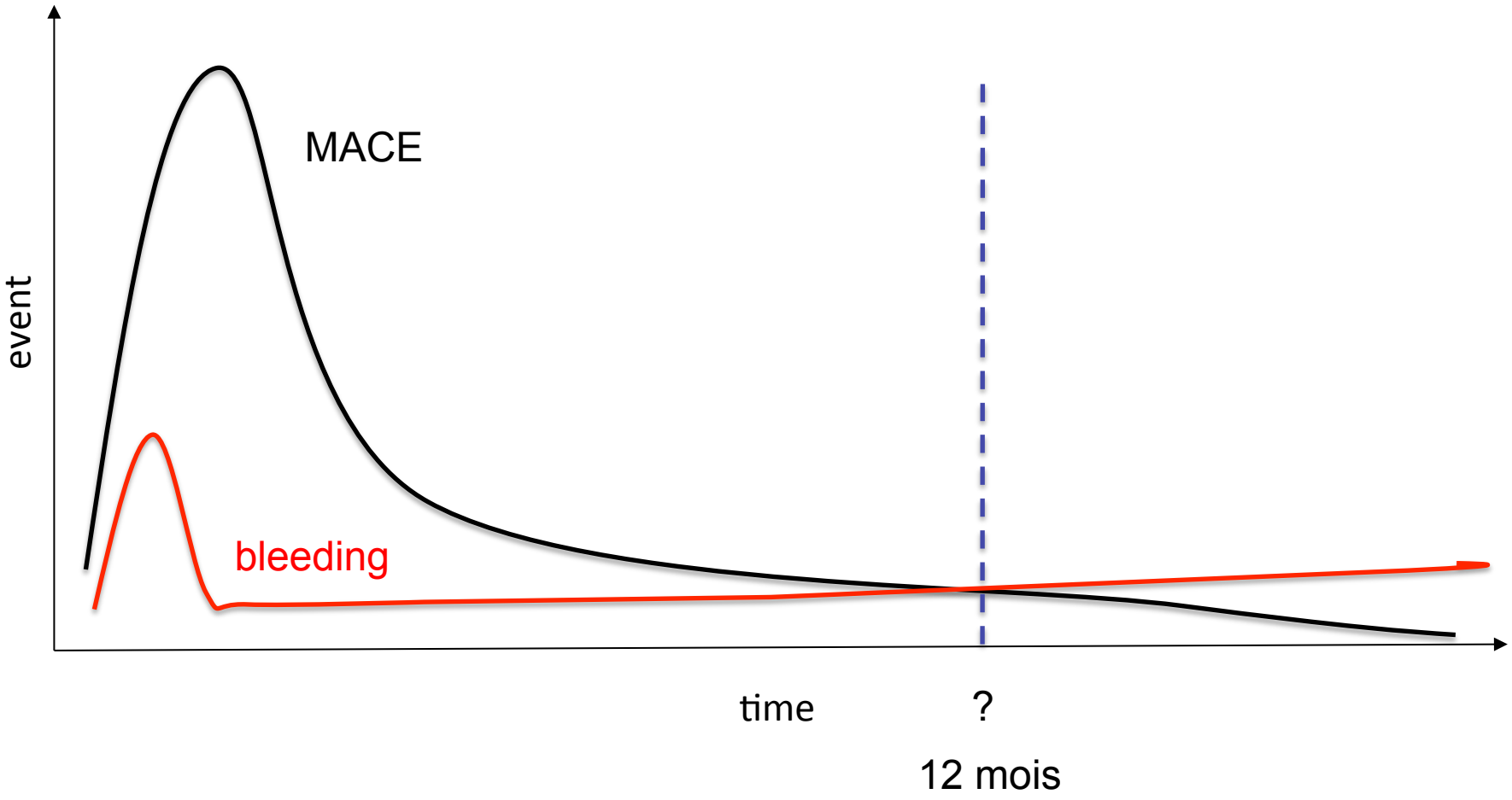




Net clinical benefit

Antman et al JACC 2008

DAPT : optimal duration



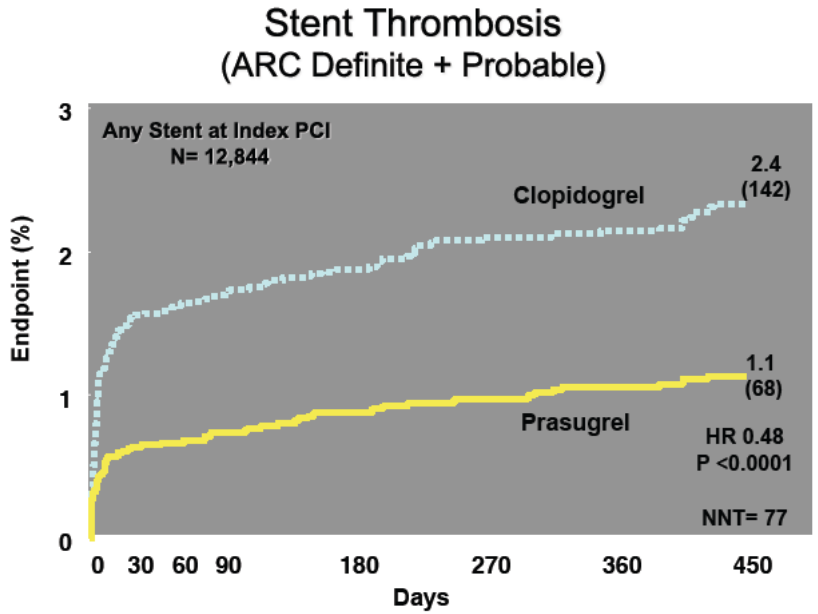
La durée optimale de la DAP : facteurs d'hétérogénéité

Hétérogénéité selon le type d'inhibiteur du récepteur P2Y12

	Ticagrelor (n=6,732)	Clopidogrel (n=6,676)	HR for ticagrelor (95% CI)	p value*
Stent thrombosis, %				
Definite	**1.0**	**1.6**	**0.62 (0.45–0.85)**	**0.003**
Probable or definite	**1.7**	**2.3**	**0.72 (0.56–0.93)**	**0.01**
Possible, probable, or definite	**2.2**	**3.1**	**0.72 (0.58–0.90)**	**0.003**

PLATO invasive

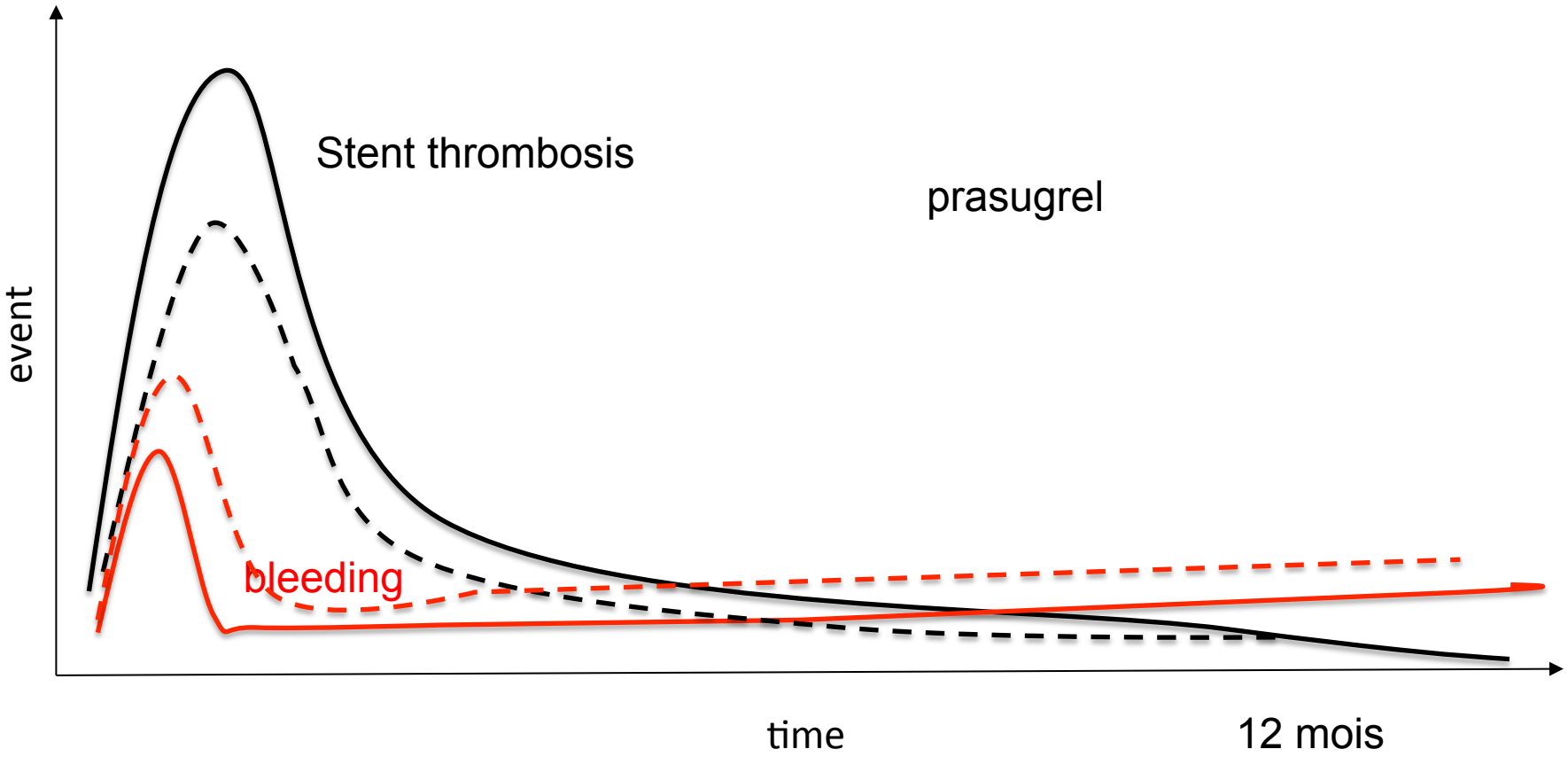
- 28 % de thrombose de stent



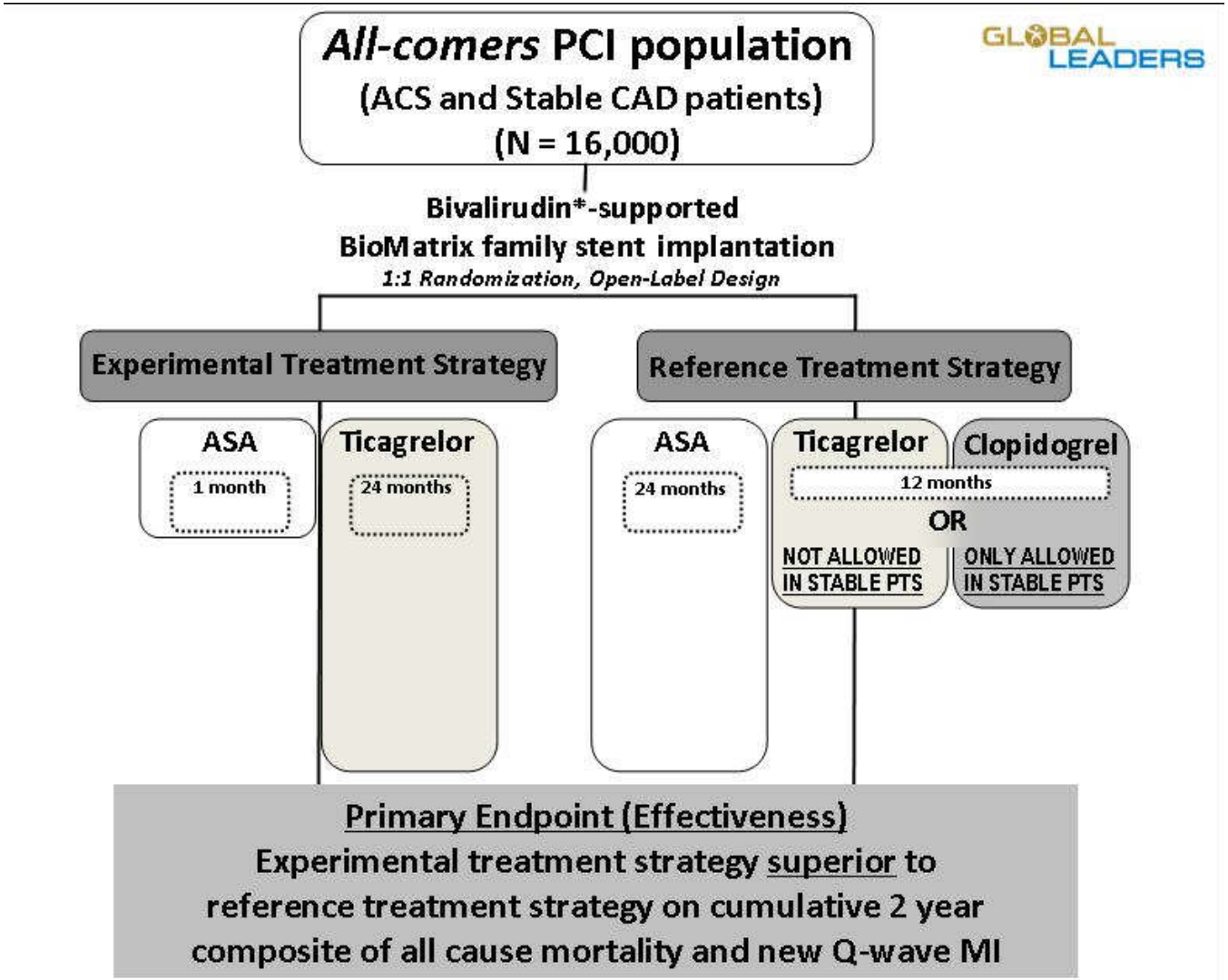
TRITON TIMI 38

- 50 % de thrombose de stent

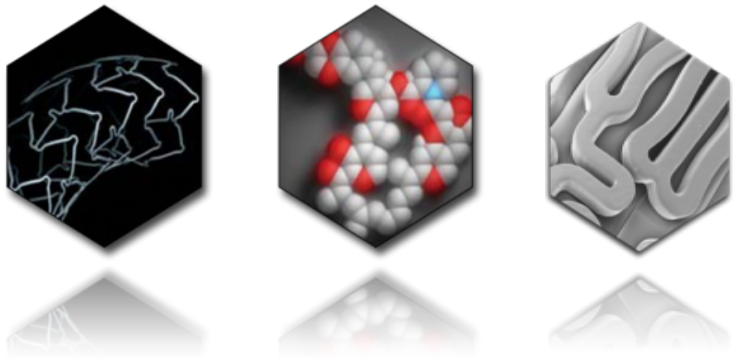
DAPT : optimal duration



Etudes à venir

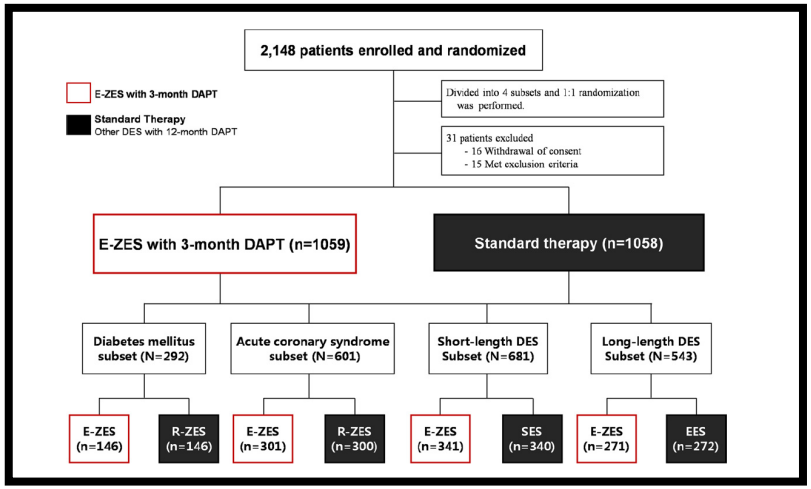


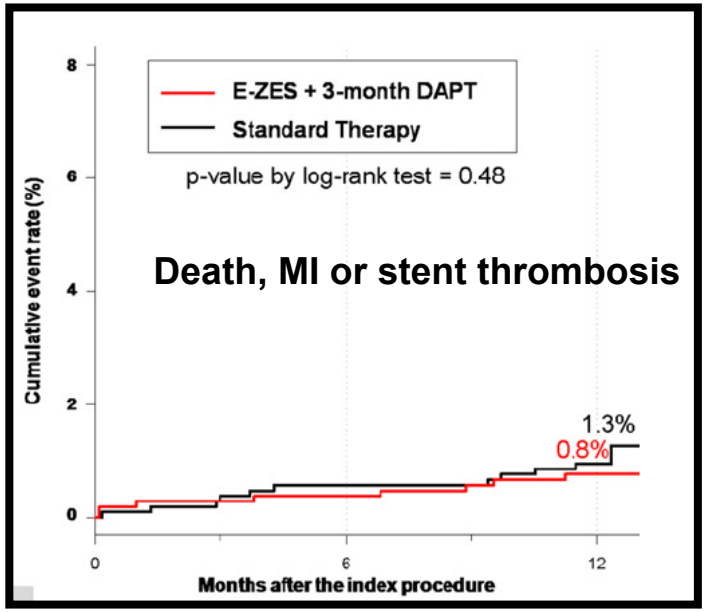
Hétérogénéité selon le type de stent



=> Stents de dernière génération
- Meilleure délivrabilité
- Mailles plus fines
- Polymères biocompatibles
- Délivrance de la molécule antiproliférative

The RESET trial



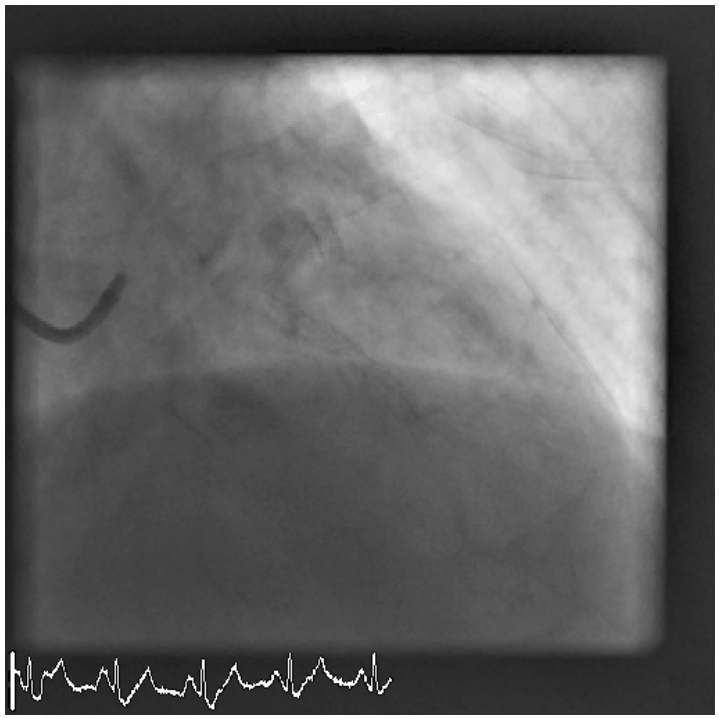


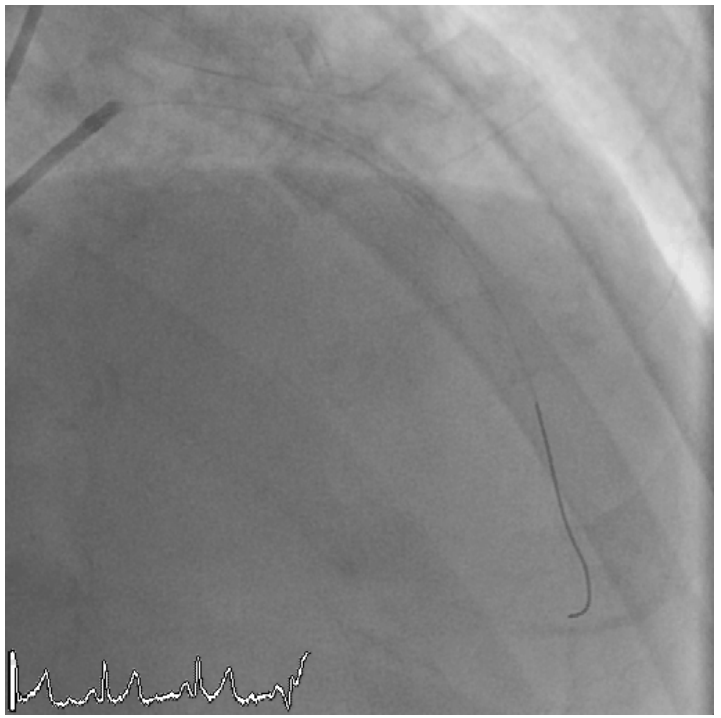
Hypothesis : Non inferiority of 3 months DAPT with ZES vs12 months with other DES

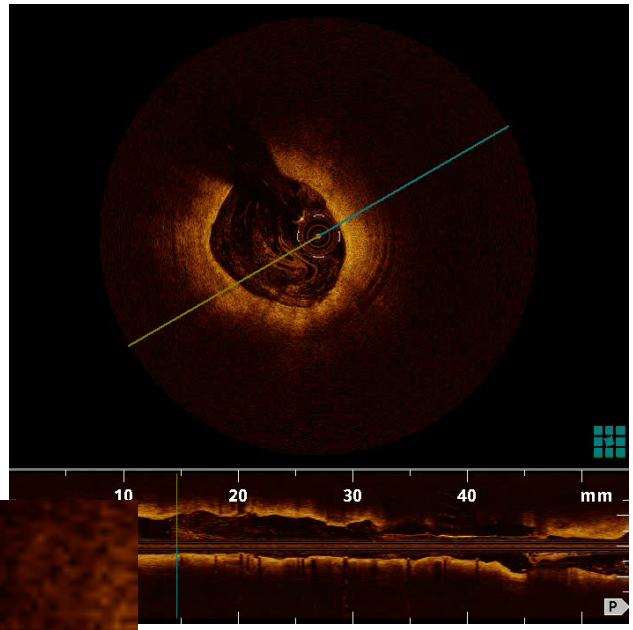
Kim et al – JACC 2012

Hétérogénéité selon le type de stent

Mr P
64 ans
SCA ST+ antérieur
ATCD : Angioplastie IVA1 (2 CYPHER 3x23 et 3x8) et Cx (BMS) **en 2005**



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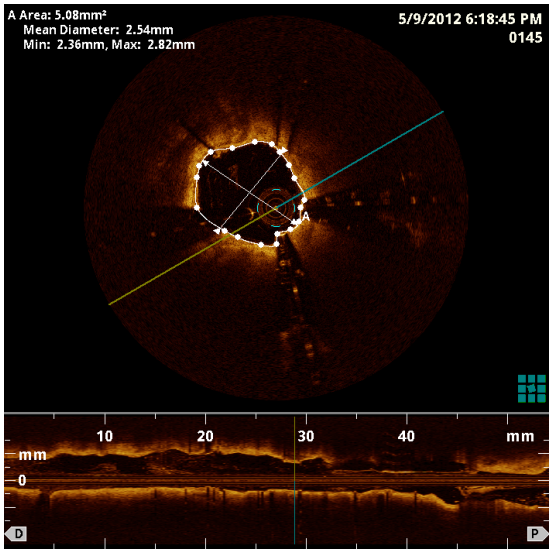
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Min: 2.36mm, Max: 2.82mm
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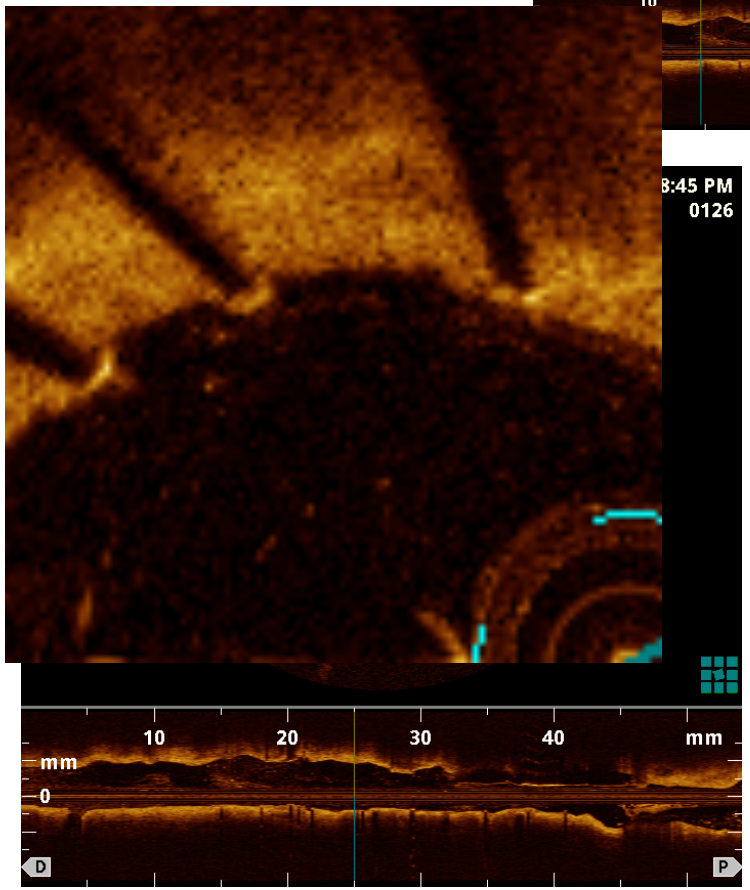
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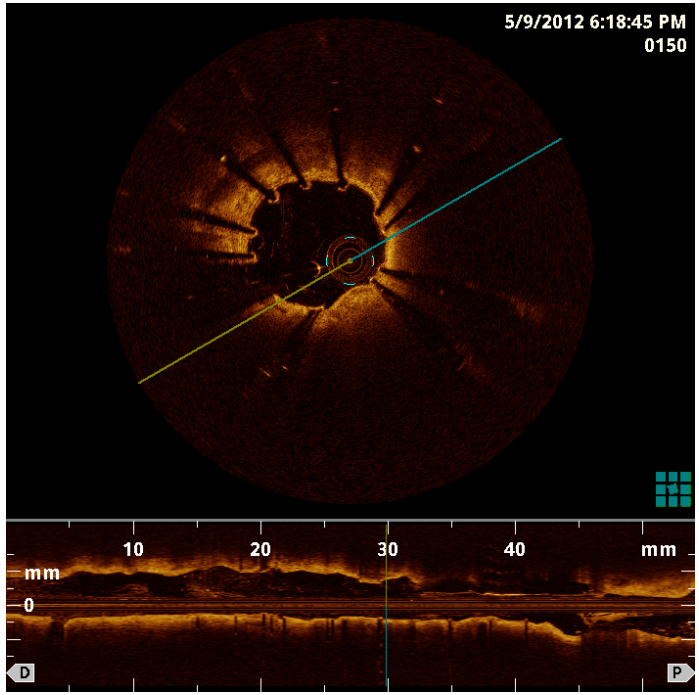
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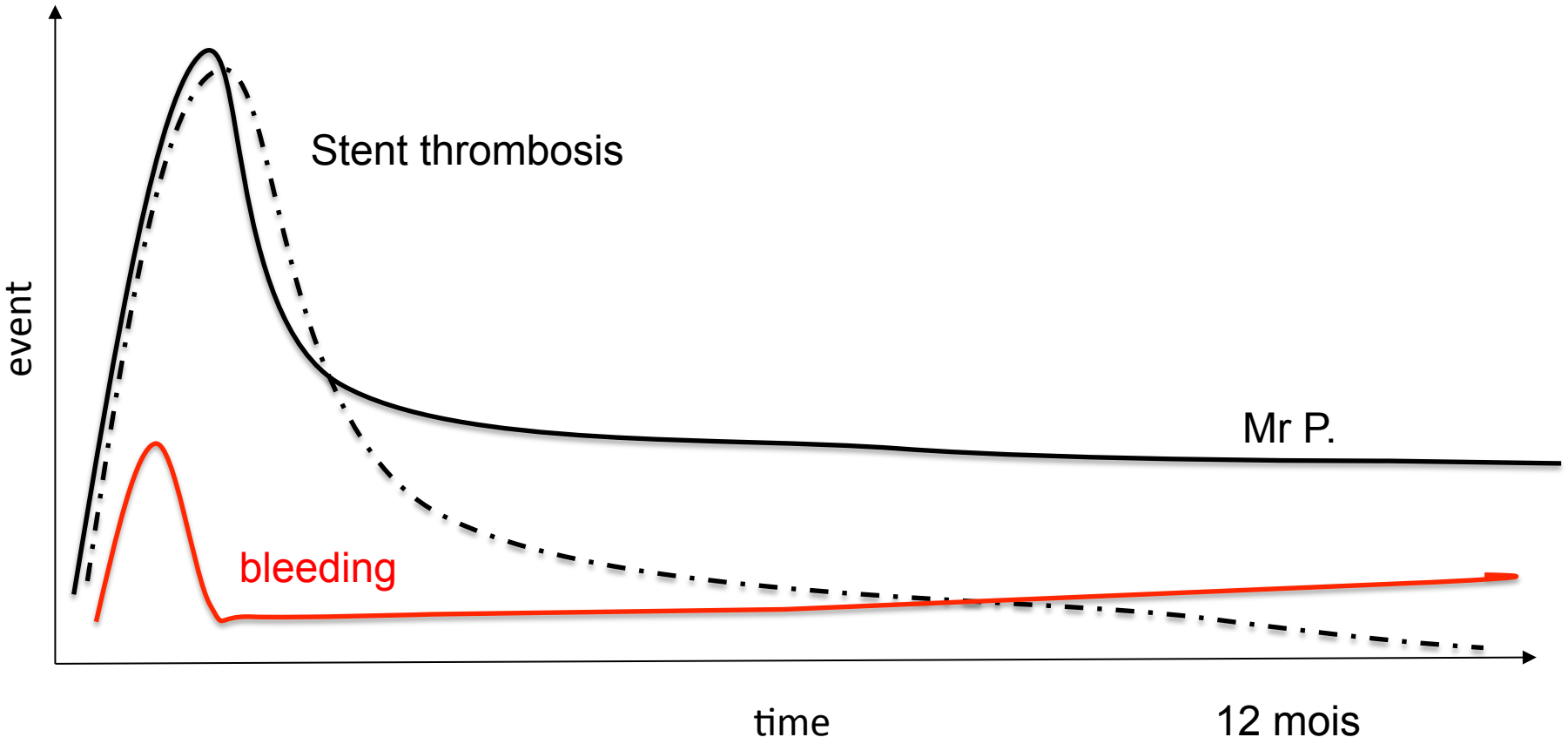
DAPT : optimal duration



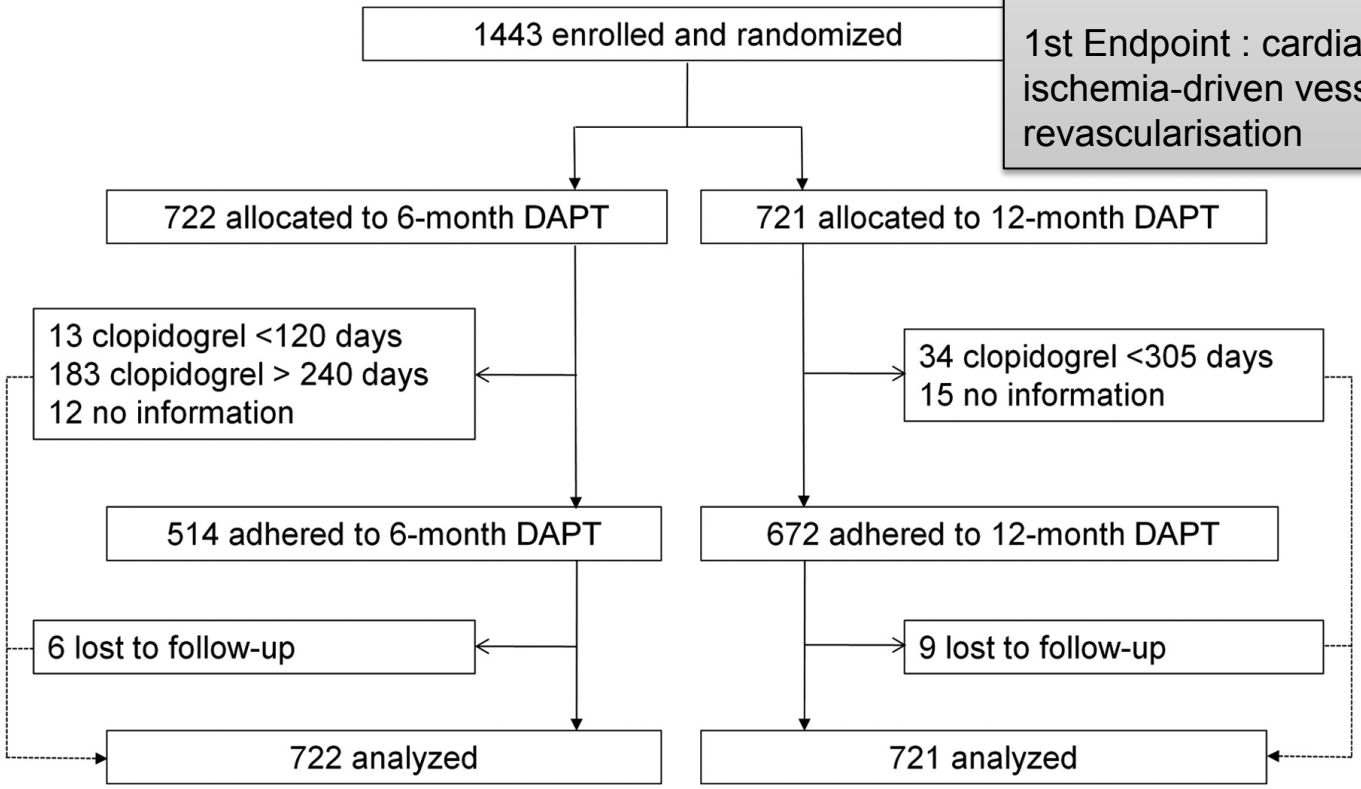
Hétérogénéité selon la procédure / le patient : le cas des diabétiques

The EXCELLENT trial

Hypothesis : 6 months DAPT is non inferior to 12 months DAPT after DES implantation

All comer PCI
DES (EES and SES)

1st Endpoint : cardiac death, MI or ischemia-driven vessel revascularisation

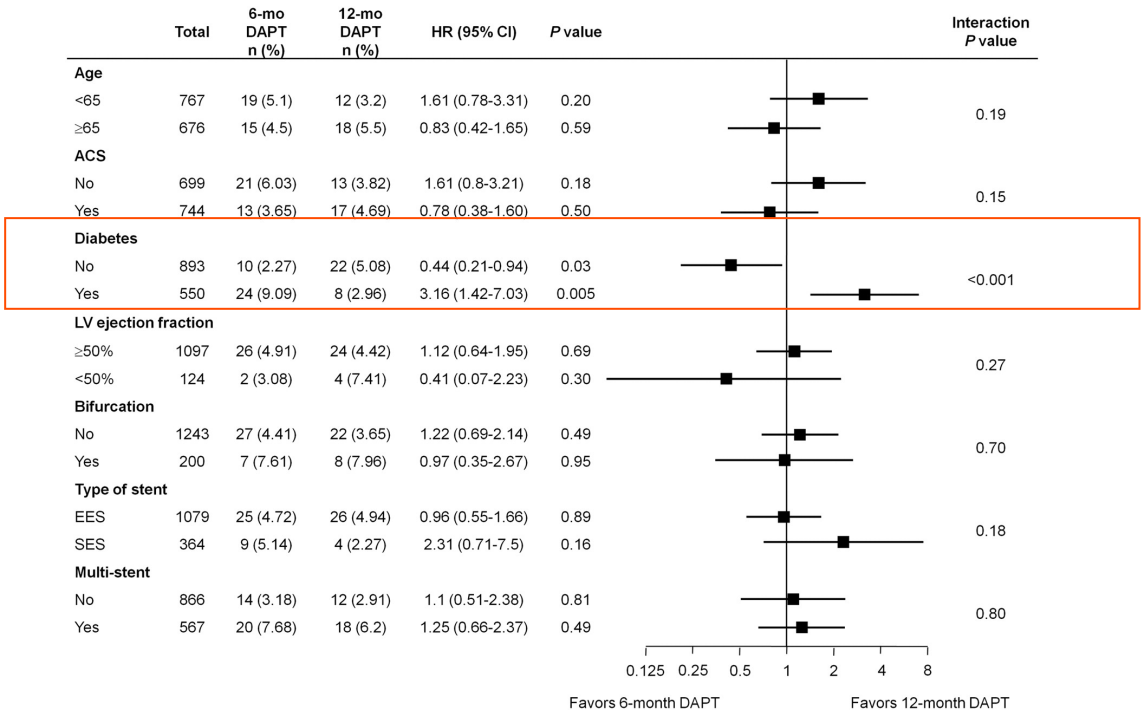


Gwon H et al. Circulation 2012

Hétérogénéité selon la procédure / le patient : le cas des diabétiques

The EXCELLENT trial

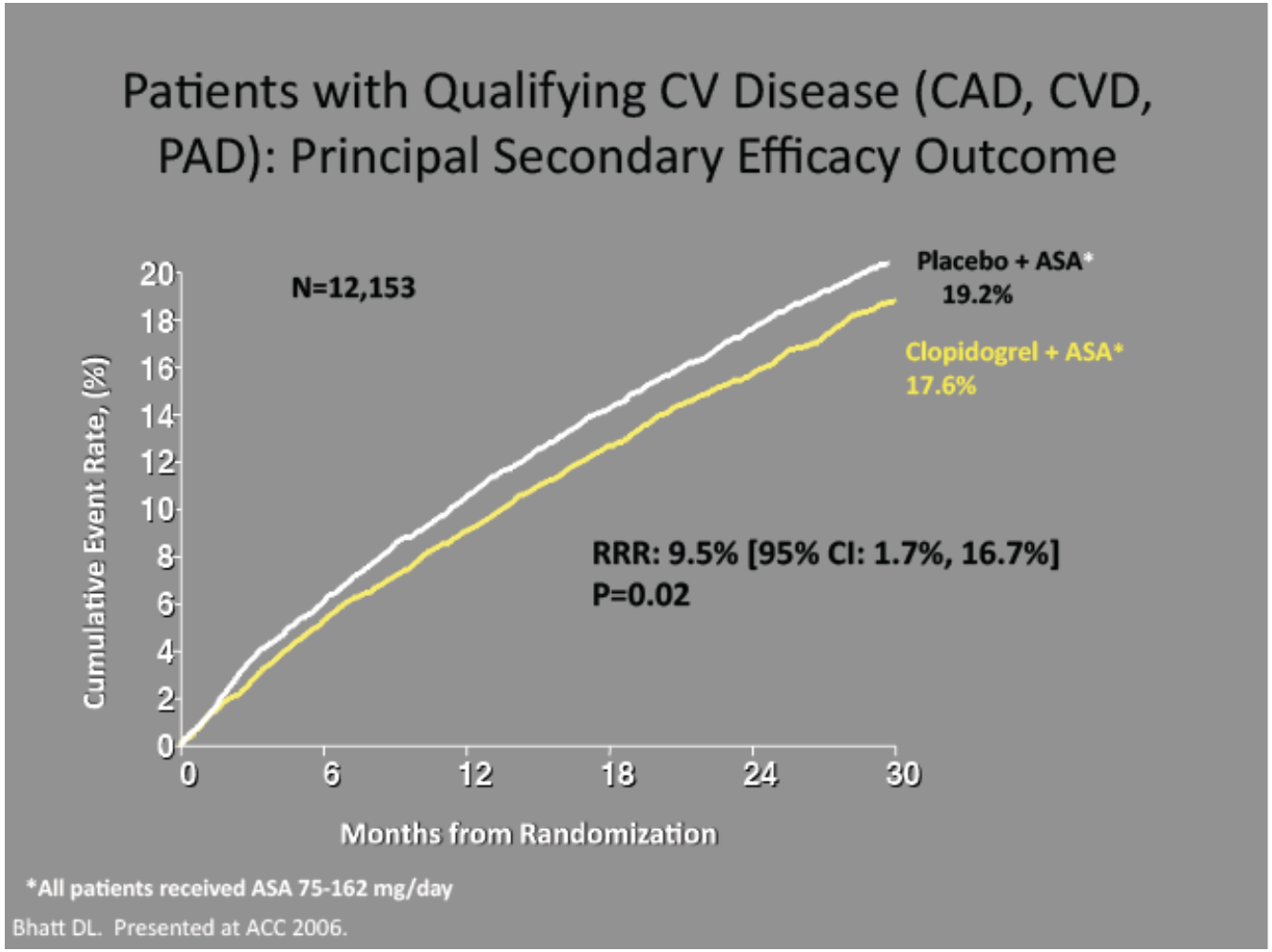
Subgroup analyses of the primary end point.



Gwon H et al. Circulation 2012

Concept de la double AA plaquettaire prolongée chez les patients à très haut risque

Etude CHARISMA



=> Le SCA « par lui même » identifie une population de patient à haut risque d'événement.

Bhatt DL. Presented at ACC 2006.

La gestion de l’arrêt de la DAP

Hétérogénéité selon le mode d'arrêt

Risque associé avec l'arrêt de la double antiagrégation dans la 1ère année qui suit l'implantation d'un DES : the ACDC study

Adjusted Risk of Major Cardiac Event

	HR	95% CI	p Value
Antiplatelet therapy discontinuation	1.32	0.56–3.12	0.526
Aspirin	1.33	0.32–5.49	0.696
Clopidogrel	1.29	0.31–5.34	0.725
Both	1.34	0.32–5.63	0.685
Age (each 10 yrs)	1.37	1.10–1.70	0.005
Chronic obstructive pulmonary disease	1.81	1.04–3.14	0.035
Chronic renal impairment	2.88	1.66–4.99	<0.001
Worst Killip class III–IV during admission	1.65	1.04–2.61	0.032
Off-label indications of DES	1.85	1.10–3.09	0.020

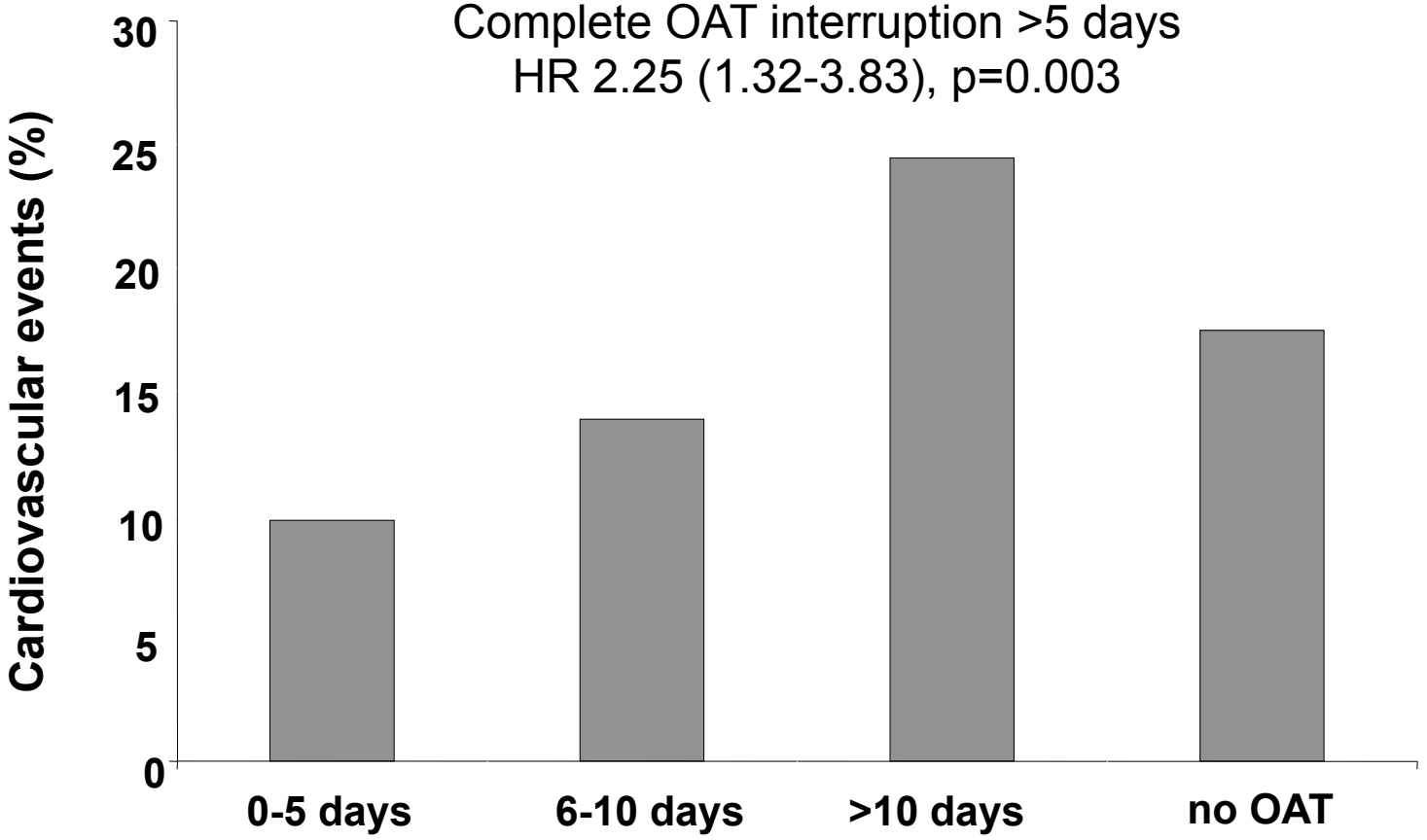
L'arrêt de la double AA est fréquent dans la 1ère année
Peu d'arrêt dans le 1er mois
Arrêt en moyenne de 7 jours de l'un des 2 AA

Ferreira-Gonzalez et al JACC 2012

Registre RECO (n=1134 stentés)

MACCE in10.5% (n=124)
3.3 ± 3.9 days (18 deaths and 17 ST)
Major bleeds in 9.5% (n=108) within 5.3±3.3 days

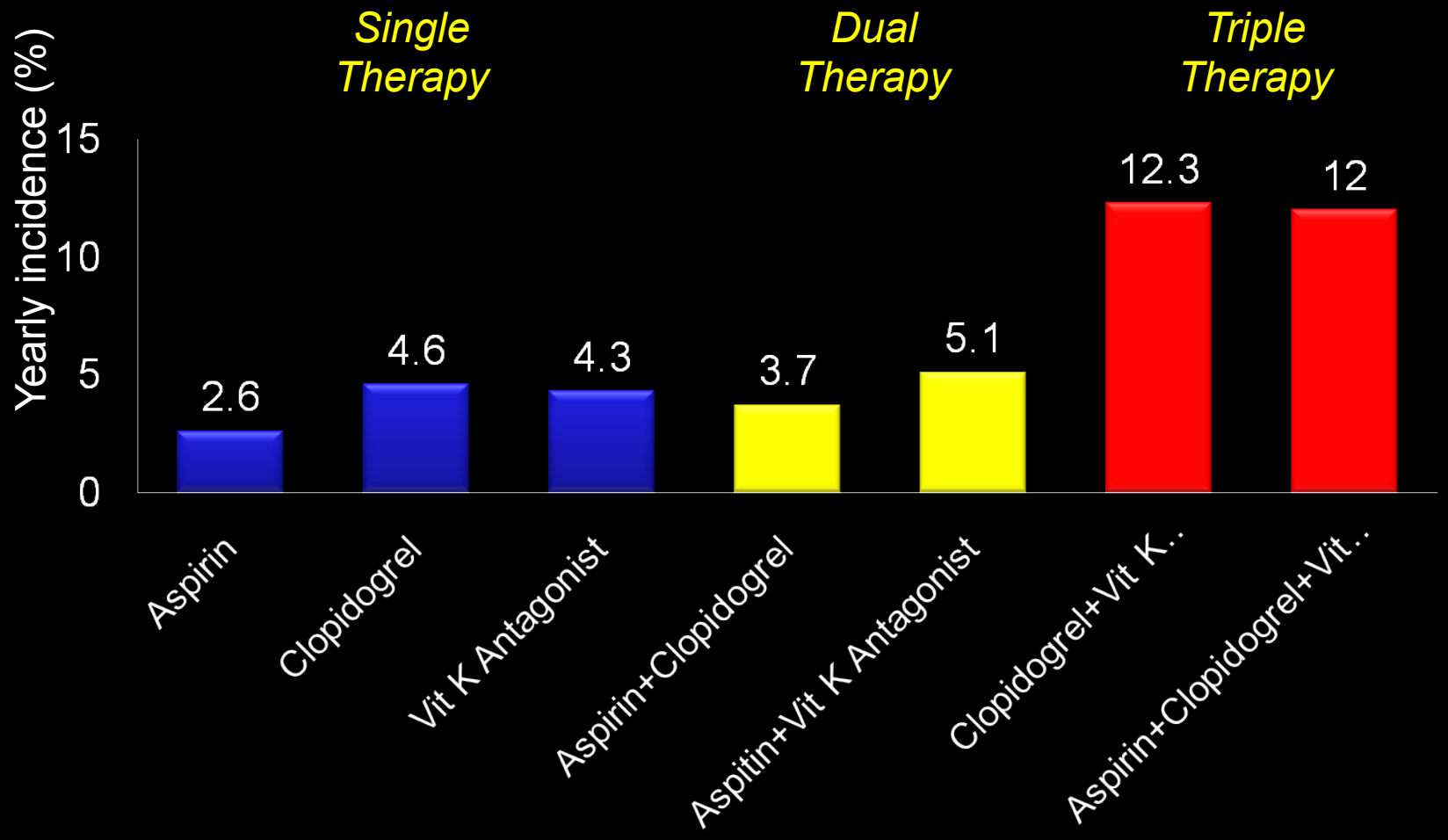
Complete OAT interruption >5 days
HR 2.25 (1.32-3.83), p=0.003



Albaladejo et al. Interventional Cardiology2013

Incidence of Bleeding in Relation to Antithrombotic Therapy

Sørensen R et al. Lancet 2009;374:1967-74



40 812 patients with MI between 2005-2008

Conclusion

- Peu d'arguments pour une durée fixe à 12 mois si ce n'est médicolégal….
- Hétérogénéité de la durée optimale de la double AA en fonction "du risque ischémique" : type de stent et de lésion, de la procédure, du patient.
- Prendre en compte le risque hémorragique
- Durée optimale et durée minimale.