Le stent à polymère biodégradable
état de l'art

Docteur Pierre Meyer
Institut Arnault Tzanck
Saint Laurent du Var
France

Pourquoi un stent partiellement ou totalement biodégradable ?

- Le stent n'est qu'un tuteur, visant à sécuriser et maîtriser la dilacération de l'artère athéromateuse par le ballon

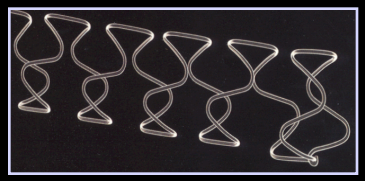
- La disparition partielle ou totale de cet étayage, une fois l'artère cicatrisée avec un bon résultat durable, permettrait une rénovation parfaite du vaisseau, régénérant son aspect et ses fonctionnalités d'origine.

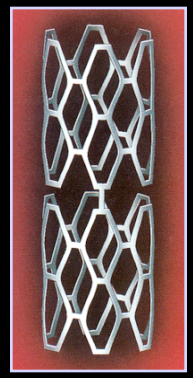
- L'évolution vers des matériaux biodégradables répond à un fantasme de s'inscrire dans le sens du progrès…

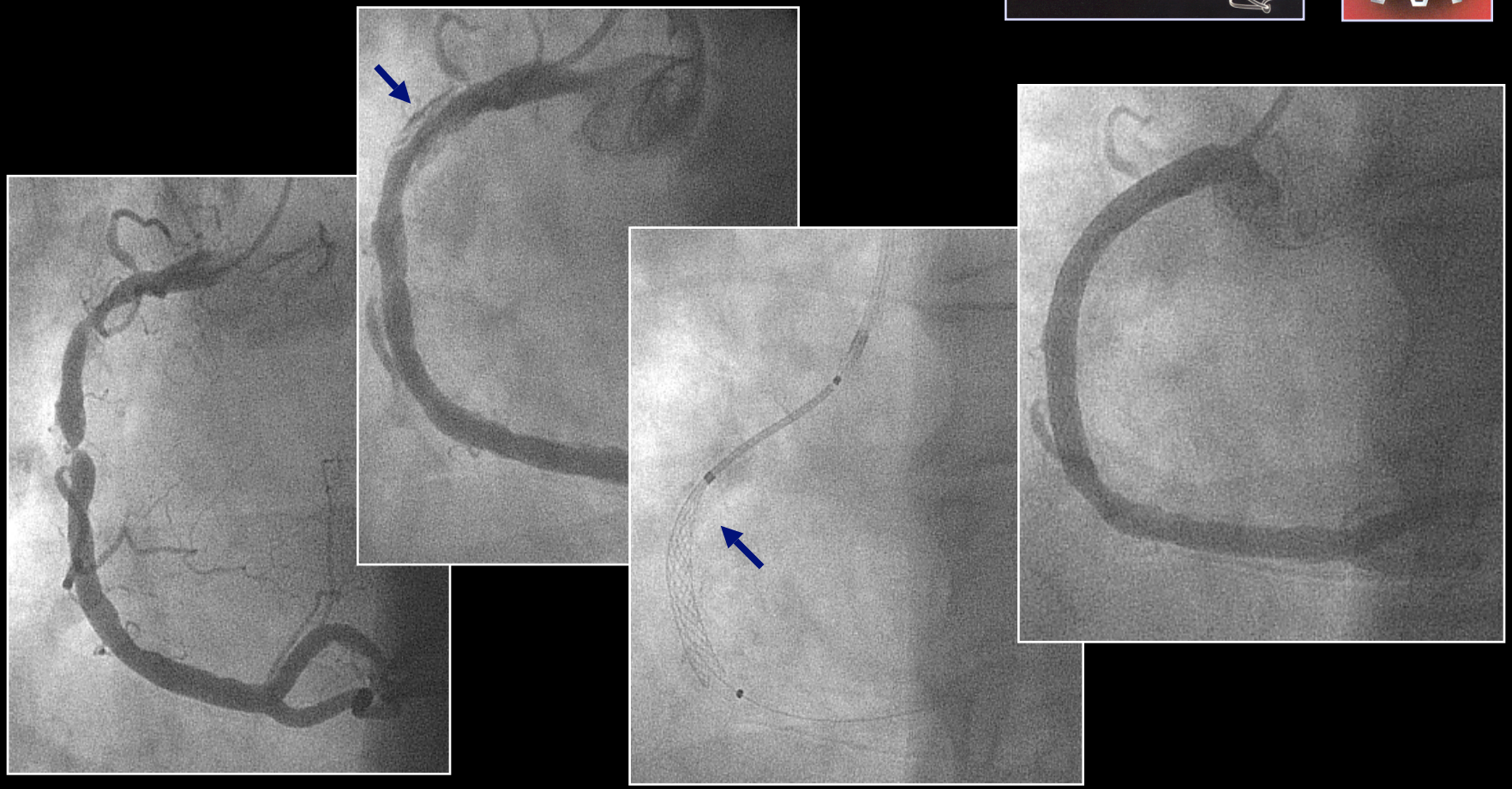
- Une innovation comme le polymère résorbable correspond à une attente de l'utilisateur et doit être replacée dans le contexte où elle a pu apparaître pour qu'on en comprenne la finalité…

Il y a 25 ans, le stent révolutionnait la cardiologie interventionnelle en sécurisant l'angioplastie, nous libérant du stand-by…

- ✓ il garantissait un résultat immédiat satisfaisant

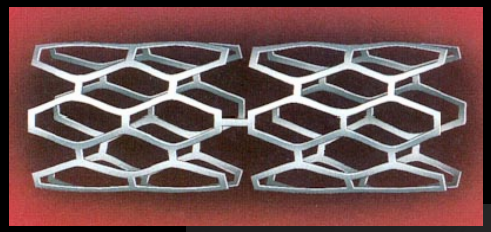






La thrombose de stent affectait 6 à 12% des premiers patients traités par endoprothèse, malgré un protocole agressif (AVK, ASA…)

- Roubin GS, Cannon AD, Agrawal SK et al. Intracoronary stenting for acute and threatened closure complicating percutaneous transluminal coronary angioplasty. *Circulation. 1992;85:916–927.*
- Foley JB, Brown RI, Penn IM. Thrombosis and restenosis after stenting in failed angioplasty. *Am Heart J. 1994;128:12–20.*
- Schomig A, Kastrati A, Mudra H et al. Four-year experience with Palmaz-Schatz stenting in coronary angioplasty complicated by dissection with threatened or present vessel closure. *Circulation. 1994;90:2716–2724.*
- Leon MB, Baim DS, Popma JJ et al. A clinical trial comparing three antithrombotic-drug regimens after coronary-artery stenting. *N Engl J Med. 1998;339:1665–1671.*



L'endoprothèse sécurise l'angioplastie et diminue le risque de resténose

		STENT	BALLON
1.	Benestent I :	22%	32%
2.	Stress :	32%	42%

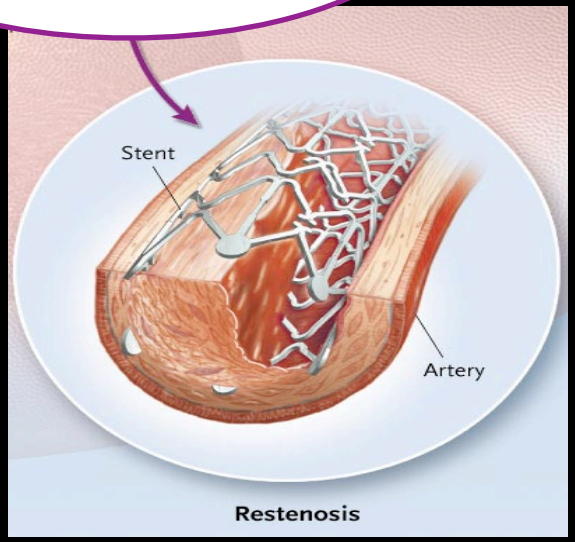
en améliorant la qualité du résultat immédiat

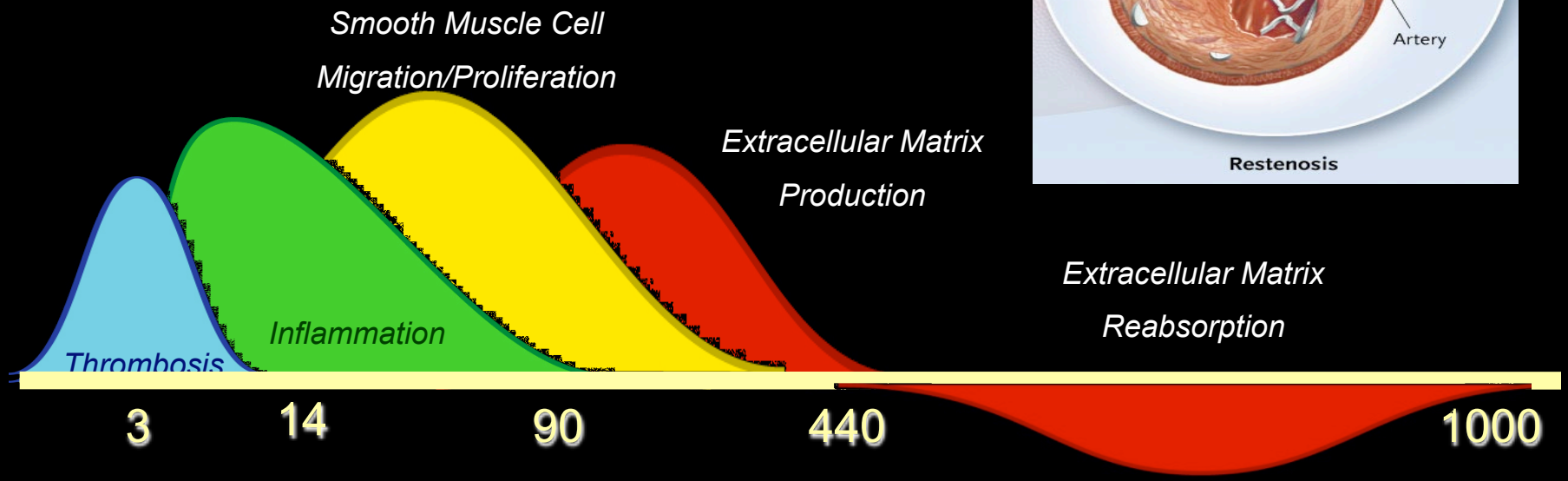
en s'opposant au remodelage cicatriciel constrictif tardif…

1. Serruys PW. N Engl J Med 1994 ; 331 : 489-95
2. Fischman DL. N Engl J Med 1994 ; 331 : 496-501

La réaction fibro-prolifératice cicatricielle est la résultante de plusieurs mécanismes dont les composantes sont variables d'un patient à l'autre et d'une lésion à l'autre

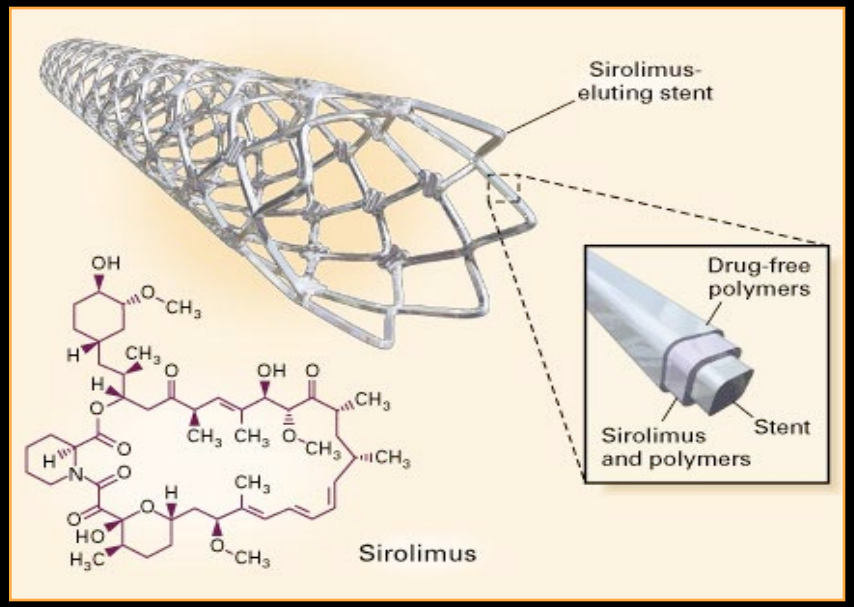
L'endoprothèse stimule la réaction néointimale fibro-prolifération cicatricielle



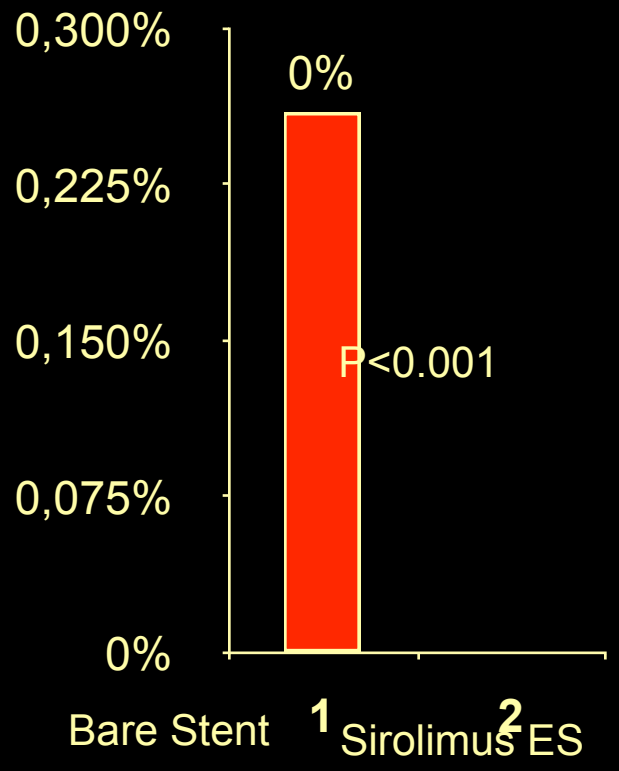


RAVEL : *Long-Term Results*

Morice MC. N Engl J Med 2002 ; 346 : 1773-80

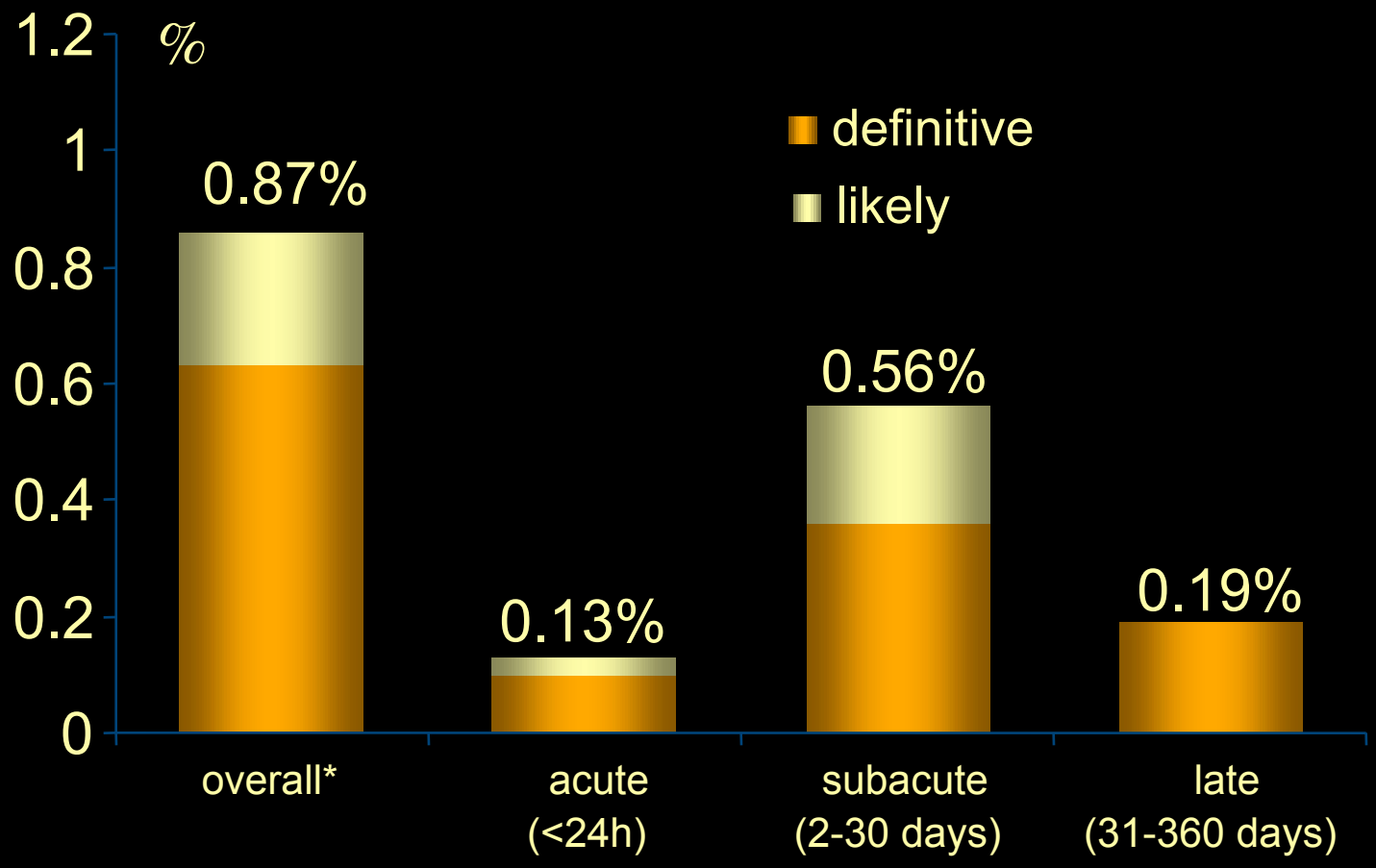


Cordis Cypher stent



Angiographic Restenosis at 6 Months

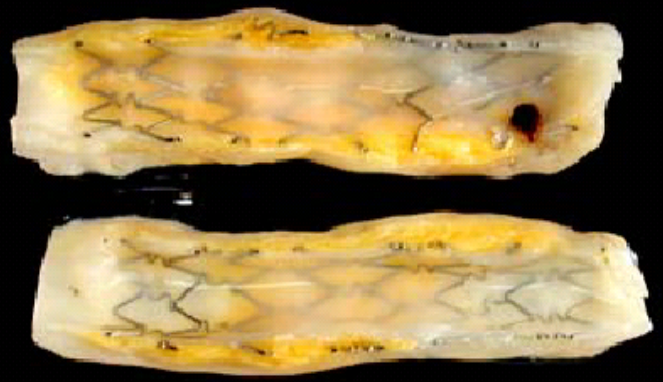
360 days FU : stent thrombosis



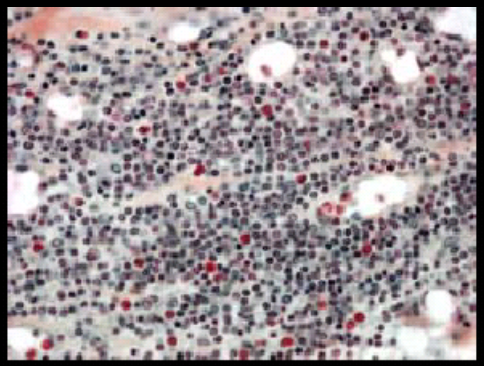
All cases with reported death, MI, TLR or stent thrombosis were reviewed and adjudicated by the CEC: ST was considered "definite" if supporting documentation was available and "likely" up to 30 day s in case of cardiac death and/or target vessel MI without angio graphy .

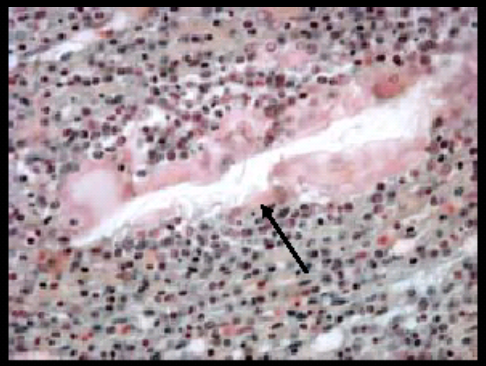
Circulation 2006

Guagliumi G. Circulation 2003 ; 107 : 1340-1.



Sirolimus 16 Months after Deployment





Localized Hypersensitivity and Late Coronary Thrombosis Secondary to a Sirolimus-Eluting Stent. Should We Be Cautious?

Virmani R. *Circulation.* 2004 ; 109 : 701-5.

Late thrombosis in drug eluting coronary stents after discontinuation of antiplatelet therapy

Mc Fadden E.P et al. Lancet 2004 ; 364 : 1519-21.

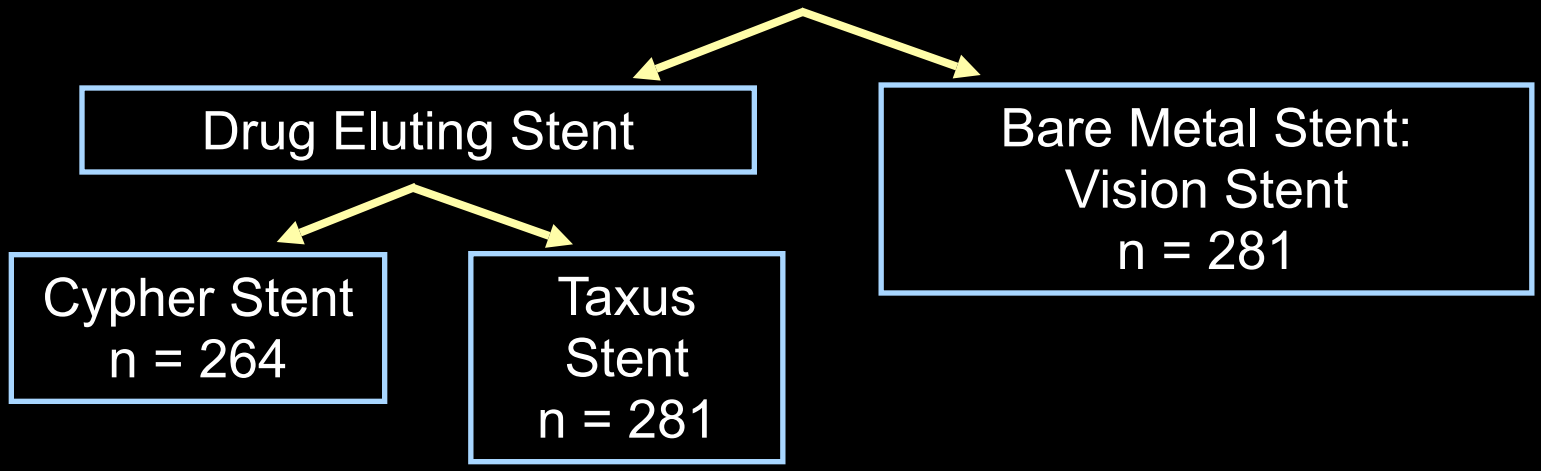
BASKET Trial : Kaiser C et al. *Lancet* 2005; 366:921-9.

826 undergoing primary PCI irrespective of indication for PCI

mean follow-up 18 months ; mean age 64 years, 21% female

Concomitant medications : clopidogrel for 6 months (irrespective of stent type), aspirin and statin therapy ; 26% with glycoprotein IIb/IIa inhibitors

19% Diabetic, 27% prior MI, 69% with triple vessel disease, 52% LAD lesions,



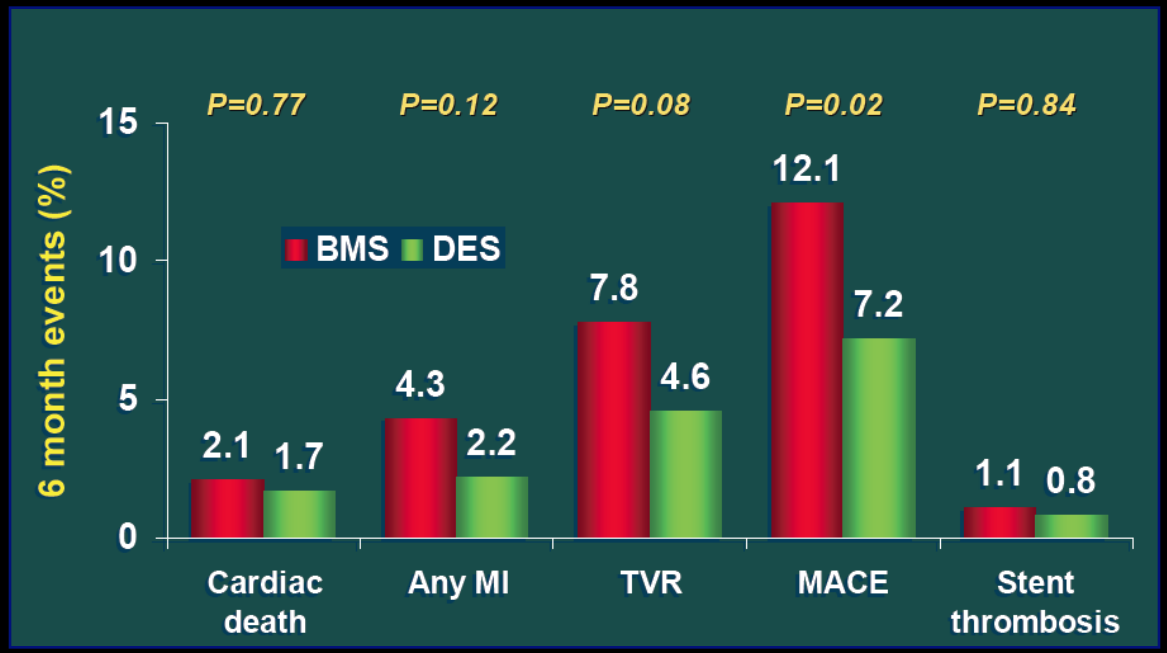
Primary Endpoint:

Cost-effectiveness after 6 months, with effectiveness defined as reduction of major adverse cardiac events for the comparison of drug-eluting stent vs bare metal stent.

BASKET Trial : primary outcome

Kaiser C et al. *Lancet* 2005 ; 366 : 921-9.

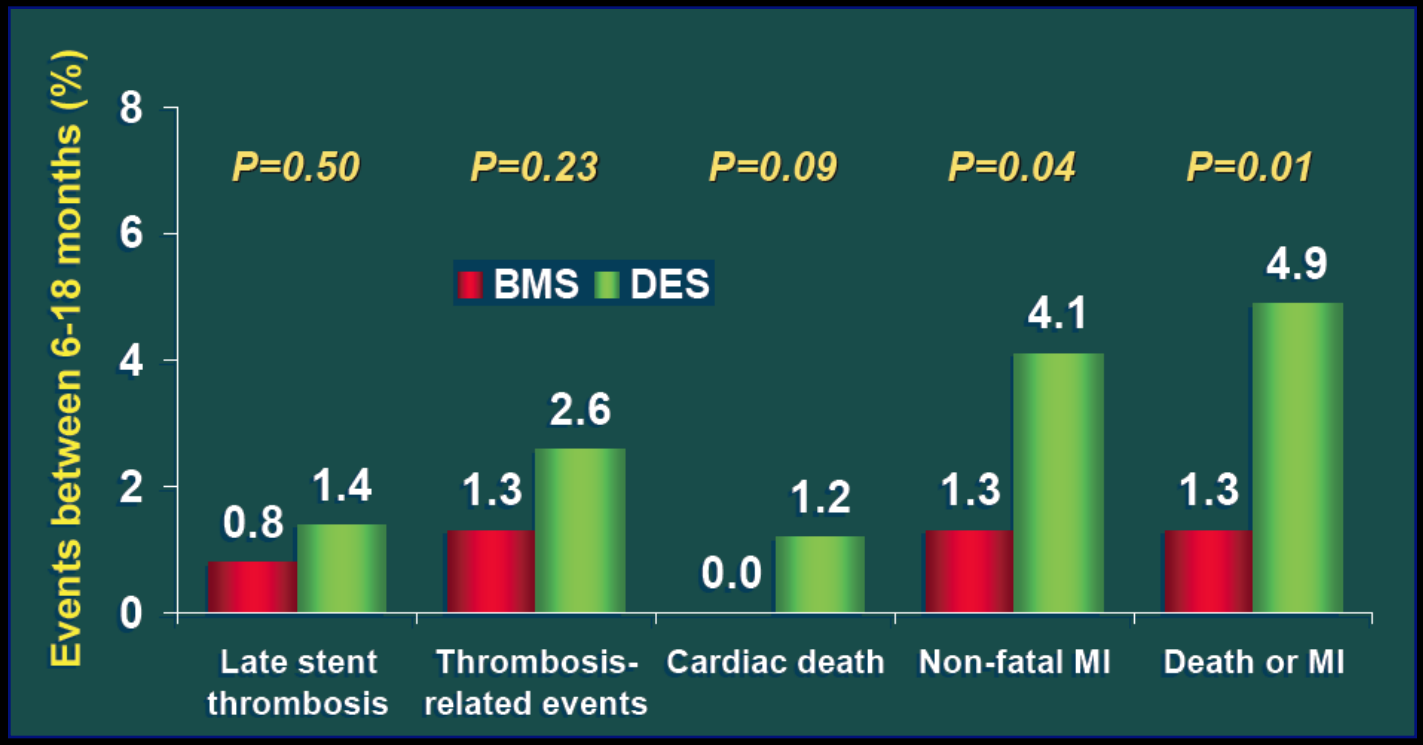
- A reduction in TVR with both drug-eluting stents, with no significant difference between the two stents
- No difference in the three therapies for death and MI



BASKET late. *Pfisterer ME et al. ACC 2006*

Major cardiac events between 7 and 18 months

Clopidogrel was stopped at six months



"I think what we see is an early clinical benefit, restenosis, followed by a loss of this benefit over time due to the increase in death/MI."

Dr Lars Wallentin ESC 2006

the ESC *firestorm*

"What kills a patient, I think, is a large vessel with a drug-eluting stent"

Renu Virmani. ESC 2006

TUESDAY

ESC Congress News

WORLD HEART FEDERATION

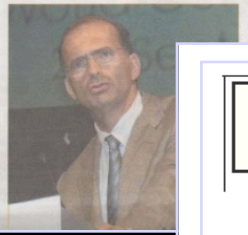
World Congress of Cardiology 2006

The unique meeting of the European Society of Cardiology Congress 2006 and the World Heart Federation's XVth World Congress of Cardiology

Do drug-eluting stents increase deaths?

TWO SEPARATE, independent meta-analyses, presented in Hot Line session I, suggest drug-eluting stents (DES) may increase death, Q-wave myocardial infarction (clinical surrogates of in-stent thrombosis) and cancer deaths, bringing the long-term safety of DES firmly into the spotlight. Discussant Salim Yusuf (McMaster University, Canada) hailed the data as one of the most important presentations to come out of this year's meeting.

"Six million people in the world have been implanted with DES, yet their long-term safety and efficacy is unknown," said Yusuf. "I've a feeling the data we're seeing today is only the tip of the iceberg. We need to encourage more public access to the data."

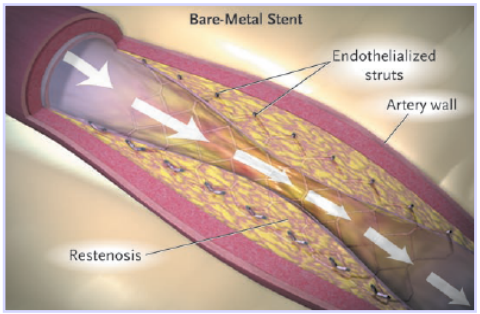


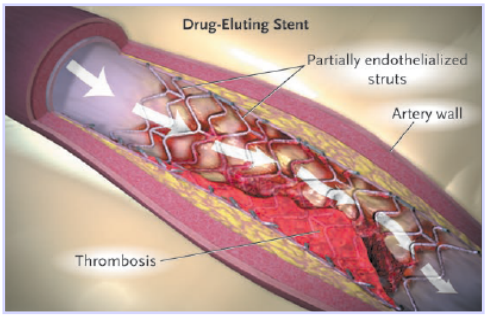
obtain this data from the manufacturer," said Nordmann. He speculated that the increase in cancer might be due to a rapid impairment of

EDITORIAL March 2007

Drug-Eluting Coronary Stents — Promise and Uncertainty

Gregory D. Curfman, M.D., Stephen Morrissey, Ph.D., John A. Jarcho, M.D., and Jeffrey M. Drazen, M.D.





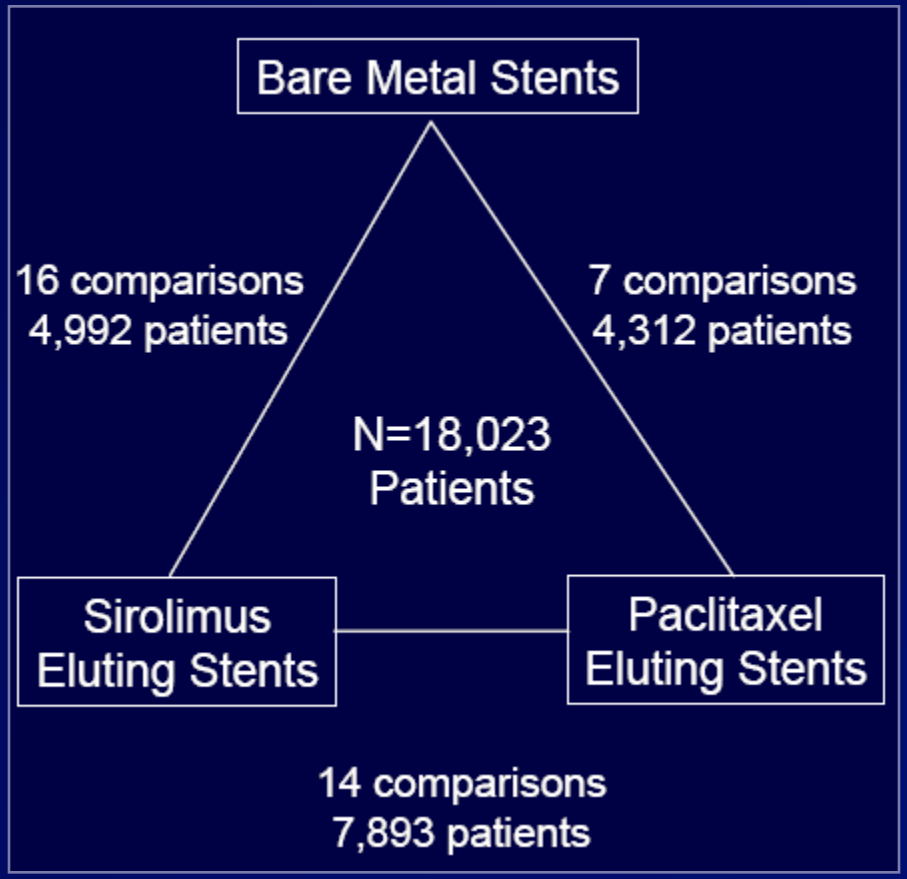
Network Meta-Analysis
38 RCT's Comparing 1st generation DES with BMS

Stettler C et al. Lancet 2007;370:937-48

Off label use : 19 trials with 9,881 patients

On label use : 19 trials with 8,142 patients

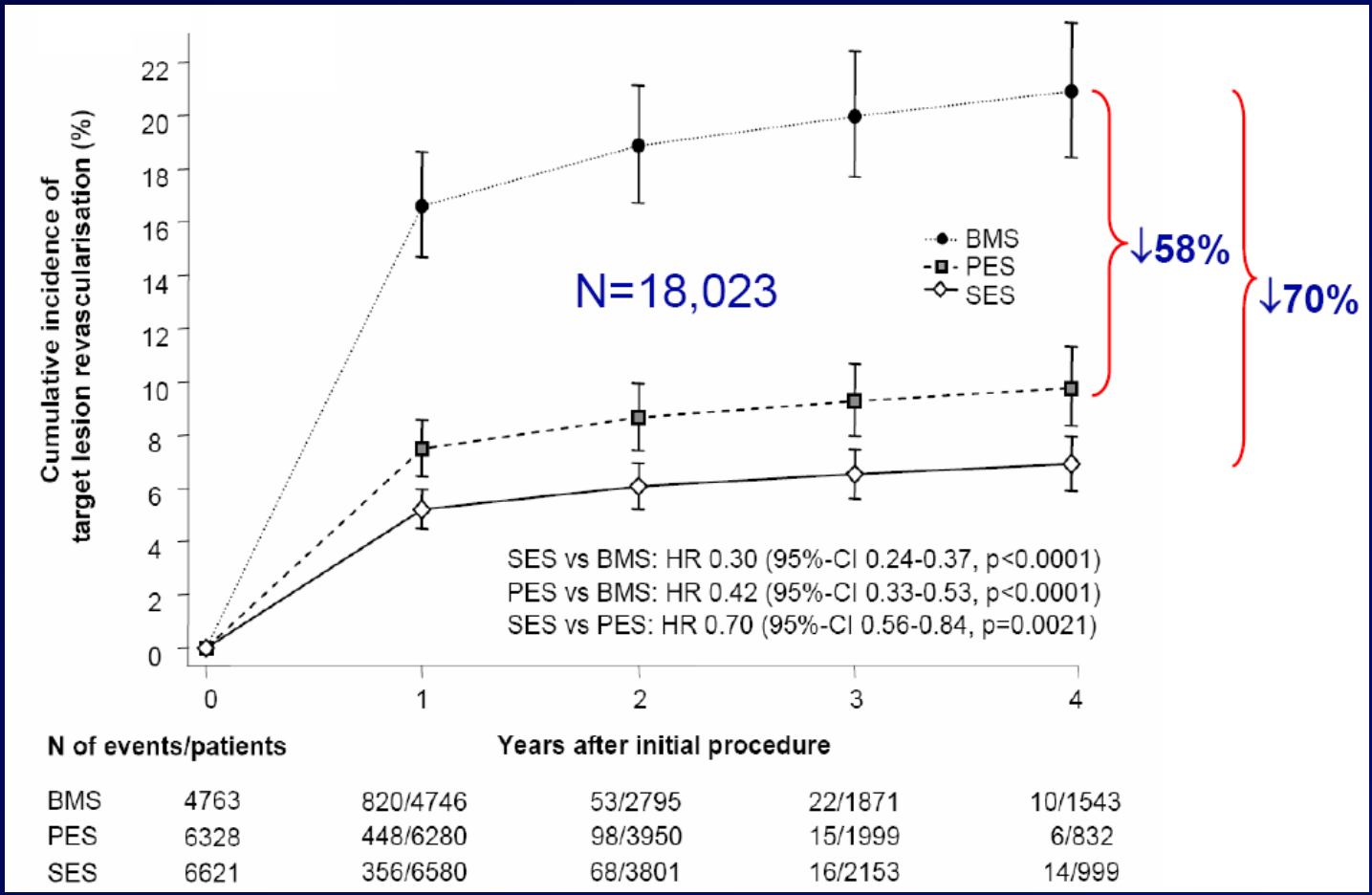
TAXUS I, II, IV, V, VI, PASSION, HAAMU, RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS, SES-SMART, DIABETES, Pacheet al, PRISON II, SCANDSTENT, TYPHOON, SESAMI, DECODE, SCORPIUS, MISSION, Ortolani et al, RRISC, TAXi, ISAR-DESIRE, ISAR-DIABETES, ISAR-SMART 3, SIRTAX, CORPAL, BASKET, REALITY, Zhang et al, LONG DES II, PROSIT, SORT OUT II, Cervinka et al, Petronio et al, Han et al



Target Lesion Revascularization

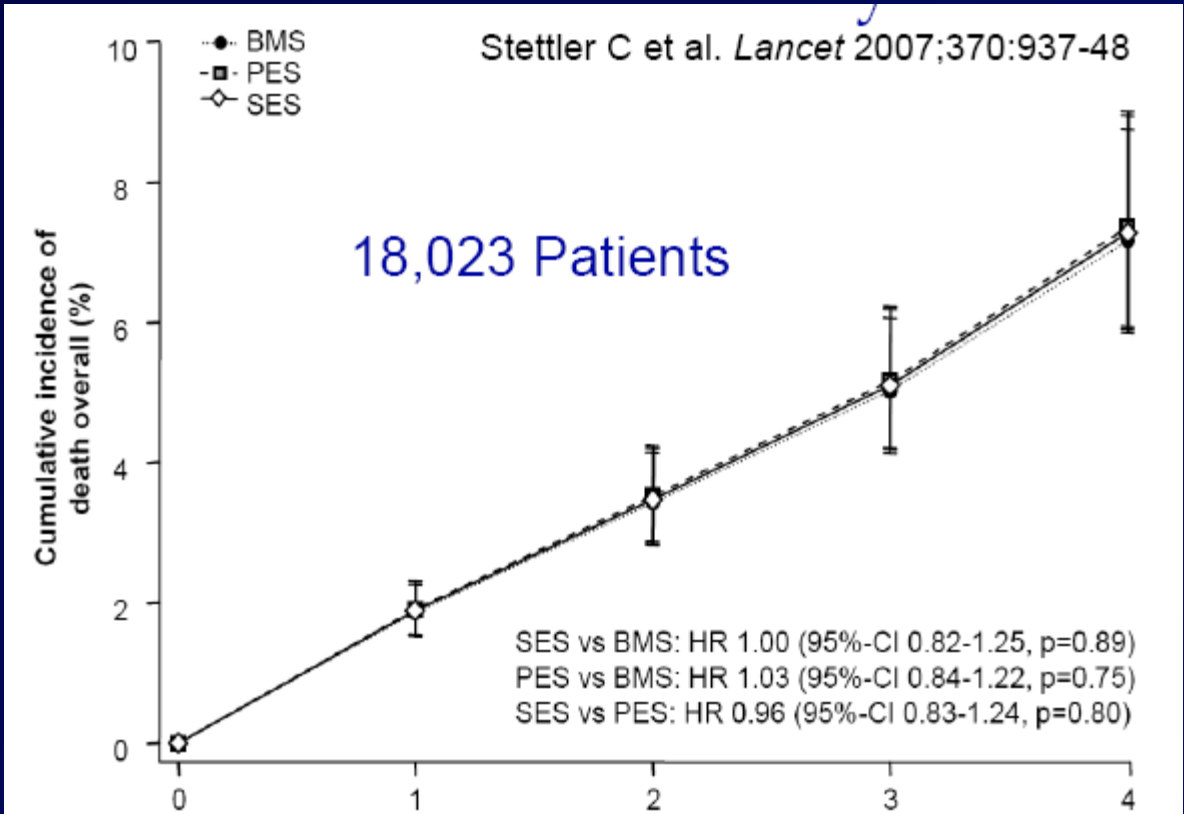
Network Meta-Analysis: DES vs BMS

Stettler C et al. Lancet 2007;370:937-48



N of events/patients					
BMS	4763	820/4746	53/2795	22/1871	10/1543
PES	6328	448/6280	98/3950	15/1999	6/832
SES	6621	356/6580	68/3801	16/2153	14/999

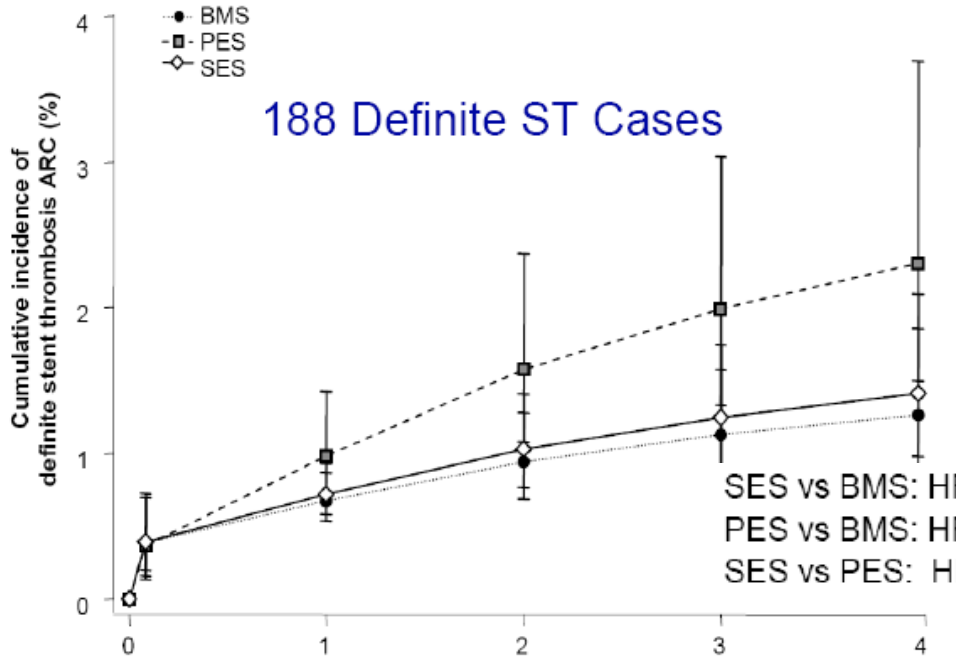
All causes mortality
Network Meta-Analysis: DES vs BMS
Stettler C et al. Lancet 2007;370:937-48



N of events/patients					
BMS	4921	109/4904	48/3340	31/2264	44/1875
PES	6331	138/6283	78/4263	32/2187	15/869
SES	6771	139/6730	72/4041	38/2340	24/1081

Definite Stent Thrombosis (ARC)
Network Meta-Analysis: DES vs BMS

Stettler C et al. Lancet 2007;370:937-48



Paclitaxel

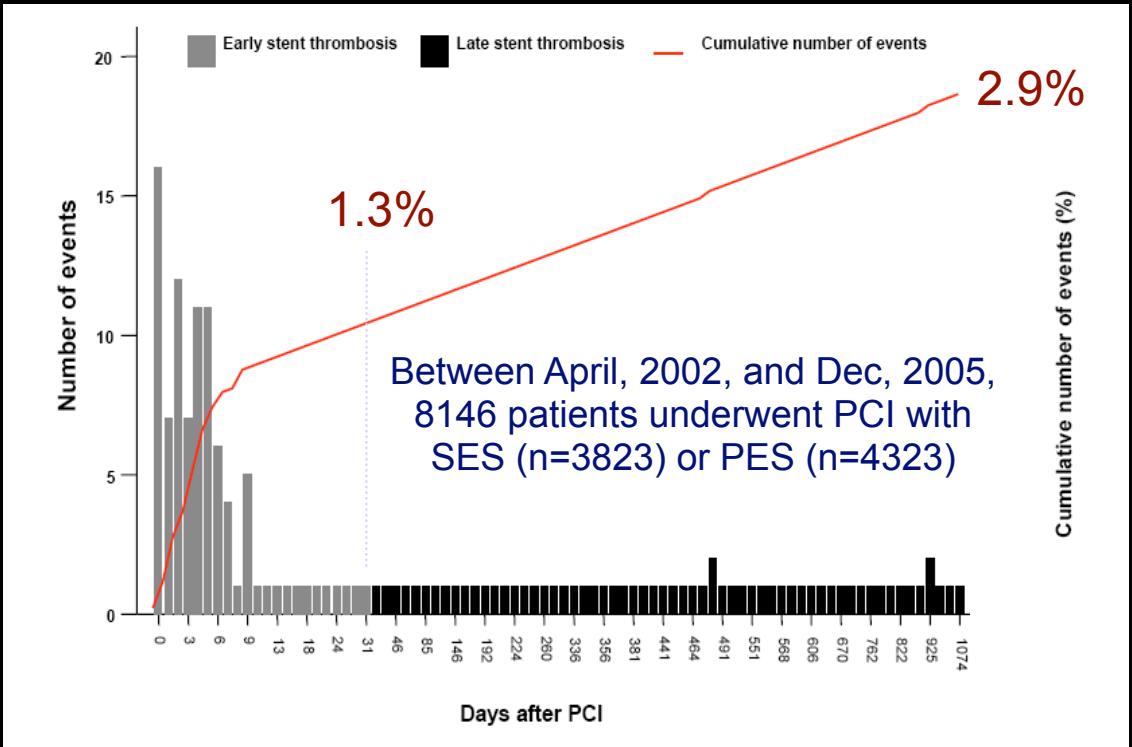
Sirolimus
Bare Metal stent

SES vs BMS: HR 1.00 (95%-CI 0.68-1.63, p=1.00)
PES vs BMS: HR 1.38 (95%-CI 0.96-2.24, p=0.14)
SES vs PES: HR 0.71 (95%-CI 0.48-1.13, p=0.21)

N of events/patients					
BMS	4003	42/4000	4/3048	3/1928	1/1806
PES	4327	46/4321	20/3711	5/1853	1/762
SES	4643	52/4642	9/3804	3/2257	2/1070

Bern-Rotterdam Registry

Daemen et al. Lancet. 2007 ; 369: 667 – 78.



- Late stent thrombosis occurred steadily at a constant rate of 0.6% per year up to three years after stent implantation. *Only angiographically documented cases of stent thrombosis were counted, which might have underrepresented the actual incidence of stent thrombosis*
- Independent predictors of overall stent thrombosis were acute coronary syndrome at presentation (hazard ratio 2·28, 95% CI 1·29–4·03) and diabetes (2·03, 1·07–3·83).

Predictors of stent thrombosis after DES implantation

I.Iakovou et al. JAMA 2005;293:2126-30

3 centers, 2229 patients, 2272 SES + 2223 PES, 9 months clinical FU

✓ Premature AP therapy stop	89.8 (29.9 – 269.6)	<.001
✓ Renal failure	6.5 (2.5 – 26.3)	<.001
✓ Bifurcation lesion	6.4 (2.9 – 14.1)	<.001
✓ Diabetes	3.7 (1.7 – 7.9)	=.001
✓ LVEF decrease by 10%	1.09 (1.05 – 1.13)	
<0.01		

Procedure-Related Risk Factors for Stent Thrombosis

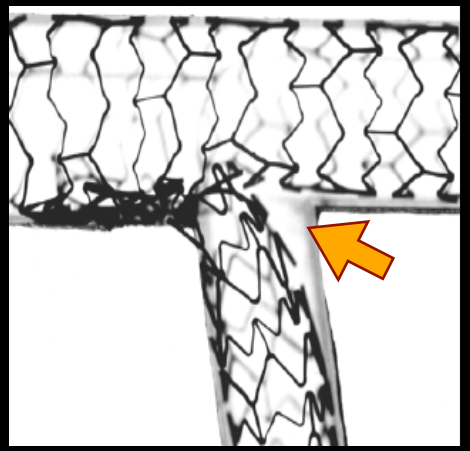
HONDA Y. *Circulation.* 2003;108:2.

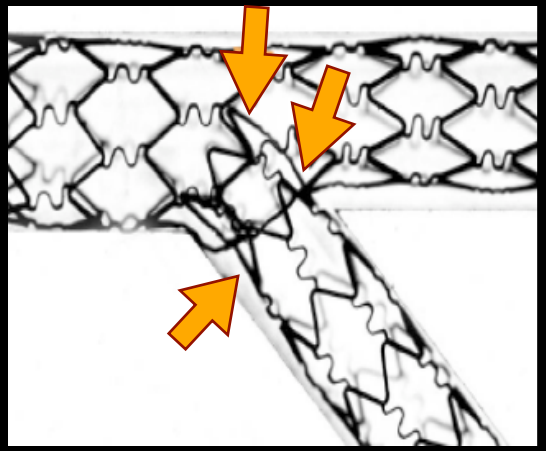
Series (Years Performed)				ssment	Risk factor (*multivariate predictor)
Karrillon et al (1992–1995)					Bailout stenting,* smaller balloon size*
De Servi et al (1995–1996)					Unplanned stenting,* lower maximal inflation pressure*
Schuhlen et al (1992–1997)					Residual dissections,* stent overlap,* longer stent length*
Cutlip et al (1995–1999)					Smaller final lumen diameter,* residual dissections,* longer stent length*
Moussa et al (1993–1995)				VUS	Smaller final lumen dimensions, smaller balloon size, multiple stents, residual dissections,* persistent slow flow,* combined use of different stent designs*
Uren et al (1991–1996)				VUS	Dissections, incomplete apposition, in-stent thrombus (in combination with stent underexpansion)
Werner et al (1995–1996)	215	4 (1.9%)	0,83	IVUS	Smaller lumen dimensions,* plaque burden*
Cheneau et al (1993–2002)	7484 (69 as control)	27 (0.4%)	1	IVUS	Smaller final lumen dimensions (in combination with dissections, thrombus, or tissue prolapse)

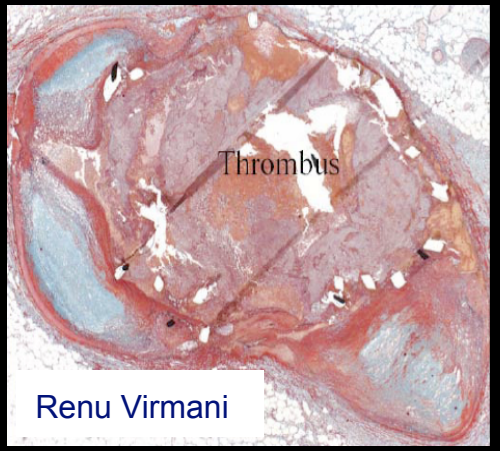
- Low pressure inflation
- Incomplete apposition
- Stent underexpansion
- Residual dissection
- tissue/thrombus prolapse
- Smaller balloon size
- Smaller final diameter
- Longer stents
- Multiple stents
- Stent overlap
- Persistent slow flow
- Bail out stenting

Bifurcation stenting increases the risk of abrupt closure

- ✓ major injury to the arterial wall generating
- ✓ proinflammatory and prothrombotic state
- ✓ stent malapposition and under-expansion
- ✓ lake of endothelialisation of the carena

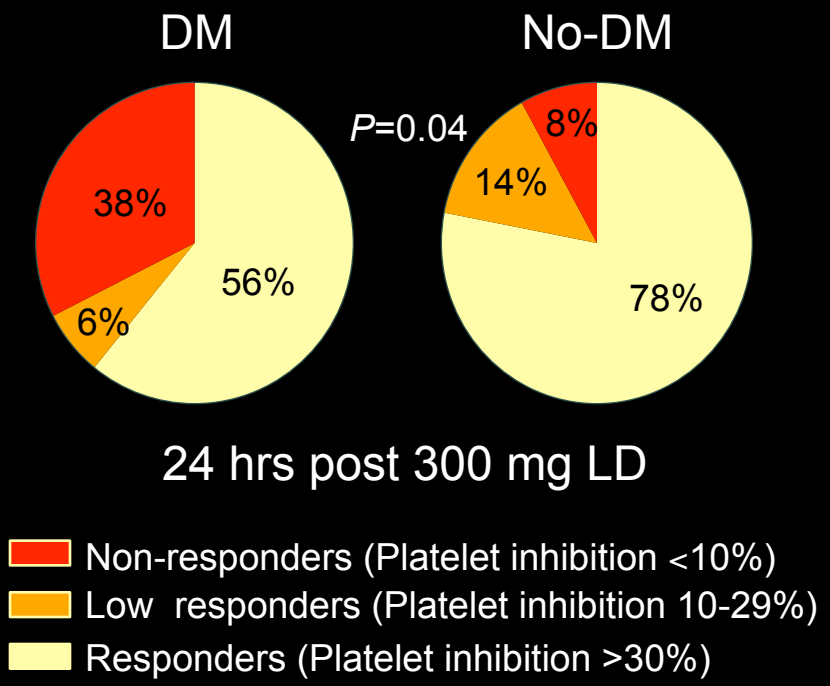






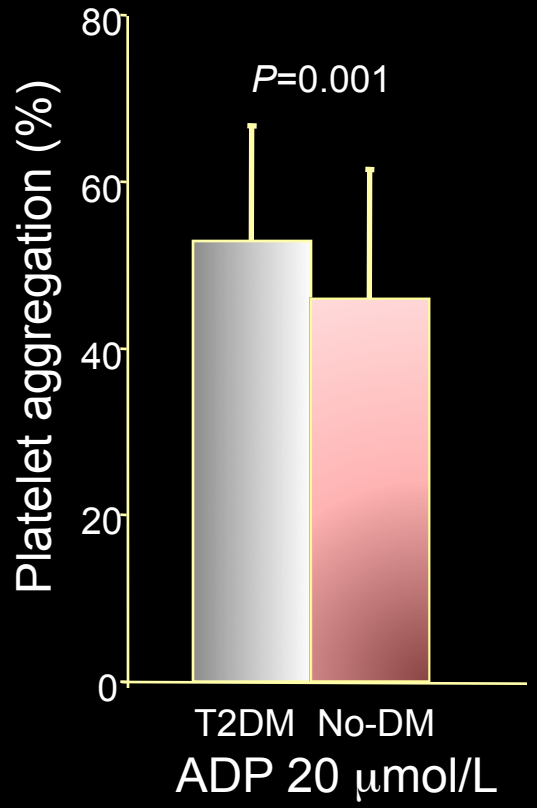
Influence of Diabetes Mellitus on Clopidogrel-induced Antiplatelet Effects

Acute phase of treatment



Angiolillo DJ et al. *Diabetes.* 2005;54:2430-5.

Long-term phase of treatment



Angiolillo DJ et al. *J Am Coll Cardiol* 2006;48 298-304.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dose Comparisons of Clopidogrel and Aspirin in Acute Coronary Syndromes

The CURRENT–OASIS 7 Investigators*

RESULTS

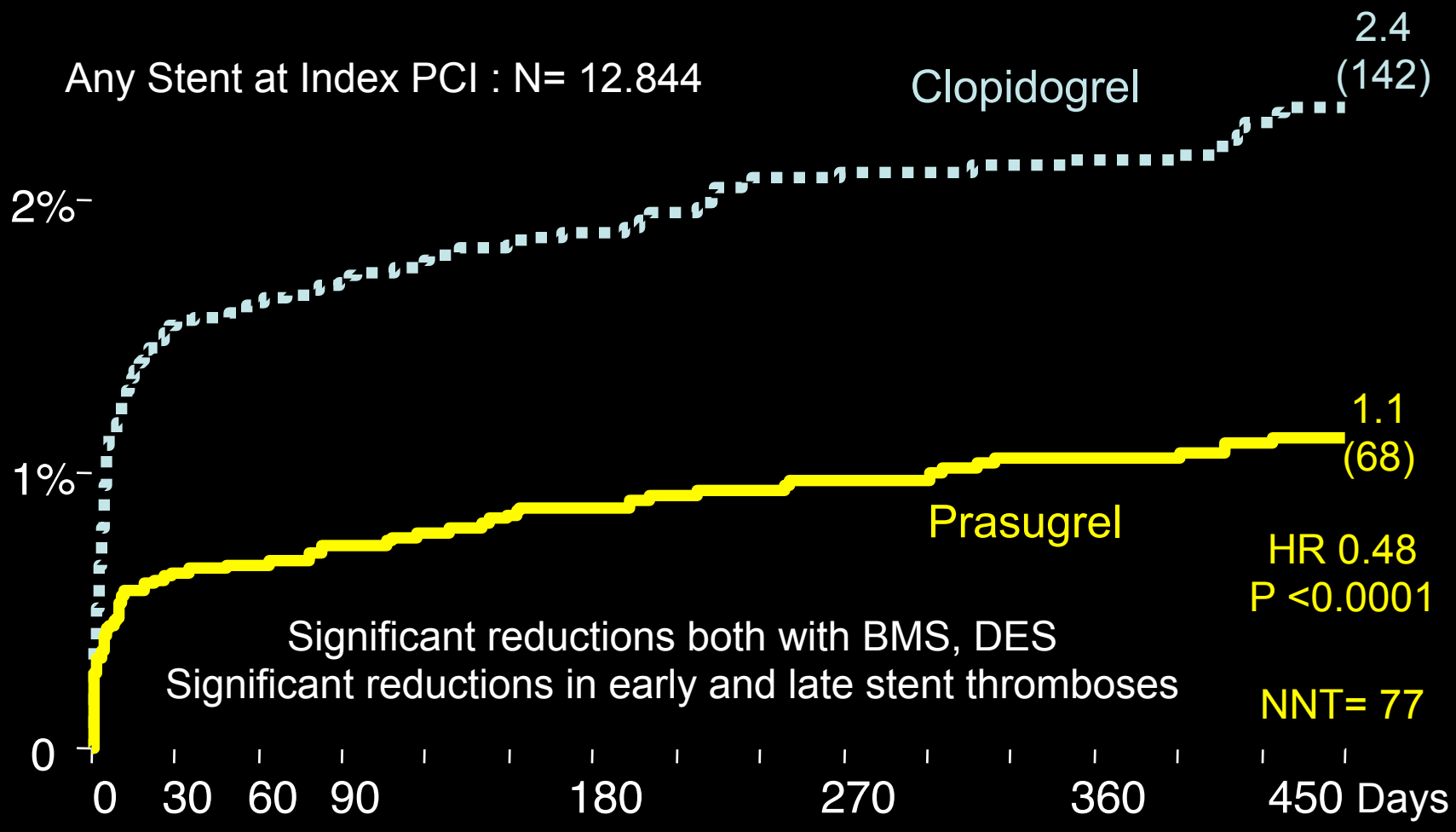
The primary outcome occurred in 4.2% of patients assigned to double-dose clopidogrel as compared with 4.4% assigned to standard-dose clopidogrel (hazard ratio, 0.94; 95% confidence interval [CI], 0.83 to 1.06; P=0.30). Major bleeding occurred in 2.5% of patients in the double-dose group and in 2.0% in the standard-dose group (hazard ratio, 1.24; 95% CI, 1.05 to 1.46; P=0.01). Double-dose clopidogrel was associated with a significant reduction in the secondary outcome of stent thrombosis among the 17,263 patients who underwent PCI (1.6% vs. 2.3%; hazard ratio, 0.68; 95% CI, 0.55 to 0.85; P=0.001). There was no significant difference between higher-dose and lower-dose aspirin with respect to the primary outcome (4.2% vs. 4.4%; hazard ratio, 0.97; 95% CI, 0.86 to 1.09; P=0.61) or major bleeding (2.3% vs. 2.3%; hazard ratio, 0.99; 95% CI, 0.84 to 1.17; P=0.90).

TRITON TIMI-38

Wiviott SD et al Lancet 2008

Stent Thrombosis
(ARC Definite + Probable)

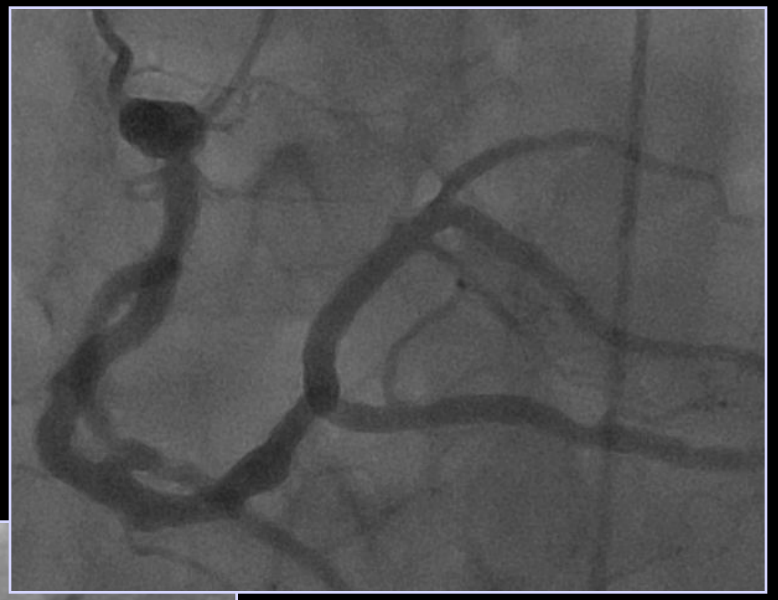
Any Stent at Index PCI : N= 12.844

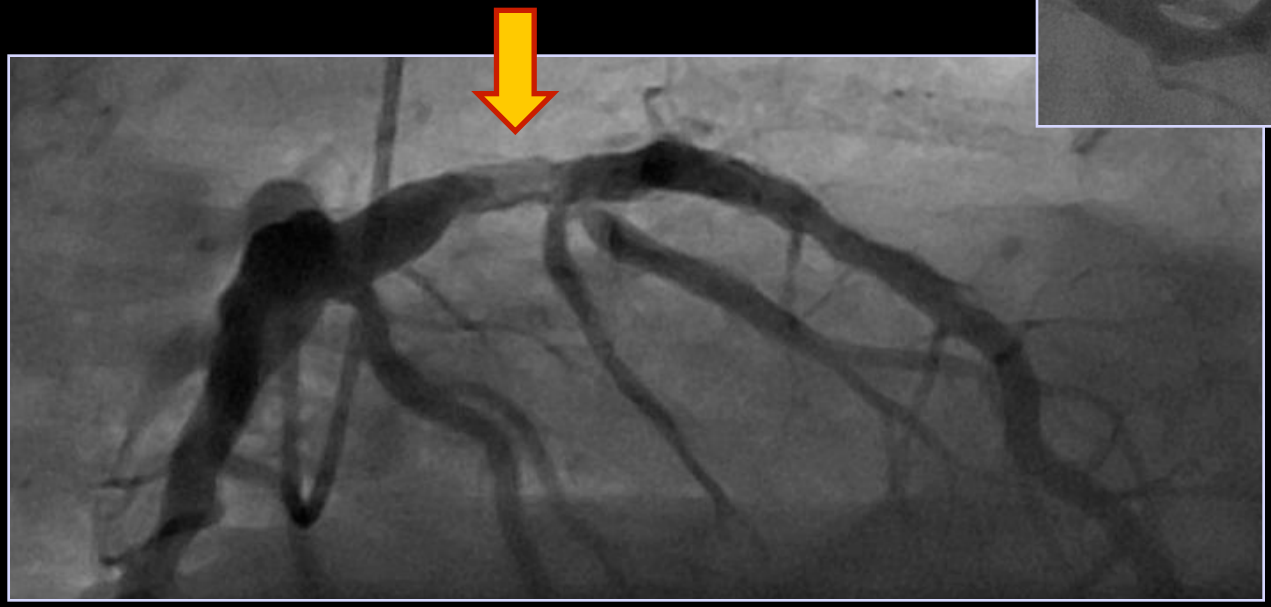


Mr P…61 ans

Angioplastie de l'IVA par un Cypher et de la droite au ballon (IVP) 7 ans auparavant

Infarctus antérieur non transmural après avoir jardiné 3 heures au soleil, 1 mois après diminution des doses d'aspirine (1j/2) motivée par une gastrite





Interventional Cardiology

Correlation of Intravascular Ultrasound Findings With Histopathological Analysis of Thrombus Aspirates in Patients With Very Late Drug-Eluting Stent Thrombosis

Stéphane Cook, MD*; Elena Ladich, MD*; Gaku Nakazawa, MD; Parham Eshtehardi, MD; Michel Neidhart, PhD; Rolf Vogel, MD, PhD; Mario Togni, MD; Peter Wenaweser, MD; Michael Billinger, MD; Christian Seiler, MD; Steffen Gay, MD; Bernhard Meier, MD; Werner J. Pichler, MD; Peter Jüni, MD; Renu Virmani, MD; Stephan Windecker, MD

Circulation. 2009;120:391-9

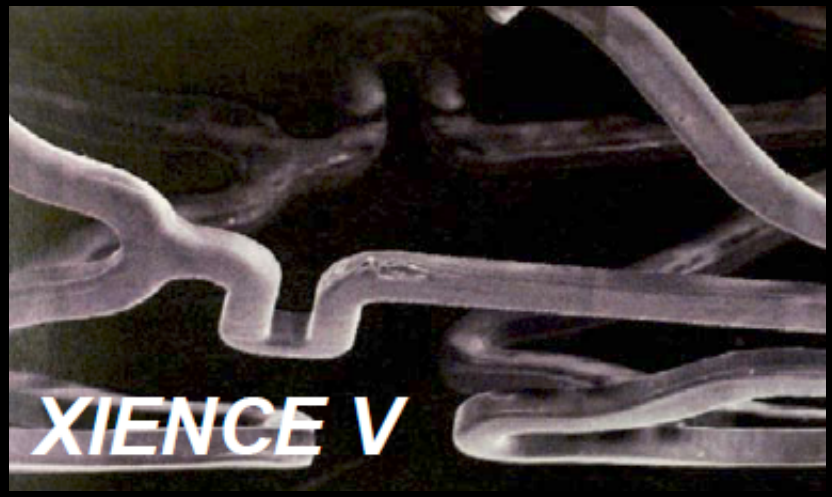
The present study sought to correlate histopathology of thrombus aspirates with intravascular ultrasound findings in 10 patients with very late DES ST (1020 ± 283 days after implantation) who underwent both thrombus aspiration and intravascular ultrasound investigation.

Incomplete Stent Apposition was present in 73% of cases with evidence of vessel remodeling

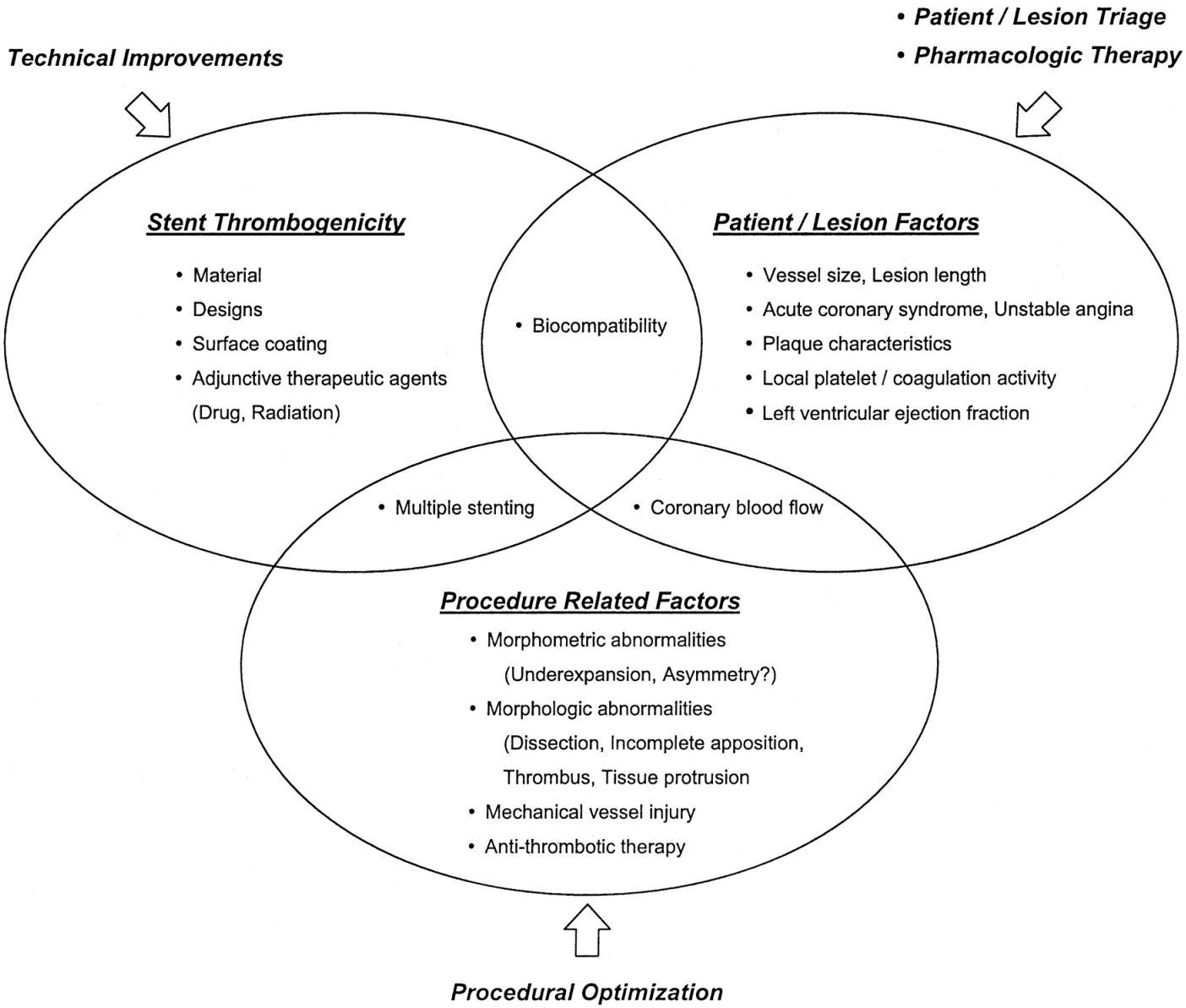
Conclusions

Very late DES thrombosis is associated with histopathological signs of inflammation and intravascular ultrasound evidence of vessel remodeling. Compared with other causes of myocardial infarction, eosinophilic infiltrates are more common in thrombi harvested from very late DES thrombosis, particularly in sirolimus-eluting stents, and correlate with the extent of stent malapposition.

Le polymère est le point faible du stent actif…



HONDA Y. *Circulation.* 2003;108:2.

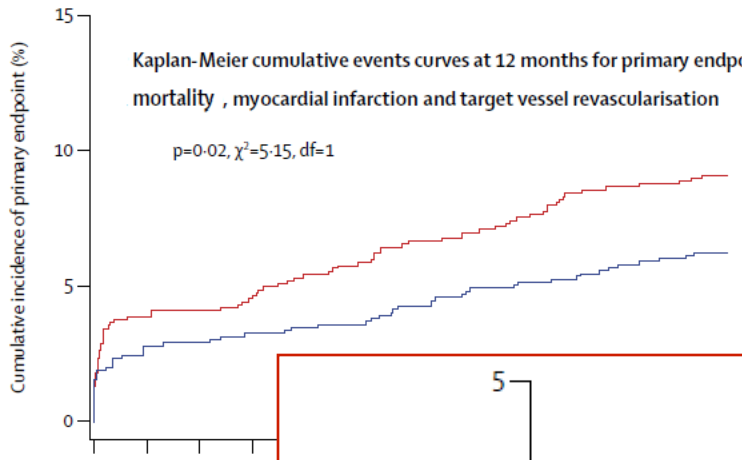


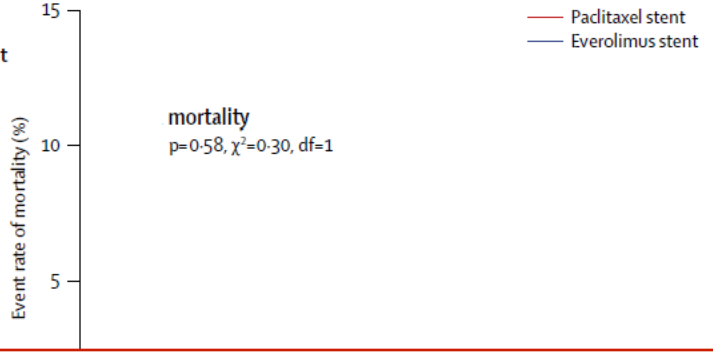
Lessons I . *S Windecker. Hot Line session ESC 2010*

- Non randomized study comparing two consecutive series of patients,
  - the first treated with the sirolimus-eluting stent over a two-year period, then a second period, during which time consecutive patients were treated with an everolimus-eluting stent.
  - Both series were then propensity matched, yielding two groups of 1342 matched pairs that were then followed out to three years.

End point	Everolimus (%)	Sirolimus (%)	HR (95% CI)	p
Death, MI, TVR*	14.9	18	0.83 (0.68-1.0)	0.056
MI	3.3	5.0	0.62 (0.42-0.92)	0.017
TVR	7.0	9.6	0.76 (0.57-0.99)	0.039
Definite stent thrombosis	0.5	1.6	—	0.010
Definite or probable stent thrombosis	2.5	4.0	—	0.041

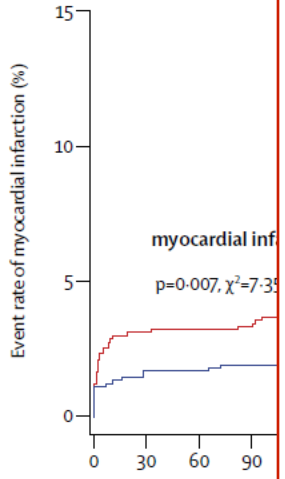
*Primary end point





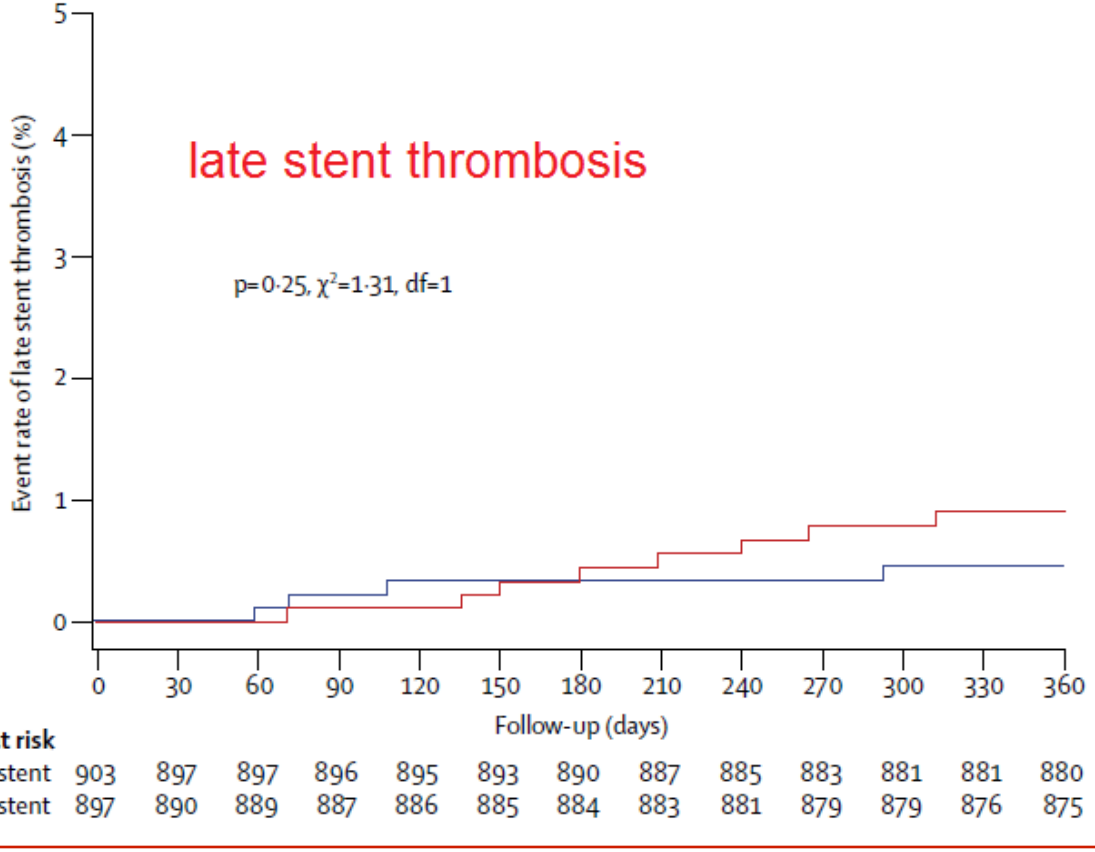
Number at risk

Paclitaxel stent	903	868	865	861
Everolimus stent	897	894	884	883



Number at risk

Paclitaxel stent	903	870	868	867
Everolimus stent	897	876	874	872

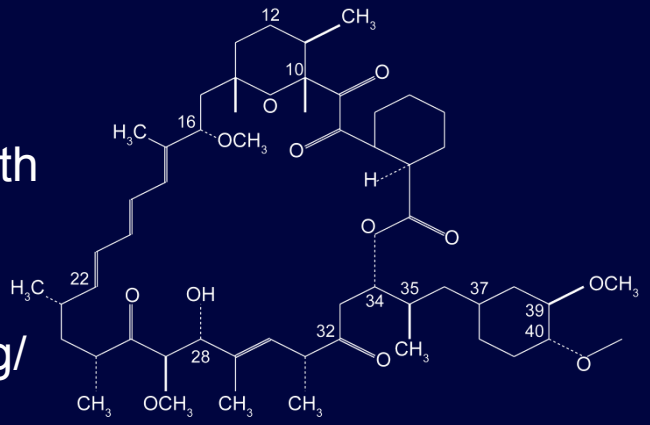


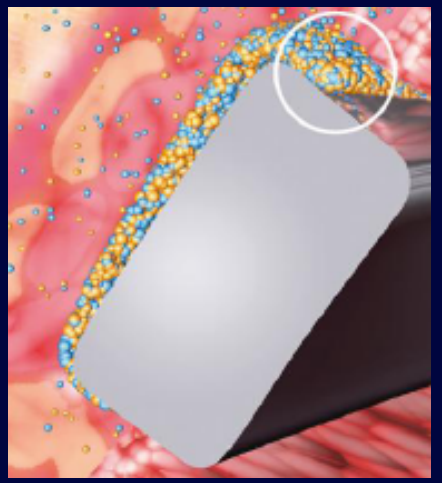
Number at risk

Paclitaxel stent	903	897	897	896	895	893	890	887	885	883	881	881	880
Everolimus stent	897	890	889	887	886	885	884	883	881	879	879	876	875

Biolimus-A9™ Eluting Stent

- Biolimus is a semi-synthetic sirolimus analogue with 10x higher lipophilicity and similar potency as sirolimus.
- Biolimus is immersed at a concentration of 15.6 μg/mm into a biodegradable polymer, polylactic acid, and applied solely to the abluminal stent surface by a fully automated process.
- Polylactic acid is co-released with biolimus and completely desolves into carbon dioxide and water during a 6-9 months period.
- The stainless steel stent platform has a strut thickness of 112 μm with a quadrature link design.





LEADERS

LEADERS

Lancet, september 1, 2008

Biolimus-eluting stent with biodegradable polymer versus sirolimus-eluting stent with durable polymer for coronary revascularisation (LEADERS): a randomised non-inferiority trial

Stephan Windecker, Patrick W Serruys, Simon Wandel, Pawel Buszman, Stanislaw Trznadel, Axel Linke, Karsten Lenk, Thomas Ischinger, Volker Klauss, Franz Eberli, Roberto Corti, William Wijns, Marie-Claude Morice, Carlo di Mario, Simon Davies, Robert-Jan van Geuns, Pedro Eerdmans, Gerrit-Anne van Es, Bernhard Meier, Peter Jüni

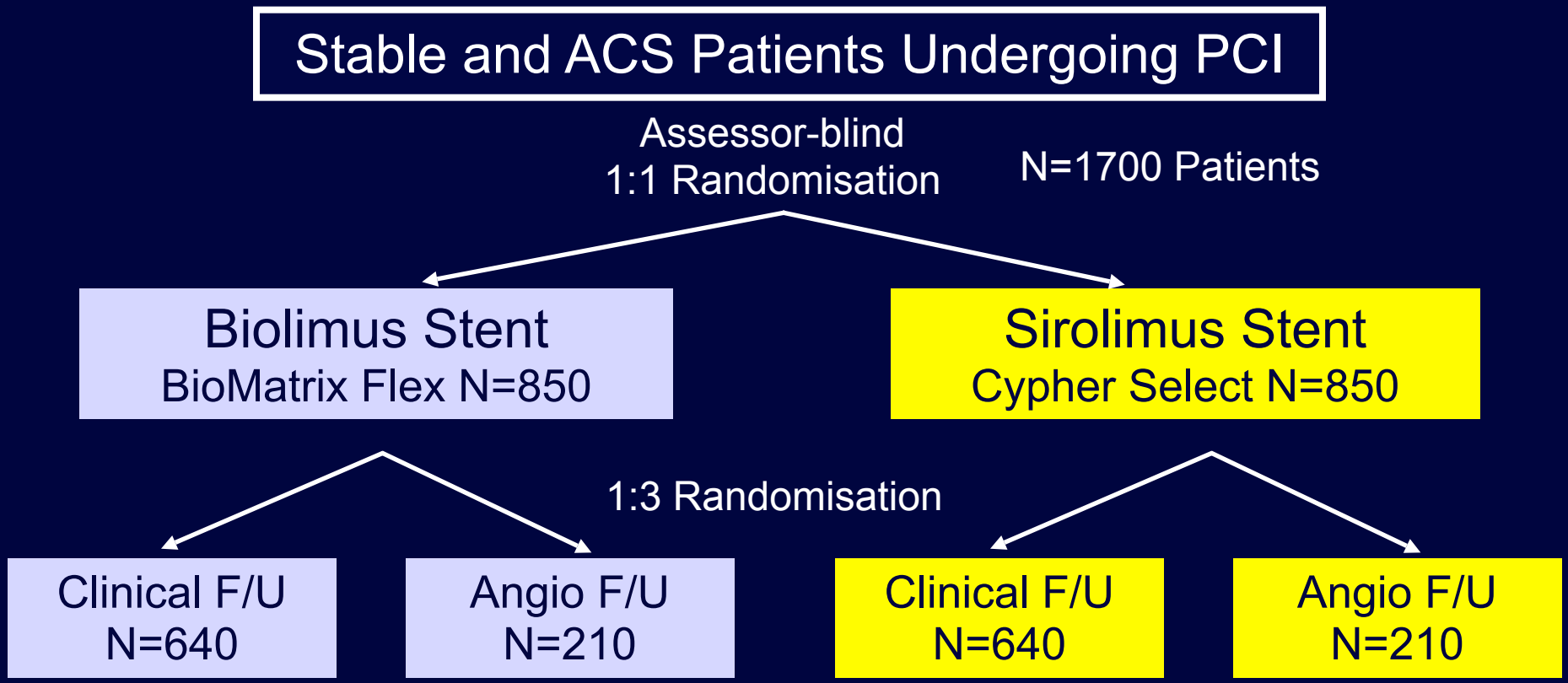
Summary

Background A novel stent platform eluting biolimus, a sirolimus analogue, from a biodegradable polymer showed promising results in preliminary studies. We compared the safety and efficacy of a biolimus-eluting stent (with biodegradable polymer) with a sirolimus-eluting stent (with durable polymer).

Methods We undertook a multicentre, assessor-blind, non-inferiority study in ten European centres. 1707 patients aged 18 years or older with chronic stable coronary artery disease or acute coronary syndromes were centrally randomised by a computer-generated allocation sequence to treatment with either biolimus-eluting (n=857) or sirolimus-eluting (n=850) stents. The primary endpoint was a composite of cardiac death, myocardial infarction, or clinically-indicated target vessel revascularisation within 9 months. Analysis was by intention to treat. 427 patients were randomly allocated to angiographic follow-up, with in-stent percentage diameter stenosis as principal outcome measure at 9 months. The trial is registered with ClinicalTrials.gov, number NCT00389220.

Lancet 2008; 372: 1163–73
Published Online
September 1, 2008

Trial Design



1º endpoint:	CV death, MI, clinically-indicated TVR
2º endpoints:	Death, CV death, MI, TLR, TVR
	Stent Thrombosis according to ARC
Angiographic study:	In-stent % diameter stenosis
	Late loss, binary restenosis

LEADERS

Patient Eligibility

Inclusion Criteria

Coronary artery disease

- Stable angina
- Silent ischemia
- Acute coronary syndrome (UA, NSTEMI and STEMI)

At least one lesion with

- Diameter stenosis ≥ 50%
- RVD: 2.25-3.5 mm
- Number of lesions: no limitation
- Number of vessels: no limitation
- Vessel length: no limitation

Written informed consent

Exclusion Criteria

Known allergy to

- aspirin, clopidogrel, heparin, stainless steel, sirolimus, biolimus, contrast material

Planned, elective surgery within 6 months of PCI unless

- dual APT could be maintained

Pregnancy

Participation in another trial

LEADERS

Patient Demographics

Stent	Biolimus Stent	Sirolimus
Patients	850 Patients	857
Age in years	65 ± 11	65 ± 11
Male gender	75%	75%
Arterial hypertension	74%	73%
Diabetes mellitus	26%	23%
- insulin-dependent	10%	9%
Hypercholesterolemia	65%	68%
Family history	40%	44%
Smoking	24%	25%
Previous MI	32%	33%

LEADERS

Patient Characteristics

	Biolimus Stent 857 Patients	Sirolimus Stent 850 Patients
Acute coronary syndrome	55%	56%
- Unstable angina	22%	20%
- Non-ST-elevation MI	18%	19%
- ST-elevation MI	16%	17%
Left ventricular ejection fraction	56 ± 11%	55 ± 12%
Number of lesions per patient	1.5 ± 0.7	1.4 ± 0.7
Lesions per patient		
- 1 lesion	63%	69%
- 2 lesions	29%	22%
- > 3 lesions	8%	10%
De novo lesions	92%	91%
Long lesions (>20 mm)	31%	27%
Small vessels (RVD ≤2.75 mm)	68%	69%
Off label use	81%	78%

LEADERS

Procedural Characteristics

	Biolimus Stent 1257 Lesions	Sirolimus Stent 1215 Lesion	*P*
# stents per lesion	1.3 ± 0.7	1.3 ± 0.7	0.36
Maximal stent diameter (mm)	3.0 ± 0.4	3.0 ± 0.4	0.96
Stent length per lesion (mm)	24.7 ± 15.5	24.6 ± 14.8	0.95
Direct stenting (%)	40.4%	39.9%	0.76
Implantation of study stent (%)	97.5%	95.7%	0.05
Device success (%)	95.8%	94.2%	0.11
Lesion success (%)	98.6%	97.8%	0.15

LEADERS

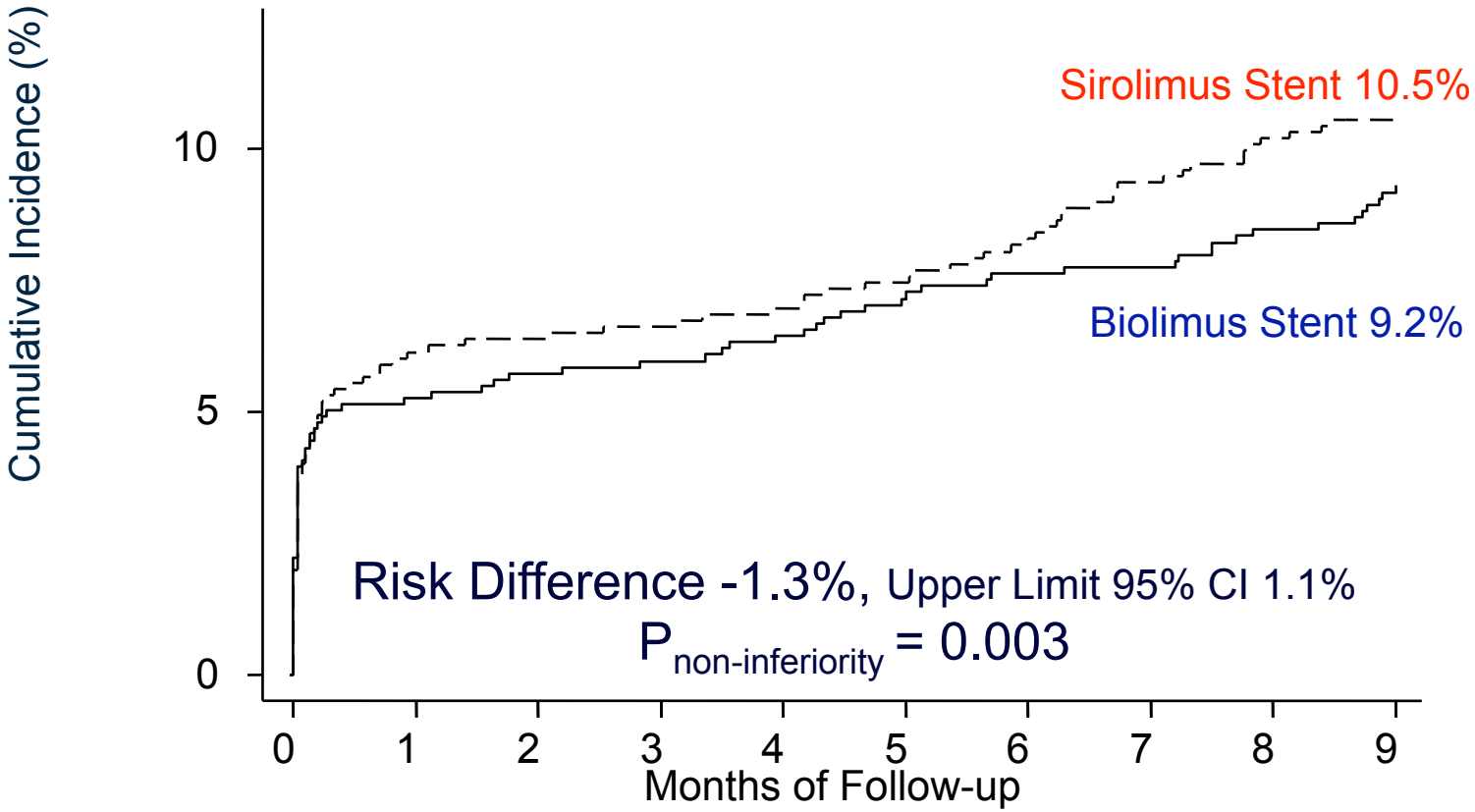
LEADERS – Pre- and Post Procedural QCA

Pre-procedure	Biolimus Stent 1257 lesions	Sirolimus Stent 1215 lesions	*P*
RVD (mm)	2.60 ± 0.61	2.60 ± 0.57	
MLD (mm)	0.91 ± 0.50	0.95 ± 0.52	
% DS	64.6 ± 17.9	63.3 ± 18.2	
Lesion length (mm)	12.7 ± 8.1	12.4 ± 8.5	
Acute gain (mm)			
In-segment	1.11 ± 0.58	1.10 ± 0.56	0.41
In-stent	1.41 ± 0.57	1.37 ± 0.54	0.07
MLD (mm)			
In-segment	2.03 ± 0.53	2.05 ± 0.52	0.60
In-stent	2.33 ± 0.52	2.33 ± 0.50	0.78
% Diameter Stenosis			
In-segment	23.3 ±10.9	22.9 ± 11.3	0.41
In-stent	15.1 ± 9.8	15.1 ± 10.2	0.91

LEADERS

Primary Endpoint

Cardiac Death, MI, or TVR @ 9 months

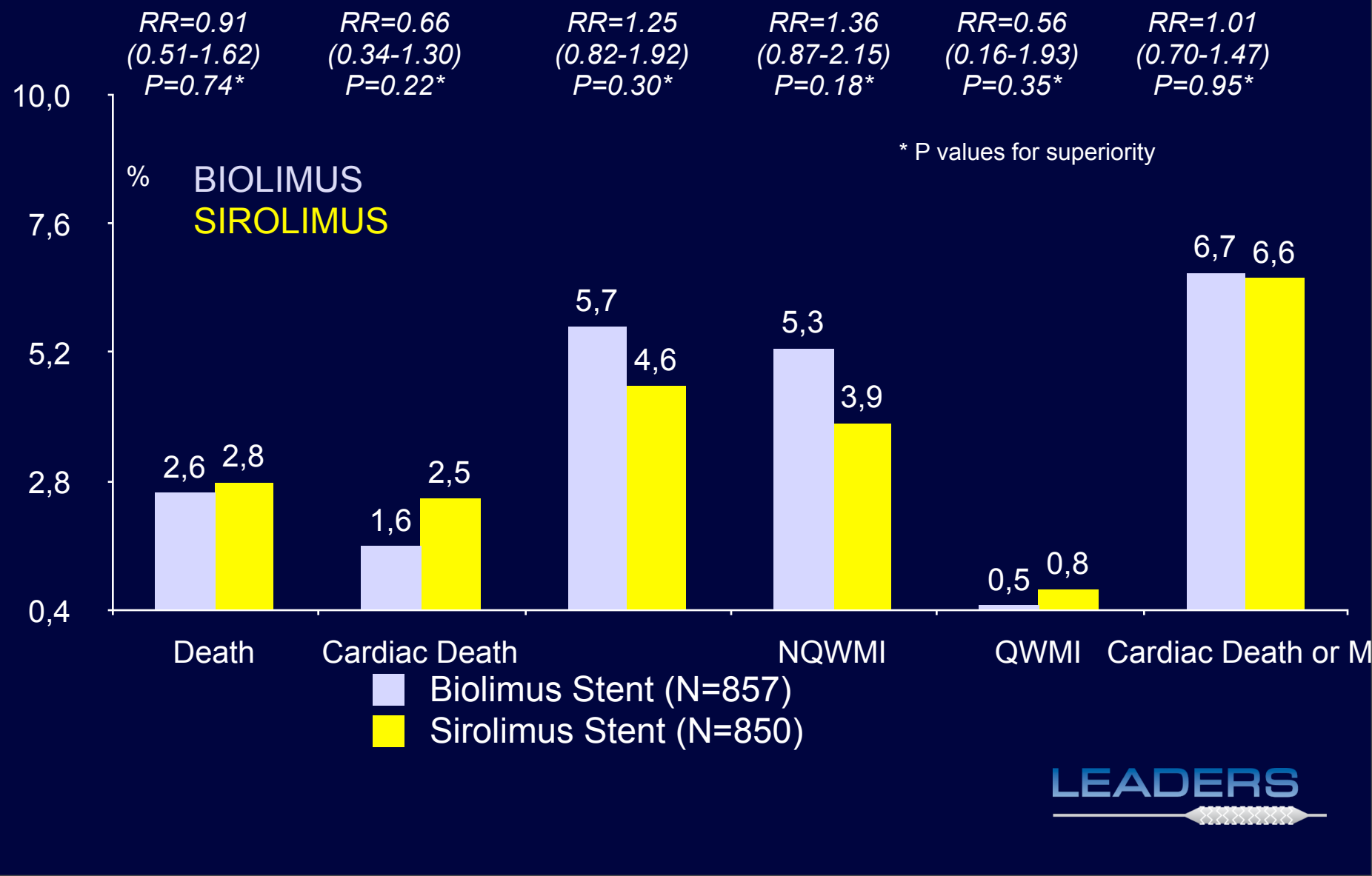


No. at risk

BE	857	806	798	796	792	784	779	777	771	761
SES	850	791	786	784	781	777	771	758	751	746

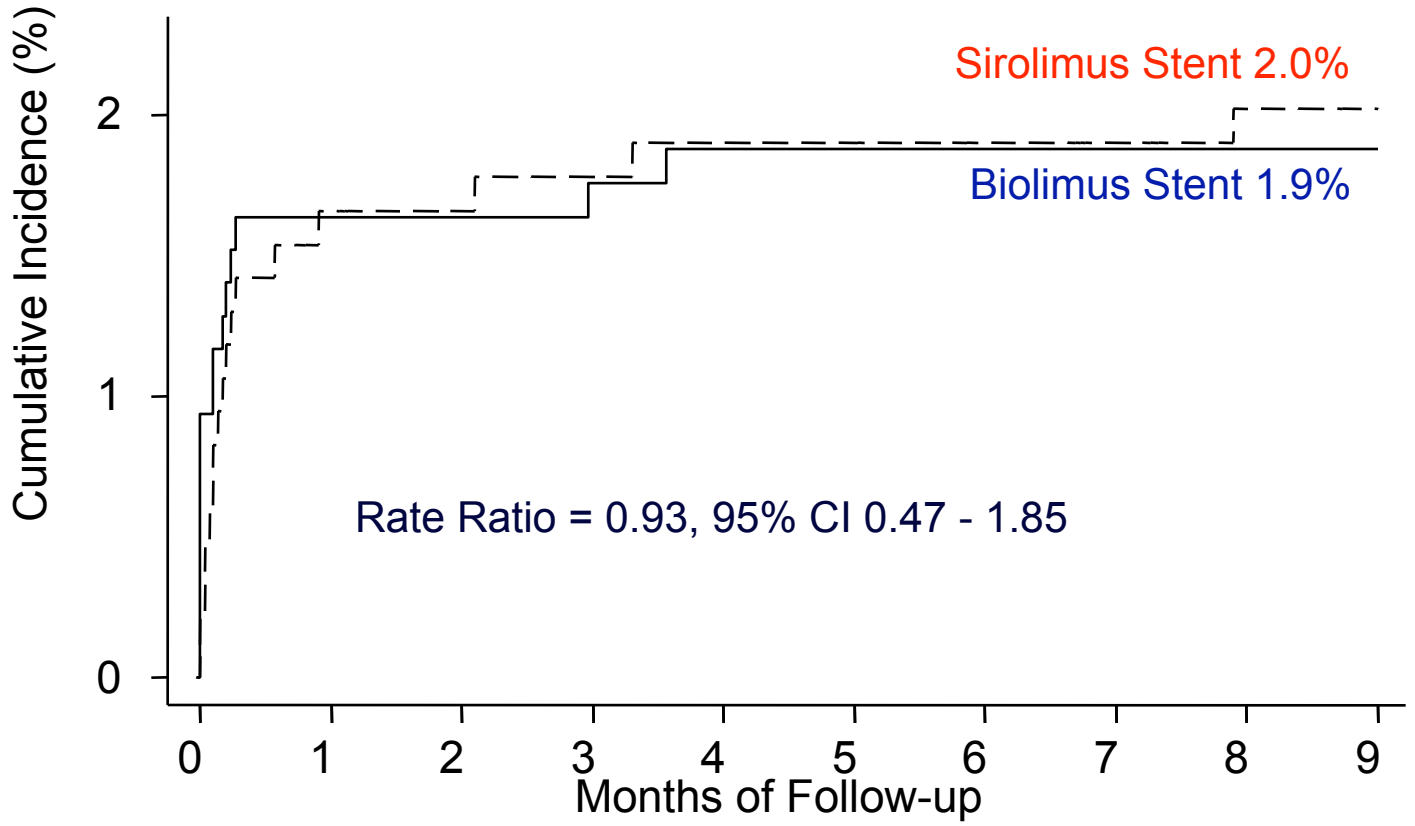
LEADERS

Safety Endpoints @ 9 Months



LEADERS

Definite Stent Thrombosis



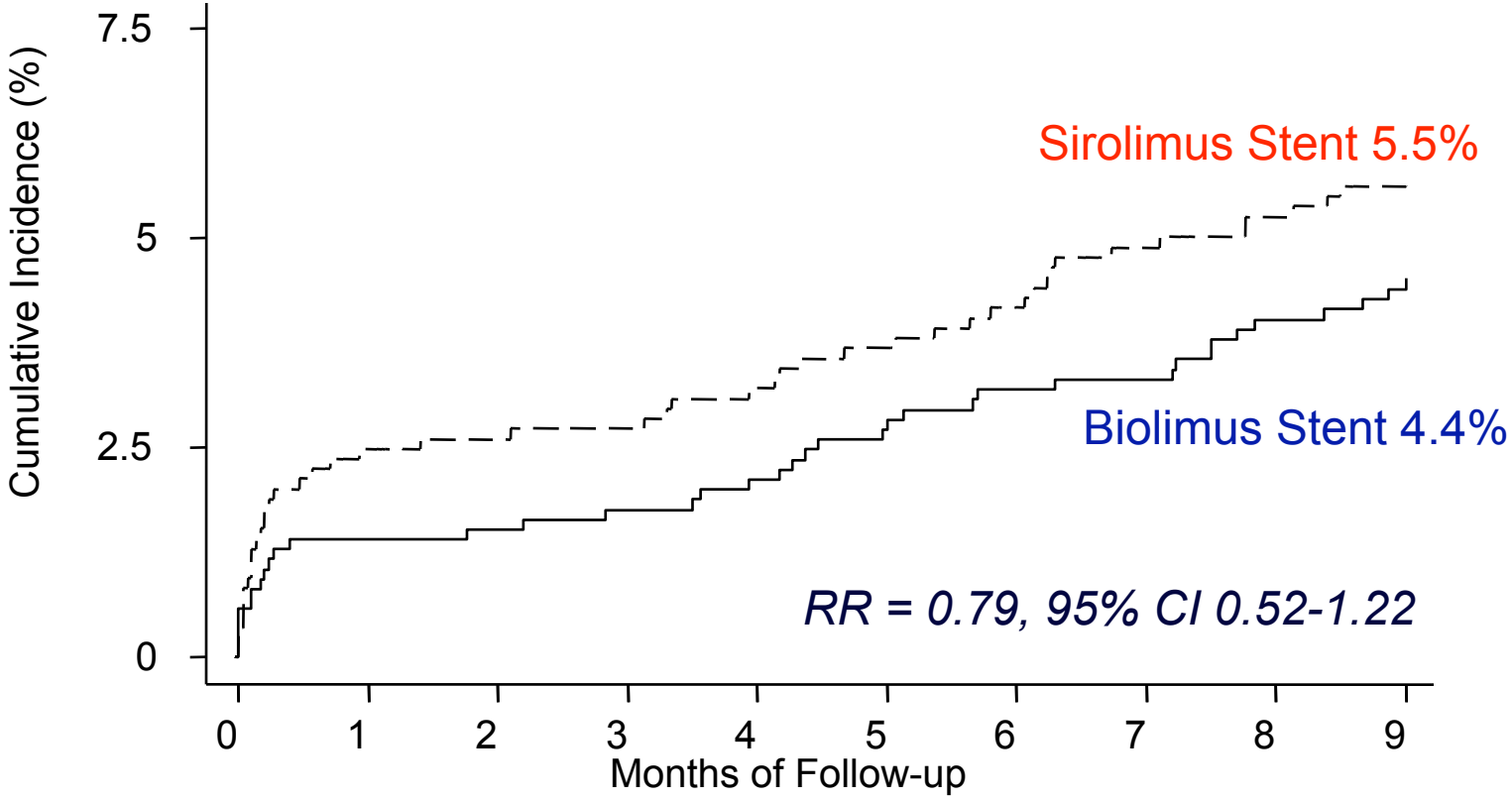
Number at risk

BES	857	833	826	825	824	821	818	817	816	808
SES	850	822	818	816	815	815	813	806	803	799

LEADERS

Efficacy Endpoint

Clinically-Indicated Target Vessel Revascularization



Number at risk

BES	857	835	827	825	822	814	808	806	800	791
SES	850	815	810	808	804	800	794	781	776	770

LEADERS

Angiographic Follow-up Results

	Biolimus Stent 255 lesions	Sirolimus Stent 233 lesions	*P**
MLD			
in-stent (mm)	2.23 ± 0.64	2.11 ± 0.70	0.08
in-segment (mm)	2.01 ± 0.59	1.87 ± 0.64	0.03
Diameter stenosis			
in-stent (%)	20.9 ± 17.5	23.3 ± 19.6	0.26
in-segment (%)	27.1 ± 16.4	29.9 ± 18.5	0.14
Late lumen loss			
in-stent (mm)	0.13 ± 0.46	0.19 ± 0.50	0.34
in-segment (mm)	0.08 ± 0.45	0.15 ± 0.46	0.12
Binary restenosis			
in-stent (%)	5.5	8.7	0.20
in-segment (%)	6.7	10.8	0.15

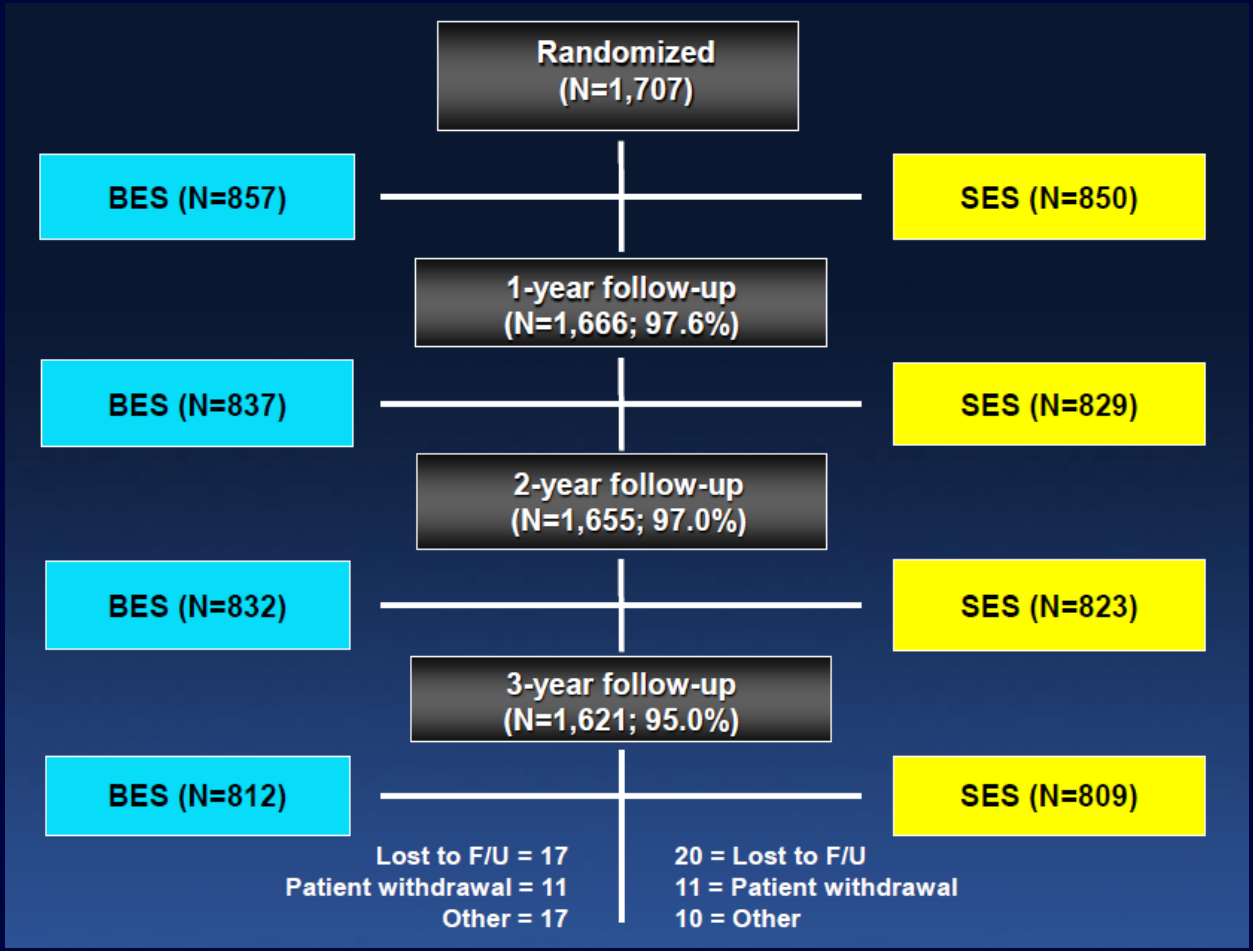
* P values for superiority

LEADERS

LEADERS – 3 Year Clinical Follow-Up

Patrick W. Serruys TCT 2010

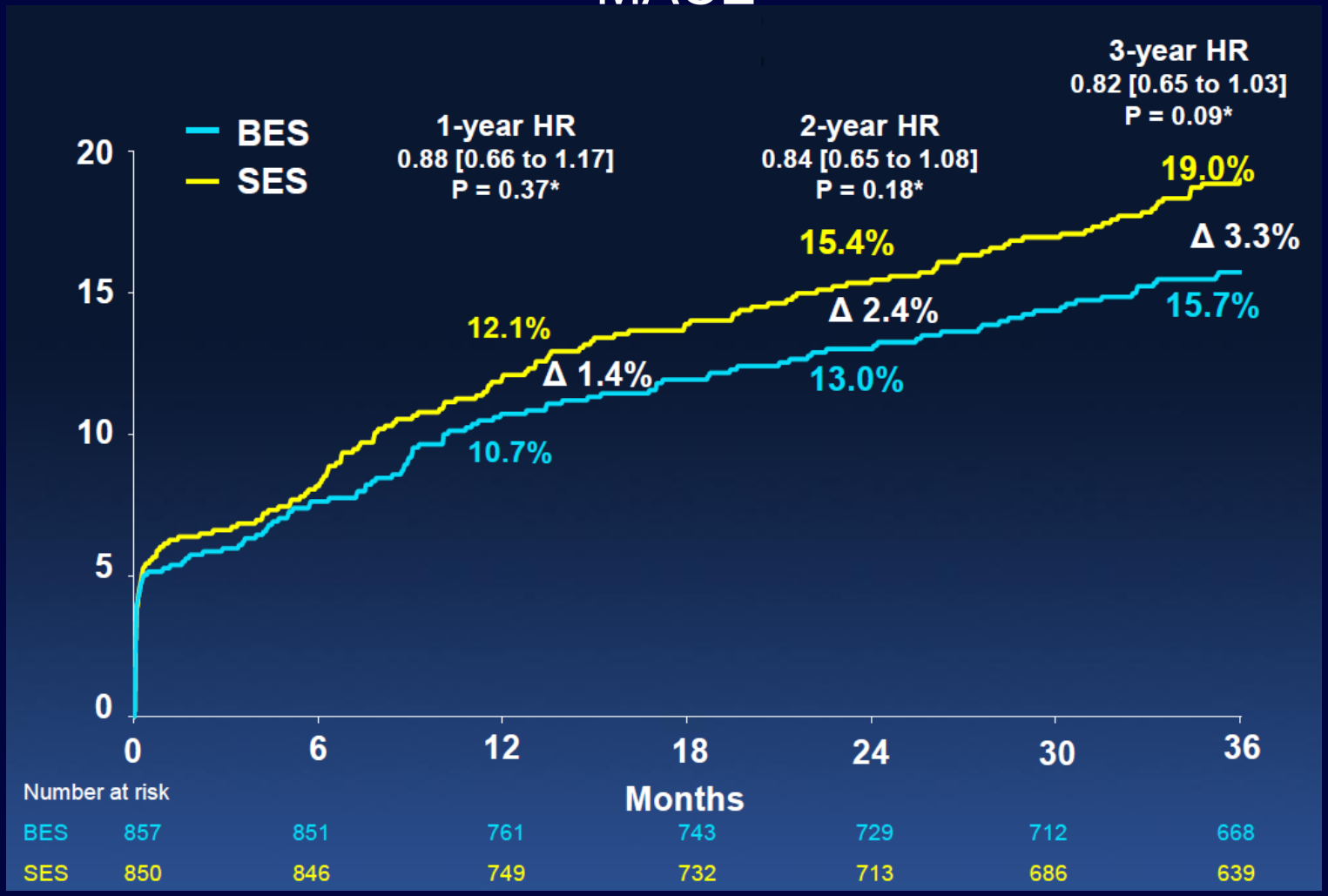
Patient Flow -Clinical



LEADERS

LEADERS 3 year clinical follow-up :

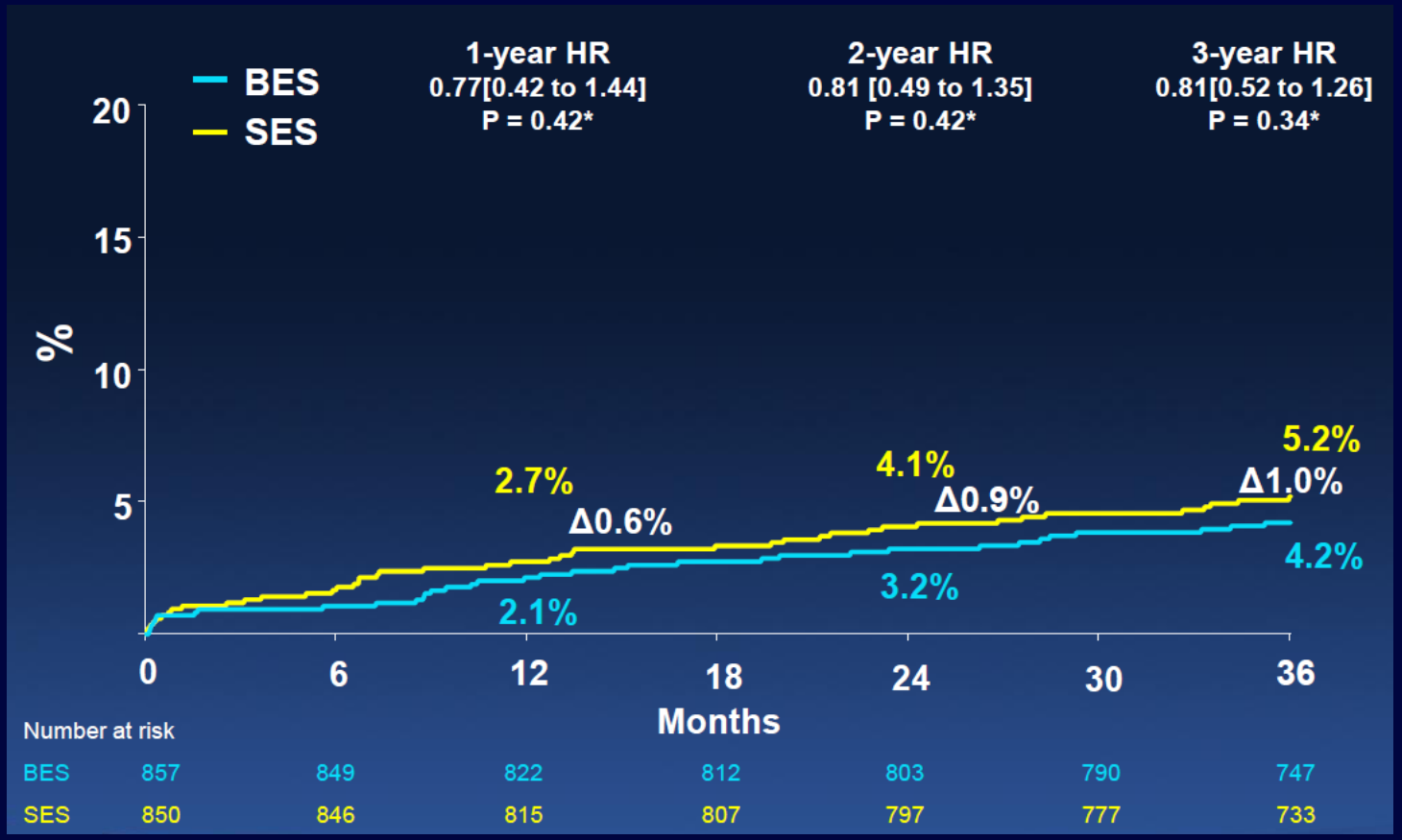
MACE



LEADERS

LEADERS 3 year clinical follow-up :

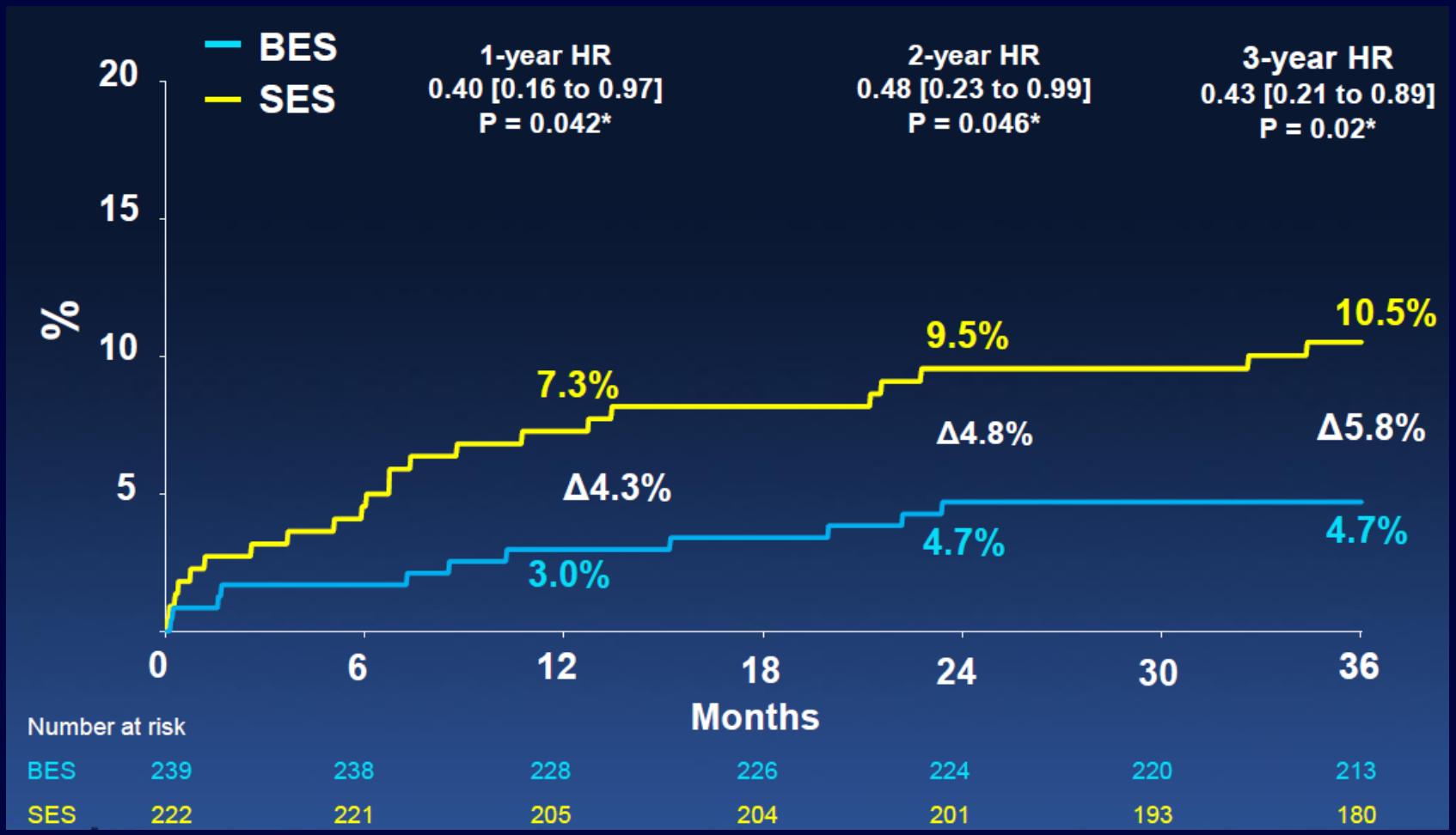
Cardiac Death



LEADERS

LEADERS 3 year clinical follow-up :

Cardiac Death in High Syntax Score (>16)



LEADERS

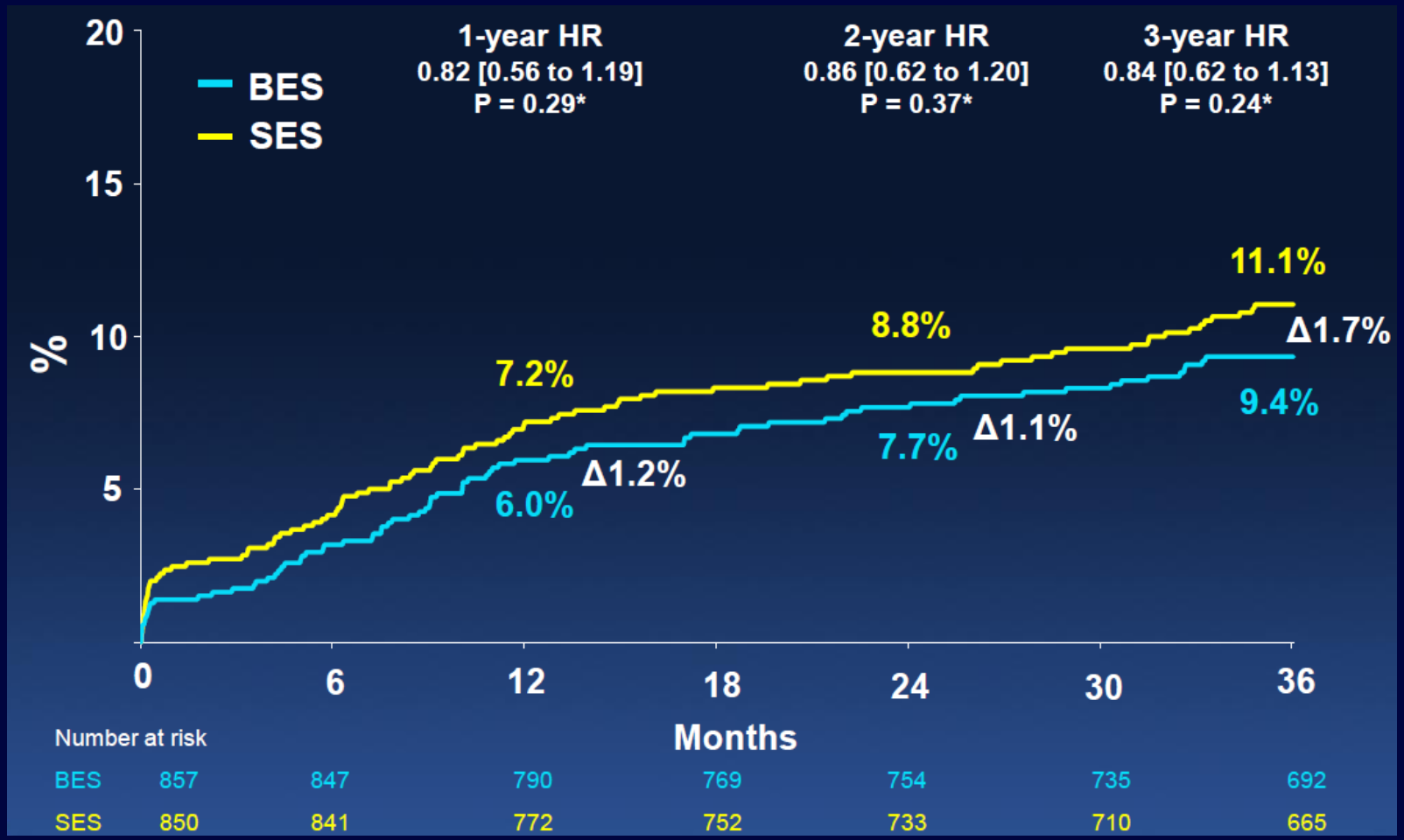
LEADERS 3 year clinical follow-up :

All Myocardial Infarction

LEADERS

LEADERS 3 year clinical follow-up :

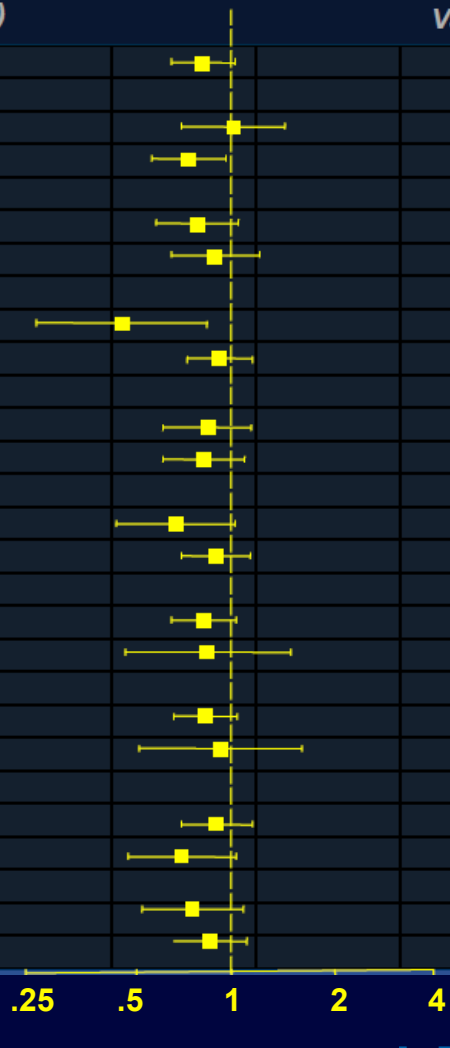
Clinically-Indicated TVR



LEADERS

LEADERS : Stratified Analysis of MACE @ 3 Years

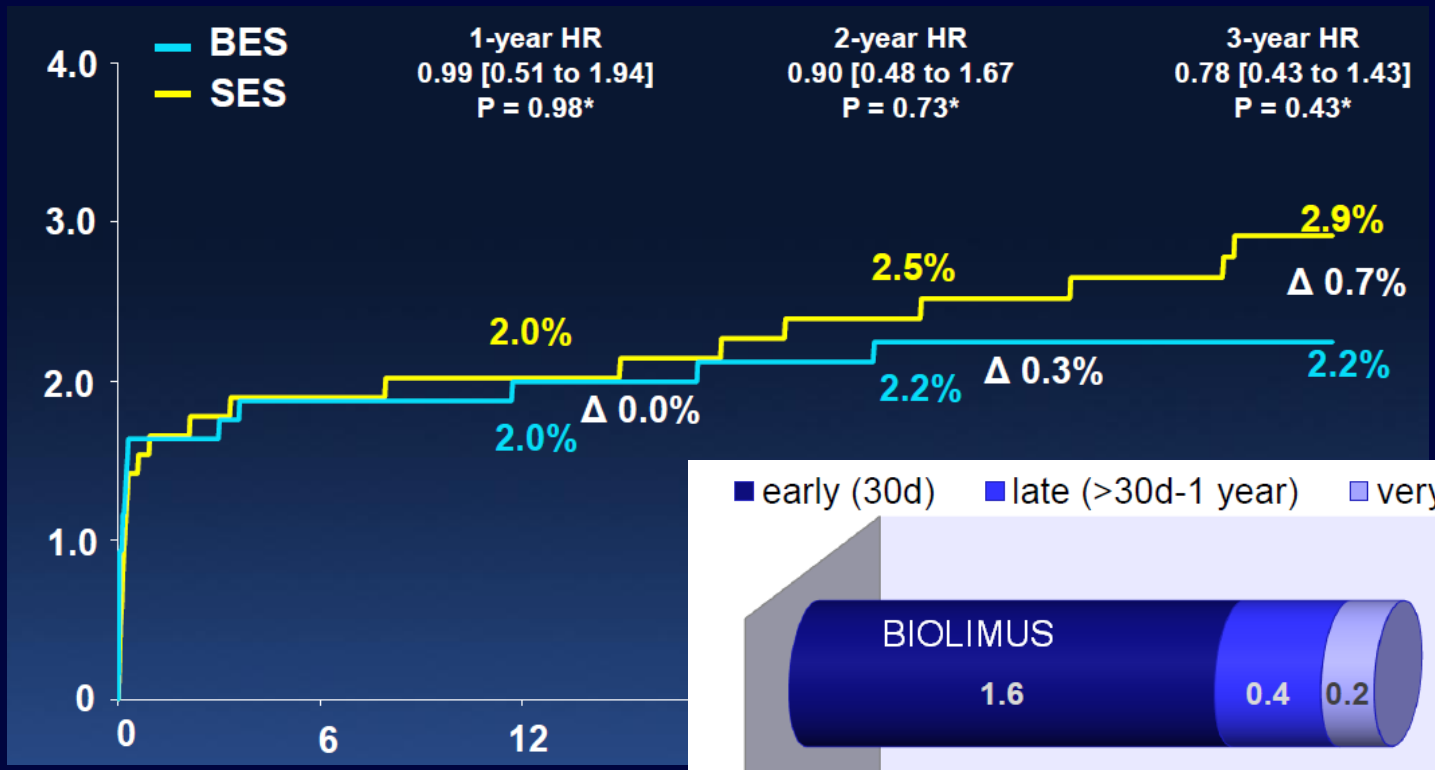
	BES	SES	Risk Ratio (95% CI)	P Value	P Int
Overall	132/857	157/850	0.80 (0.63 to 1.03)		ns
Diabetes mellitus					ns
Yes	53/223	45/191	1.02 (0.68 to 1.52)	0.92	
No	79/634	112/659	0.72 (0.54 to 0.96)	0.02	
Acute coronary					ns
Yes	68/470	87/473	0.77 (0.56 to 1.06)	0.11	
No	64/387	70/377	0.88 (0.63 to 1.25)	0.48	
ST-elevation MI					0.03
Yes	13/135	29/140	0.43 (0.22 to 0.83)	0.01	
No	119/722	128/710	0.91 (0.71 to 1.18)	0.48	
Left anterior					ns
Yes	59/407	71/417	0.84 (0.59 to 1.17)	0.32	
No	73/449	86/431	0.81 (0.59 to 1.11)	0.18	
Multivessel disease					ns
Yes	33/209	42/176	0.65 (0.41 to 1.03)	0.06	
No	99/648	115/674	0.89 (0.68 to 1.16)	0.39	
Off-label use					ns
Yes	116/696	135/665	0.81 (0.63 to 1.04)	0.09	
No	16/160	22/183	0.83 (0.44 to 1.59)	0.58	
De-novo lesions					ns
Yes	114/788	136/774	0.82 (0.64 to 1.05)	0.11	
No	18/68	21/74	0.92 (0.49 to 1.73)	0.79	
Small-vessel disease					ns
Yes	96/585	104/568	0.89 (0.68 to 1.18)	0.43	
No	36/271	53/280	0.68 (0.45 to 1.04)	0.08	
Long lesions					ns
Yes	46/262	52/225	0.74 (0.50 to 1.10)	0.14	
No	86/594	105/623	0.85 (0.64 to 1.13)	0.27	

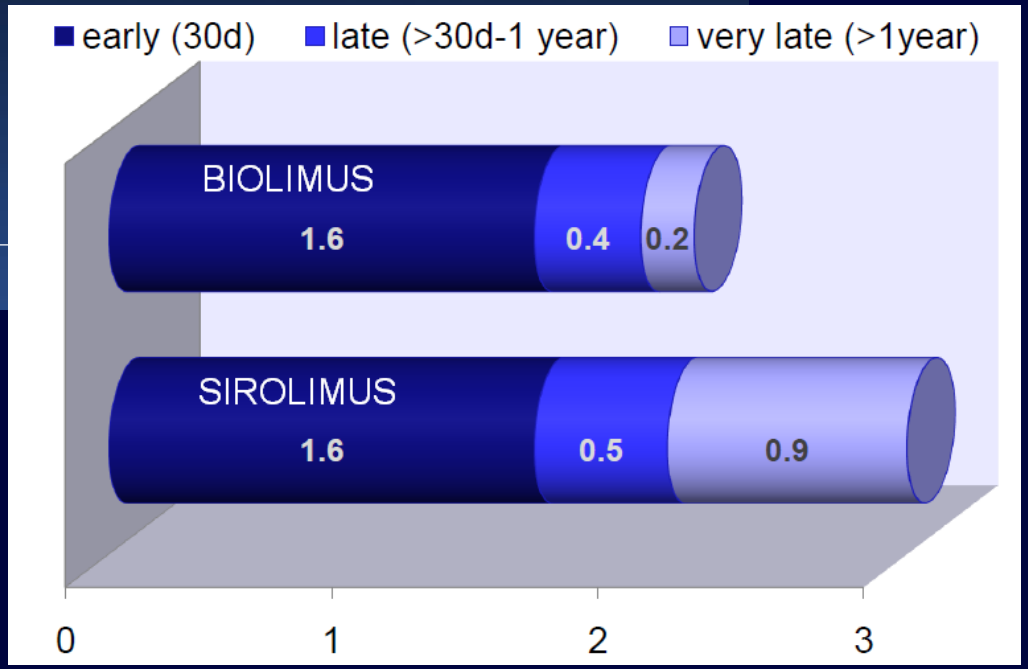


LEADERS

LEADERS 3 year clinical follow-up :

Definite ST through 3 years





LEADERS 3 year clinical follow-up :

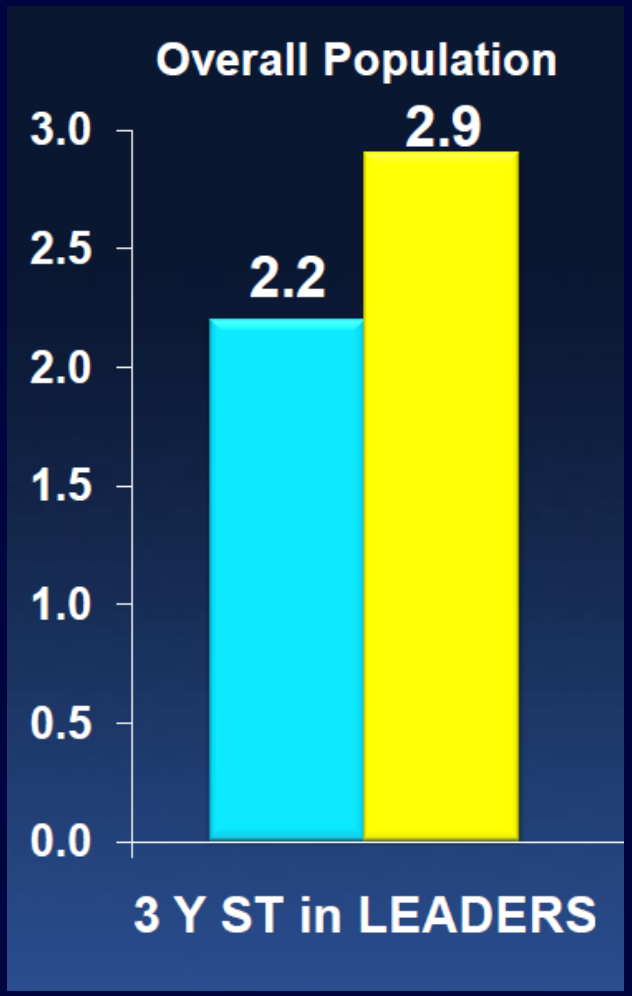
Definite Antiplatelet Agent Utilization

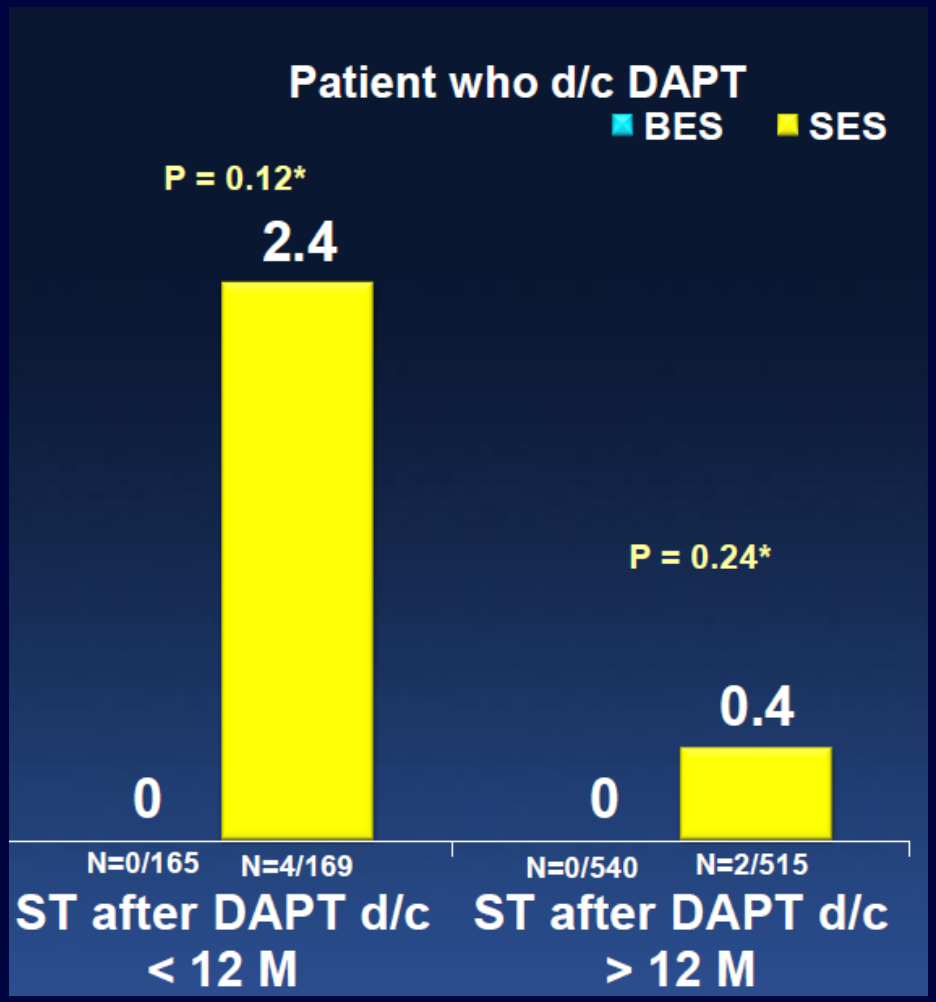
	BES	SES	P value
Aspirin			
- At 9 months	96.6% (n=818)	97.4% (n=798)	**0.39**
- At 12 months	97.0% (n=810)	96.1% (n=801)	**0.34**
- At 24 months	94.9% (n=789)	94.2% (n=778)	**0.58**
- At 36 months	94.3% (n=757)	94.8% (n=746)	**0.73**
Clopidrogel/Thienopyridine			
- At 9 months	95.6% (n=818)	95.2% (n=798)	**0.81**
- At 12 months	68.1% (n=810)	66.5% (n=801)	**0.52**
- At 24 months	23.4% (n=789)	24.3% (n=778)	**0.72**
- At 36 months	19.6% (n=757)	20.4% (n=747)	**0.75**

LEADERS

LEADERS 3 year clinical follow-up :

Definite ST through 3 years - Effect of DAPT Discontinuation





LEADERS

LEADERS 3 year clinical follow-up : Conclusions

Patrick Serruys – TCT Sept 2010

Overall population

- The biolimus eluting stent with abluminal biodegradable polymer compared against the sirolimus eluting stent with durable polymer resulted in non-inferior safety, efficacy and angiographic outcome at 9 months and this result was sustained up to 3 years.

- In this overall non-restricted LEADER patient population there were similar outcomes for BES and SES with respect to MACE, Cardiac Death, MI and clinically-indicated TVR.

- The Kaplan-Meier curves for MACE continue to diverge showing lower event rates for BES

LEADERS

LEADERS 3 year clinical follow-up : Conclusions

Patrick Serruys – TCT Sept 2010

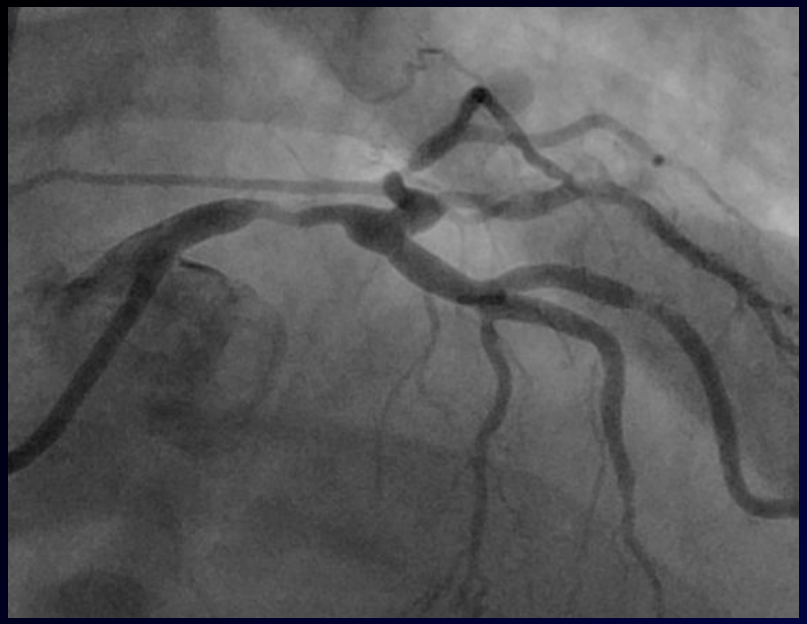
Subgroup analysis

- STEMI patients have a significant reduction of MACE with BES compared to SES *(9.6% vs 20.7% Psup= 0.01)*

Very Late Stent Thrombosis

- Although this was an all-comers study, definite very late stent thrombosis events were rare *(BES 0.2% vs SES 0.9% PSup=0.43)*
- There were no VLST events in patients where a BES was implanted in native coronary arteries

LEADERS



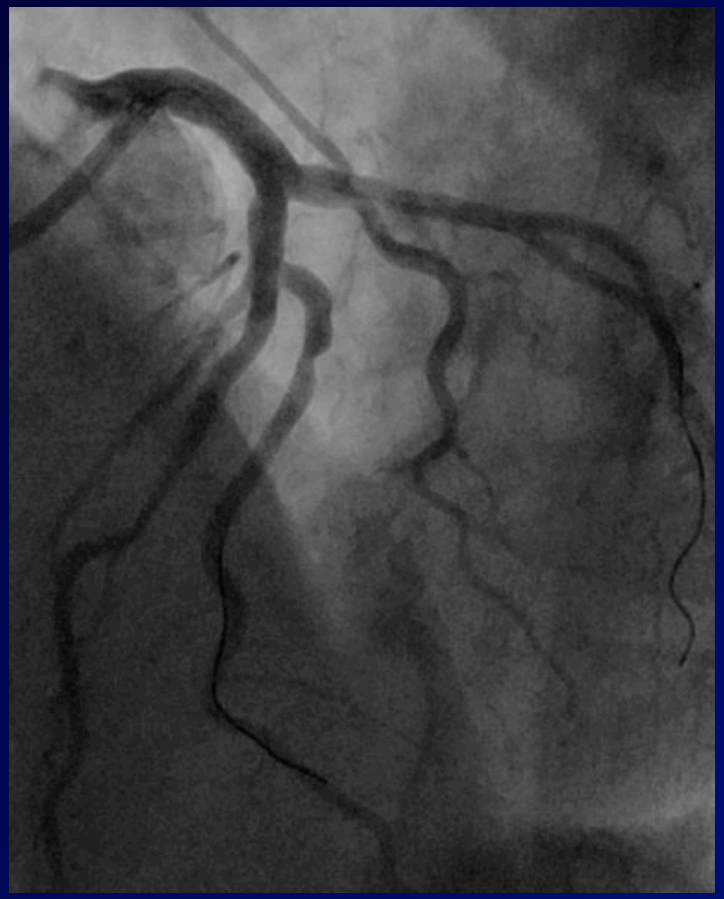
Stent Biomatrix 3.5 x 18 à 22B

Mr C…60 ans

Angor crescendo

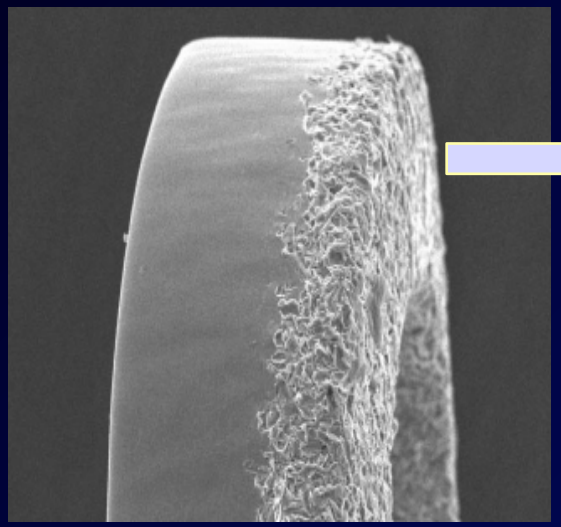
FR : dyslipidémie

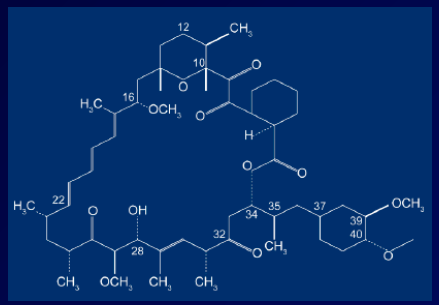
Ergo + 60 W



Stent actif sans polymère : le BioFreedom

- Offre l'avantage de s'affranchir de la fragilité du polymère et de son effet potentiellement thrombogène, permettant d'envisager des durées de bithérapie sensiblement écourtées.
- Le stent doit cependant assurer une élution efficace et progressive du principe actif : le biolimus A9. Pour ce faire, il dispose d'une surface micro poreuse délivrant la drogue du coté abluminal

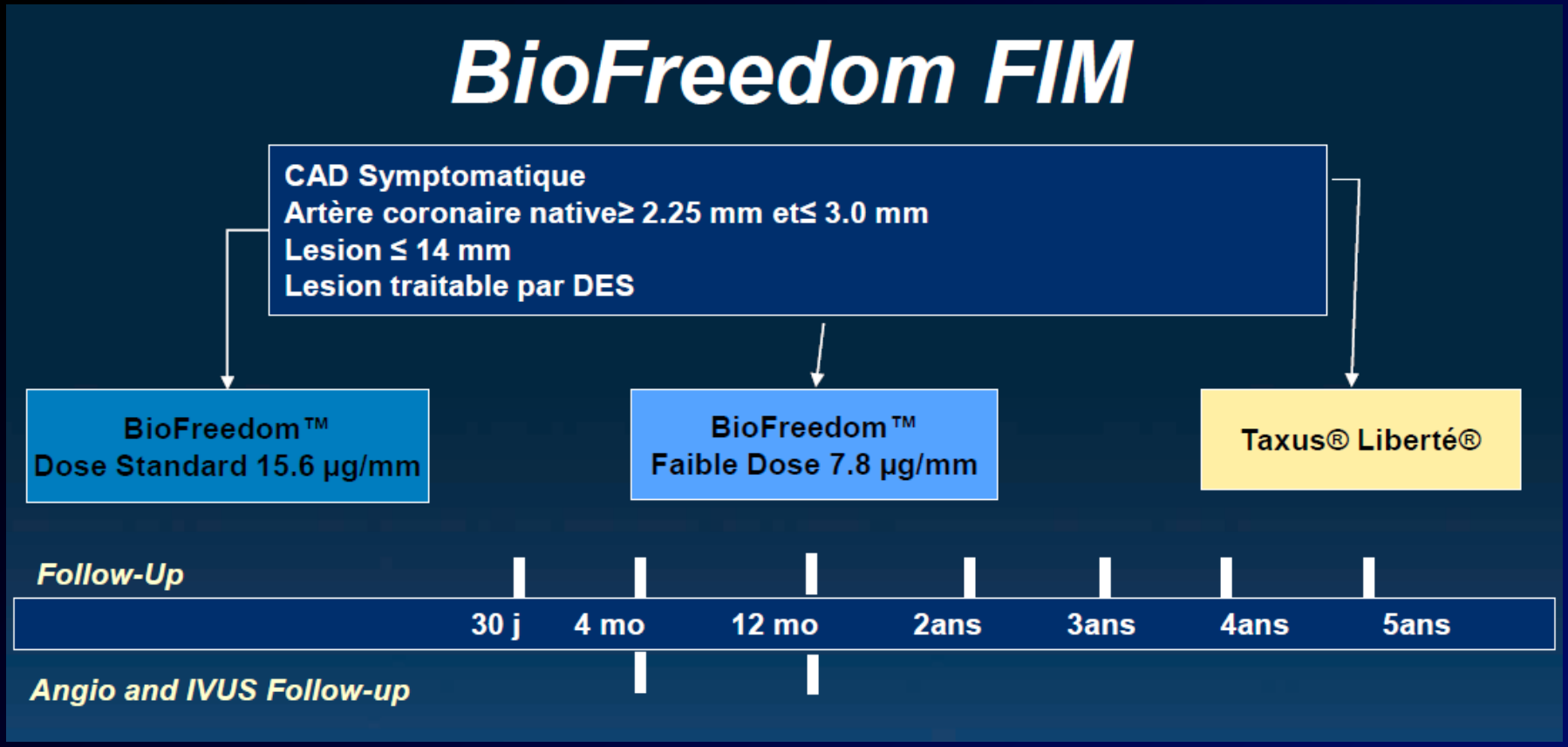




Le Biolimus A9, dérivé de la rapamycine est un puissant anti inflammatoire et immunosuppresseur

Très lipophile et hydrophobe, propriétés lui assurant un faible relargage dans le flux sanguin.

BioFreedom FIM

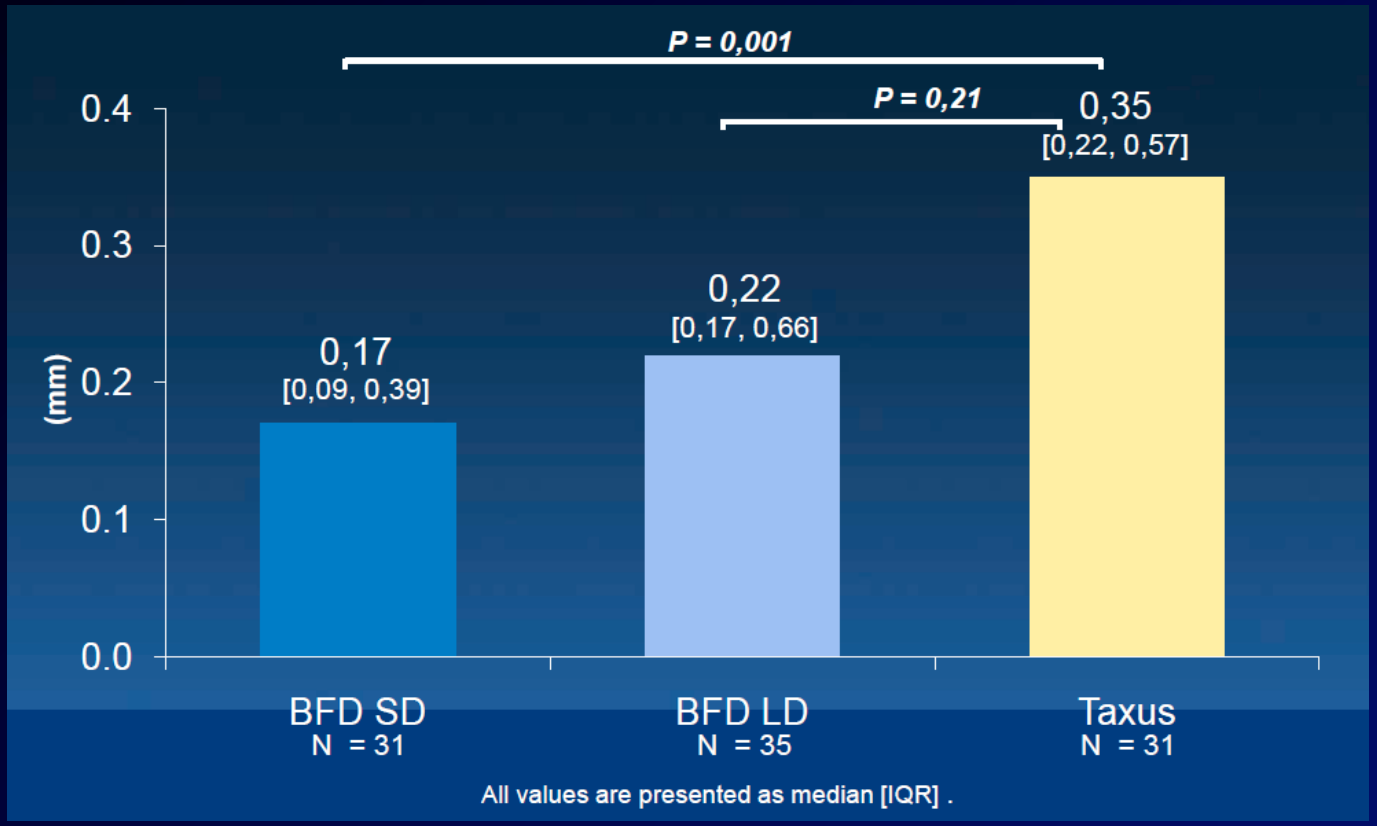


Primary Endpoint : In-stent Late Lumen Loss (LL) at 12 months (second cohort)

Non inferiority trial

DAPT : at least 6 months.

Primary end-point : 12 month in stent late lumen loss



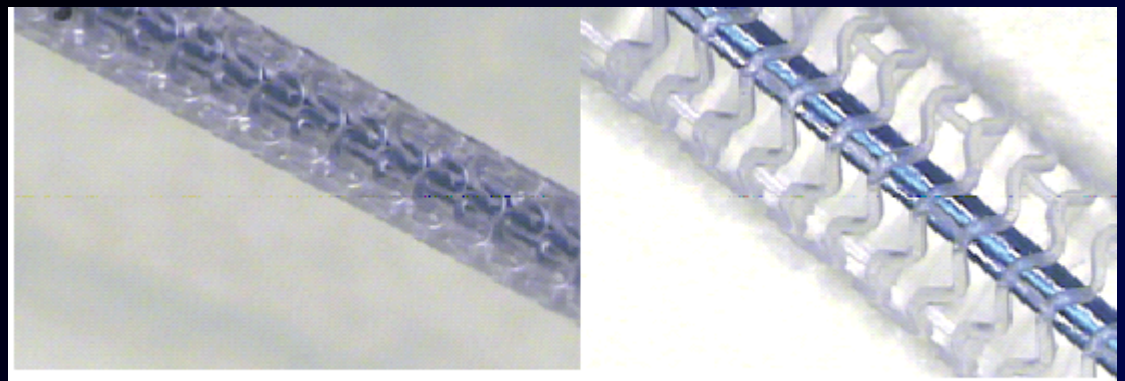
12 Month Follow-up : MACE (cohorts 1 & 2)

	BFD SD N = 60	BFD LD N = 62	Taxus N = 60
MACE	**3** (6.1%)	**7** (11.6%)	**3** (5.5%)
Deaths (all causes)	**1** (1.8%)	**0** (0.0%)	**0** (0.0%)
Myocardial infarction	**1** (1.8%)	**1** (1.6%)	**0** (0.0%)
Q Waves MI	**0** (0.0%)	**0** (0.0%)	**0** (0.0%)
Non Q Waves MI	**1** (1.8%)	**1** (1.6%)	**0** (0.0%)
CABG	**0** (0.0%)	**0** (0.0%)	**0** (0.0%)
TLR	**1** (1.8%)	**6** (10.0%)	**3** (5.5%)
Stent thrombosis	**0** (0%)	**0** (0%)	**0** (0%)

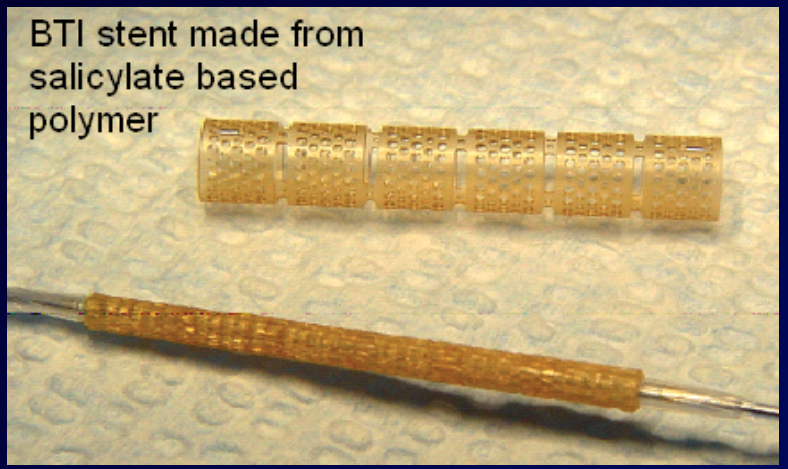
Biofreedom : conclusions de l'étude First in man

- Le stent Biofreedom est le premier stent actif sans polymère démontrant une non infériorité par rapport au stent historique qu'est le Taxus dont le principe actif est libéré progressivement par un polymère
- La perte tardive à un an est similaire à celle du TAXUS.
- Sur ces petits échantillons, aucun surcroît de sécurité n'apparaît …
- Il faudrait désormais évaluer l'intérêt de ce concept sur des populations plus larges, incluant tous types de situations cliniques, et notamment chez les patients ne prenant pas une double antiagrégation prolongée.

L’étape suivante est le stent entièrement dégradable…



stent pre-mounted on a 3.0mm delivery system in crimped and deployed states.



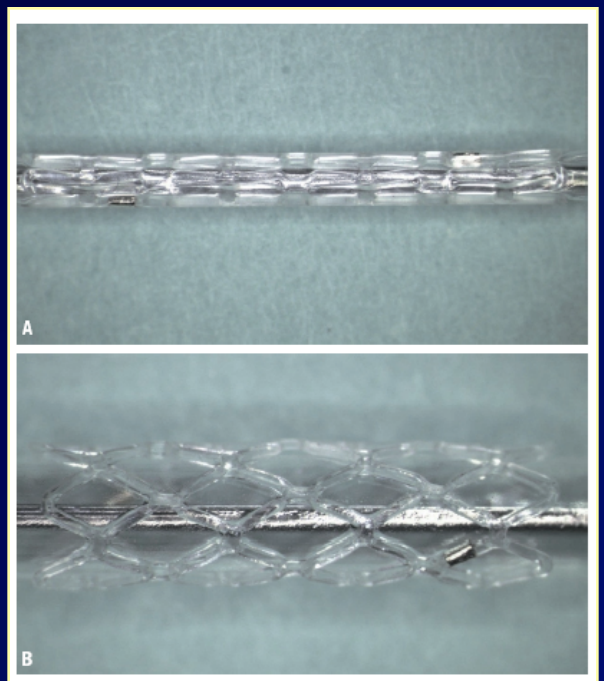


Figure 1. A. PLA stent gently crimped on the balloon resulting in neither strut cracks nor crazing; B. PLA expanded stent deployment presenting neither strut cracks nor crazing.

CONCLUSIONS :

Les progrès réalisés dans l'efficacité et la sécurité de l'angioplastie sont spectaculaires depuis 20 ans :

Le stent conventionnel a sécurisé le traitement et atténué de 20 à 30% le risque de resténose, pour les meilleures prothèses

Le stent délivrant un principe actif a effondré le risque de resténose

L'amélioration des matériaux, les polymères résorbables, voire les stents actifs dépourvus de polymère, augmentent certainement la sécurité à long terme sur les lésions complexes et chez les patients à haut risque d'évènements tardifs.

Les stents à polymères résorbables permettent probablement de s'affranchir des bithérapies prolongées sans sur-risque de thrombose tardive de stent. Une étude randomisée est en cours…

Le stent résorbable semble prometteur, s'il arrive à atteindre la qualité mécanique et l'efficacité des DES de dernière génération