INFARCTUS AIGU: STENT ACTIF OU STENT NU ?

DR M. PANSIERI

Session GACI

APPAC 10/06/2010

Facteurs pronostiques dans l'infarctus aigu (ST+)

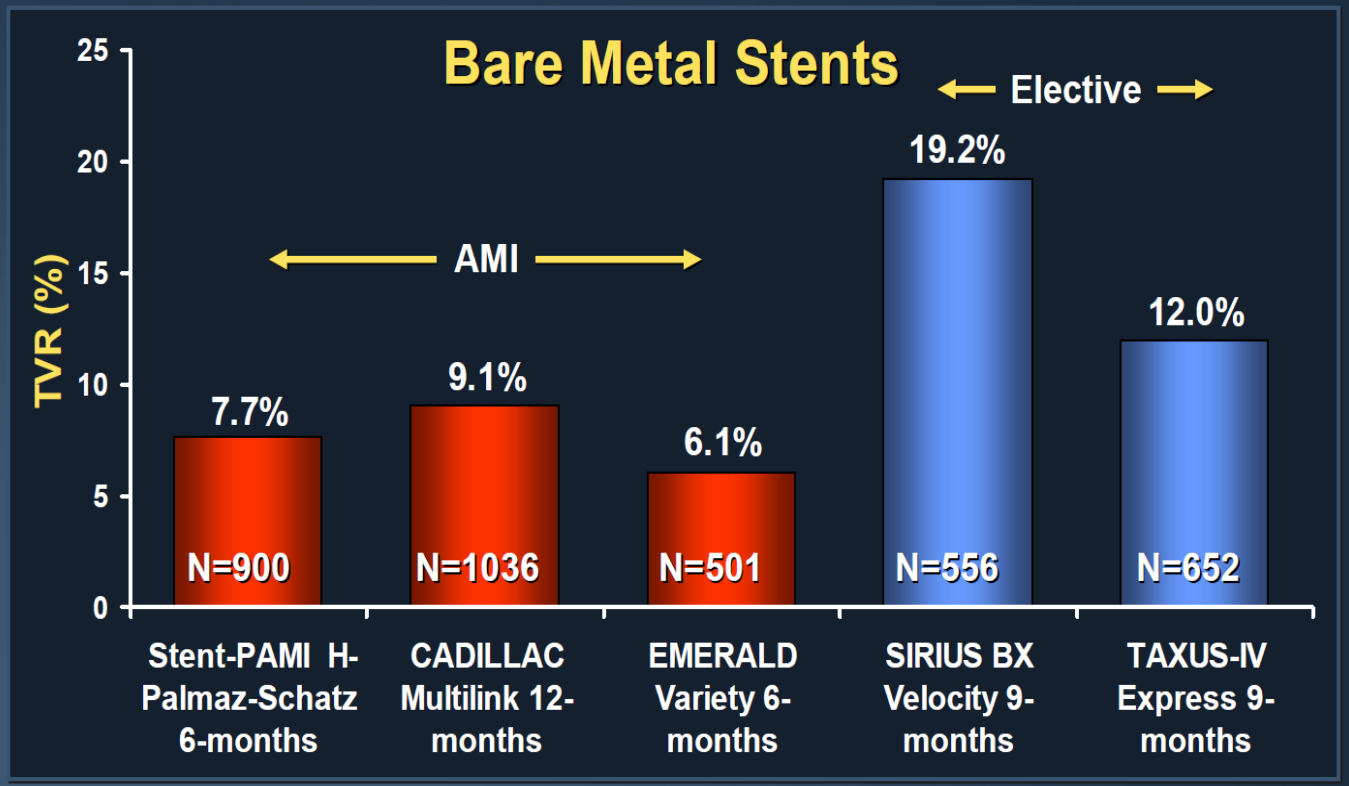
- Localisation de l'infarctus
- Précocité de la reperfusion
- Angioplastie primaire/lyse
- Taille de l'infarctus (ECG, tropo., IRM)
- Saignements
- Glycémie à l'admission
- Type de stent ?

Stent nu ou stent actif: les enjeux

- Stent nu: risque de resténose?
- Stent actif: risque de thrombose?
- Stent « bioactif »: alternative?

Resténose dans l'IDM aigu: Est-ce vraiment un problème?

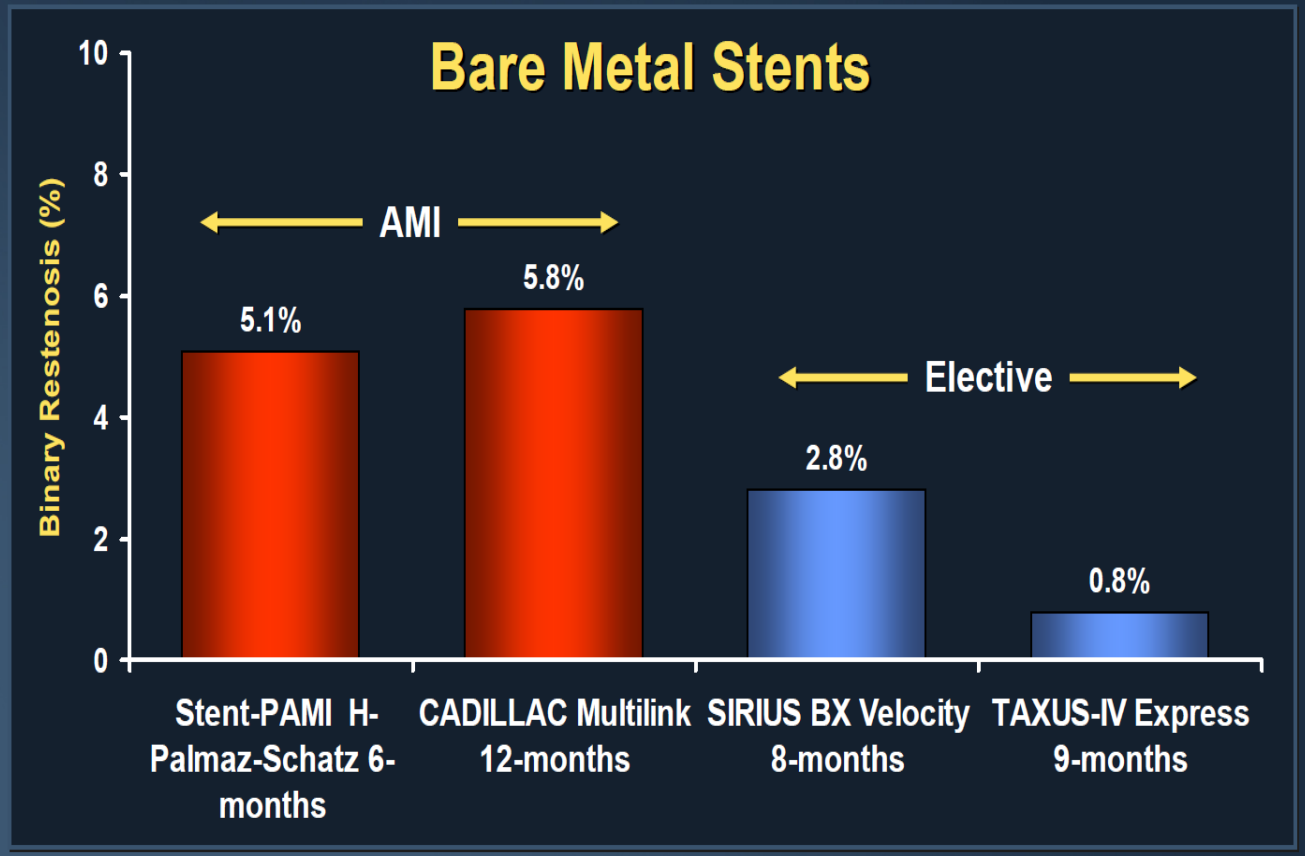
Clinical Restenosis (TVR) After Primary Stenting in AMI



CARDIOVASCULAR RESEARCH FOUNDATION

COLUMBIA UNIVERSITY MEDICAL CENTER

Target Vessel Reocclusion after Primary Stenting in AMI



Risques potentiels des D.E.S. dans l'IDM

- Cicatrisation artérielle retardée
- Malapposition tardive?
- → ↗ potentielle du risque de thrombose de stent subaigue et tardive

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 14, 2006 VOL. 355 NO. 11

TYPHOON
712 pts
TVF 1 year

Sirolimus-Eluting versus Uncoated Stents in Acute Myocardial Infarction

Christian Spaulding, M.D., Patrick Henry, M.D., Ph.D., Emmanuel Teiger, M.D., Ph.D., Kevin Beatt, M.B., B.S., Ph.D., Ezio Bramucci, M.D., Didier Carrié, M.D., Michel S. Slama, M.D., Bela Merkely, M.D., Ph.D., Andrejs Erglis, M.D., Ph.D., Massimo Margheri, M.D., Olivier Varenne, M.D., Ph.D., Ana Cebrian, Ph.D., Hans-Peter Stoll, M.D., David B. Snead, Ph.D., and Christoph Bode, M.D., for the TYPHOON Investigators*

ABSTRACT

BACKGROUND

Sirolimus-eluting stents reduce rates of restenosis and reintervention, as compared with uncoated stents. Data are limited regarding the safety and efficacy of such stents in primary percutaneous coronary intervention (PCI) for acute myocardial infarction with ST-segment elevation.

METHODS

We performed a single-blind, multicenter, prospectively randomized trial to compare sirolimus-eluting stents with uncoated stents in primary PCI for acute myocardial infarction with ST-segment elevation. The trial included 712 patients at 48 medical centers. The primary end point was target-vessel failure at 1 year after the procedure, defined as target-vessel–related death, recurrent myocardial infarction, or target-vessel revascularization. A follow-up angiographic substudy was performed at 8 months among 174 patients from selected centers.

RESULTS

The rate of the primary end point was significantly lower in the sirolimus-stent group than in the uncoated-stent group (7.3% vs. 14.3%, P=0.004). This reduction was driven by a decrease in the rate of target-vessel revascularization (5.6% and 13.4%, respectively; P<0.001). There was no significant difference between the two groups in the rate of death (2.3% and 2.2%, respectively; P=1.00), reinfarction (1.1% and 1.4%, respectively; P=1.00), or stent thrombosis (3.4% and 3.6%, respectively; P=1.00). The degree of neointimal proliferation, as assessed by the mean (±SD) in-stent late luminal loss, was significantly lower in the sirolimus-stent group (0.14±0.49 mm, vs. 0.83±0.52 mm in the uncoated stent group; P<0.001).

CONCLUSIONS

Among selected patients with acute myocardial infarction, the use of sirolimus-eluting stents significantly reduced the rate of target-vessel revascularization at 1 year. (ClinicalTrials.gov number, NCT00232830.)

From Assistance Publique–Hôpitaux de Paris (AP–HP) Cochin Hospital, Paris 5 Medical School Rene Descartes University and INSERM U780, Paris (C.S., O.V.); AP–HP Lariboisiere Hospital, Paris 7 Medical School University Denis Diderot, Paris (P.H.); AP–HP Henri Mondor Hospital, Paris 12 Medical School, Créteil (E.T.); Hospital Rangueil, Toulouse (D.C.); and AP–HP Antoine Béclère Hospital, Paris 12 Medical School Paris Sud University, Clamart (M.S.S.) — all in France; Mayday University Hospital, London (K.B.); Istituto di Ricovero e Cura a Carattere Scientifico Policlinico San Matteo, Pavia (E.B.), and Azienda Universitaria Ospedaliera Careggi, Florence (M.M.) — both in Italy; Semmelweis University, Budapest (B.M.); Pauls Stradins University Hospital, Riga, Latvia (A.E.); Cordis (Johnson & Johnson), Waterloo, Belgium (A.C., H.-P.S.) and Warren, NJ (D.B.S.); and the University of Freiburg, Freiburg, Germany (C.B.). Address reprint requests to Dr. Spaulding at Cochin Hospital, 27 rue du Faubourg St. Jacques, 75014 Paris, or at christian.spaulding@cch.ap-hop-paris.fr.

*Members of the Trial to Assess the Use of the Cypher Stent in Acute Myocardial Infarction Treated with Balloon Angioplasty (TYPHOON) are listed in the Appendix.

N Engl J Med 2006;355:1093-104.

SES BMS

Typhoon: TVF = 7.3% vs 14.3%

TVR = 5.6% vs 13.4%

LLL = 0.14 vs 0.82 mm

Multivariate analysis of the primary end point was performed to control for all significant variables in Tables 1 and 2, including the use of clopidogrel, at 6 months. On the basis of this adjusted analysis, patients in the sirolimus-stent group were less than half as likely as those in the uncoated-stent group to have target-vessel failure (odds ratio, 0.41; P=0.001).

ANGIOGRAPHIC FOLLOW-UP STUDY

Of the 210 patients included in the angiographic substudy, 174 underwent angiography at 8 months (82.8%) and 170 had qualifying angiograms (81.0%) (Fig. 1 and Table 4). Patients in the angiographic study, as compared with those not in the study, tended to have higher rates of target-vessel failure (13.3% vs. 9.8%, P=0.19) and revascularization (12.4% vs. 8.4%, P=0.12), although these differences were not significant. However, the reduction in target-vessel failure in the sirolimus-stent groups was similar whether or not follow-up angiography was performed. At 8 months, sirolimus-eluting stents, as compared with uncoated stents, were associated with significant mean reductions in in-stent late luminal loss (0.14±0.49 mm vs. 0.83±0.52 mm, P<0.001) and in-stent restenosis (3.5% vs. 20.3%, P=0.001).

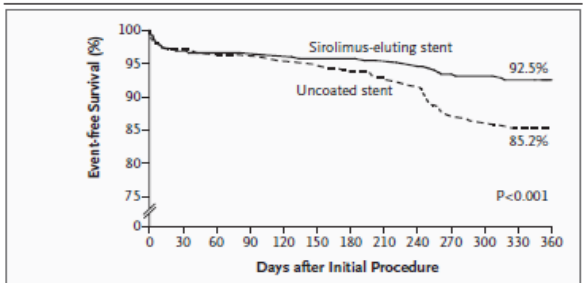


Figure 2. Actuarial Rate of Survival Free from Target-Vessel Failure among Patients Who Received Either a Sirolimus-Eluting Stent or an Uncoated Stent.

The rate of event-free survival was significantly higher in the group receiving a sirolimus-eluting stent than in the uncoated-stent group (P<0.001 by the log-rank test).

DISCUSSION

nition that we used in our trial, cumulative rates of stent thrombosis ranged from 0 to 1.1%.[1-3,10] A higher rate (2.0%) was reported for sirolimus-eluting stents in the Sirolimus-Eluting Stent Compared with Paclitaxel-Eluting Stent for Coronary Revascularization (SIRTAX) trial (a comparison of the Cypher stent and the Taxus stent), which included both patients with and those without acute

PASSION: Taxus pas mieux qu'Express

PASSION

Clinical events at 1 year

	TAXUS® (n = 310)	Express2/Liberte® (n = 309)
MACE	8.8%	12.8%
		RR 0.69 (0.43-1.10); *P* = 0.12
Cardiac death	3.9%	6.2%
		RR 0.63 (0.31-1.27); *P* = 0.20
Recurrent MI	1.7%	2.0%
		RR 0.83 (0.13-5.34); *P* = 0.74
Stent thrombosis	1.0%	1.0%
		RR 1.00 (0.20-4.91); *P* = 0.99

Laarman, Suttorp, Dirksen *et al* NEJM 2006

olvg

Taxus<Cypher ou Express>BX ???

PASSION

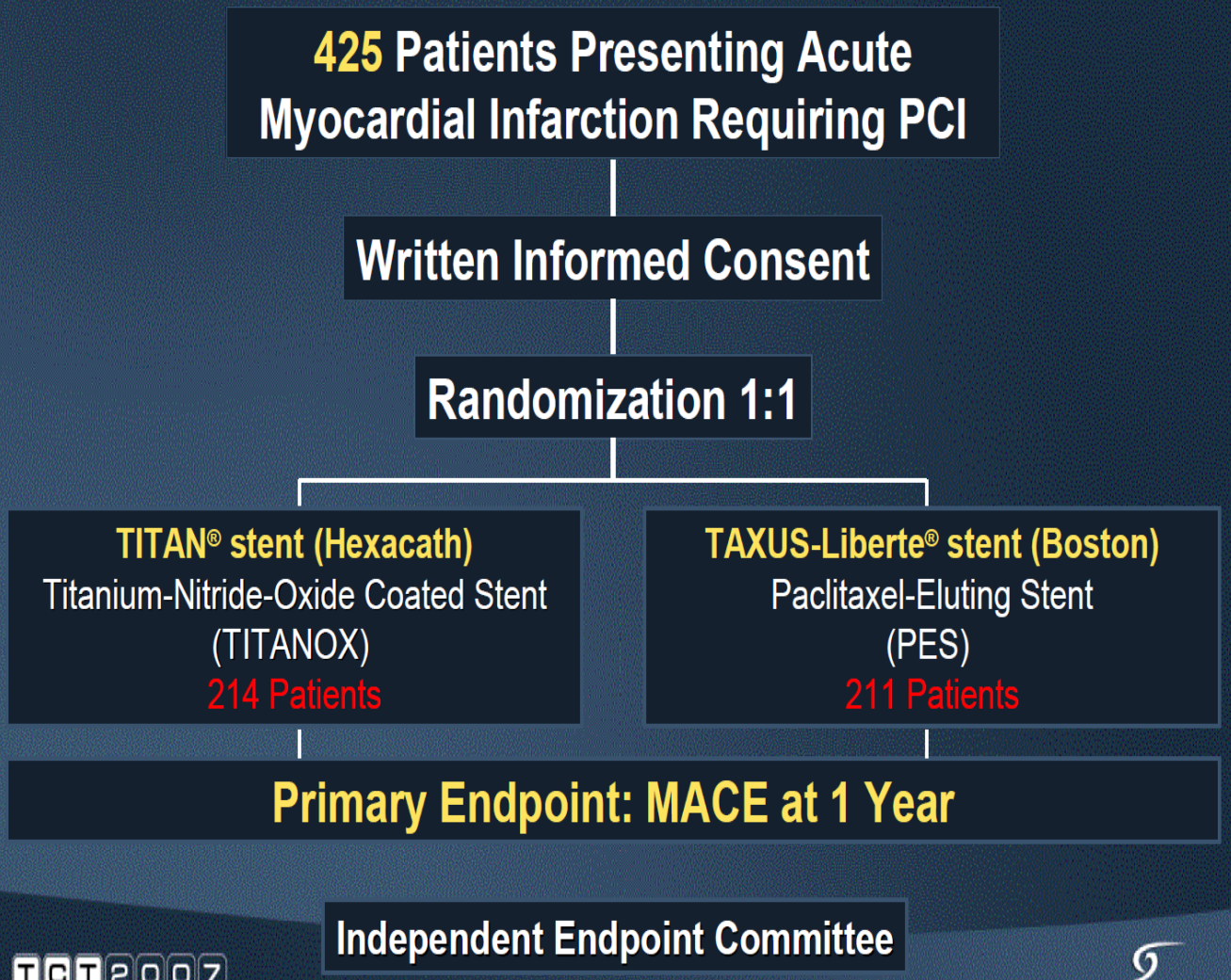
Clinical events at 1 year

	TAXUS® (n = 310)	Express2/Liberte® (n = 309)
TLR	5.3%	7.8%
		RR 0.69 (0.37-1.27); *P* = 0.23
PCI of TLR	2.0%	3.4%
		RR 0.59 (0.22-1.61); *P* = 0.23
CABG of TVR	3.3%	5.1%
		RR 0.66 (0.30-1.44); *P* = 0.30

Laarman, Suttorp, Dirksen *et al* NEJM 2006

olvg

TITAX AMI trial: Study Design

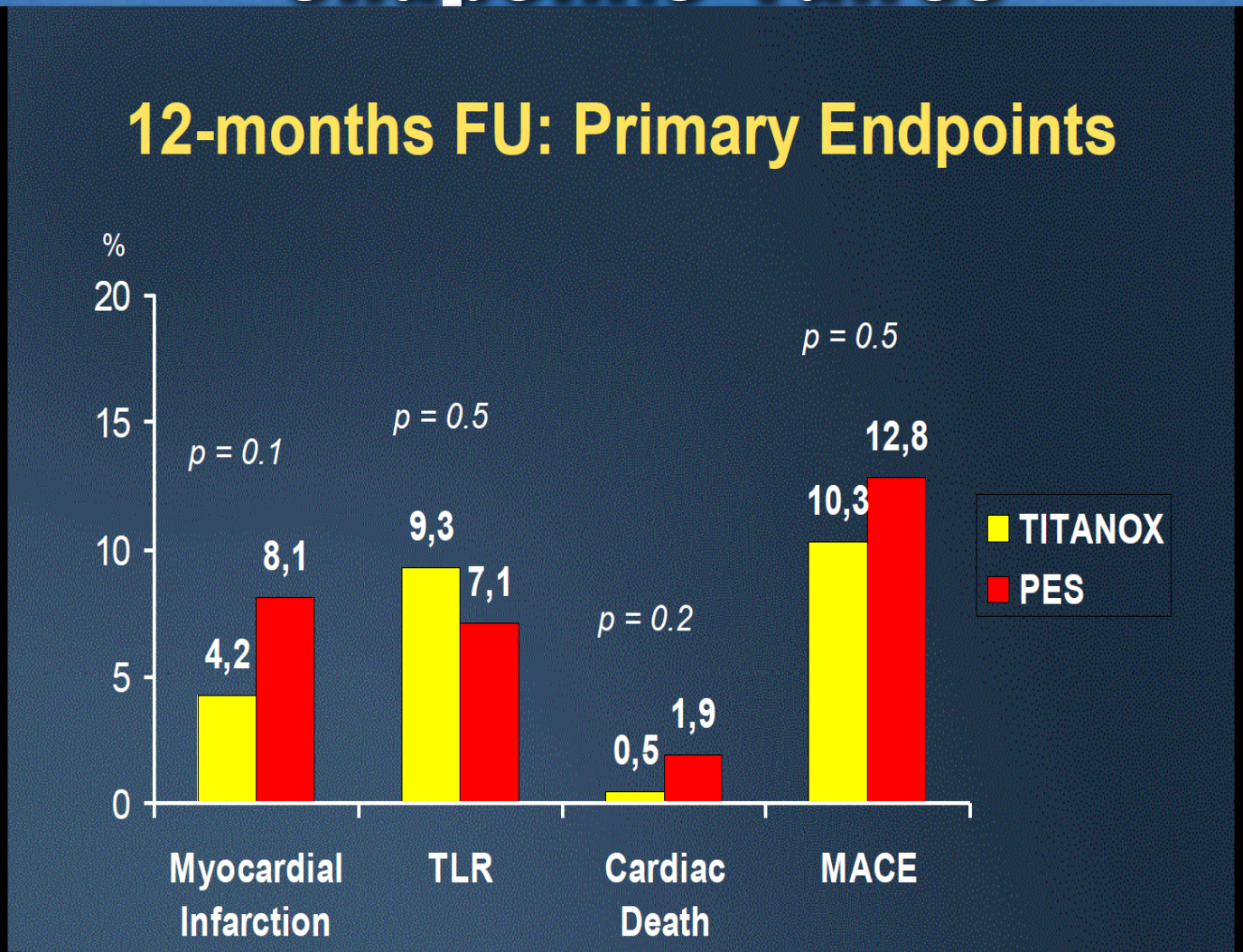


TITAX AMI

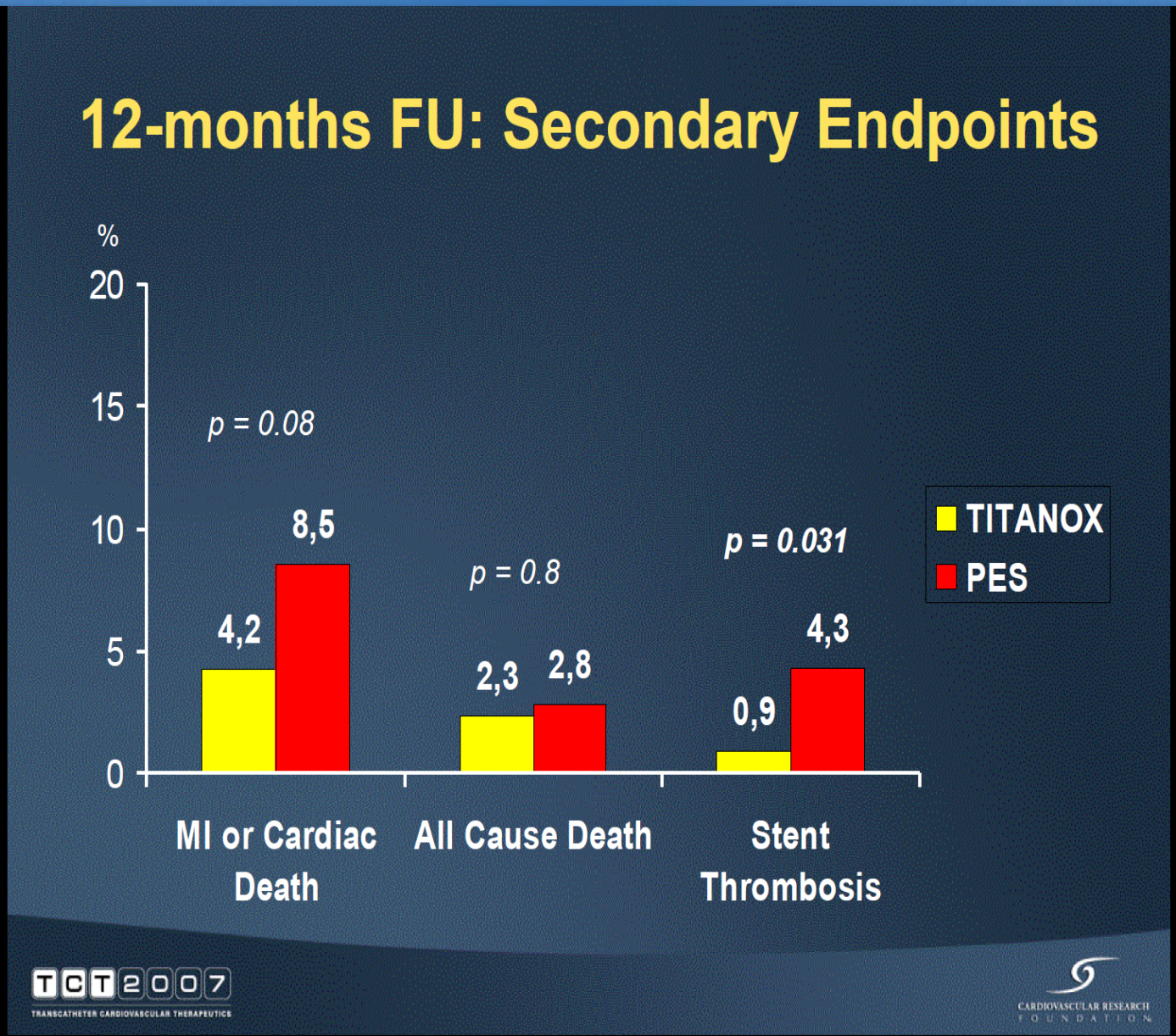
Procedural and Lesion Characteristics

	TITANOX (214)	PES (211)	P Value
RVD, (mm)	3.16 ± 0.45	3.11 ± 0.50	0.35
Lesion length, (mm)	13.6 ± 5.6	13.2 ± 6.4	0.47
Stent diameter, (mm)	3.16 ± 0.42	3.11 ± 0.45	0.19
Stent length, (mm)	17.4 ± 4.5	17.7 ± 5.3	0.48
Total stent length, (mm)	18.5 ± 6.4	19.2 ± 7.2	0.26
No of stents per lesion, n (%)	1.1 ± 0.3	1.1 ± 0.4	0.24
Acute Procedural Success, n (%)	213 (99.5)	207 (98.1)	0.21
Multivessel PCI, n (%)	30 (14)	19 (9)	0.13

Pas de ≠ à 12 mois sur les endpoints 1aires



+ de thromboses de stents groupe TAXUS



Mais…

Les — :

- Etude non dimensionnée pour la « sécurité »:

  ≠ sur SAT non retrouvée en analyse multivariée
- Patients thrombolysés non exclus (+ côté Taxus)

Les + :

- Etude indépendante
- Le stent Titan® peut être une alternative si on veut éviter une bithérapie prolongée(ex:sujet âgé)

HORIZONS AMI STUDY: 3000 pts
Follow up clinique:
Ischemia driven Rev.
À 12 mois
Follow up angio 13 m.

ORIGINAL ARTICLE

Paclitaxel-Eluting Stents versus Bare-Metal Stents in Acute Myocardial Infarction

Gregg W. Stone, M.D., Alexandra J. Lansky, M.D., Stuart J. Pocock, Ph.D., Bernard J. Gersh, M.B., Ch.B., D.Phil., George Dangas, M.D., Ph.D., S. Chiu Wong, M.D., Bernhard Witzenbichler, M.D., Giulio Guagliumi, M.D., Jan Z. Peruga, M.D., Bruce R. Brodie, M.D., Dariusz Dudek, M.D., Martin Möckel, M.D., Andrzej Ochala, M.D., Alison Kellock, B.S., Helen Parise, Sc.D., and Roxana Mehran, M.D., for the HORIZONS-AMI Trial Investigators*

ABSTRACT

BACKGROUND

There is no consensus regarding the safety and efficacy of drug-eluting stents, as compared with bare-metal stents, in patients with ST-segment elevation myocardial infarction who are undergoing primary percutaneous coronary intervention (PCI).

METHODS

We randomly assigned, in a 3:1 ratio, 3006 patients presenting with ST-segment elevation myocardial infarction to receive paclitaxel-eluting stents (2257 patients) or otherwise identical bare-metal stents (749 patients). The two primary end points of the study were the 12-month rates of target-lesion revascularization for ischemia (analysis powered for superiority) and a composite safety outcome measure of death, reinfarction, stroke, or stent thrombosis (powered for noninferiority with a 3.0% margin). The major secondary end point was angiographic evidence of restenosis at 13 months.

RESULTS

Patients who received paclitaxel-eluting stents, as compared with those who received bare-metal stents, had significantly lower 12-month rates of ischemia-driven target-lesion revascularization (4.5% vs. 7.5%; hazard ratio, 0.59; 95% confidence interval [CI], 0.43 to 0.83; P=0.002) and target-vessel revascularization (5.8% vs. 8.7%; hazard ratio, 0.65; 95% CI, 0.48 to 0.89; P=0.006), with noninferior rates of the composite safety end point (8.1% vs. 8.0%; hazard ratio, 1.02; 95% CI, 0.76 to 1.36; absolute difference, 0.1 percentage point; 95% CI, −2.1 to 2.4; P=0.01 for noninferiority; P=0.92 for superiority). Patients treated with paclitaxel-eluting stents and those treated with bare-metal stents had similar 12-month rates of death (3.5% and 3.5%, respectively; P=0.98) and stent thrombosis (3.2% and 3.4%, respectively; P=0.77). The 13-month rate of binary restenosis was significantly lower with paclitaxel-eluting stents than with bare-metal stents (10.0% vs. 22.9%; hazard ratio, 0.44; 95% CI, 0.33 to 0.57; P<0.001).

CONCLUSIONS

In patients with ST-segment elevation myocardial infarction who were undergoing primary PCI, implantation of paclitaxel-eluting stents, as compared with bare-metal stents, significantly reduced angiographic evidence of restenosis and recurrent ischemia necessitating repeat revascularization procedures. No safety concerns were apparent at 1 year. (ClinicalTrials.gov number, NCT00433966.)

From Columbia University Medical Center and New York–Presbyterian Hospital and the Cardiovascular Research Foundation (G.W.S., A.J.L., G.D., A.K., H.P., R.M.), and New York–Presbyterian Hospital and Weill Cornell Medical Center (S.C.W.) — all in New York; London School of Hygiene and Tropical Medicine, London (S.J.P.); Mayo Clinic, Rochester, MN (B.J.G.); Charité Campus Benjamin Franklin (B.W.) and Charité Campus Virchow-Klinikum (M.M.) — both in Berlin; Ospedali Riuniti di Bergamo, Bergamo, Italy (G.G.); Medical University, Lodz (J.Z.P.), Jagiellonian University, Krakow (D.D.), and Silesian Medical Academy, Katowice (A.O.) — all in Poland; and LeBauer Cardiovascular Research Foundation and Moses Cone Hospital, Greensboro, NC (B.R.B.). Address reprint requests to Dr. Stone at Columbia University Medical Center, Cardiovascular Research Foundation, 111 E. 59th St., 11th Fl., New York, NY 10022, or at gs2184@columbia.edu.

*The investigators, institutions, and research organizations participating in the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial are listed in the Appendix.

N Engl J Med 2009;360:1946-59.

Taxus(T) vs Express(E) 1 year: ↘TVR 40% /DC IDM= /Re IDM= /SAT=

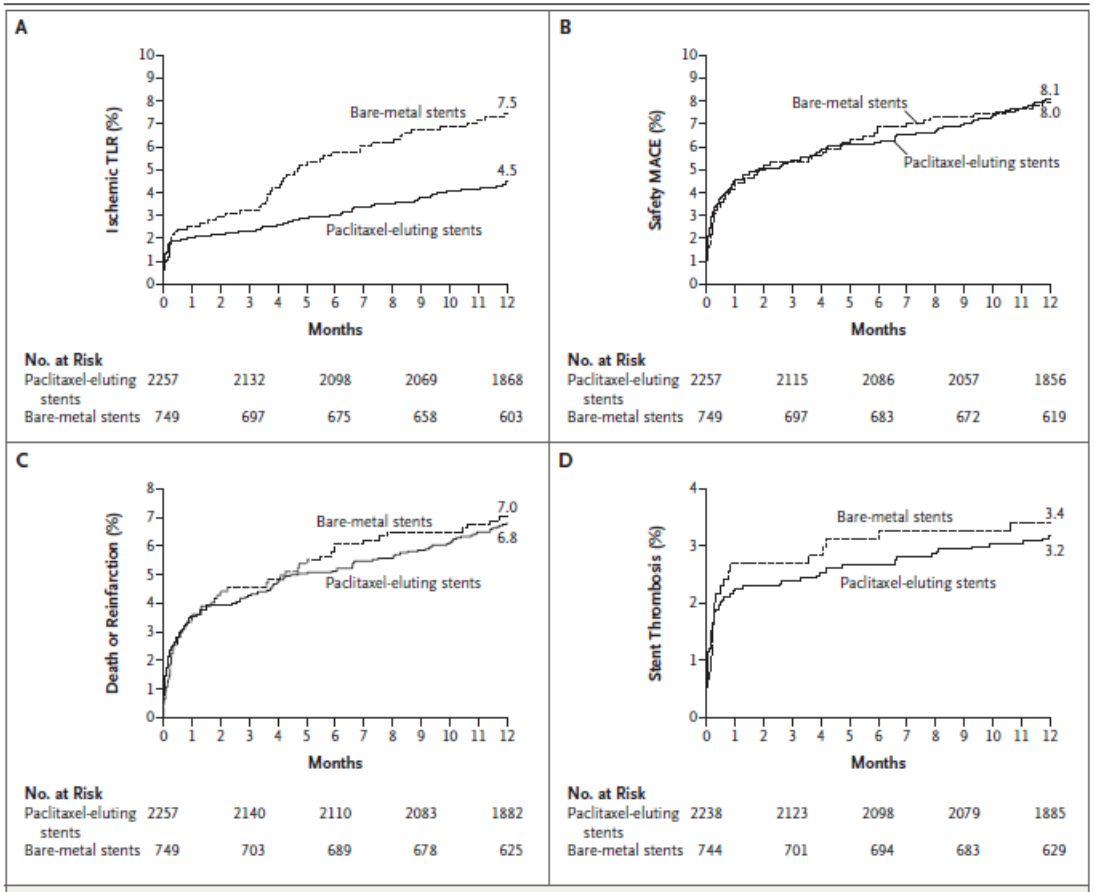
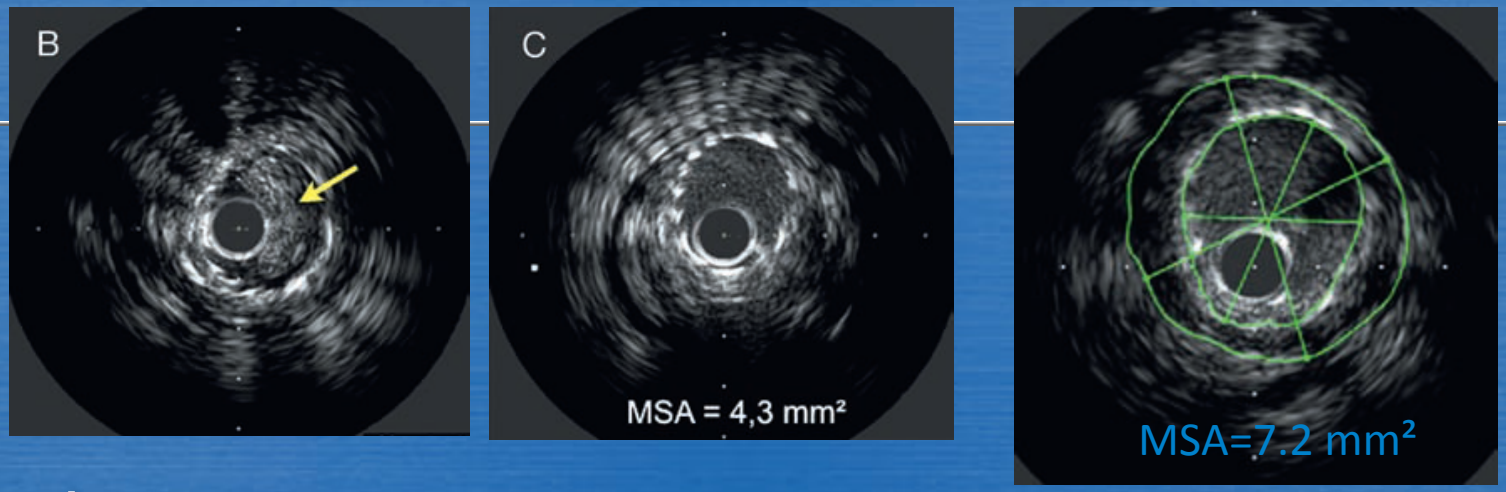


Figure 2. Kaplan–Meier Time-to-Event Curves for Primary End Points and Three Components of the Primary Composite Safety End Point.

Time-to-event curves through 1 year are shown for ischemia-driven target-lesion revascularization (TLR) (Panel A), the composite safety end point of major adverse cardiovascular events (MACE), consisting of death, reinfarction, stroke, and stent thrombosis (Panel B), death or reinfarction (Panel C), and stent thrombosis (definite or probable, defined according to the Academic Research Consortium classification) (Panel D). Treatment with paclitaxel-eluting stents as compared with bare-metal stents resulted in a lower 12-month rate of ischemia-driven target-lesion revascularization (4.5% vs. 7.5%; hazard ratio, 0.59; 95% CI, 0.43 to 0.83; P=0.002), a noninferior 12-month rate of the safety composite end point of major adverse cardiovascular events (8.1% vs. 8.0%; hazard ratio, 1.02; 95% CI, 0.76 to 1.36; P=0.01 for noninferiority; P=0.92 for superiority), and nonsignificantly different 12-month rates of death or reinfarction (6.8% vs. 7.0%; hazard ratio, 0.97; 95% CI, 0.70 to 1.32; P=0.83) and of stent thrombosis (3.2% vs. 3.4%; hazard ratio, 0.93; 95% CI, 0.59 to 1.47; P=0.77).

HORIZONS : ETUDE IVUS (Circ nov 09)



- 400 pts
- % obstruction 13 m.: 6.5% T vs 15.6% E p=0.0001
- Late malapposition : 29.6% T vs 7.9% E p=0.0005
- Dûe à un remodelage positif du vaisseau
- Nécessite un suivi clinique prolongé
- HORIZONS 2 ans: pas de ≠ DC, IDM, Thrombose S.

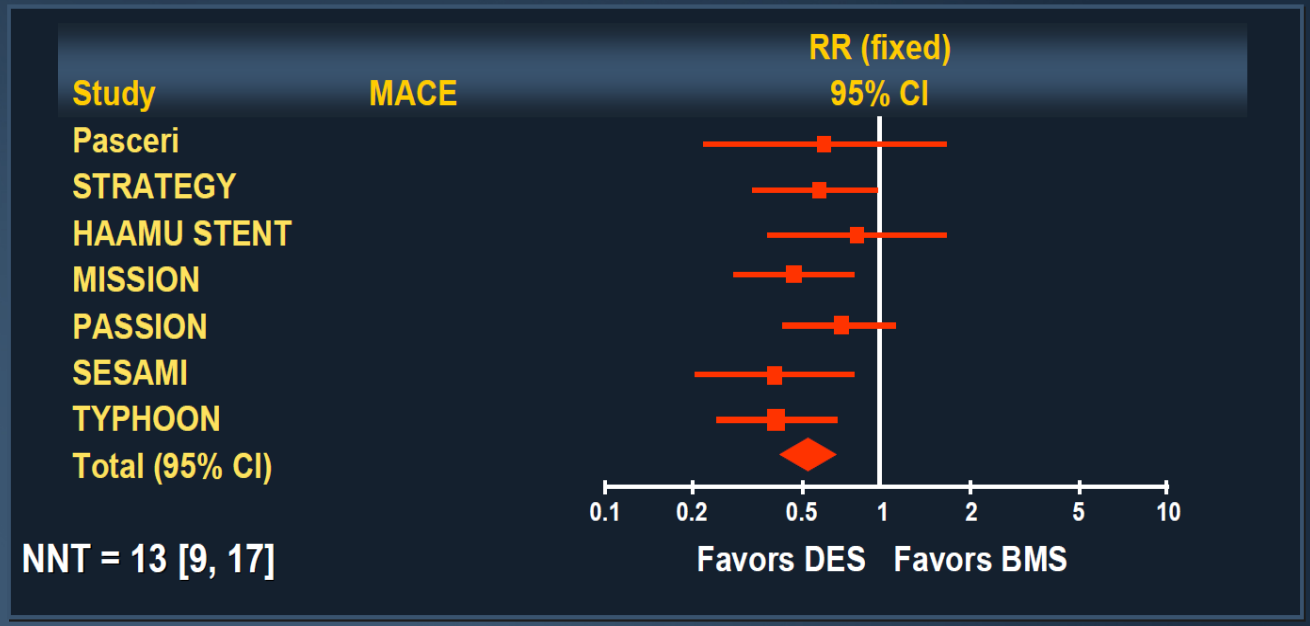
META ANALYSES A 1 AN

7 DES vs. BMS RCTs in AMI (n=2,357)

MACE at 8–12 Months*

DES vs. BMS: 9.3% vs. 17.6%

RR [95%CI] = 0.53 [0.43, 0.66], P<0.0001



NNT = 13 [9, 17]

*MACE = Death, Reinfarction, or TVR for all trials, except TLR for PASSION

Adapted from Pasceri V et al. AHJ 2007;153:749–54

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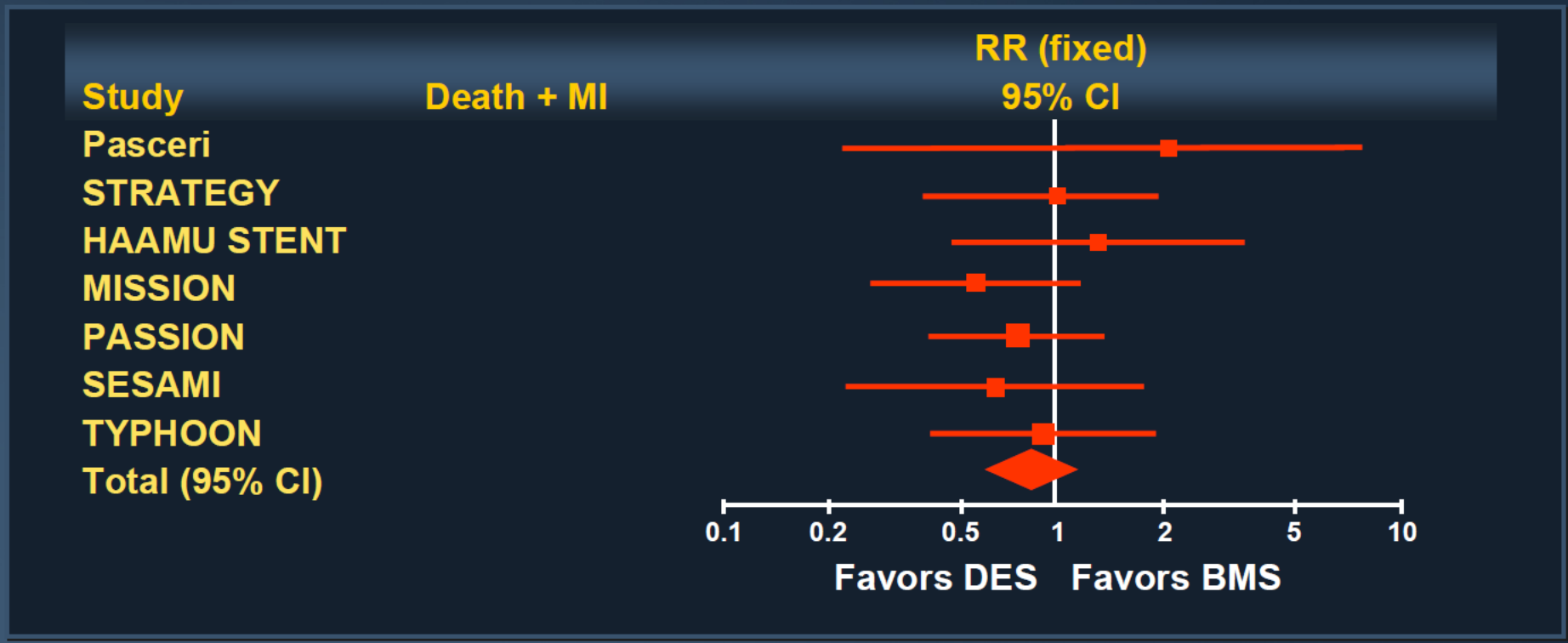
7 DES vs. BMS RCTs in AMI (n=2,357)

Death or Reinfarction at 8–12 Months

DES vs. BMS: 5.8% vs. 6.9%

RR [95%CI] = 0.84 [0.62, 1.15], P=0.28



Mortality at 1 year (5 trials; N=1857)

2.8% vs. 3.1%, 0.90 [0.53, 1.51], P=NS

Adapted from Pasceri V et al. AHJ 2007;153:749–54

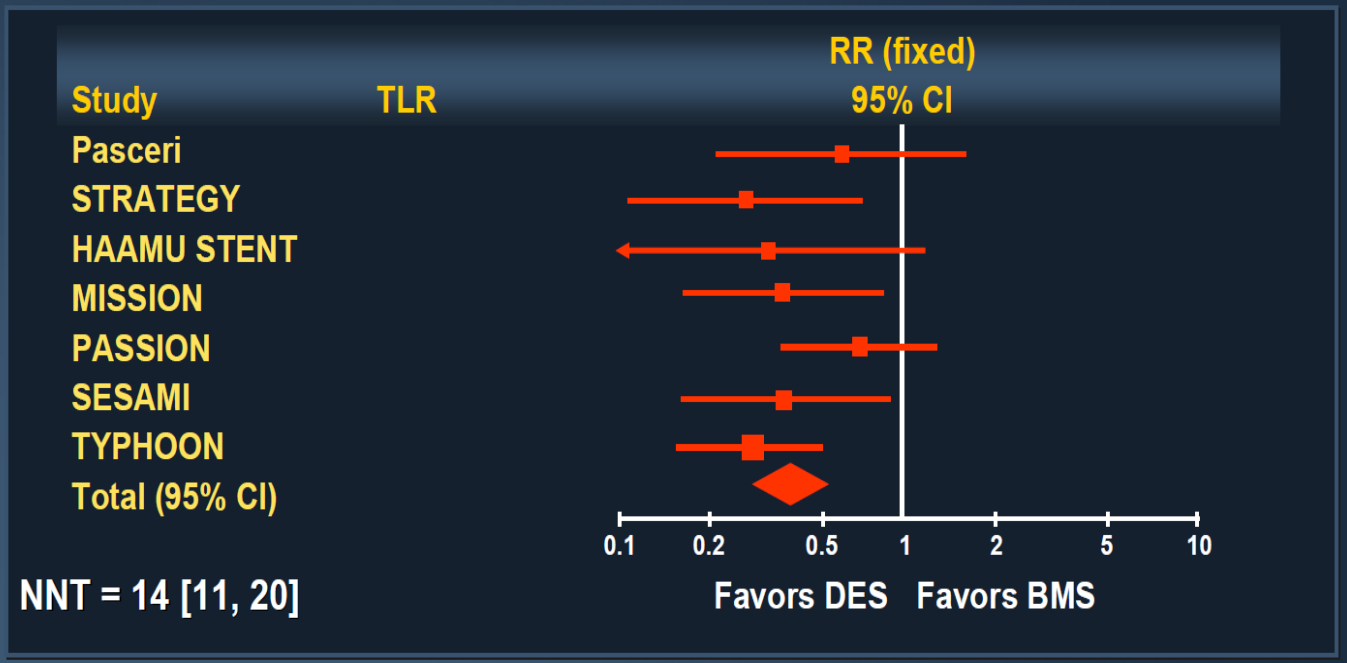
EFFICACITE A 1 AN

7 DES vs. BMS RCTs in AMI (n=2,357)

TLR at 8–12 Months

DES vs. BMS: 4.8% vs. 12.0%

RR [95%CI] = 0.40 [0.30, 0.54], P<0.0001



NNT = 14 [11, 20]

Adapted from Pasceri V et al. AHJ 2007;153:749–54

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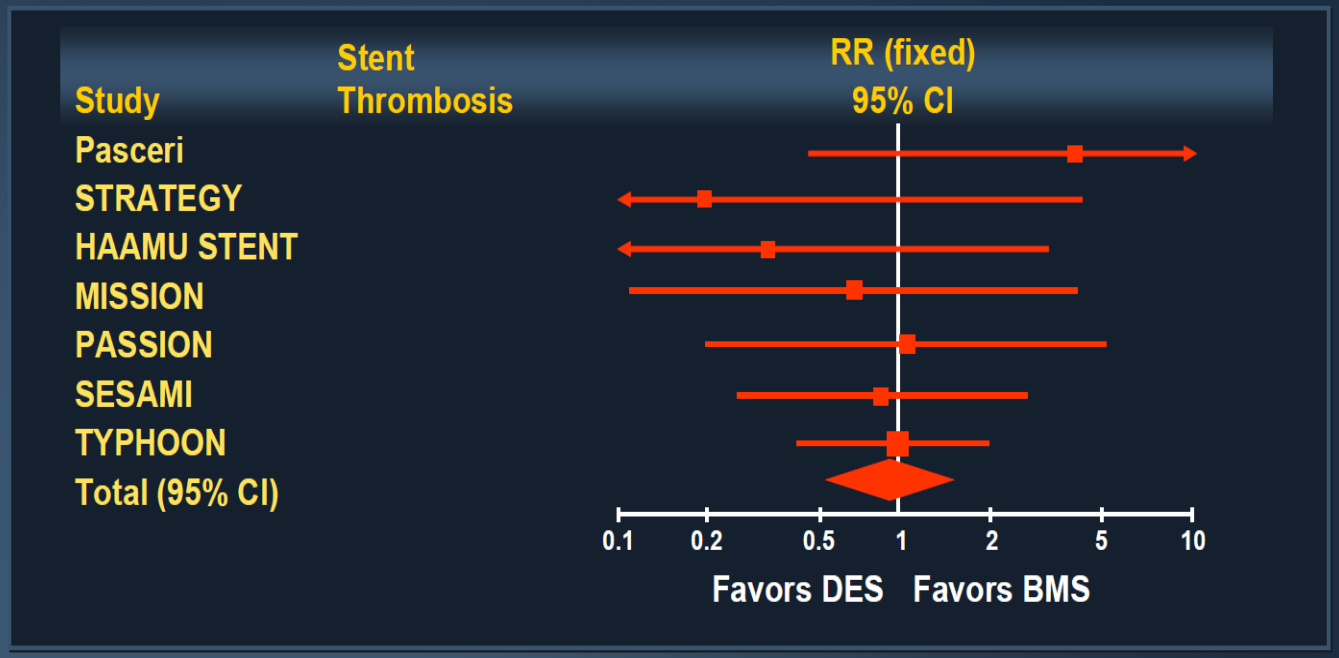
SECURITE à 1 AN

7 DES vs. BMS RCTs in AMI (n=2,357)

Stent Thrombosis at 8–12 Months

DES vs. BMS: 2.3% vs. 2.6%

RR [95%CI] = 0.87 [0.53, 1.45], P=0.60



Adapted from Pasceri V et al. AHJ 2007;153:749–54

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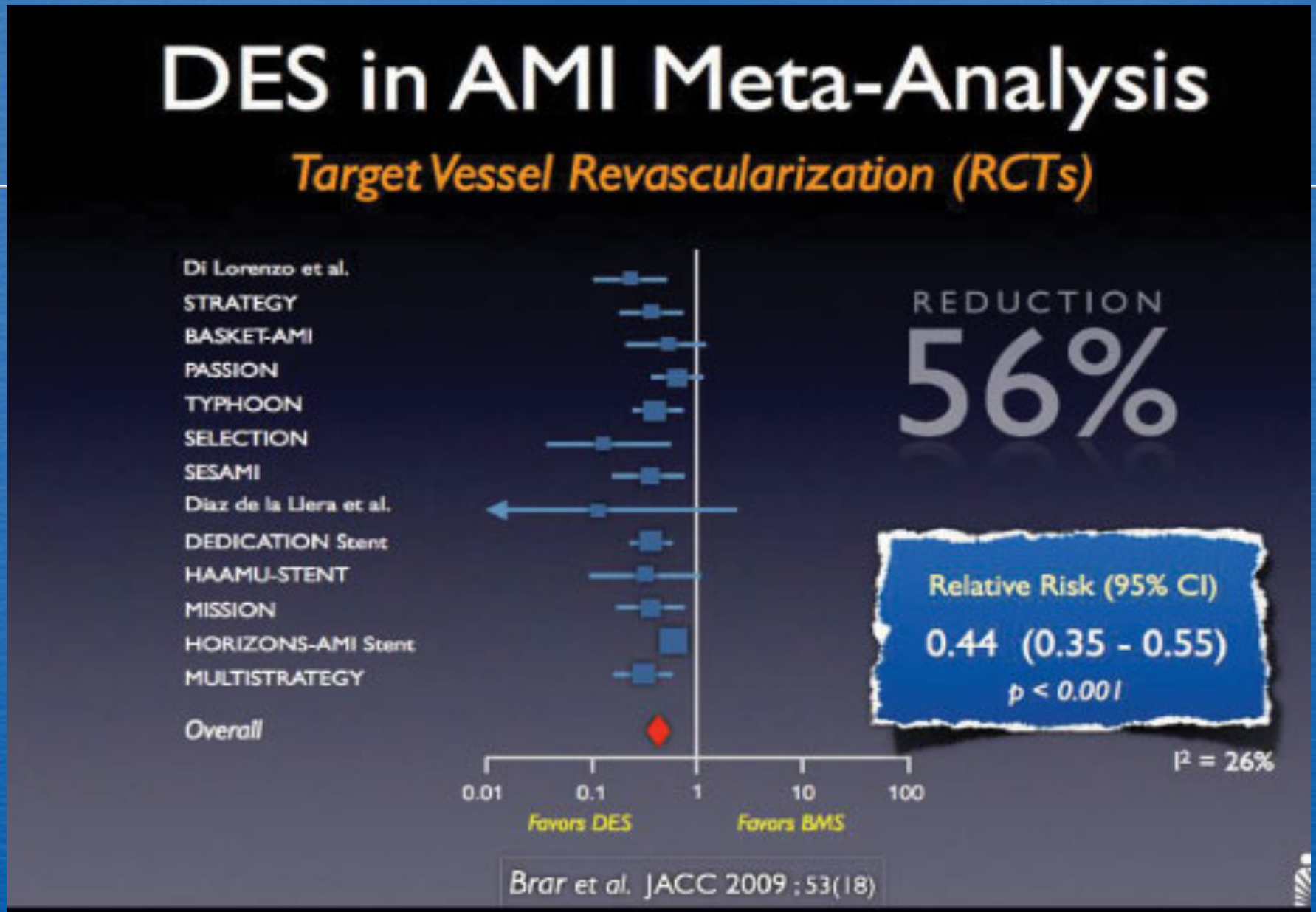
META ANALYSE 2009: 13 RCT's



Figure

LES REGISTRES : GRACE
5093 STEMI PTS SUIVI A 2 ANS

European Heart Journal (2009) **30**, 321–329
doi:10.1093/eurheartj/ehn604

CLINICAL RESEARCH
Acute coronary syndrome

Mortality following placement of drug-eluting and bare-metal stents for ST-segment elevation acute myocardial infarction in the Global Registry of Acute Coronary Events

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Received 17 July 2008; revised 25 October 2008; accepted 16 December 2008; online publish-ahead-of-print 15 January 2009

Aims To assess mortality after drug-eluting stent (DES) or bare-metal stent (BMS) for ST-segment elevation myocardial infarction (STEMI).

Methods and results In this multinational registry, 5093 STEMI patients received a stent: 1313 (26%) a DES and 3780 (74%) only BMS. Groups differed in baseline characteristics, type, or timing of percutaneous coronary intervention, with a higher baseline risk for patients receiving BMS. Two-year follow-up was available in 55 and 60% of the eligible BMS and DES patients, respectively. Unadjusted mortality was lower during hospitalization, similar for the first 6 months after discharge, and higher from 6 months to 2 years, for DES patients compared with that of BMS patients. Overall, unadjusted 2-year mortality was 5.3 vs. 3.9% for BMS vs. DES patients ($P = 0.04$). In propensity- and risk-adjusted survival analyses (Cox model), post-discharge mortality was not different up to 6 months ($P = 0.21$) or 1 year ($P = 0.34$). Late post-discharge mortality was higher in DES patients from 6 months to 2 years (HR 4.90, $P = 0.01$) or from 1 to 2 years (HR 7.06, $P = 0.02$). Similar results were observed when factoring in hospital mortality.

Conclusion The observation of increased late mortality with DES vs. BMS suggests that DES should probably be avoided in STEMI, until more long-term data become available.

Keywords Risk score • STEMI • Drug-eluting stent • Bare-metal stent

Mortalité non ajustée
à 2 ans: 5.3% BMS
3.9% DES p 0.04

Après ajustement
↗ mortalité DES entre
6 et 24 mois (HR 4.9!)

Mais 55 à 60% de suivi
à 2 ans!

Registre Massachussets, ACC 09

- 5258 Pts suivi à 2 ans
- Mortalité brut : DES 9% BMS 14% p 0.001
- Mortalité ajustée: STEMI D 8% B 11.7% p 0.001

(propensity score matching)

ALORS QUI CROIRE ?????????

Meta analyse BRAR (JACC 10)

- Analyse de 18 registres : 26500 pts!
- ↘ TVR = 46% groupe DES
- IDM: Pas de ≠
- Thrombose stent: =
- DC : DES mieux à 1 an mais = à 2 ans
- Ce sont les patients les plus à risque de resténose qui bénéficient le plus des DES

PASEO: suivi à très long terme (Circ sept 09)

- 270 pts STEMI, 90 SES, 90 PES, 90 BMS
- Durée moyenne suivi: 4.3 ans
- TVR BMS 22% PES 6.7% SES 5.6% $p < 0.005$
- Pas de ≠ DC - IDM

TYPHOON 4 ANS

	SES		BMS	
TVR	9.6	vs	17.2%	p 0.002
DC	4.0	vs	6.4%	ns
IDM	4.8	vs	4.0%	ns
SAT	4.4	vs	4.8%	ns

DES/BMS: coût/efficacité

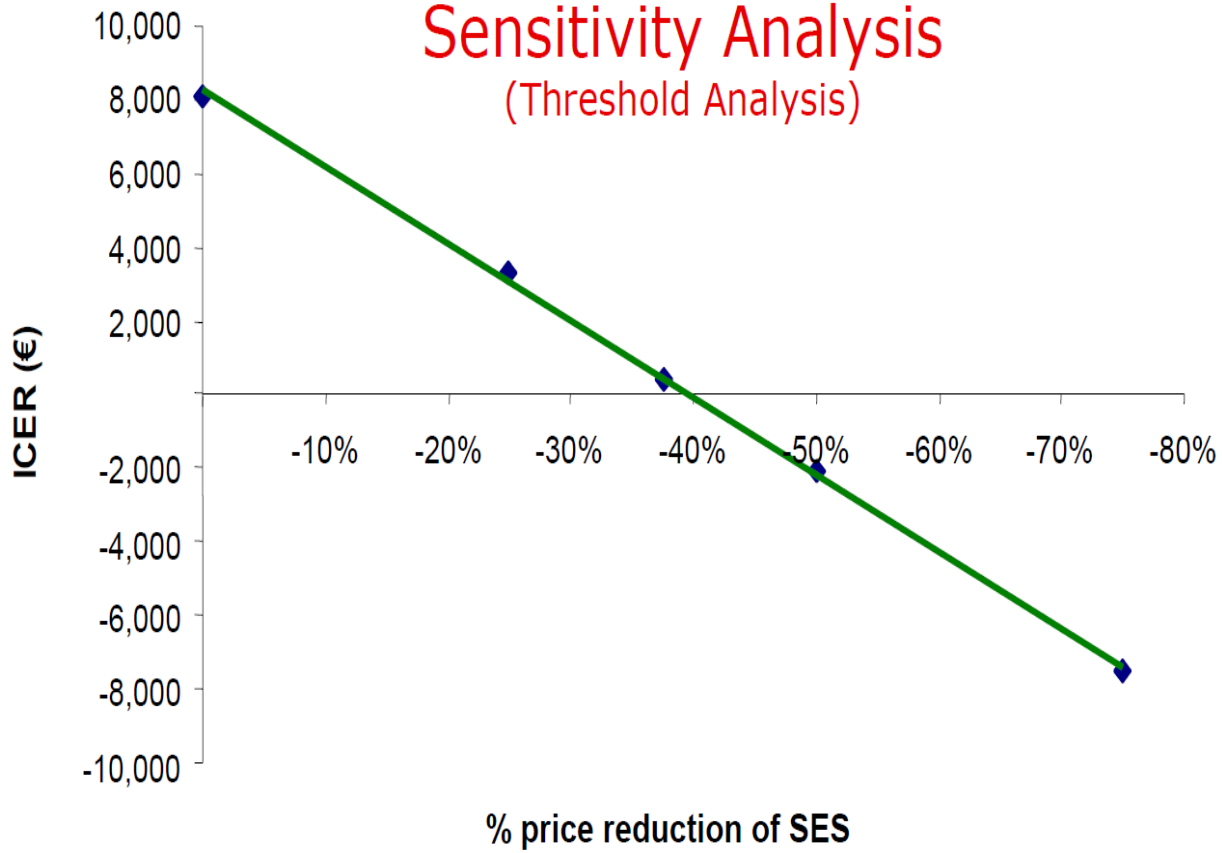
ICER: incremental cost effectiveness ratio

$$\text{CE ratio} = \frac{\text{cost}_{\text{new strategy}} - \text{cost}_{\text{current practice}}}{\text{effect}_{\text{new strategy}} - \text{effect}_{\text{current practice}}}$$

Ici: coût DES/BMS par revascularisation évitée

Dans Typhoon ICER =7321 €/ TVR évité!
(prix du Cypher 2007+ prix de la bithérapie sur 1 an)

Sensitivity Analysis
(Threshold Analysis)



For price reduction of SES higher than about 40% (from 1,500€ to 900€), it could dominate the BMS option

Conclusion

- Aucun argument en faveur d'un excès de mortalité ou d'IDM tardif après DES posé dans l'IDM < 24h Horizons 2 ans?

  Actuellement la contre indication IDM < 72h

  a disparu

  Il est raisonnable de proposer les DES dans les indications LPP (haut risque d'ISR)

  Dans les autres cas BMS ou Titan

  Sujet âgé: Bithérapie? Titan ou BMS

6-months Follow-up

	TITANOX (214)	PES (211)	P value
Complete data available, n (%)	214 (100)	211 (100)	
Myocardial infarction, n (%)	8 (3.7)	12 (5.7)	0.37
TLR, n (%)	15 (7.0)	7 (3.3)	0.12
Death from cardiac causes, n (%)	0 (0)	2 (0.9)	0.15
MACE, n (%)	16 (7.5)	15 (7.1)	1.0
Recurrent MI or cardiac death, n (%)	8 (3.7)	13 (6.2)	0.27
Death from any cause, n (%)	4 (1.9)	3 (1.4)	0.72
Stent thrombosis, n (%)	1 (0.5)	**7 (3.3)**	**0.031**
Definite, n (%)	1 (0.5)	6 (2.8)	0.06
Probable, n (%)	0 (0)	1 (0.5)	0.31