# SYMPOSIUM ASTRA ZENECA
# Biarritz le 5 juin 2014

Thibault PERRET *CH STJOSEPH SAINT LUC Lyon*

# CONFLITS D'INTERETS

- Astra zeneca
- Biotronik
- Saint jude
- Medtronic

# DOUBLE AAP : PROTEGER LE STENT ET AU DELA …

# Débat parfois houleux

- 12 mois évidemment

-6 mois !!!!

-3 mois c’ est mieux

-1 mois suffit

# DE NOMBREUX PARAMETRES

- ***1) CONTEXTE CLINIQUE***

- SCA ( ST+ ou ST-)
- angor stable/ischémie silencieuse

- ***2) CARACTERISTIQUES DU STENT***

- BMS/DES/BVS
- bifurcation-longueur stentée-diamètre –TCG
- Optimisation du stenting ( stenboost-OCT)

# DE NOMBREUX PARAMETRES

## 3) LE PATIENT

- - âge/poids/sexe
- - diabète/insuffisance rénale
- - traitement associées ( AVK-NACO- CORTICOIDE)
- - profil psychologique/observance ?

- - *un paramètre en moins : le profil génétique ..*

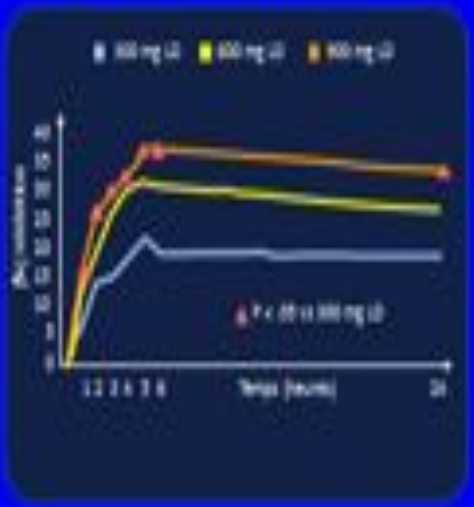
# 4 ou 30 cps de CLOPIDOGREL ?

## Effets du clopidogrel LD 900mg [1,2]

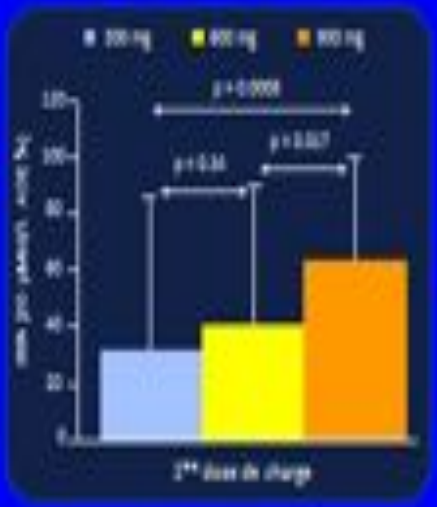
**Essai ALBION**

**Etude RELOAD**

Inhibition maximale de l'agrégation plaquettaire (ADP 20 µmol/L)



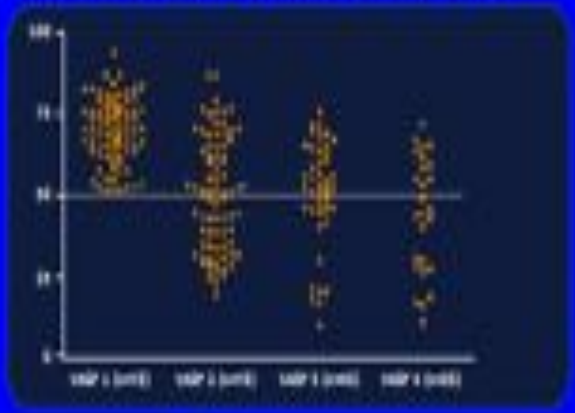
Inhibition de RPA 4 heures après la 1ère dose de charge

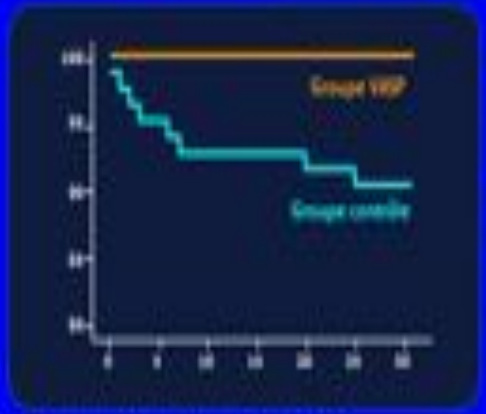



## Tester l'efficacité in vitro pour augmenter les doses [1]

**Randomisation lors d'une angioplastie :**

- dose classique
- test d'agrégation pour adapter la dose de clopidogrel

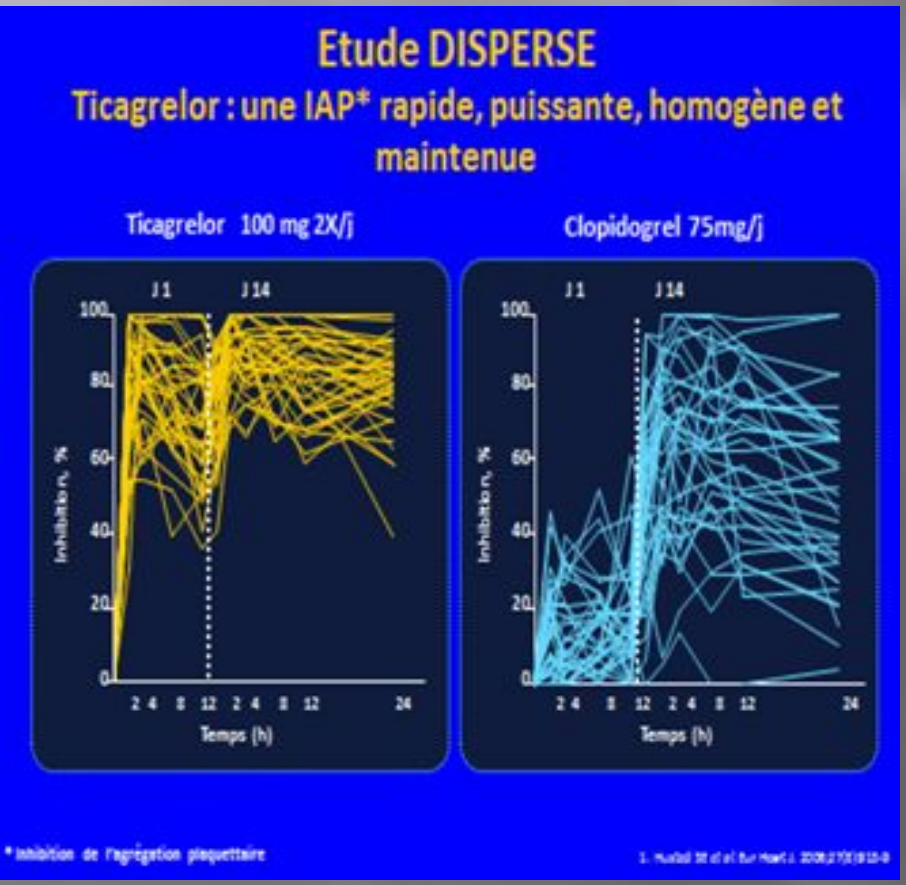




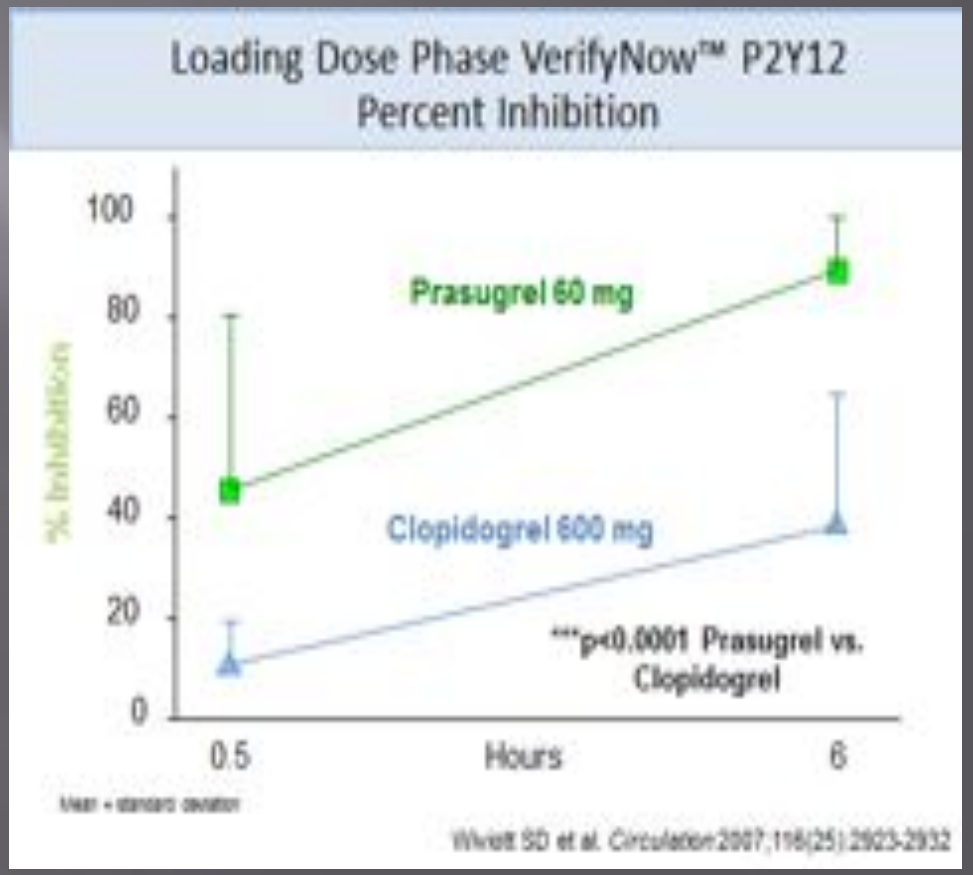

**Pratiquement inenvisageable dans une situation aiguë**

# PAS DE RESISTANCE P2Y12

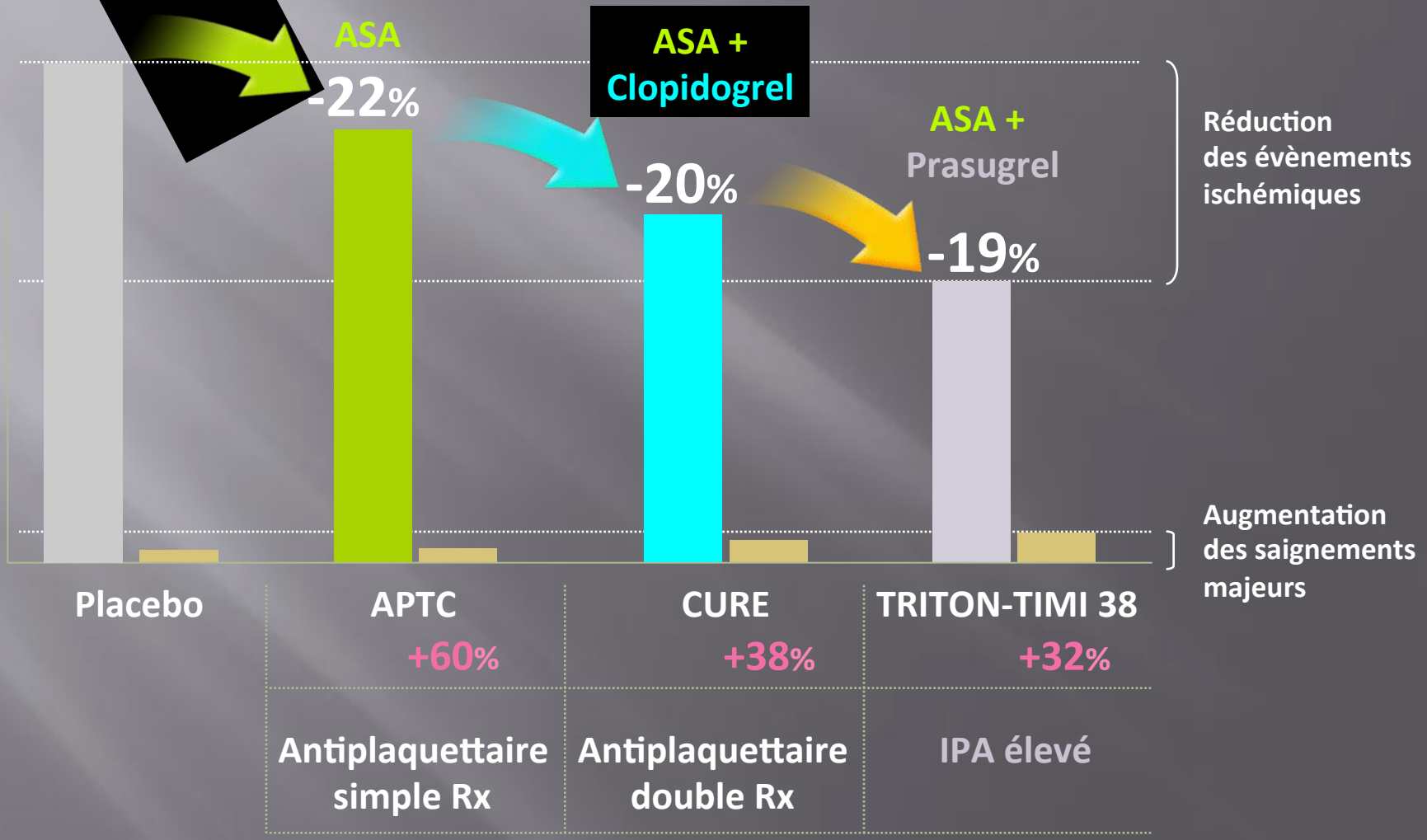
## TICAGRELOR




## PRASUGREL



# Apport des antiagrégants plaquettaires dans la prise en charge du SCA (1-3)

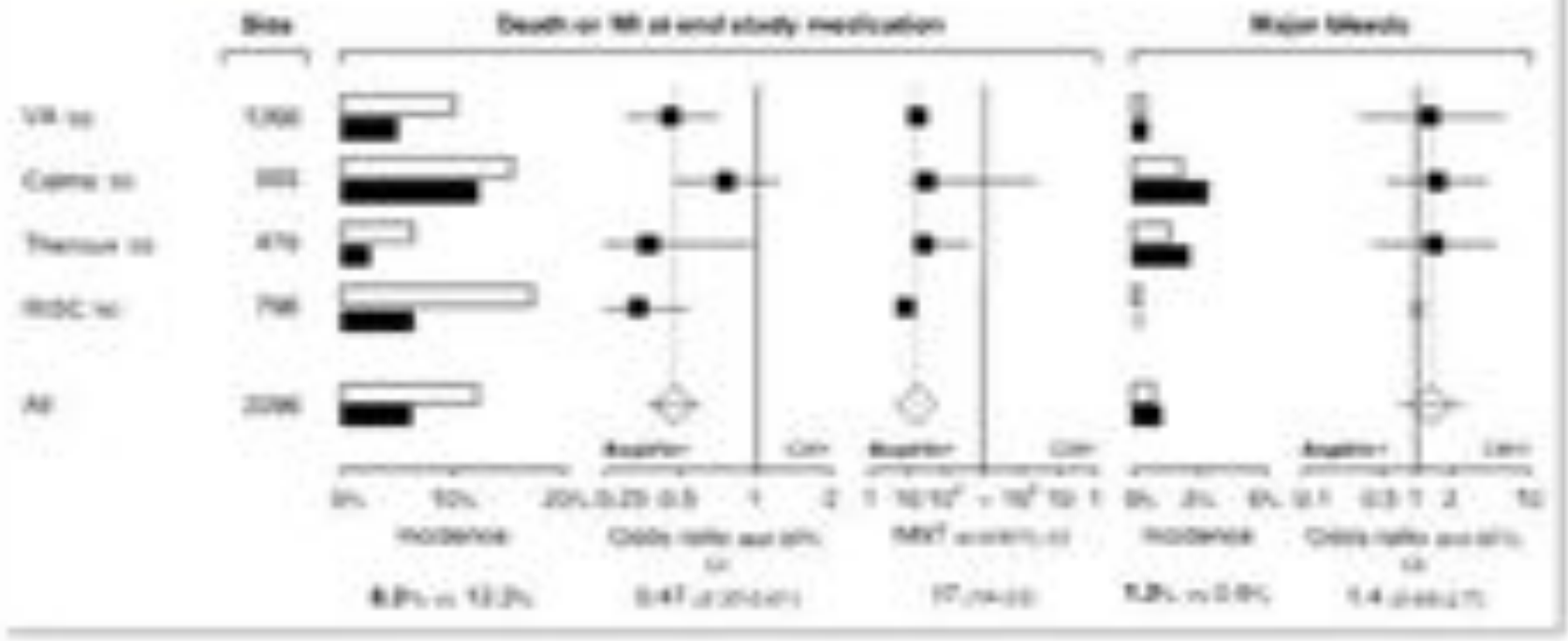




1. APTC : BMJ. 2002 12;324(7329):71-86.
2. CURE : N Engl J Med. 2001 16;345(7):494-502
3. TRITON : N Engl J Med 2007;357:2001-15

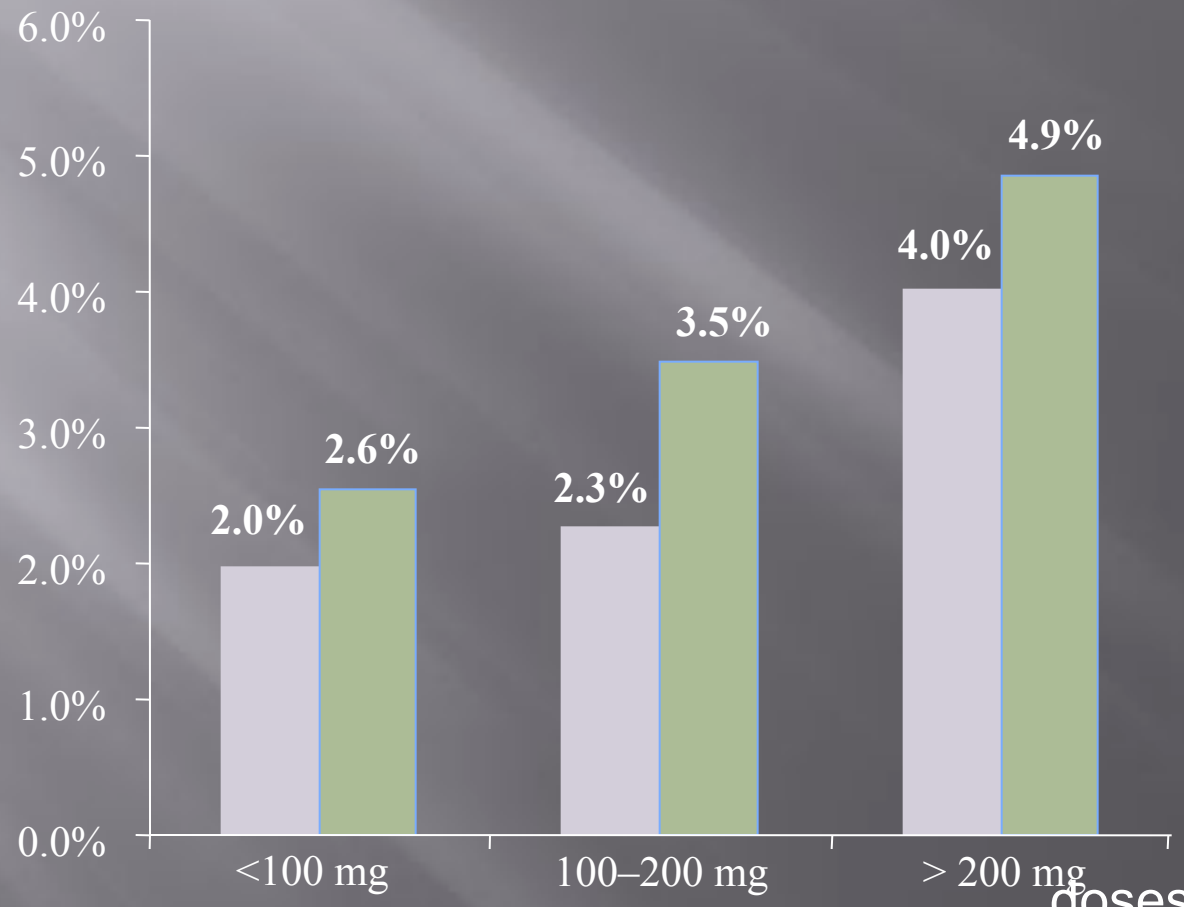
# L’aspirine reste la base

☑ Aspirine 250 à 500 mg / IVD ou PO **IA**



# A moins de 100 mg/j…

Fréquence des saignements majeurs




doses d'aspirine associées

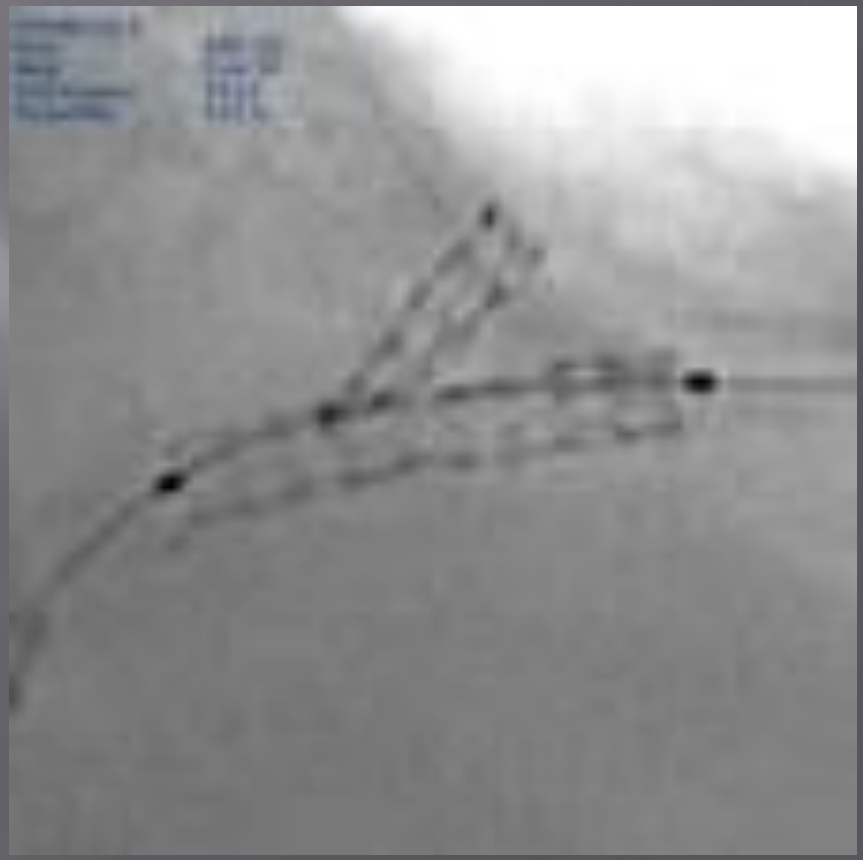
* Plavix : 300 mg en dose de charge puis 75 mg/jour

# Quels arguments pour réduire la durée de traitement ?

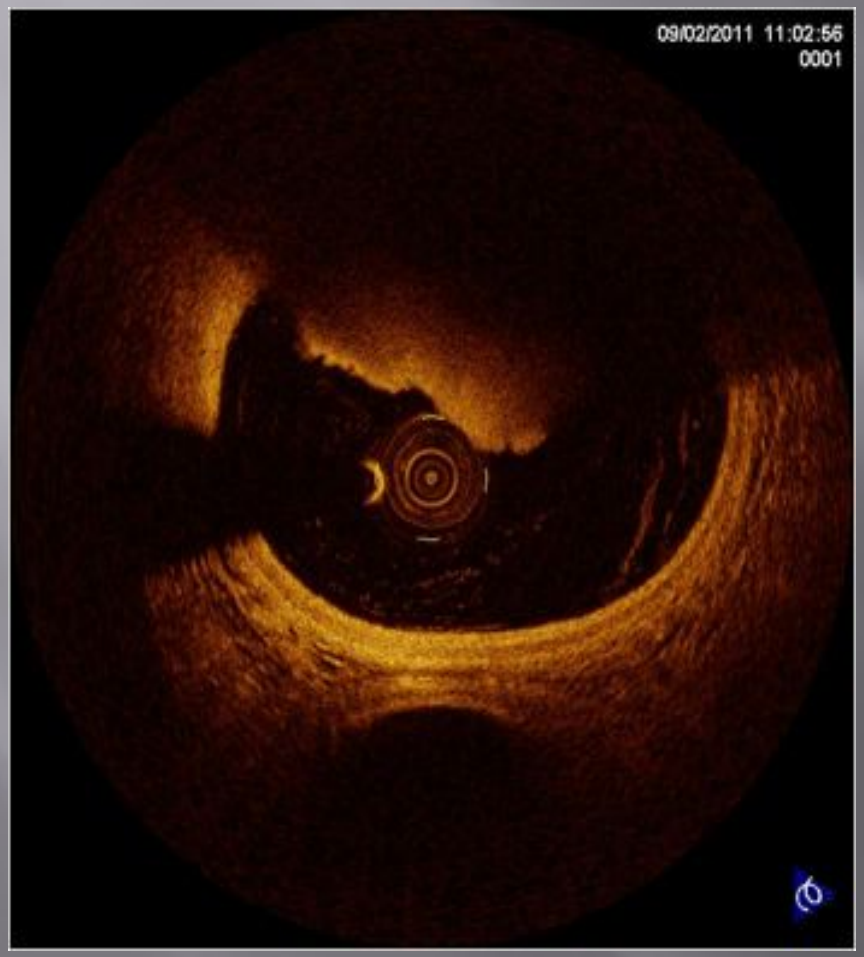
- **-réduction des hémorragies ?**
- **-meilleure observance ?**
- **-La thrombose de stent ne fait (presque ) plus peur ..**

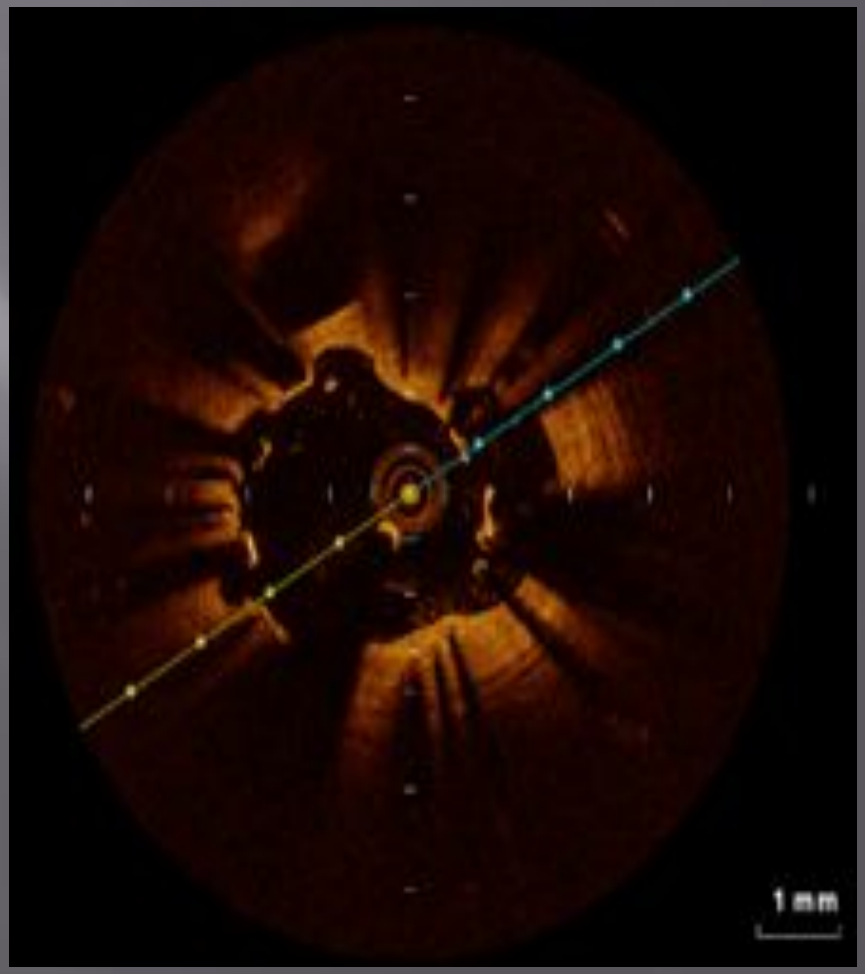
# L'OPTIMISATION de la pose du stent

- Des progrès majeurs ces derniers années
- balbutiement avec le STENTBOOST



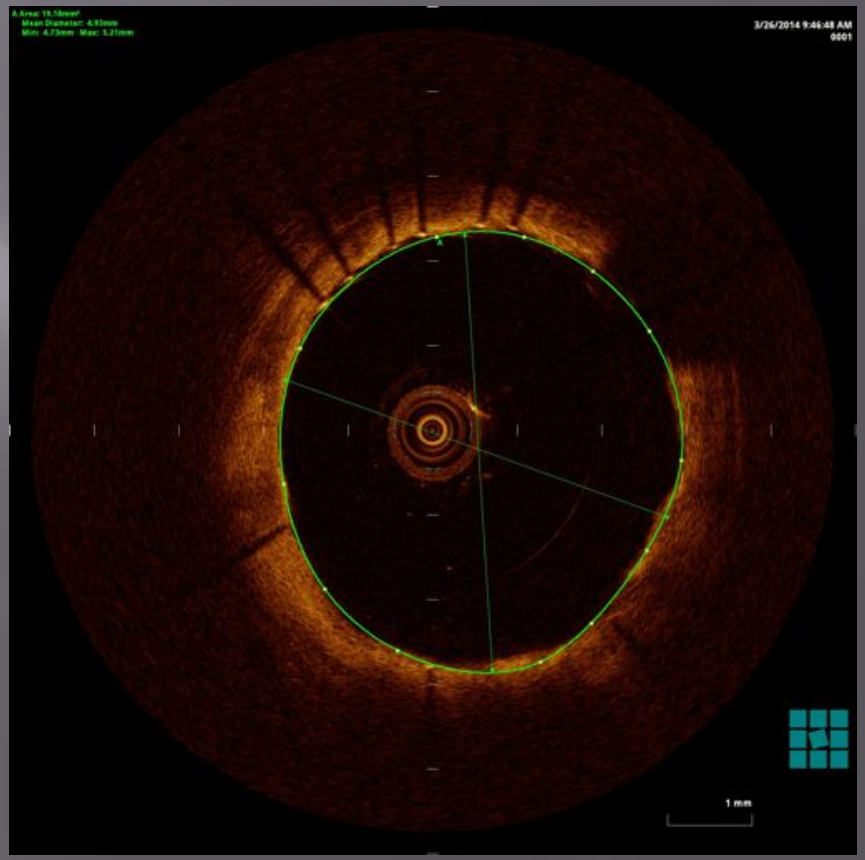
# Optimisation du stenting
# Imagerie OCT



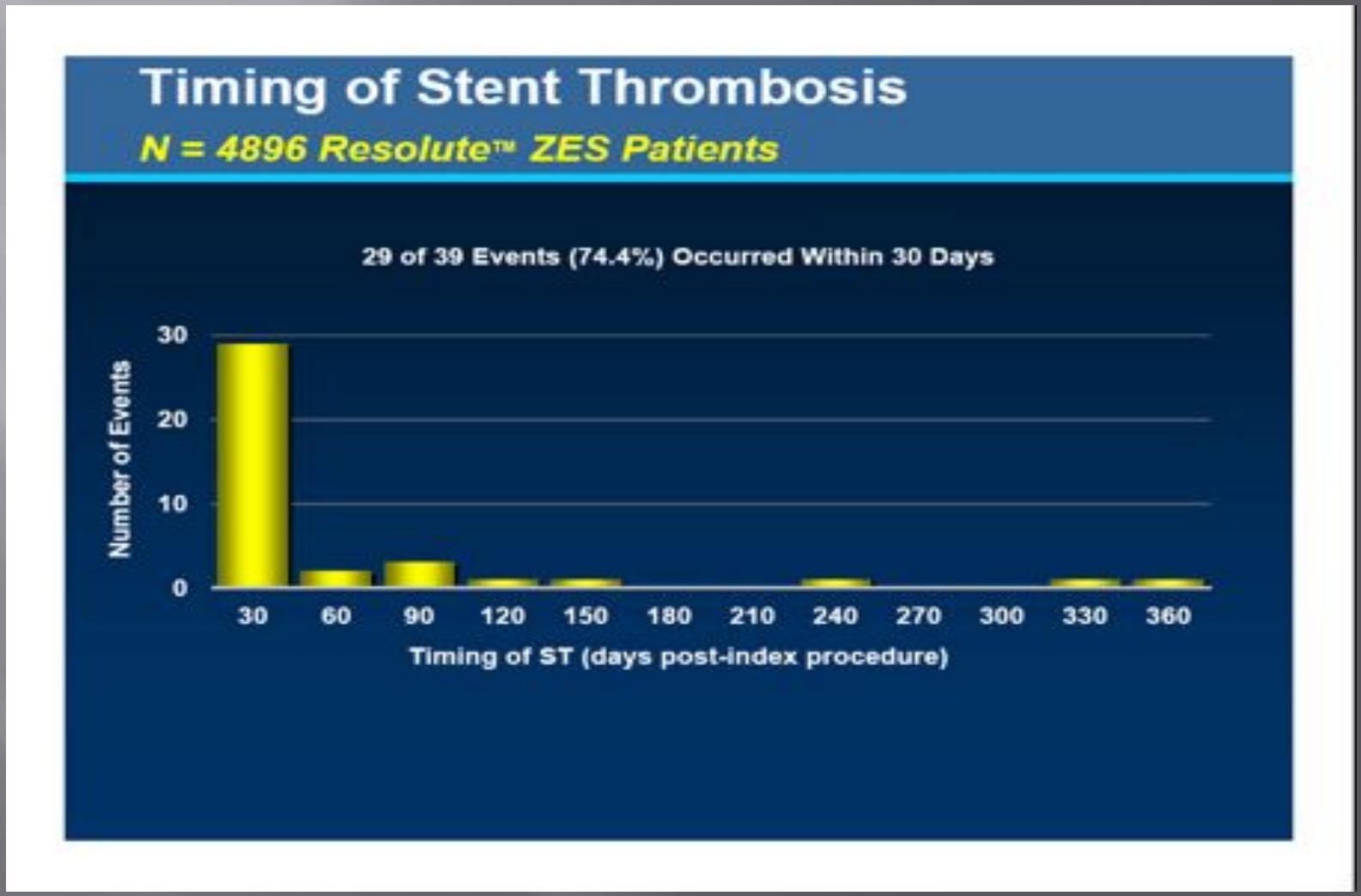
# OPTIMISATION DU STENTING en OCT

- **- Utilisation de ballon non compliant**
- **- POT ( proximal optimal technique)**
- **- stent autoexpandable**
- **-simplification de l'abord des bifurcation**



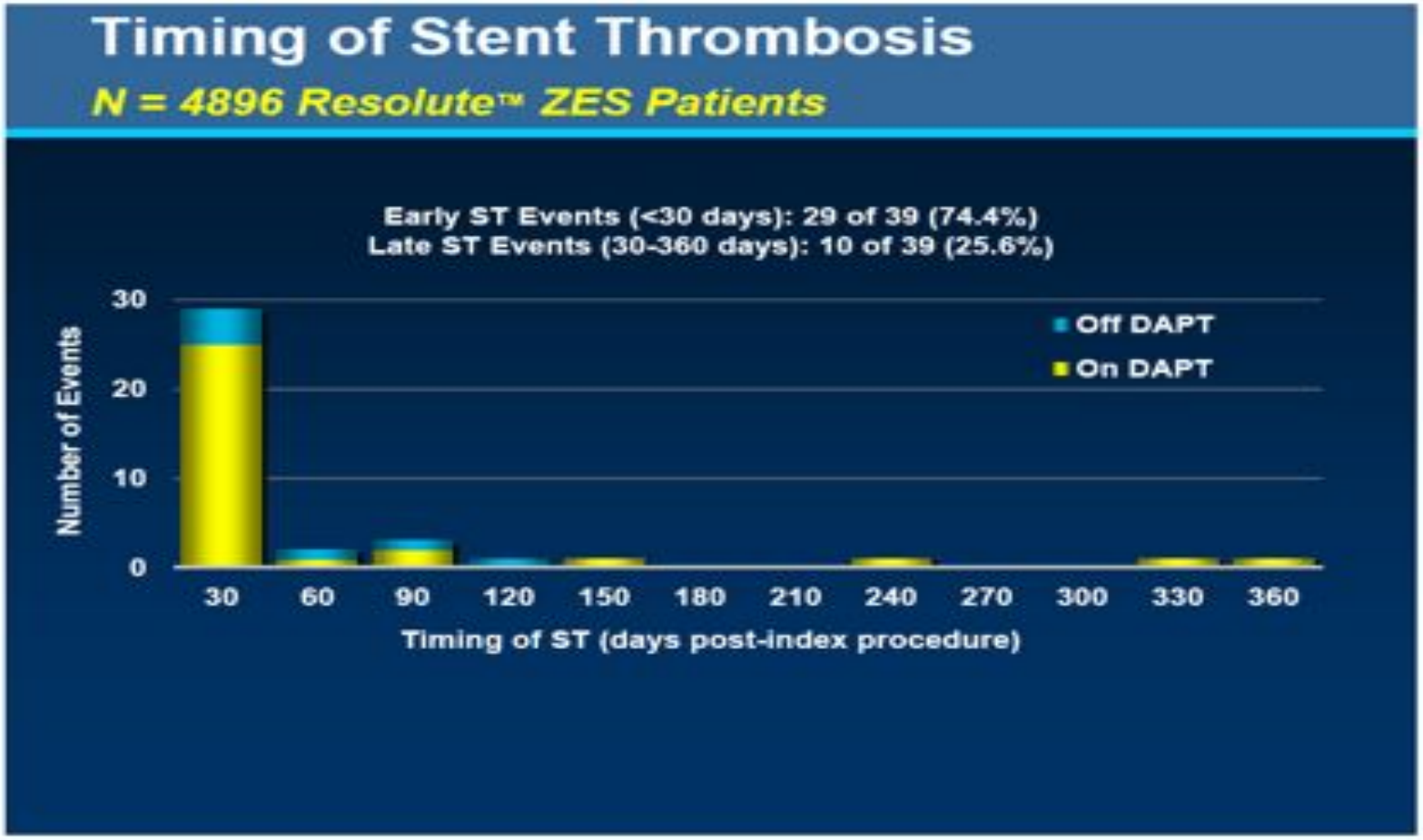
# La thrombose de stent est généralement précoce..

ACC KIRTANE mars 2013



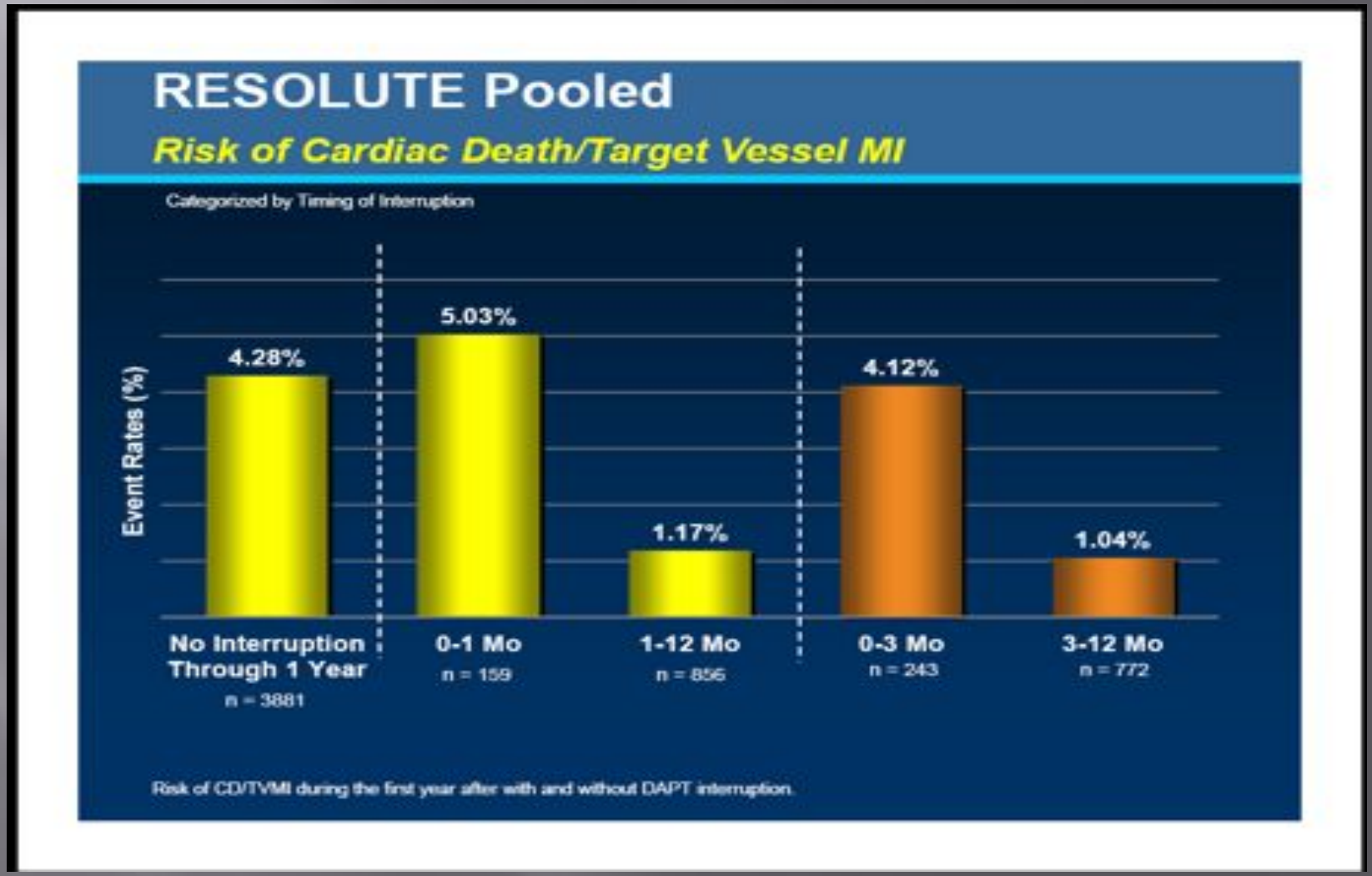
# Mais pas plus avec un arrêt prématuré de la DAAP

ACC KIRTANE mars 2013



# Pas de surisque avec les DES de seconde génération

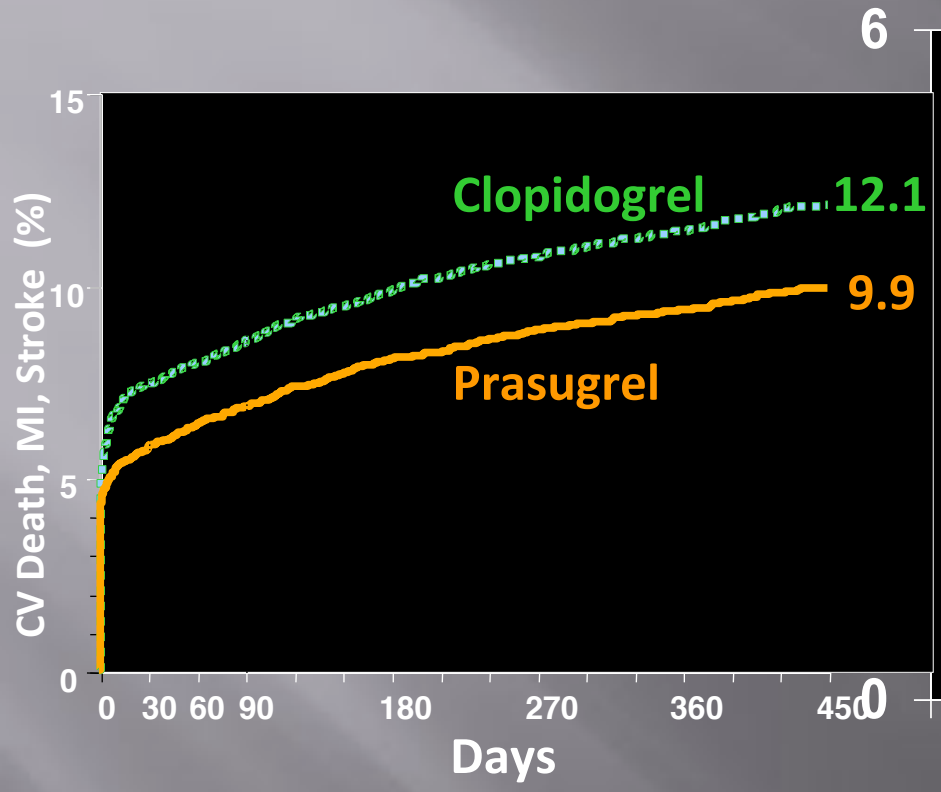
ACC KIRTANE mars 2013



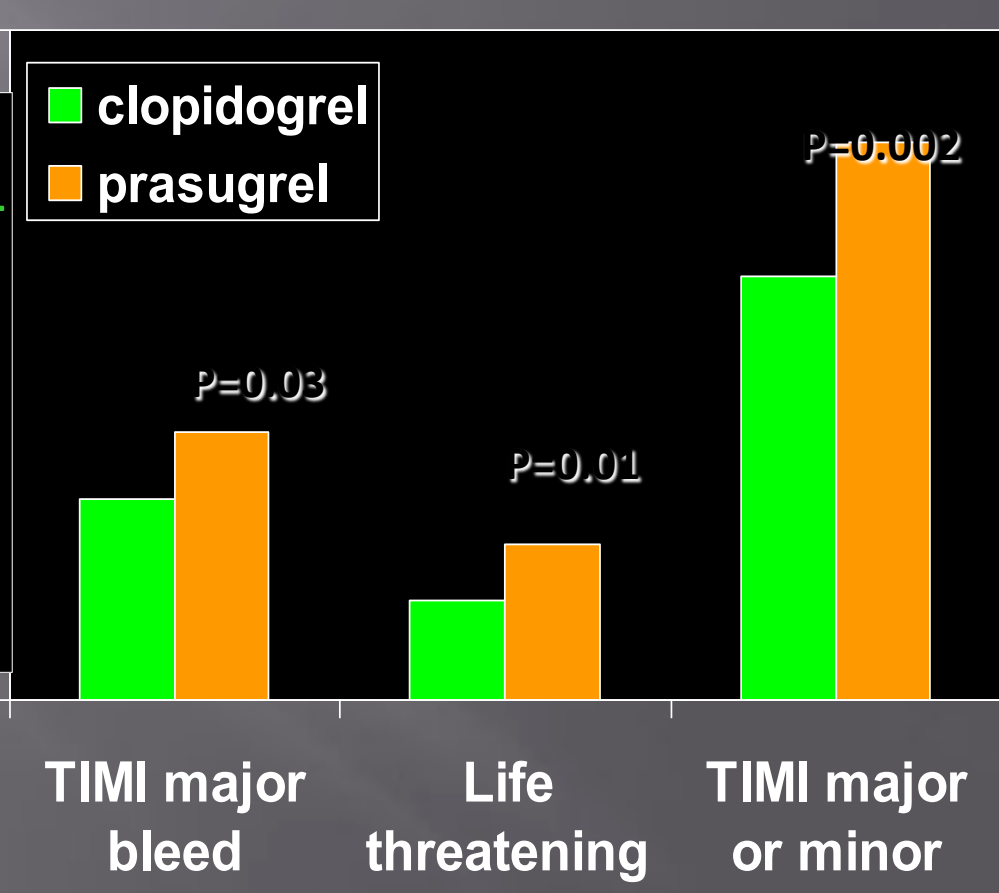
# LE SURISQUE HEMORRAGIQUE

**Plus marqué avec le Prasugrel que le Ticagrelor**

# TRITON-TIMI 38

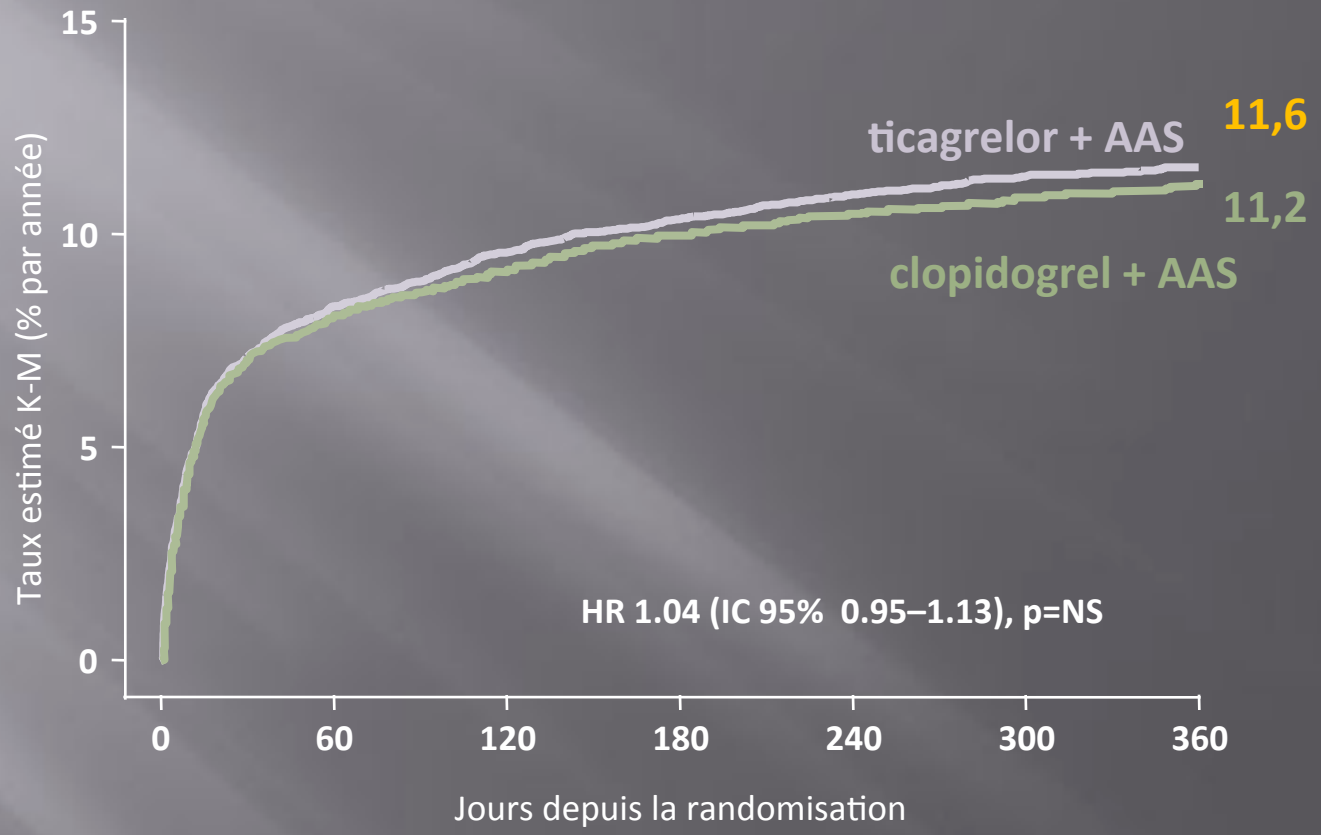



Wiviott et al. *New Engl J Med* 2007;357:2001-2015




**TRITON allowed recruitment of STEMI patients undergoing primary PCI when they presented < 12 hours of symptom onset *or* secondary PCI when they presented late**

# Etude PLATO : critère primaire de tolérance [1]



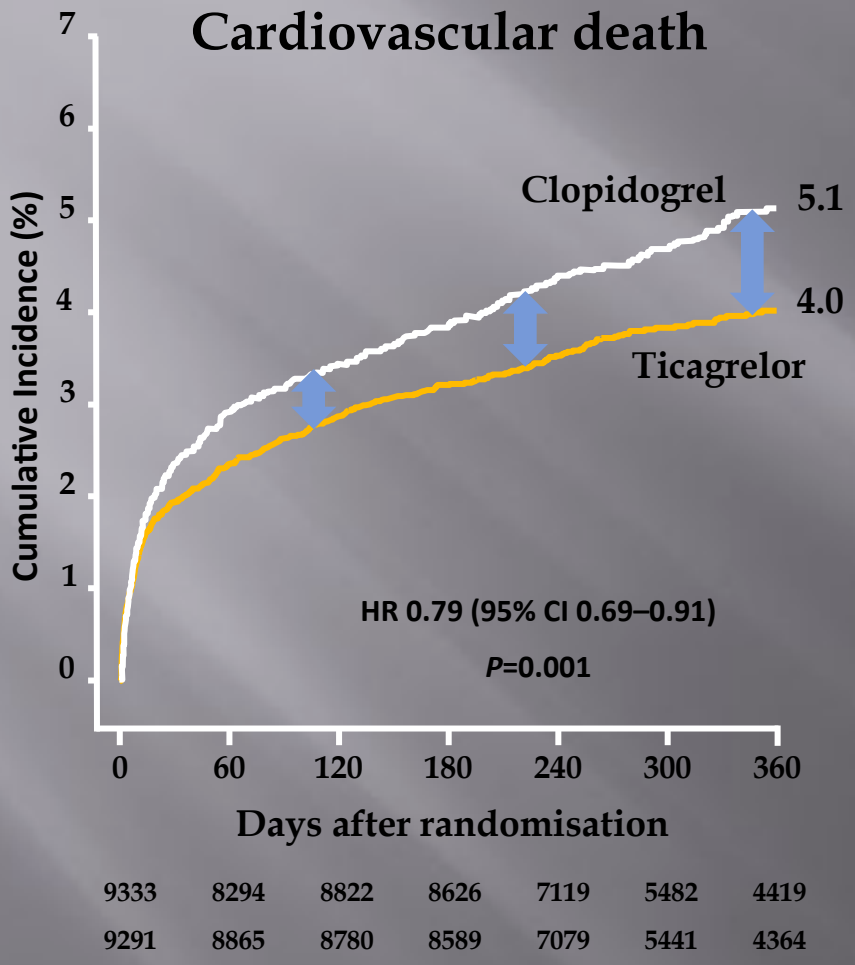

Nombre de patients à risque

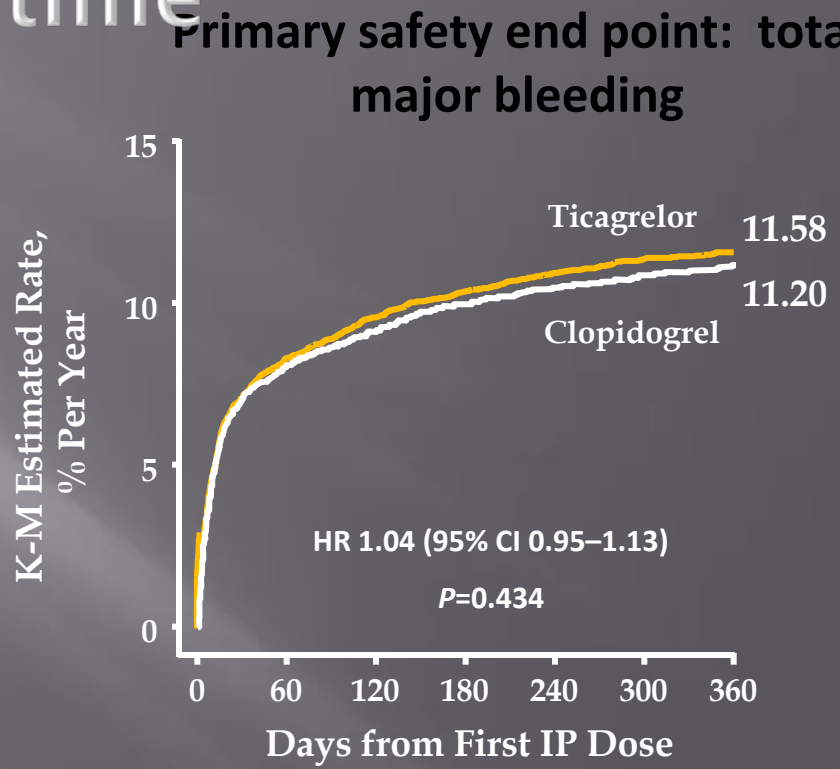
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ticagrelor + AAS | 9,235 | 7,246 | 6,826 | 6,545 | 5,129 | 3,783 | 3,433 |
| clopidogrel + AAS | 9,186 | 7,305 | 6,930 | 6,670 | 5,209 | 3,841 | 3,479 |

*Total Majeurs : incluant saignement majeur, fatal, engageant le pronostic vital et autres saignements majeurs (selon la classification de PLATO).

1. Wallentin *et al.* N Engl J Med. 2009;361(11):1045-57

# PLATO: benefits accrue over time




Wallentin L, et al. *N Engl J Med.* 2009;361:1045-57.

# L'athérosclérose évolue au delà de 6 mois.. ( PRODIGY JACC 2014)

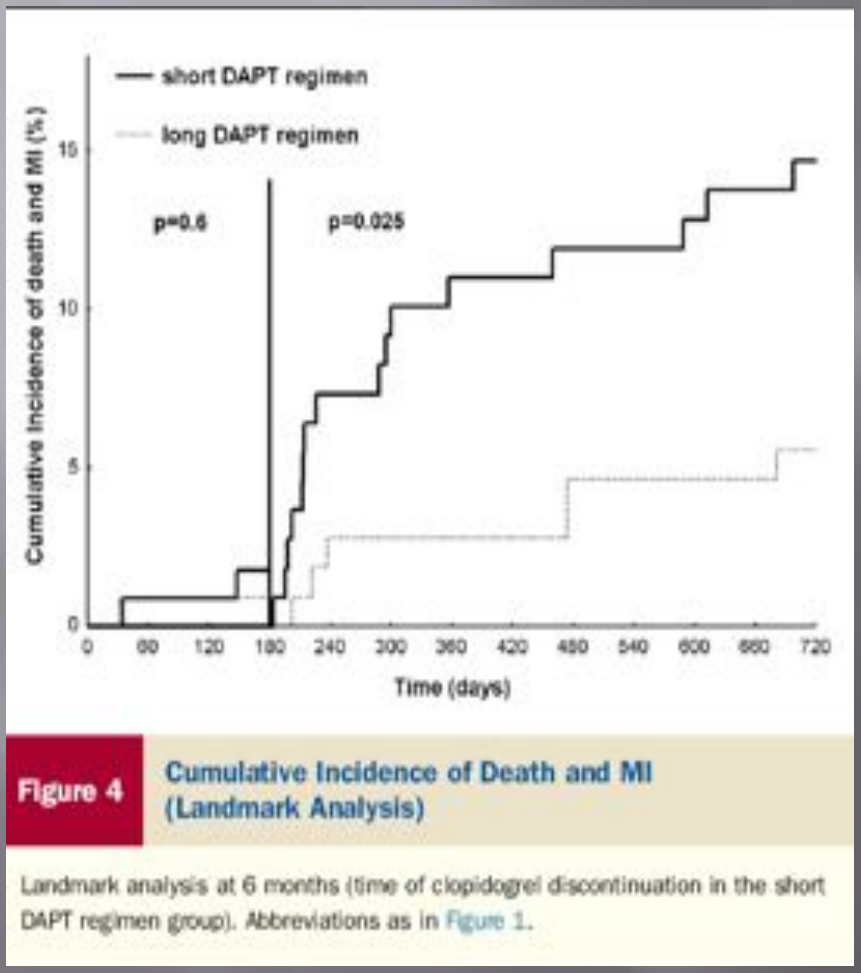



**Figure 4** Cumulative Incidence of Death and MI (Landmark Analysis)

Landmark analysis at 6 months (time of clopidogrel discontinuation in the short DAPT regimen group). Abbreviations as in Figure 1.

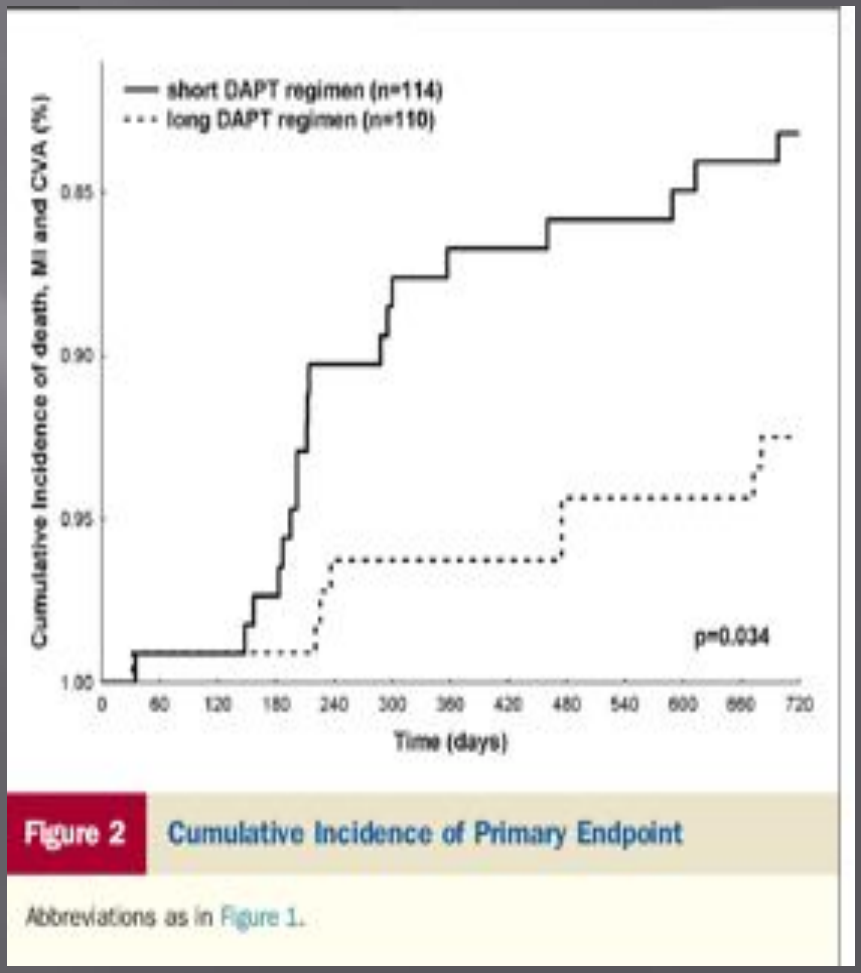



**Figure 2** Cumulative Incidence of Primary Endpoint

Abbreviations as in Figure 1.

# ET MEME APRES 12 MOIS

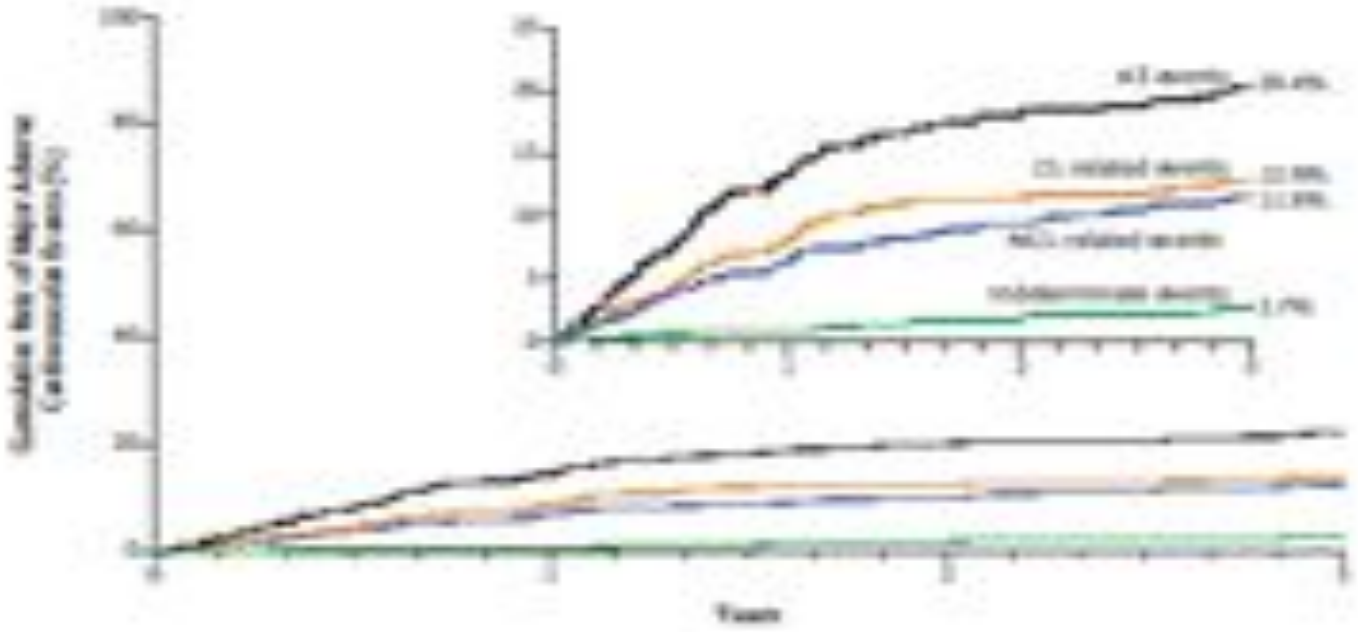
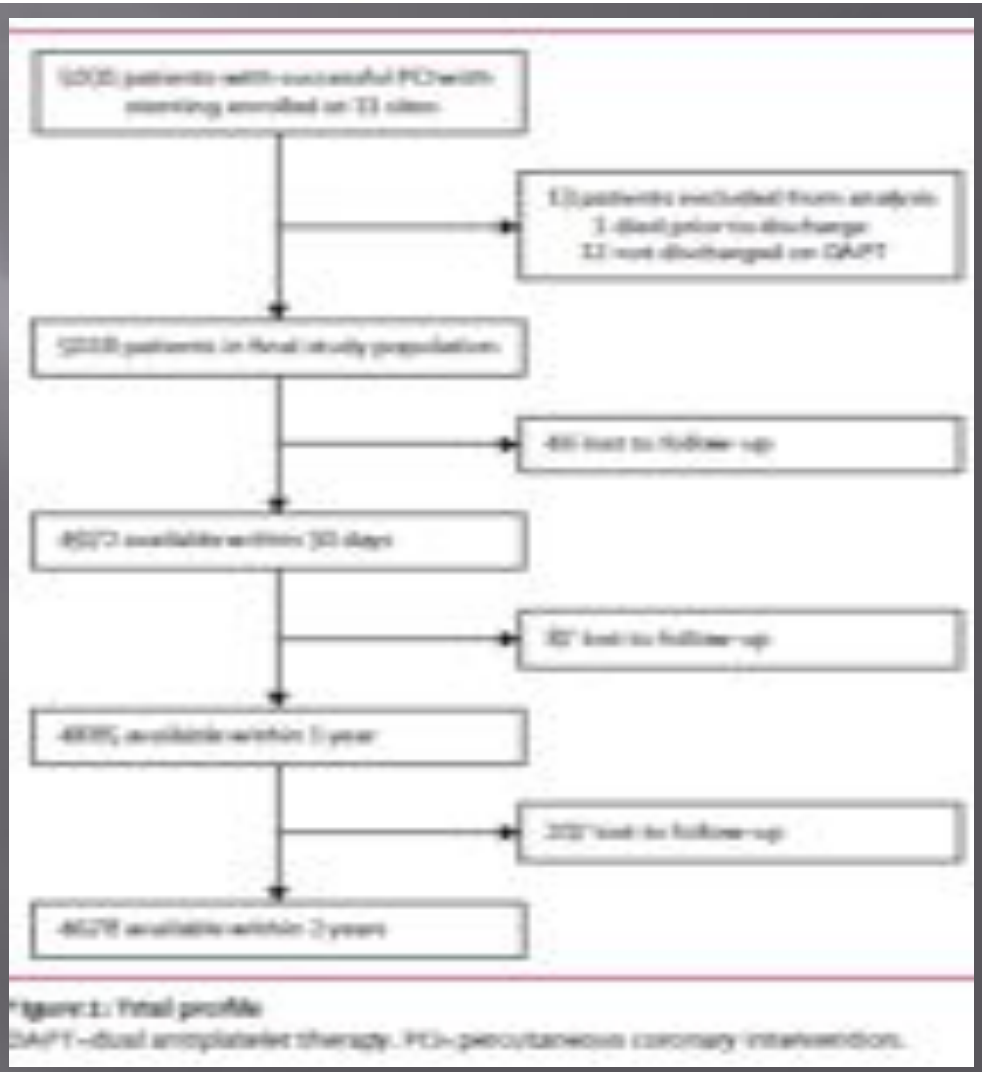


Figure 1. Time-to-Event Curves for Major Adverse Cardiovascular Events after Successful, Uncomplicated Percutaneous Coronary Intervention in 887 Patients with Acute Coronary Syndromes.

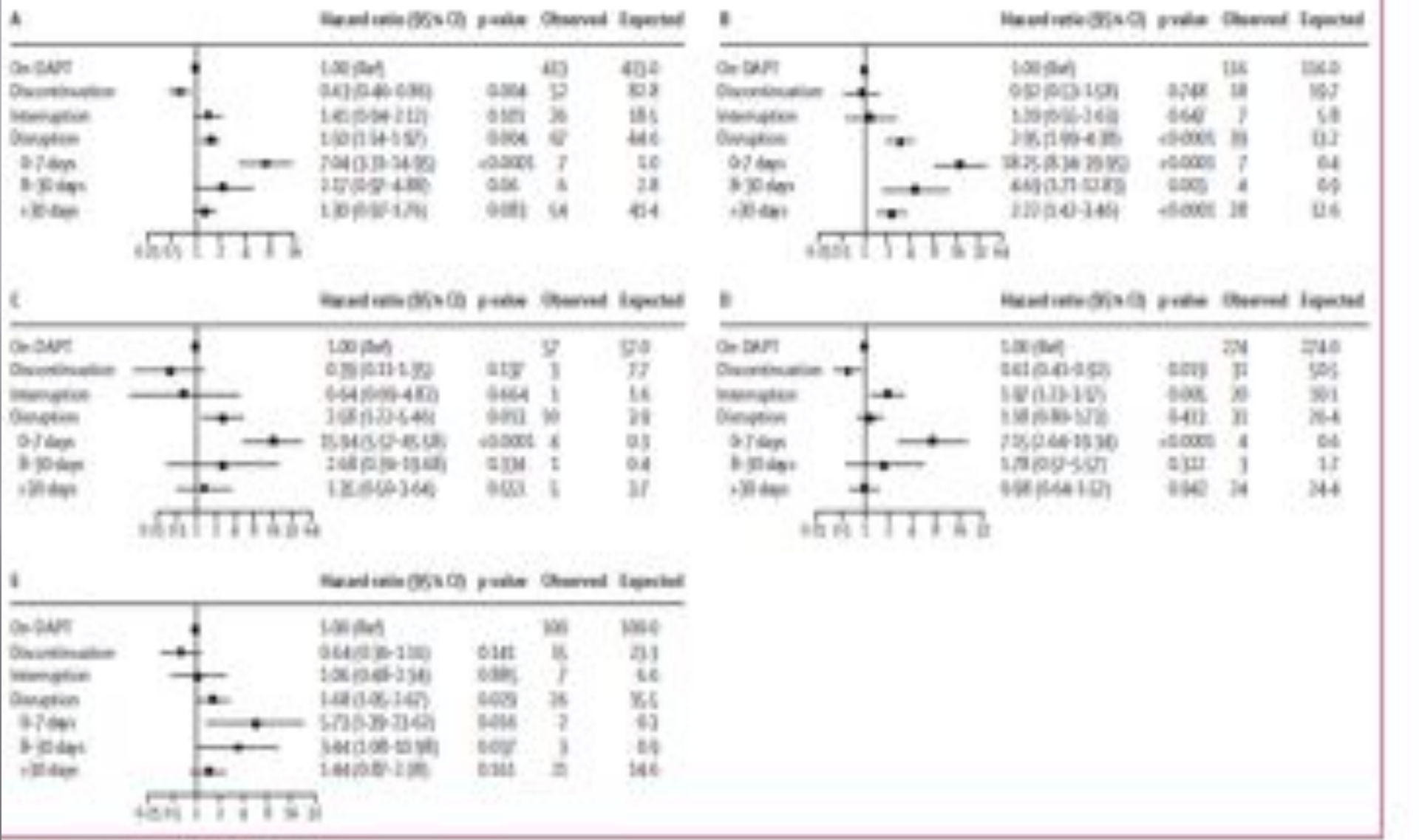
The 3-year cumulative rates of major adverse cardiovascular events are shown (Kaplan–Meier estimates). The 1-year rates were 11.2% for all such events, 7.9% for events related to culprit lesions (CL), 4.4% for events related to nonculprit lesions (NCL), and 0.9% for events of indeterminate origin. CL-related events were those adjudicated to be recurrent disease at the sites of originally treated culprit lesions, NCL-related events were adjudicated to be at sites of nonculprit lesions. Some patients had both CL-related and NCL-related events, and some patients had multiple CL-related events, multiple NCL-related events, or both at different times (in which case the first event is represented in the time-to-event curve). Major adverse cardiovascular events were defined as death from cardiac causes, cardiac arrest, myocardial infarction, and rehospitalization for unstable or progressive angina.

# Cessation of dual antiplatelet treatment and cardiac events after percutaneous coronary intervention (PARIS): 2 year results from a prospective observational study

- 5000 patients
- 200 perdus de vue
- Suivi de 24 mois
- DAAP ( Clopidogrel)



# A/ MACE - B/ STEMI - C / STENT THROMBOSIS D / REVACULARISATION - E/ DEATH



# PARIS en resumé

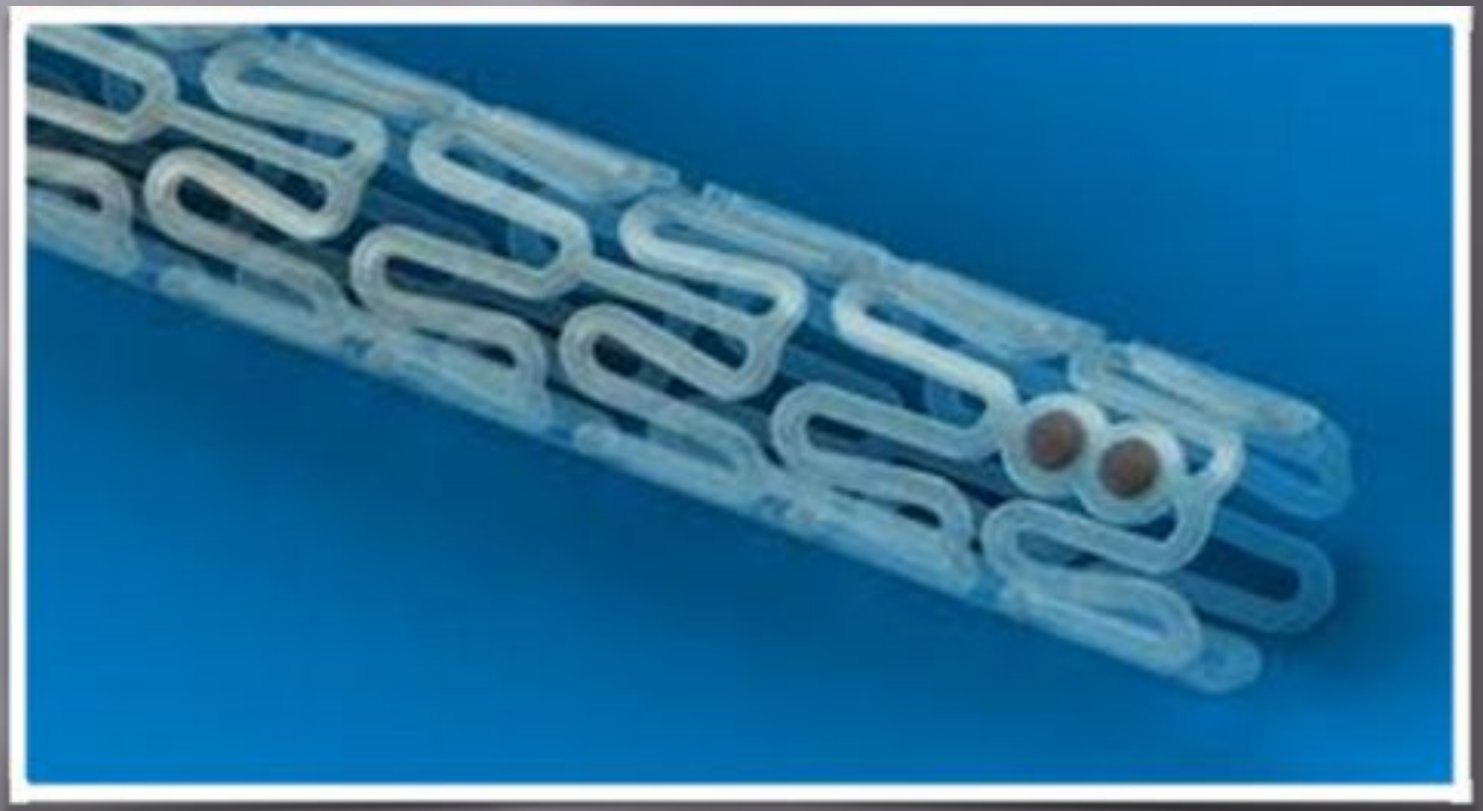
| | On-DAPT | Discontinuation | Interruption | Disruption | Total |
|---|---|---|---|---|---|
| MACE | 413 (74%) | 52 (9%) | 26 (5%) | 67 (12%) | 558 |
| Spontaneous myocardial infarction | 116 (64%) | 18 (10%) | 7 (4%) | 39 (22%) | 180 |
| Definite or probable stent thrombosis | 57 (80%) | 3 (4%) | 1 (1%) | 10 (14%) | 71 |
| Clinically indicated target lesion revascularisation | 274 (77%) | 31 (9%) | 20 (6%) | 31 (9%) | 356 |
| Cardiac death | 100 (68%) | 15 (10%) | 7 (5%) | 26 (18%) | 148 |

MACE=major adverse cardiovascular event. DAPT=dual antiplatelet therapy.

*Table 4:* Number of events for each clinical outcome by worst DAPT cessation status achieved before the MACE event

- 50 % arrêt de DAAP à 1 an ( programmé ou non)
- Pas de bénéfice évident sur les MACE au delà de 1 an
- Pas de surisque si arrêt de moins de 15 jours ( Xie)
- Majorité des thrombose de stent dans les 30 jours post disruption
- Mais 75 % des MACE sous DAAP…

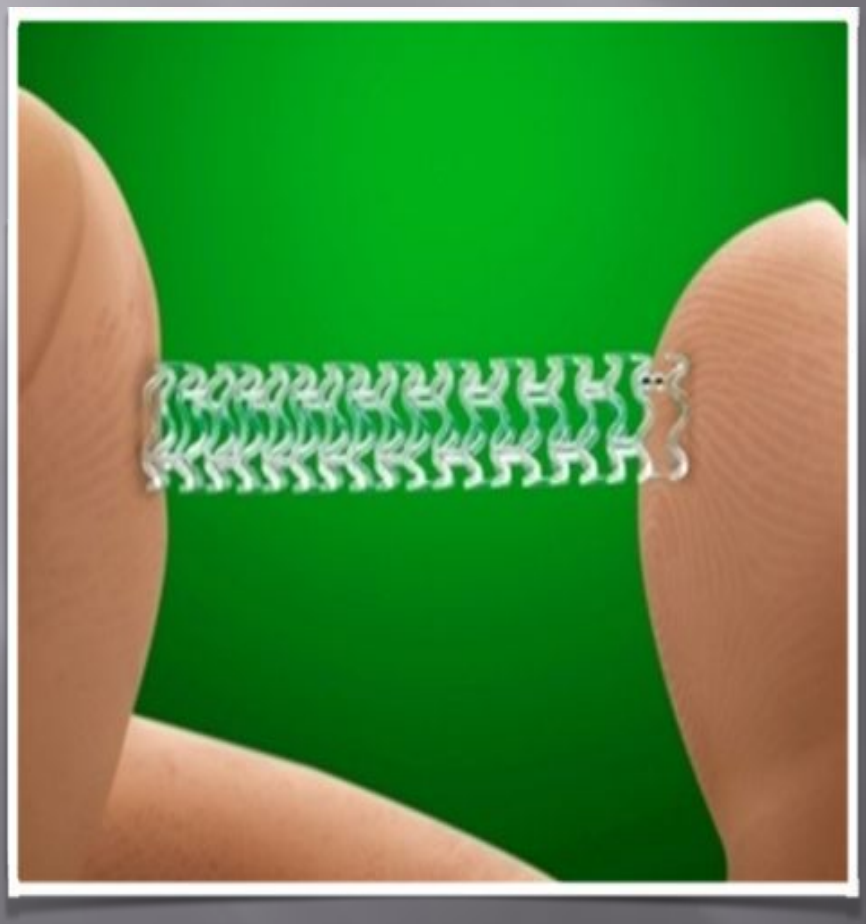
# Certains stents nécessitent une longue DAAP: les résorbables

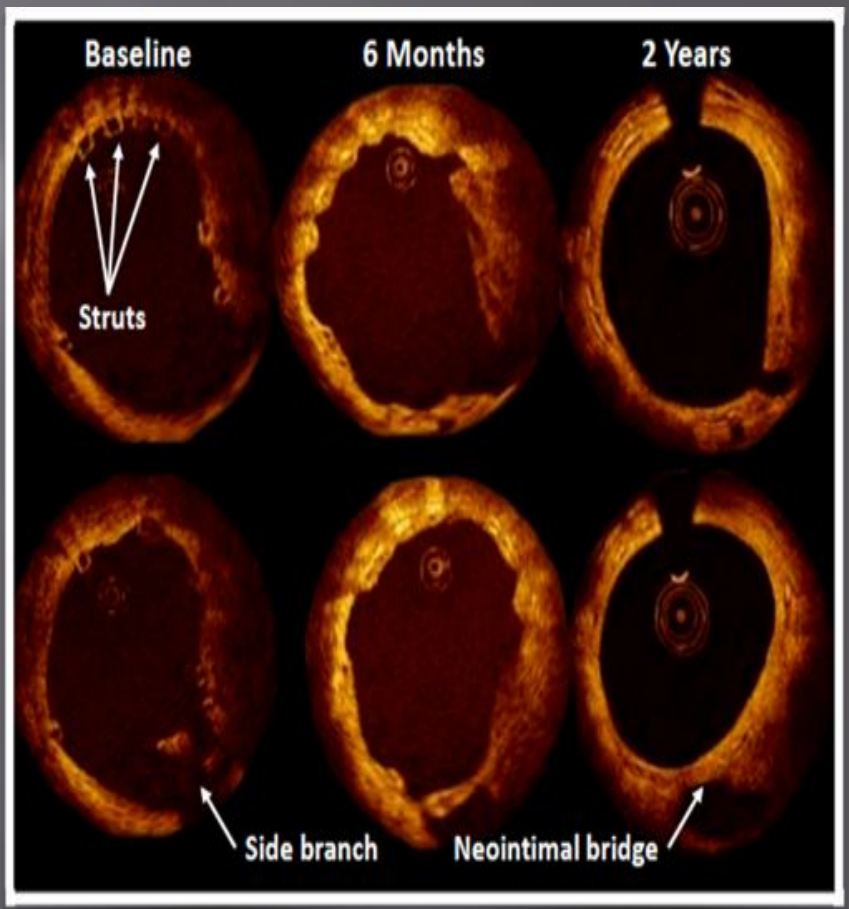


# Le stent Bioresorbable

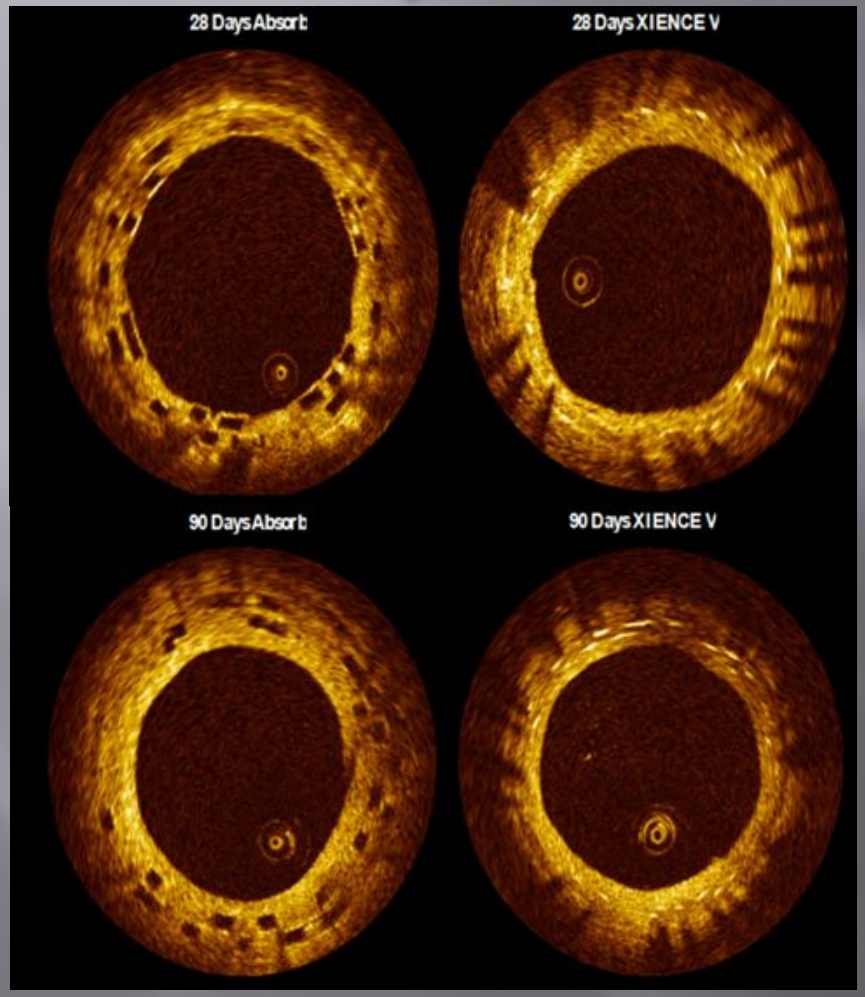
ABSORB ( ABBOT)

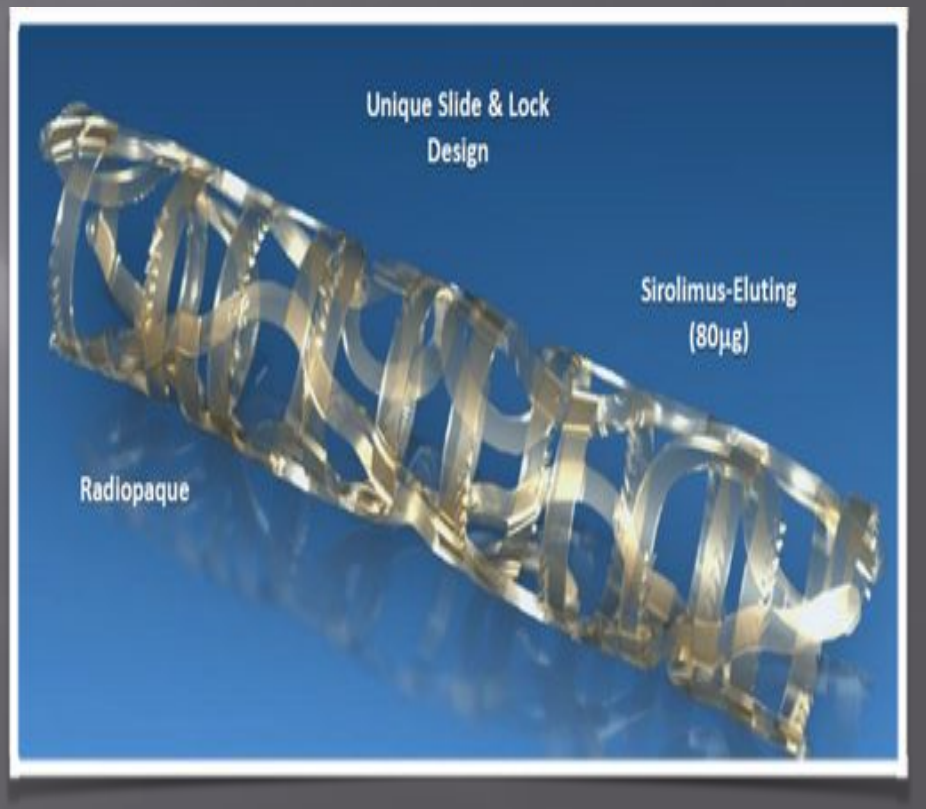
2 % DES STENTS IMPLANTES EN FRANCE





# Résorption lente en 24 à 36 mois épaisseur de 140 µm



# CE QU'IL FAUT RETENIR..

- DAAP de 1 ans reste utile
- Mais suffisante avec les stents actuels
- Balance MACE-HEMORRAGIES favorable
- ***2/3 des récidives de SCA surviennent sur les non CULPRIT lésions***
- Près de 50 % des patients à 1 ans ont stoppé leur DAAP ( interuption ou disruption …)
- Le risque de thrombose de stent s'atténue grandement après 30 jours d'arrêt

# Durée traitement AAP en cas de SCA: les recommendations

- QUELQUE SOIT LE TYPE DE SCA ET LE TYPE DE PRISE EN CHARGE : les Recommandations préconisent une bithérapie allant jusqu'à 12 mois

- *Recommandations de la société européenne de cardiologie :*

**STEMI**

| | | |
|---|---|---|
| DAPT with aspirin and an oral ADP receptor antagonist must be continued for up to 12 months after STEMI, with a strict minimum of: | I | C |
| • 1 month for patients receiving BMS | I | C |
| • 6 months for patients receiving DES | IIb | B |

**NSTEMI**

| | | |
|---|---|---|
| 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 |

- *Recommandations Françaises sur le bon usage des antiplaquettaires :*

***Post-IDM***

Durant l'année suivant un infarctus du myocarde (IDM), il est recommandé de prescrire, soit aspirine (75-160 mg/j) + clopidogrel (75 mg/j), soit aspirine (75-160 mg/j) + prasugrel (10 mg), soit aspirine (75-160 mg/j) + ticagrelor (180 mg/j) (grade A). Puis l'aspirine sera poursuivie en monothérapie au long cours.

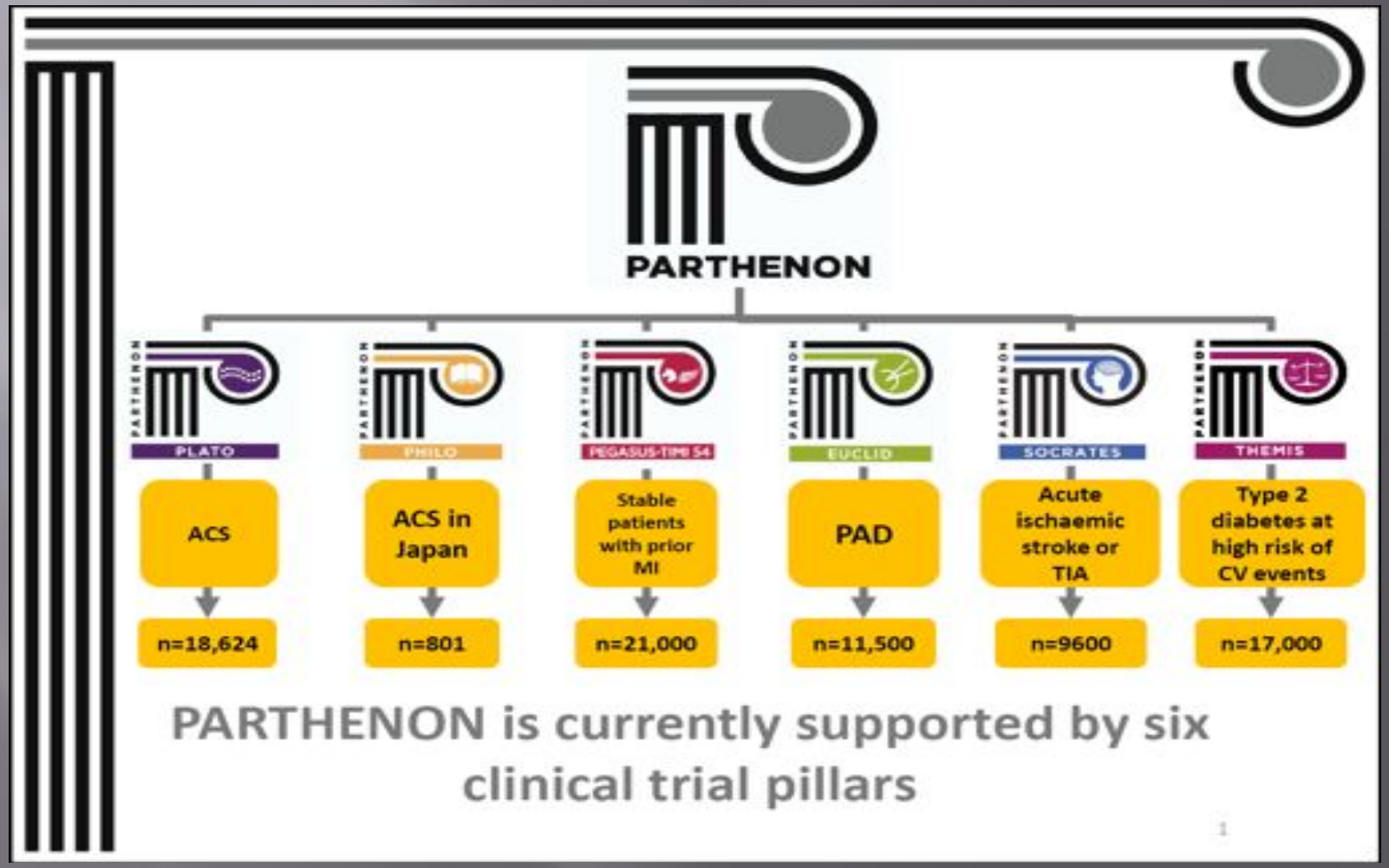
# Comme CLOPIDOGREL par le passé ..

| Acute STEMI | UA/NSTEMI | PCI | Long-term 2º (1º) Prevention |
|---|---|---|---|
| CLARITY TIMI 28 | CURE | CREDO | CAPRIE |
| COMMIT (CCS-2) | | | CHARISMA |

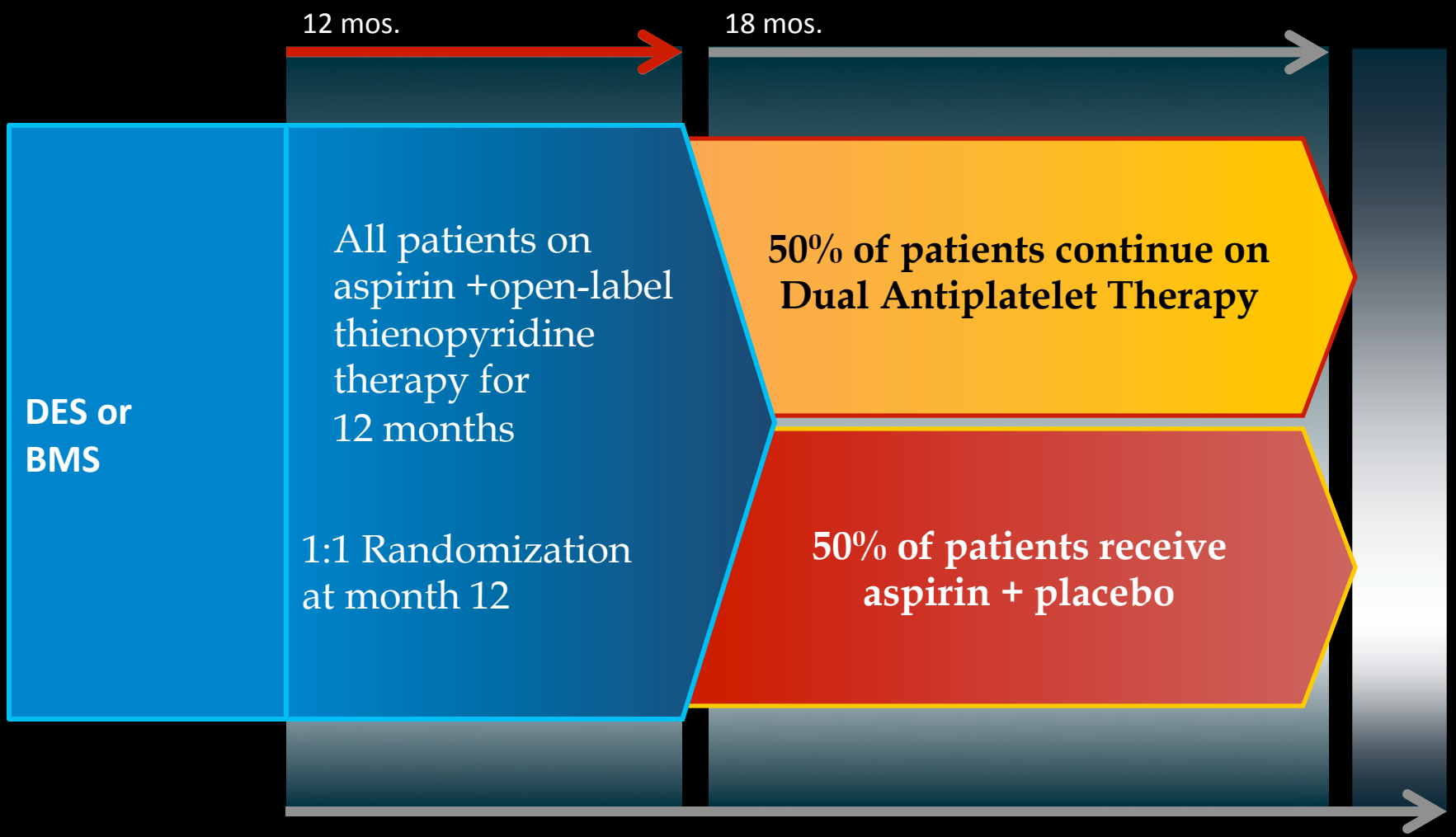
| STEMI | NSTEMI / UA | PCI | MI/Stroke/PAD | High-Risk Vascular Disease |
|---|---|---|---|---|
| 30 Days + Benefit | 1 Year + Benefit | 1 Year + Benefit | 1-3 Years + Benefit | Up to 3.5 years (ongoing) |

Cannon CP. Presented at: 54th Annual Scientific Session of the American College of Cardiology; March 9, 2005; Orlando, Fla.

# Le développement du TICAGRELOR se poursuit..



# DAPT Study Design




*Mauri, Kereiakes et al, AHJ, December 2010*

www.daptstudy.org www.clinicaltrials.gov – NCT00977938

# The PEGASUS trial

PEGASUS TIMI 54

*N ~ 21,000*

**Stable pts with history of MI 1-3 yrs prior**
**+ ≥1 additional atherothrombosis risk factor***

** Age ≥65 yrs, diabetes, 2nd prior MI, multivessel CAD, or chronic non-end stage renal dysfunction*

**RANDOMIZE**
**DOUBLE BLIND**

**Planned treatment with ASA 75 – 150 mg & Standard background care**

| Ticagrelor 90 mg bid | Ticagrelor 60 mg bid | Placebo |
|---|---|---|

**Follow-up Visits**
**Q4 mos for 1st yr, then Q6 mos**

**Min 12 mos and median 26 mos follow-up**
**Event-driven trial**

**Primary Efficacy Endpoint: CV Death, MI, or Stroke**
**Primary Safety Endpoint: TIMI Major Bleeding**