



Session: TCT Asia Pacific - DES Summit

When and How do I use DES? Clinical Considerations - Case Selection, Implantation Technique And Anti-platelet Therapy

Speaker - 15'

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It all matters about restenosis



Facts:

DES give a lower restenosis rate compared to BMS in all type of lesions. The risk varies according to the type of lesion and patient: sometimes the advantage is small

DES demand for longer duration of aspirin and clopidogrel

Late thrombosis is ill defined but "it is with us"

Preventing restenosis decreases reinterventions , AMI and occasionally death

It is difficult to make the right choice in patients with low risk of restenosis and when ischemia at follow-up is not searched aggressively



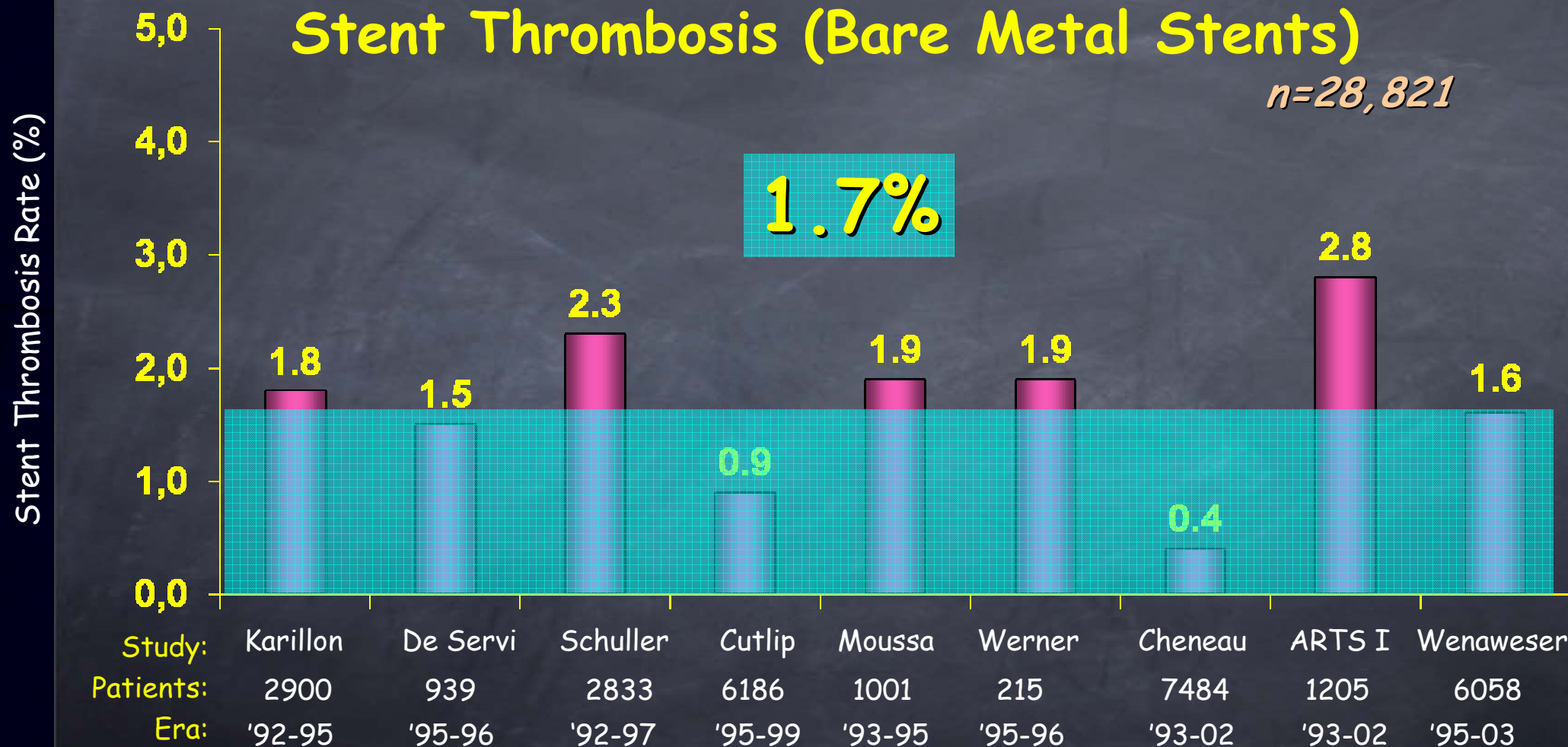
When BMS:

When there are uncertainties about the possibility the patient can continue dual antiplatelet therapy

When the patient is taking oral anticoagulants unless she/he has a lesion at a very high risk for restenosis

In most patients with AMI

FORWARD : BMS are not immune from thrombosis





Clinical research

EuroIntervention







Three-year follow-up of the ARTS-II[#] – sirolimus-eluting stents for the treatment of patients with multivessel coronary artery disease

Arterial revascularisation therapies study

Patrick W. Serruys^{1*}, MD, PhD; Joost Daemen¹, MD; Marie-Claude Morice², MD; Bernard De Bruyne³, MD, PhD; Antonio Colombo⁴, MD; Carlos Macaya⁵, MD; Gert Richardt⁶, MD; Jean Fajadet⁷, MD; Christian Hamm⁸, MD; Keith D. Dawkins⁹, MD, FRCP; Pascal Vranckx¹⁰, MD; Marco Bressers¹¹, MSc; Ron van Domburg¹, PhD; Monique Schuijjer¹¹, PhD; Kristel Wittebols¹², MSc; Magdaleen Pieters¹², MSc; Hans Peter Stoll¹², MD; on behalf of the ARTS-II Investigators

ARTS II - Baseline Demographics



	ARTS II N=607 %	ARTS I (CABG) N=605 %	ARTS I (PCI) N=600 %
Male	77	76	77
Age (years)	63 	61	61
Body mass index (kg/m ²)	28	27	27
Previous MI (Q-wave)	34 (18) 	42 (24)	44 (26)
Diabetes (IDDM)	26 (5) 	16 (3)	19 (4)
Hypertension	67 	45	45
Hypercholesterolemia	74 	58	58
Family history	36	42	39
Current smokers	19 	26	28
Ejection fraction	60	60	61
Unstable angina	37	35	37

Figures in Orange indicate statistical difference (95% CI) between ARTS II and ARTS I groups

ARTS II - Lesion Characteristics



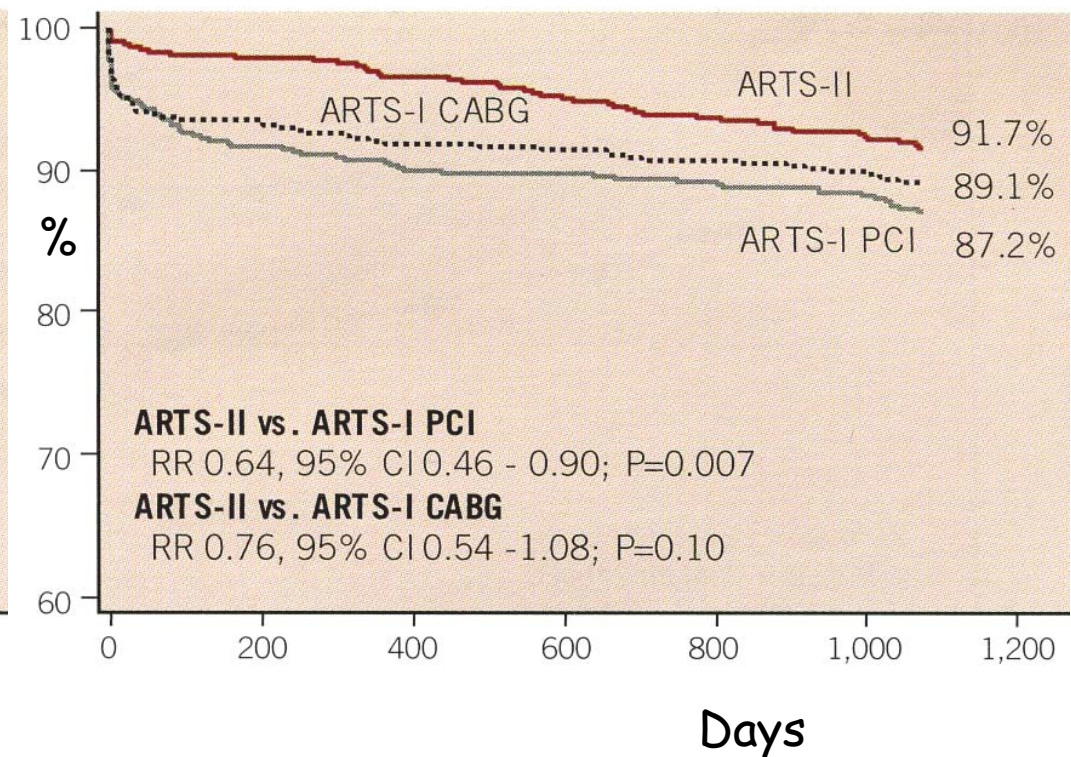
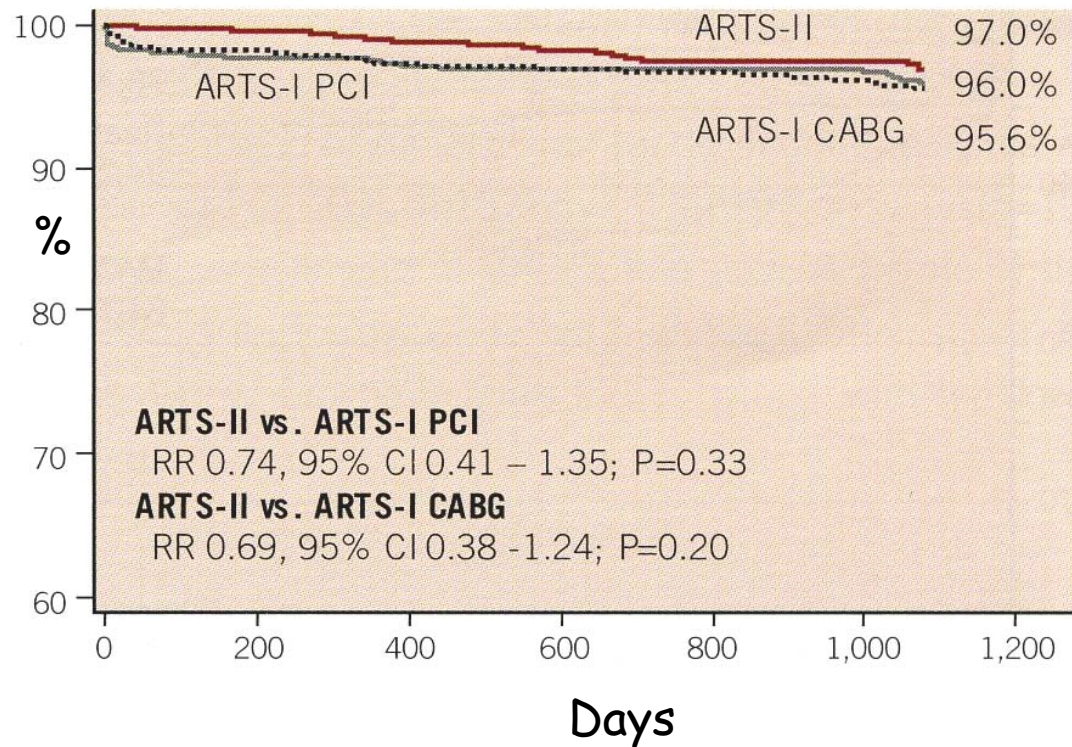
	ARTS II N=607 pts N=2160 les.	ARTS I (CABG) N=605 pts N=1638 les.	ARTS I (PCI) N=600 pts N=1606 les.
% of patients			
2-VD	46	66	69
3-VD	54 ↗	30	27
% of lesions			
LAD location	42	41	39
LCx location	29	29	29
RCA location	29	30	31
Discrete (<10mm)	61	68	66
Tubular (10-20mm)	27	25	27
Diffuse (>20mm)	12 ↗	7	7
Type C lesion	14 ↗	8	8
Side branch involvement	34	32	35



3 Years survival outcome

All Cause
Survival

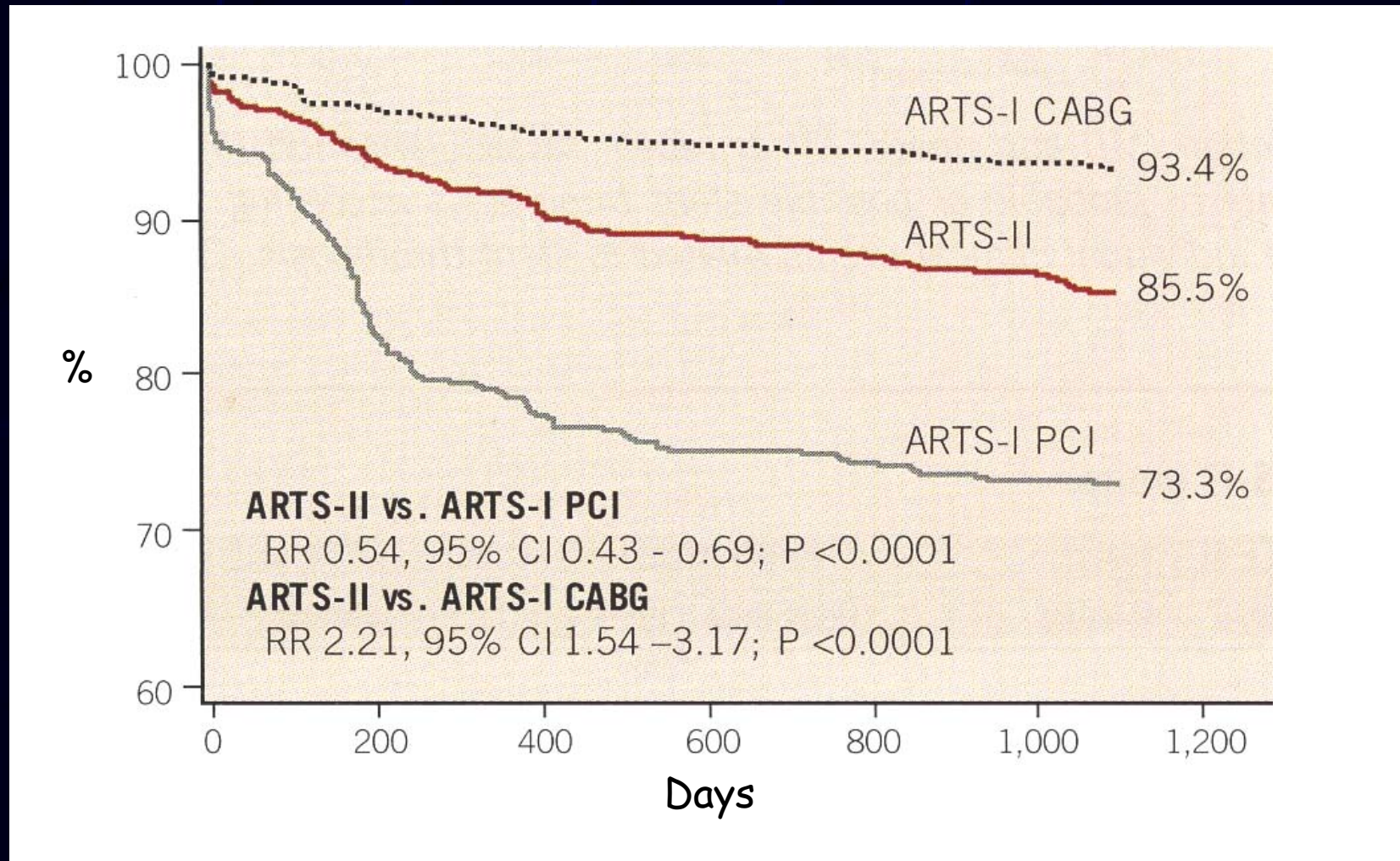
Freedom from All Cause
Death, CVA or MI





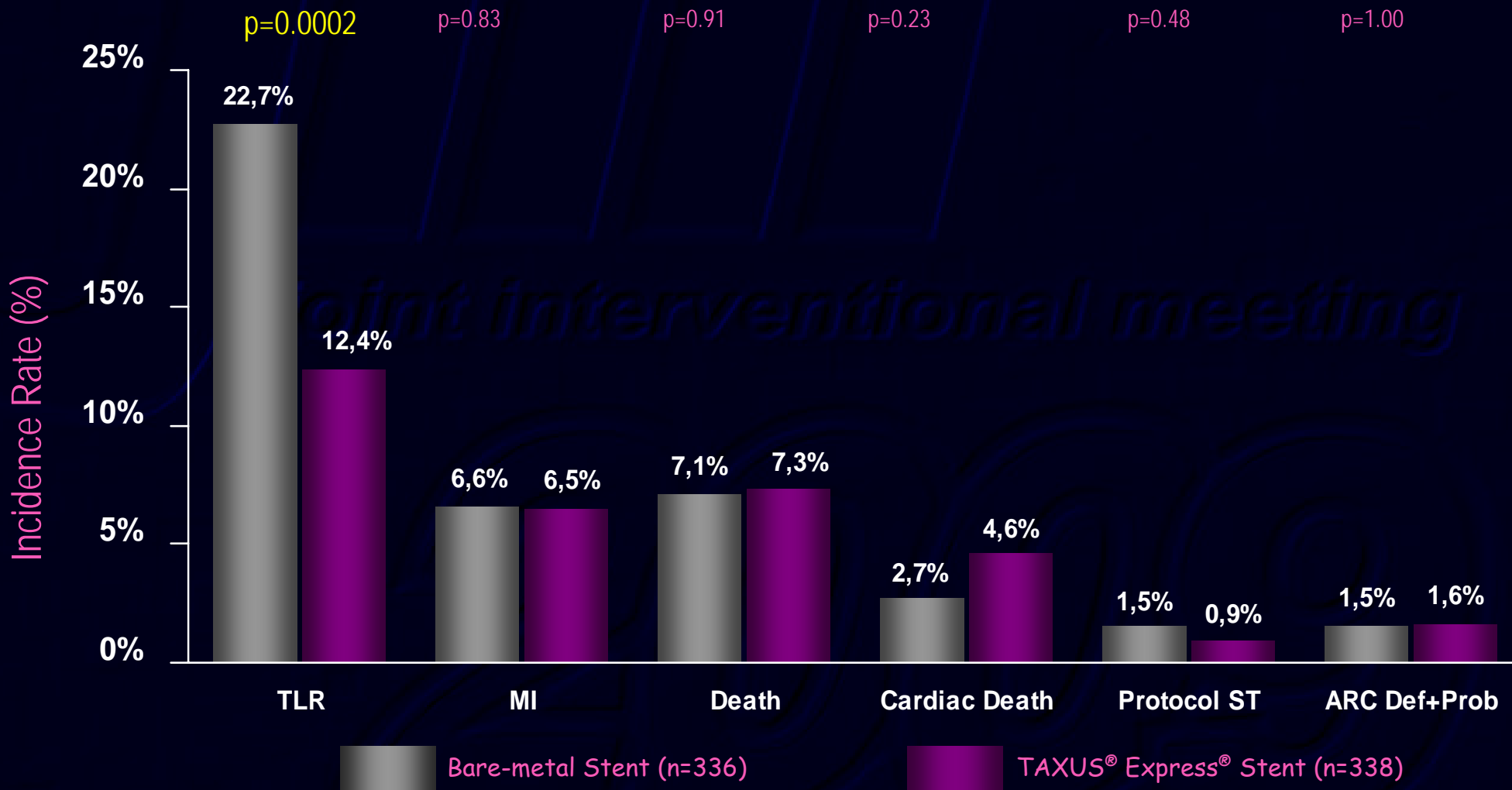
3 Years survival outcome

Freedom from Repeat Revascularization





TAXUS IV and V Diabetic Subset 3-year Clinical Results





OFF-LABEL REGISTRIES

1) Marzocchi et al. REAL Registry of 3064 pts with DES vs. 7565 pts with BMS in Emilia Romagna with 2yrs FU, Circulation 2007.

2) Jensen et al. Western Denmark Heart Registry of 3548 pts with DES vs. 8247 pts with BMS with 15 months FU, JACC 2007

3) Serruys et al. ARTS II study with 607 pts with SES vs. 600 pts with BMS with 3 yrs FU, EuroInterv 2005

No differences in Death or Myocardial Infarction in 23631 pts and reduction in the need for revascularization HR 0.5-0.7.



The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

Effectiveness and Safety of Drug-Eluting Stents in Ontario

Jack V. Tu, M.D., Ph.D., James Bowen, B.Sc.Pharm., M.Sc., Maria Chiu, M.Sc.,
Dennis T. Ko, M.D., M.Sc., Peter C. Austin, Ph.D., Yaohua He, M.D., Ph.D.,
Robert Hopkins, M.A., Jean-Eric Tarride, Ph.D., Gord Blackhouse, M.B.A., M.Sc.,
Charles Lazzam, M.D., Eric A. Cohen, M.D., and Ron Goeree, M.A.

Tu J.V. et al N Engl J Med 2007;357:1393-402



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CLINICAL RESEARCH

Interventional Cardiology

Unrestricted Use of Drug-Eluting Stents Compared With Bare-Metal Stents in Routine Clinical Practice

Findings From the National Heart,
Lung, and Blood Institute Dynamic Registry

J. Dawn Abbott, MD, FACC,* Matthew R. Voss, MD,* Mamoo Nakamura, MD,†
Howard A. Cohen, MD, FACC,‡ Faith Selzer, PhD,† Kevin E. Kip, PhD, Helen A. Vlachos, MSc,†
Robert L. Wilensky, MD, FACC,§ David O. Williams, MD, FACC*

Providence, Rhode Island; Pittsburgh and Philadelphia, Pennsylvania; and New York, New York

4 studies reporting MI rates 3.5-19.4% with treatment of restenosis



1)Chen MS, John JM, Chew DP, Lee DS, Ellis SG, Bhatt DL. Bare metal stent restenosis is not a benign clinical entity. *Am Heart J.* 2006;151:1260–1264.

2)Nayak AK, Kawamura A, Nesto RW, Davis G, Jarbeau J, Pyne CT, Gossman DE, Piemonte TC, Riskalla N, Chauhan MS. Myocardial infarction as a presentation of clinical in-stent restenosis. *Circ J.* 2006;70:1026–1029.

3)Walters DL, Harding SA, Walsh CR, Wong P, Pomerantsev E, Jang IK. Acute coronary syndrome is a common clinical presentation of in-stent restenosis. *Am J Cardiol.* 2002;89:491–494.

4)Bossi I, Klersy C, Black AJ, Cortina R, Choussat R, Cassagneau B, Jordan C, Laborde JC, Laurent JP, Bernies M, Fajadet J, Marco J. In-stent restenosis: long-term outcome and predictors of subsequent target lesion revascularization after repeat balloon angioplasty. *J Am Coll Cardiol.* 2000;35:1569–1576.



Thrombosis in bifurcations

NORDIC Bifurcation Study



Individual End Points after 6 months

	1 Stent	2 Stents	P
Patients	207	206	
Cardiac death	2 (1.0)	2 (1.0)	1.00
Myocardial infarction	0 (0.0)	1 (0.5)	0.31
Stent thrombosis	1 (0.5)	0 (0.0)	0.31



joint in-person meeting

DES in AMI

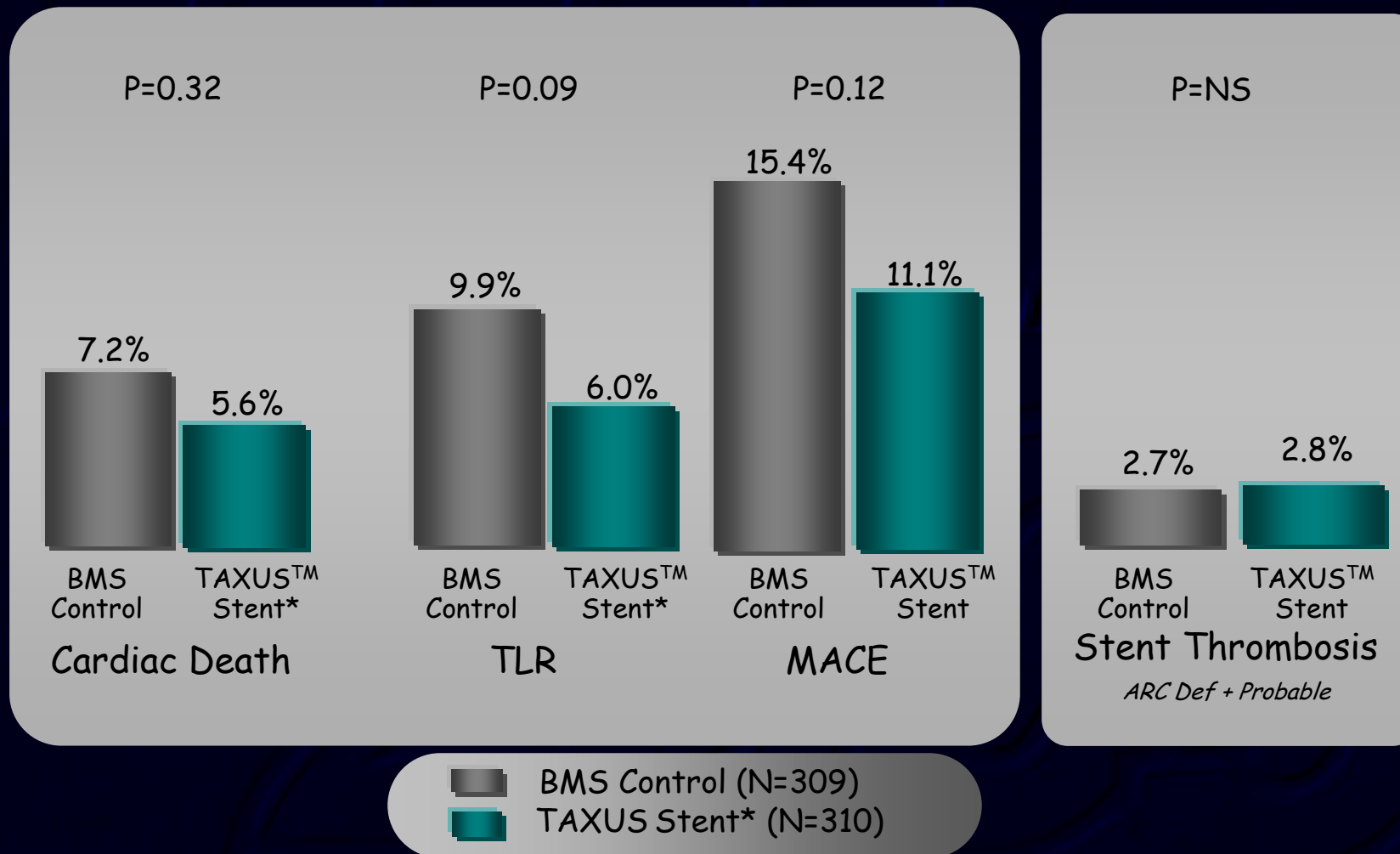
2009

PASSION Trial



Acute Myocardial Infarction (AMI)*

2-Year Results



SES/PES/BMS in AMI* Registry 3-Year Data



Primary Endpoint: MACE at 30 days, 12, 24, 36 months
Secondary endpoint: Angiographic restenosis at 12, 24 and 36 months.

Follow up: **3-year results**

Number of Patients: BMS N= 388
Cypher™ Stent N= 676
TAXUS™ Stent N= 478

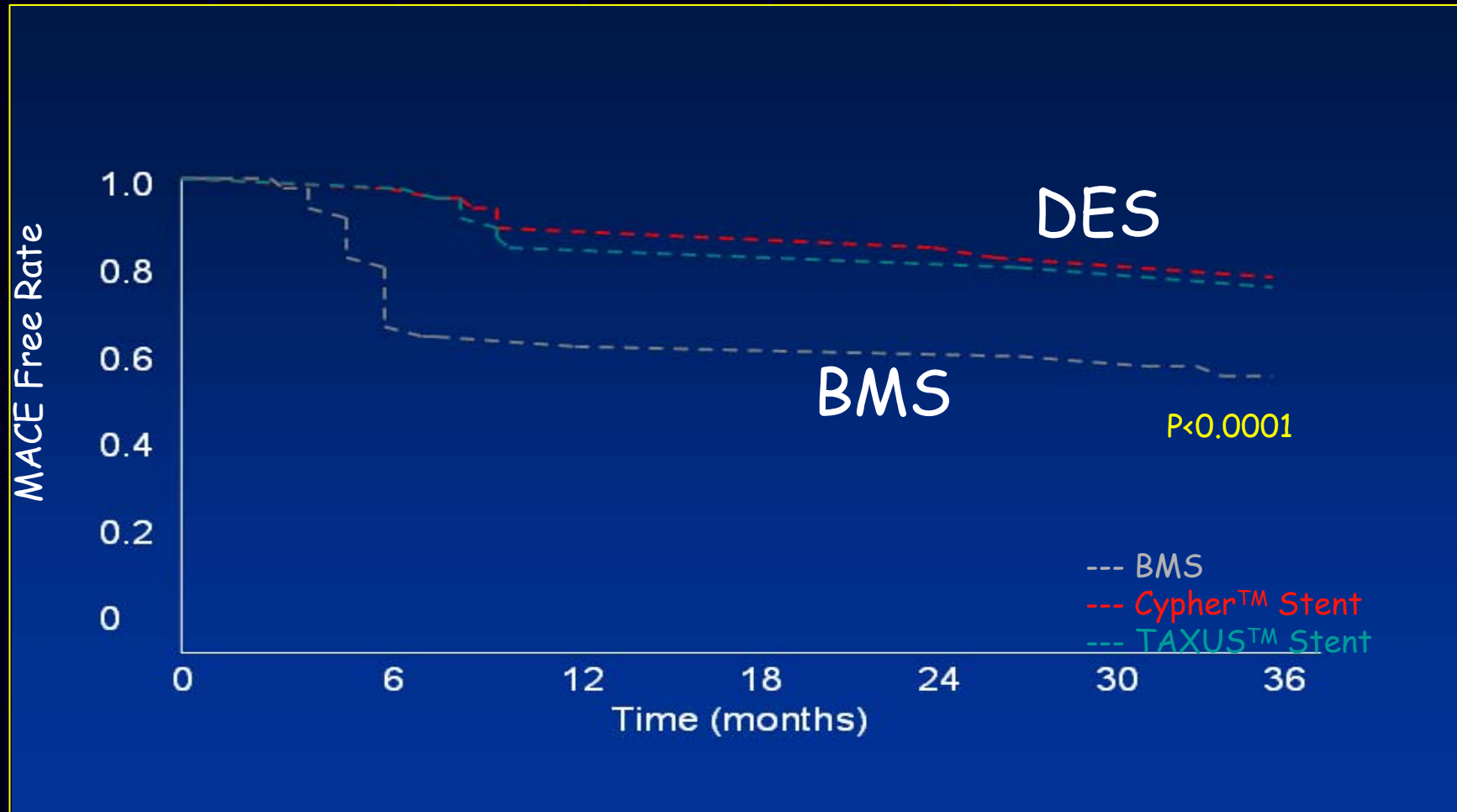
Number of Sites: 8 Centers

Study Design: Prospective, Multi-center Registry

Presented: ESC 2007 by Dr. Nakamura

* TAXUS™ Express²™ Stent System is contraindicated for use in patients with Myocardial Infarction < 72 hours prior to TAXUS index procedure

SES/PES/BMS in AMI* Registry 3-Year Data MACE (All cause death, MI, CABG, TVR, TVF)

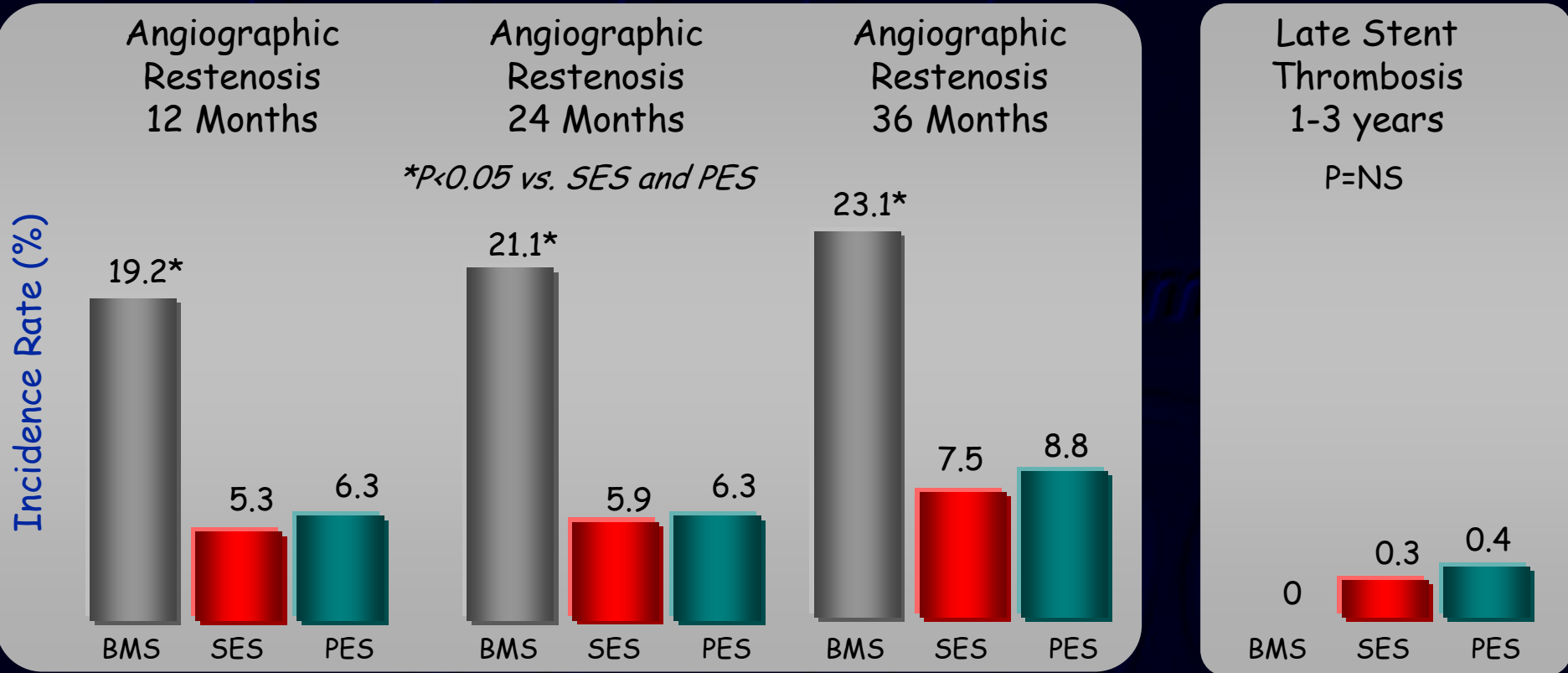




SES vs. PES

Acute Myocardial Infarction (AMI)* Registry

3-Year Results



- Bare Metal Stent (N=388)
- Cypher™ Stent (N=676)
- TAXUS™ Stent (N=478)

MASS Stent AMI DES vs. BMS 2-year Results

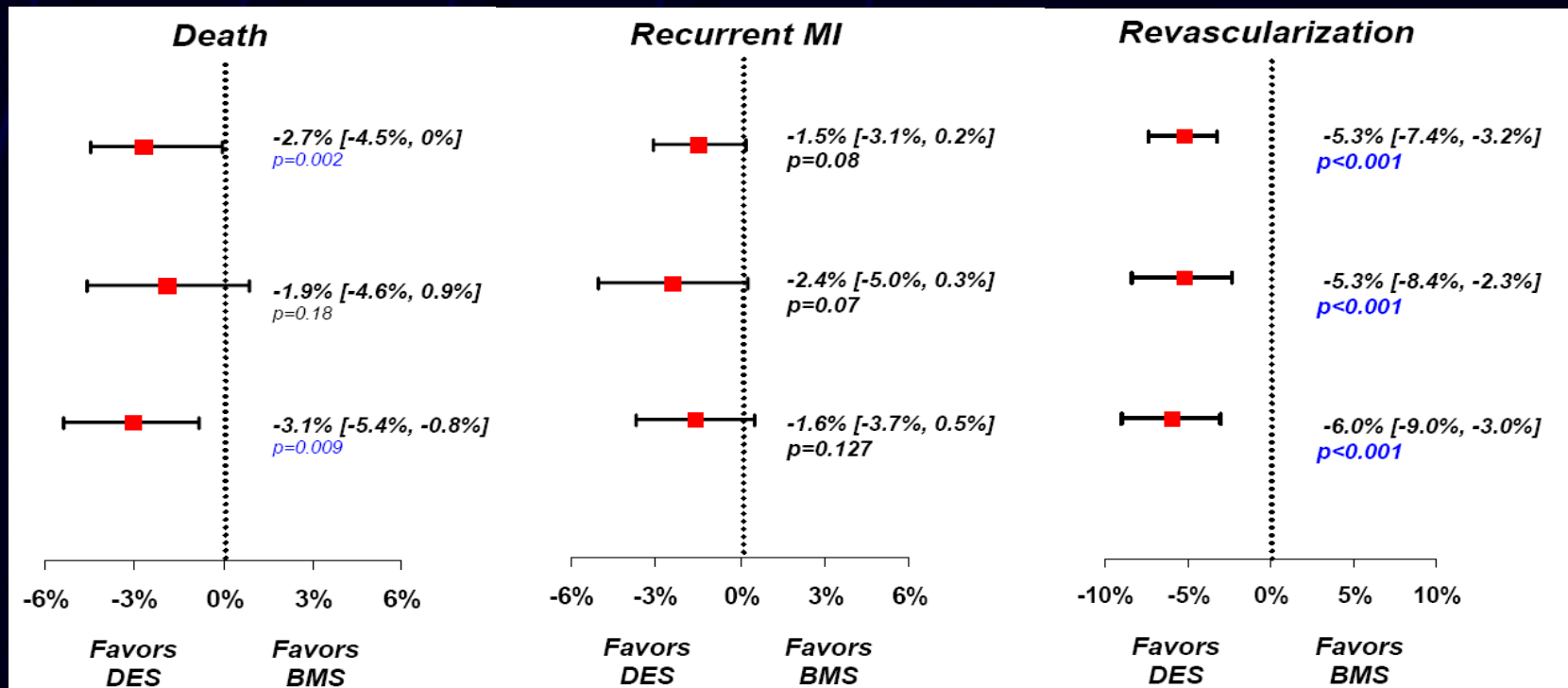


Risk Difference (95% CI), DES vs. BMS

MI
n=2629 pairs

NSTEMI
n=1221 pairs

STEMI
n=1302 pairs



GRACE Registry

Baseline Characteristics – All ACS



	BMS	DES	p-value
Number of Patients	4,321	2,126	
Percent Female	25.9	28.7	0.018
BMI (kg/m ²)	27.6	28.3	0.001
Med hx MI	19.9	26.8	0.001
Med hx CHF	3.6	6.3	0.001
Med hx PCI	14.8	25.7	0.001
Med hx CABG	7.7	11.8	0.001
Med hx Diabetes	19.1	27.2	0.001
Med hx Hypertension	56.2	62.5	0.001
Med hx Hyperlipidemia	45.1	57.0	0.001

Restenosis rates following BMS implantation in AMI are not low!!



	Pasceri et al	STRATEGY	PASSION	TYPHOON	SESAMI	HAAMU-STENT	MISSION	SELECTION	Diaz et al			
N° pts	65	175	605	712	320	164	316	80	120			
DES type	Cypher	Cypher	Taxus	Cypher	Cypher	Taxus	Cypher	Taxus	Cypher			
Angiogr Follow-up	100%	90%	N.A.	82% of 200 pts	52%	88%	82%	90%	-			
Follow-up duration	365 days	240 days	365 days	365 days	365 days	365 days	365 days	210 days	360 day			
Resten. (%)	NA	11.0 0.008	36 0.008	NA	7.1 0.02	20 0.02	9.3 0.03	21.3 0.03	NA	5.1 >0.01	37.8 0.001	NA

* Def ** Prob/poss



For how long dual antiplatelet therapy ?

2009



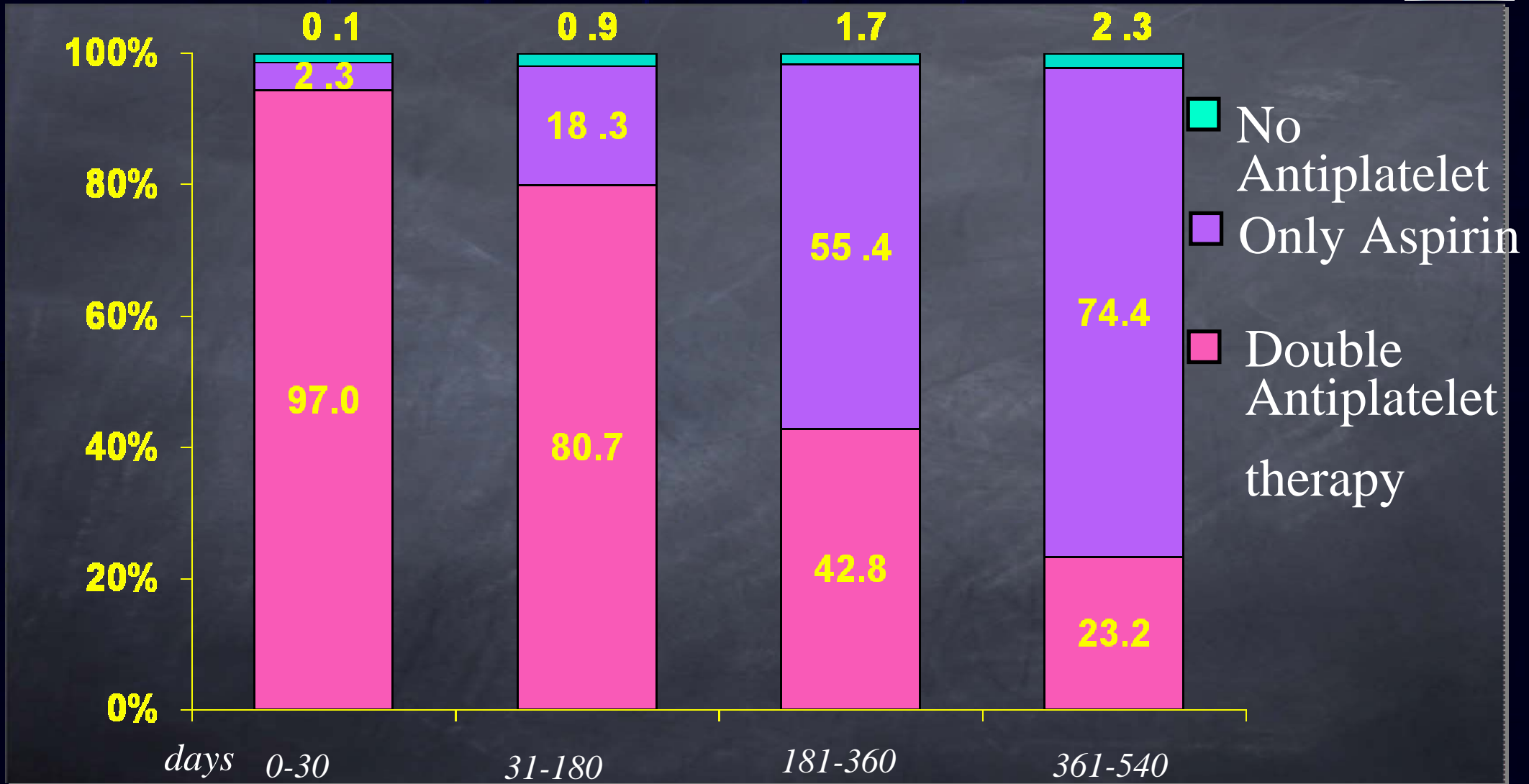
*18 month follow-up in 3021 pts. treated with
DES (Cypher /Taxus)*

in unselected indications:

58 (1.9%) thrombotic events (early and late)

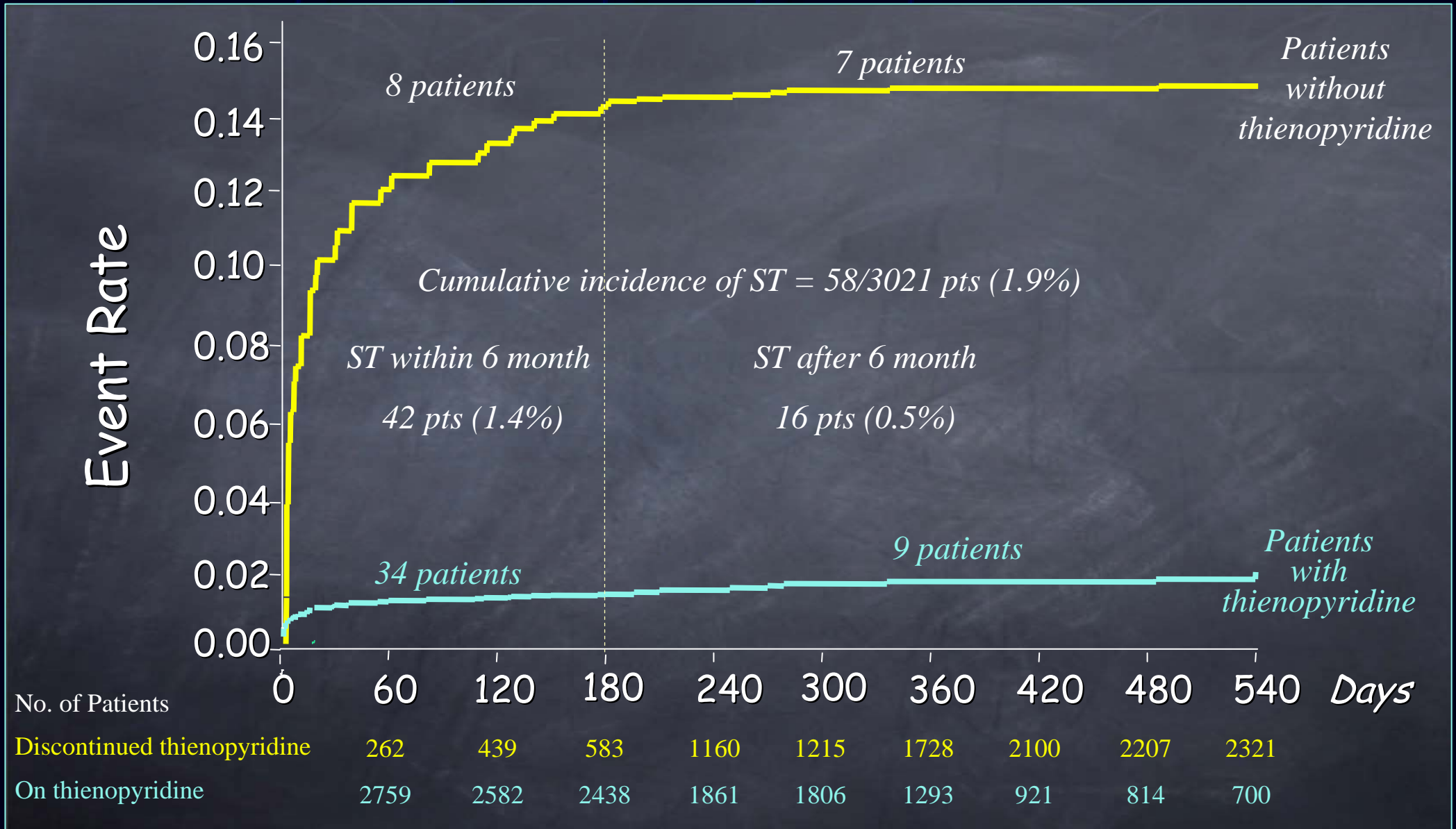
Airoldi F, Colombo A, et al Circulation 2007

Thienopyridine Therapy



Proportion of patients with double antiplatelets, only aspirin and no antiplatelets in different time periods

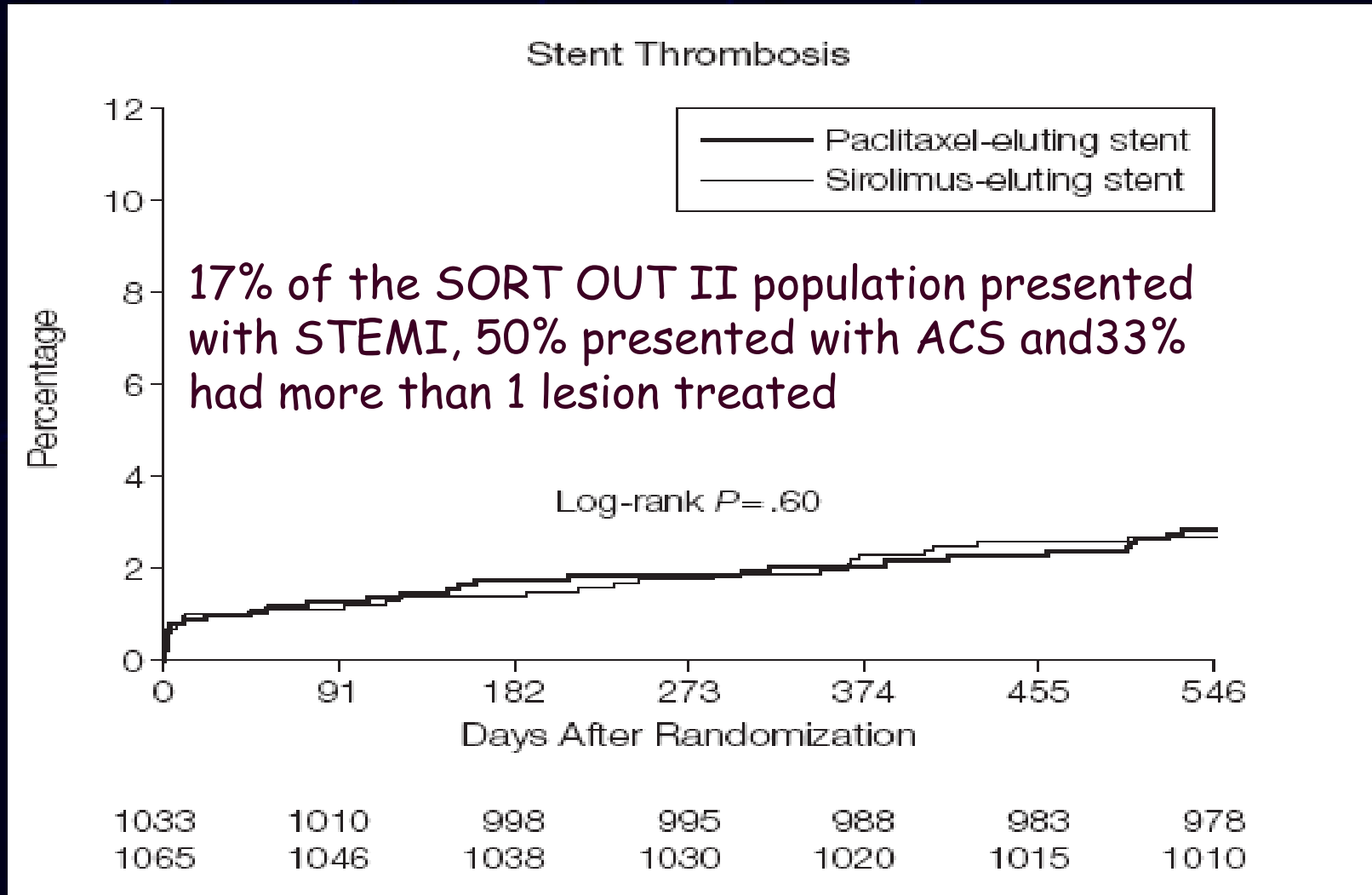
Aalen-Nelson estimate of the cumulative hazard function





Thrombosis rate at 18 months was 2.7%

Cumulative Proportions of Patients Experiencing Definite and Probable Stent Thrombosis

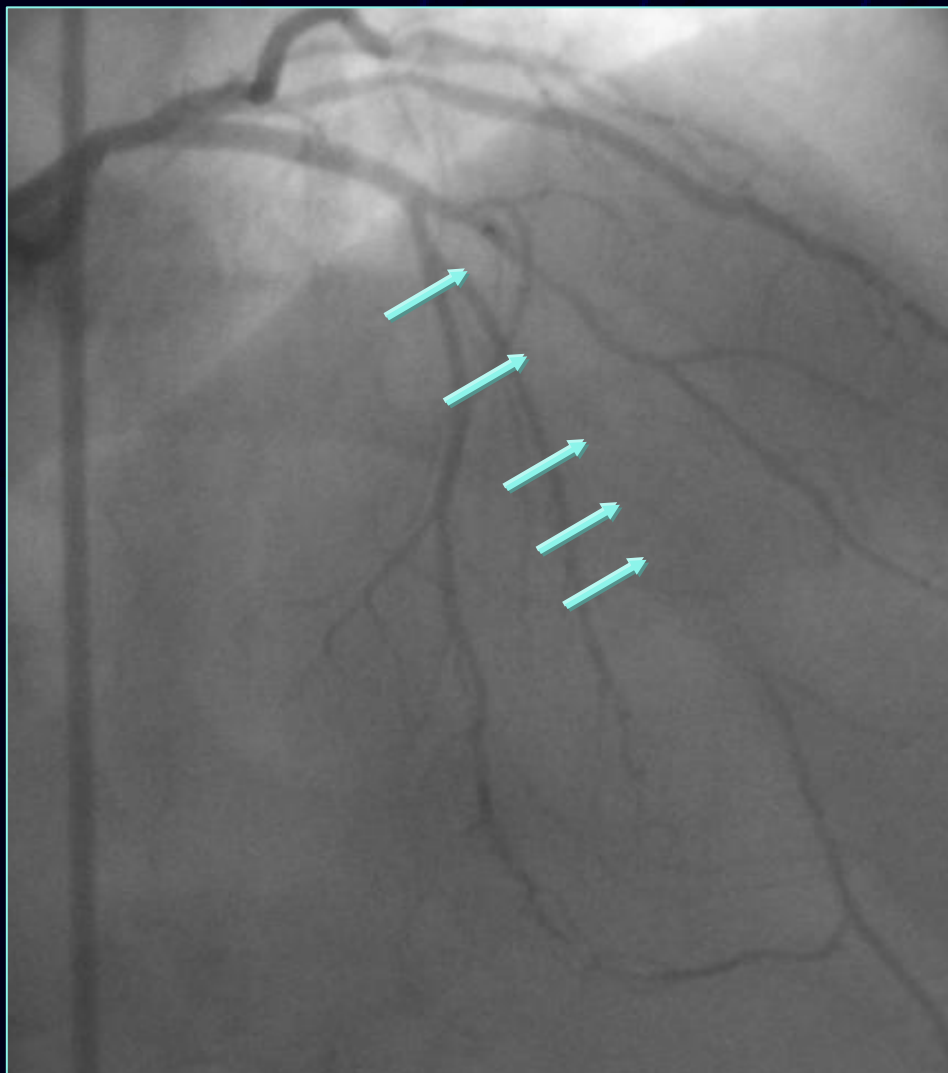


Definition of LST: a problem!

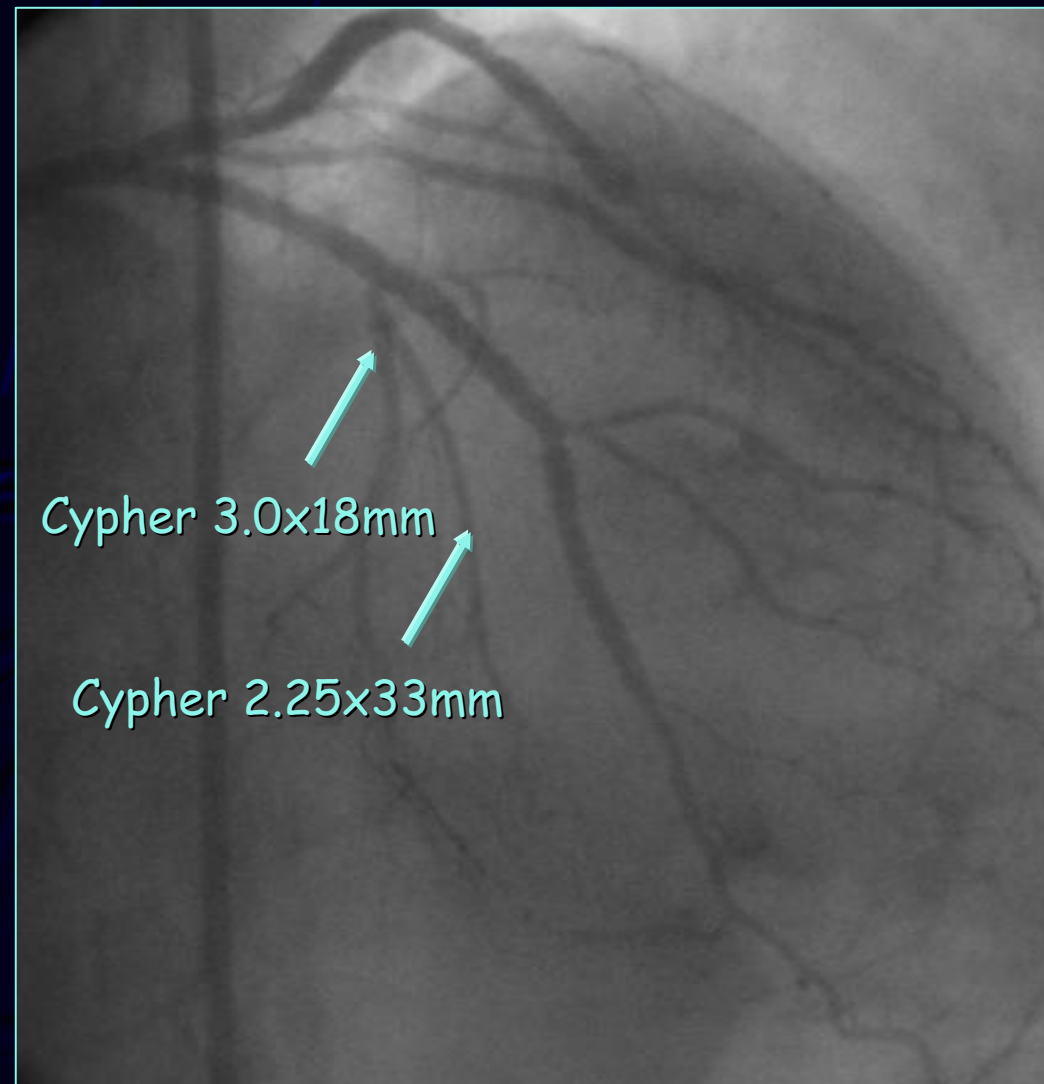


- There is an intrinsic risk for overestimation when we assign the label of “stent thrombosis” to all events which occur in *a stented and diseased coronary segment, in particular when we stent 2 or 3 vessels.*
- Treatment of multiple vessels will label any future myocardial infarction as “stent related”.

Late Stent Thrombosis?

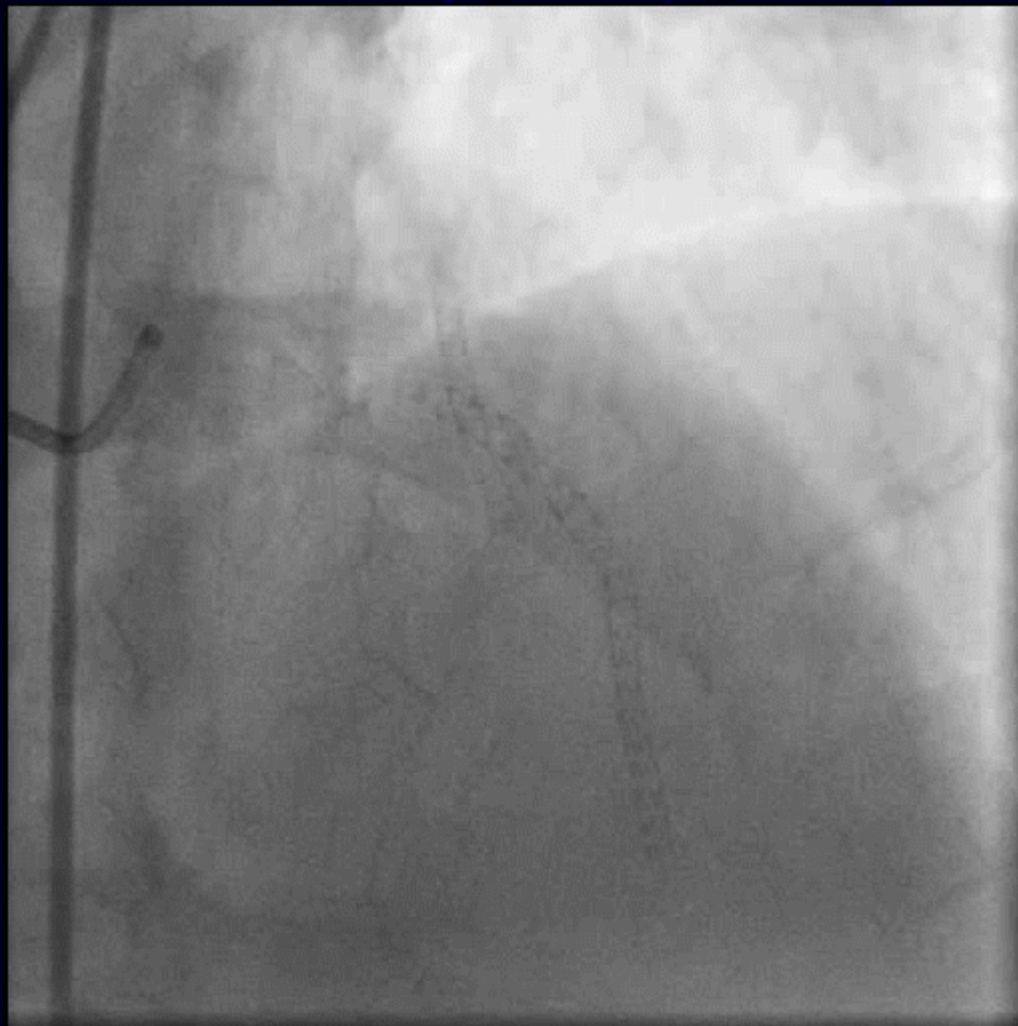


Baseline



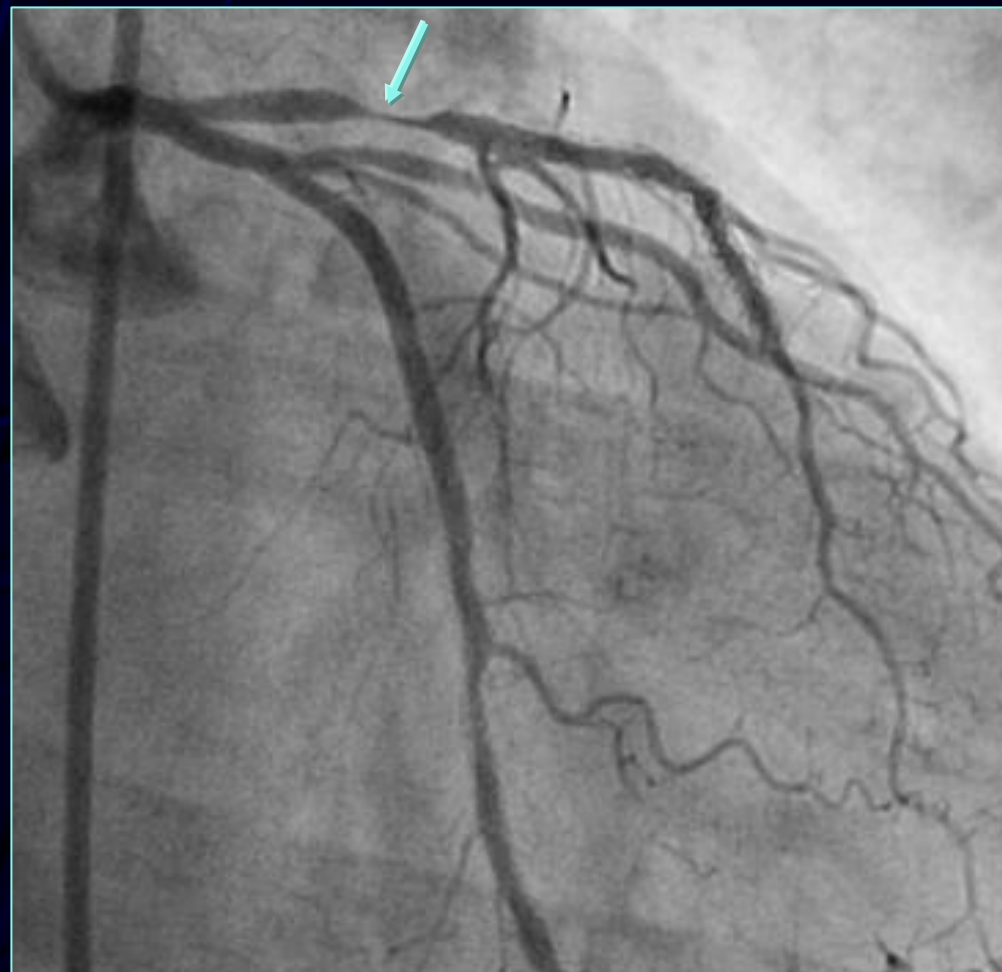
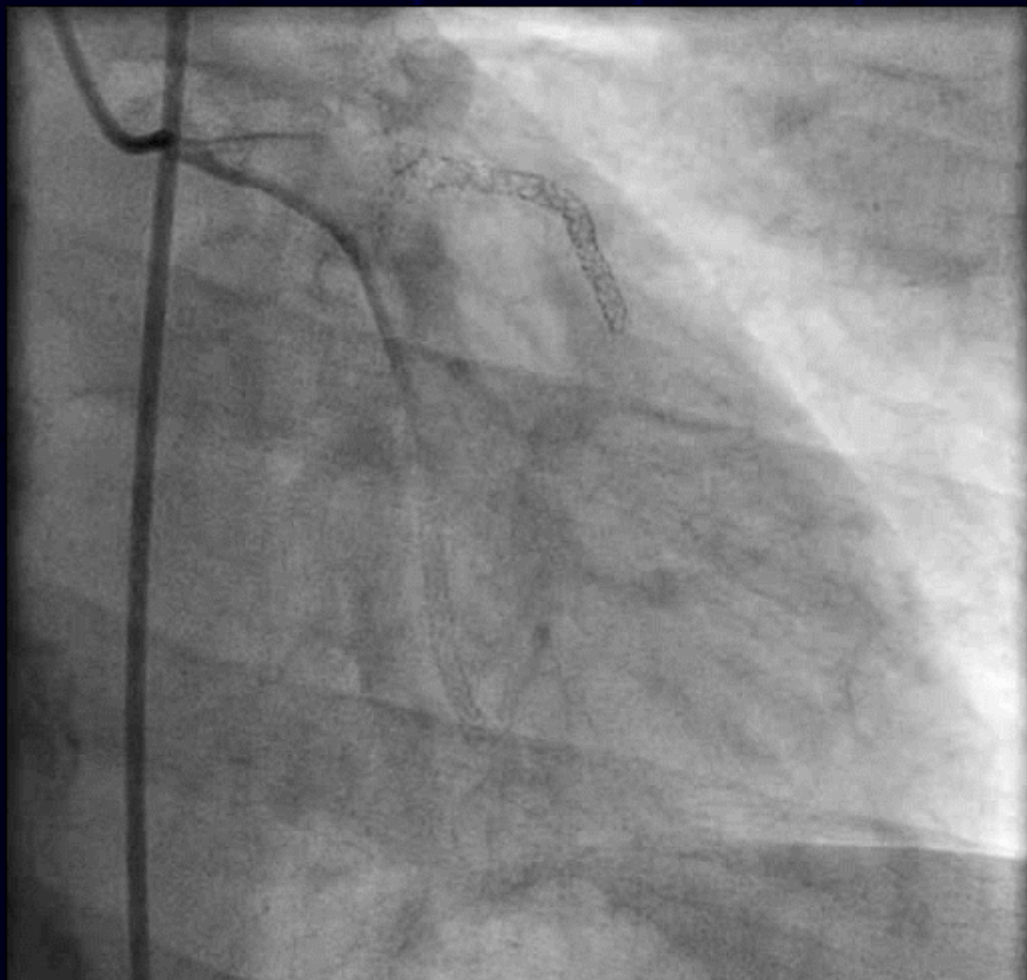
Final Result

Late Stent Thrombosis?



8 months later Follow-Up

Late Stent Thrombosis?



8 months later Follow-Up



What can we do at present time?

-New generation stents?

joint interventional meeting

-Evaluate optimal platelet inhibition

- Improve stent implantation technique:
IVUS, non compliant balloon post-dilatation

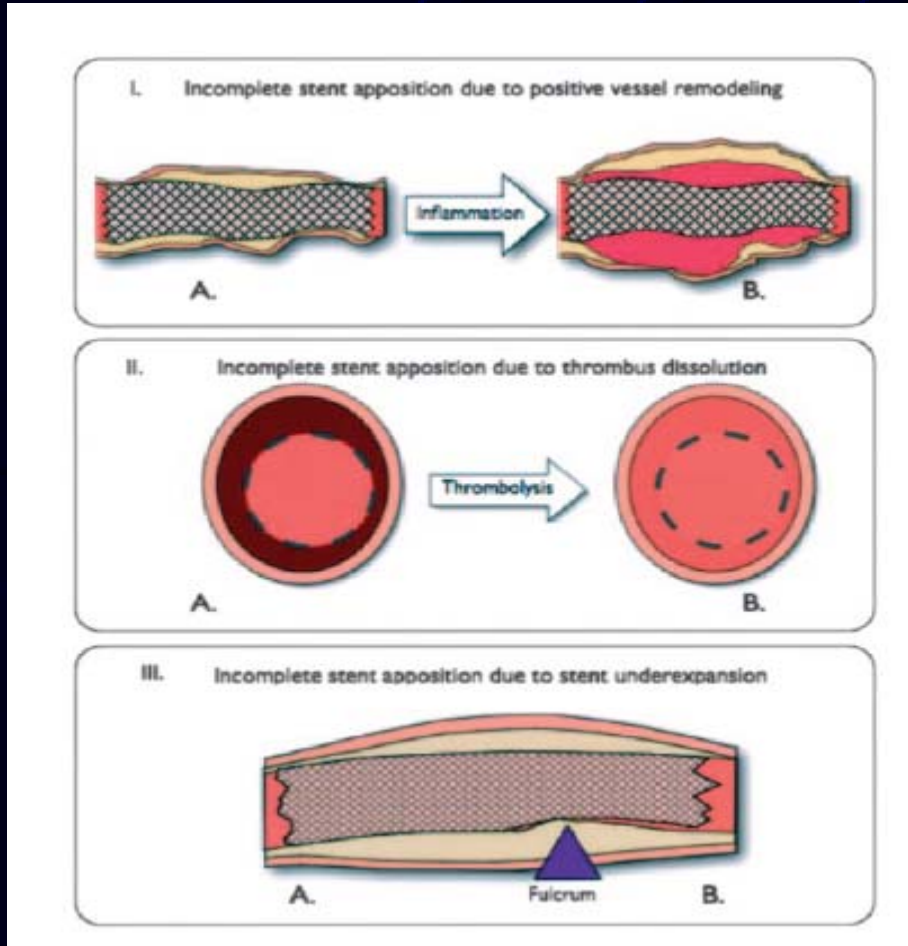
IVUS at the time of late stent thrombosis (LST)



Incomplete stent apposition was more frequent (77% versus 12%; $P 0.001$) and maximal incomplete stent apposition area was larger (8.37.5 versus 4.03.8 mm²; $P 0.03$) in patients with very late stent thrombosis compared with controls.

Out of 13 pts with LST 6 had stenting during AMI and 3 during NSTEMI

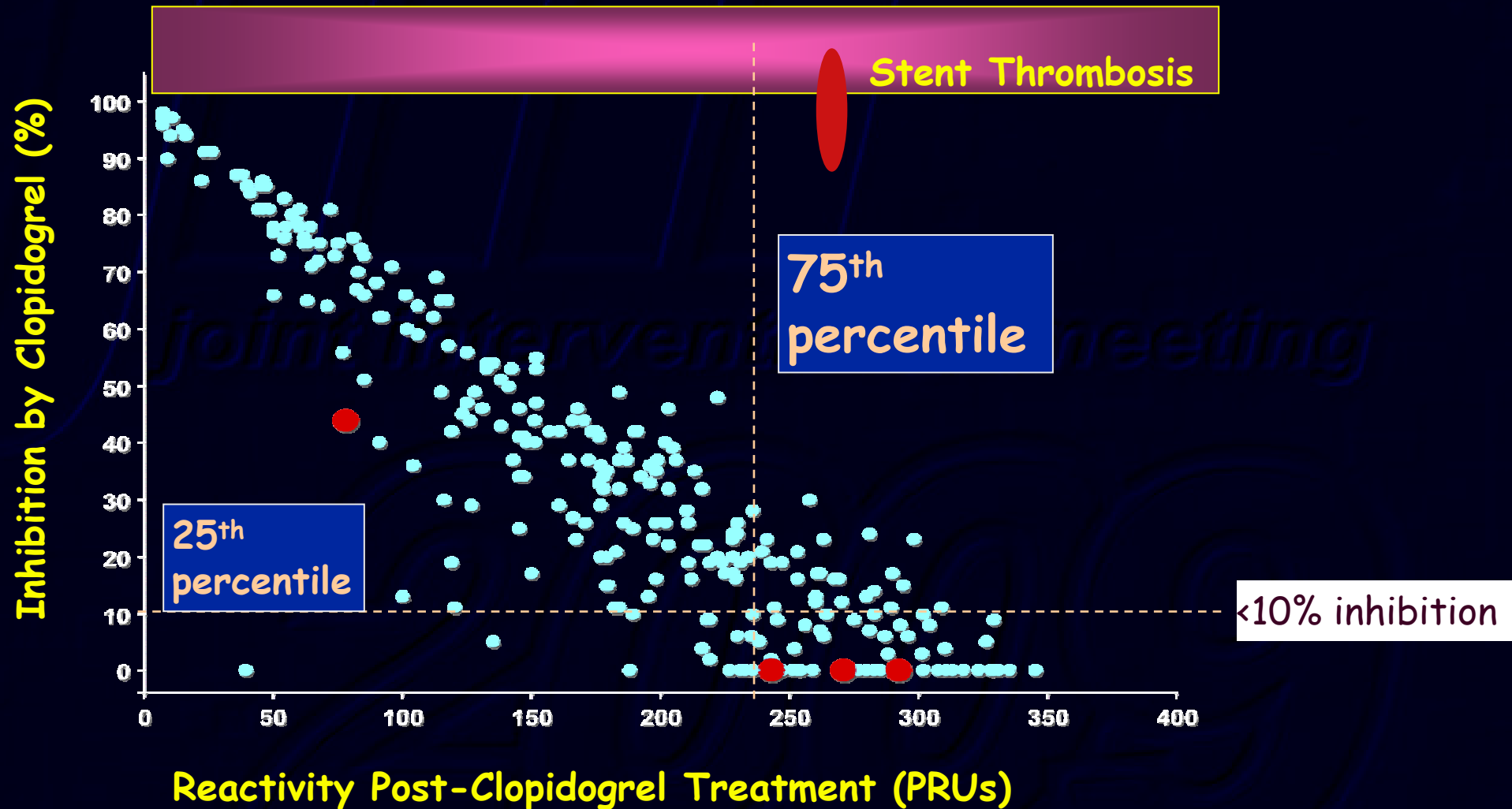
Cook, S et al. Circul 2007



Unless we know how many pts with incomplete apposition do not sustain Stent Thrombosis this issue is not going to be clear



Clopidogrel Responsiveness at the Time of PCI and ST after Cypher® Stent < 30 Days (n=280)



Price MJ et al, TCT 2006

Prasugrel versus Clopidogrel



13,608 patients

	Prasugrel	Clopidogrel
BMS	48%	47%
DES	47%	47%
Stent Thrombosis (ARC d+prob)	1.1%	2.4%

BMS HR 0.52 (95% CI 0.35 - 0.77) P < 0.001

DES HR 0.43 (95% CI 0.28 - 0.66) P < 0.001

Prasugrel versus Clopidogrel

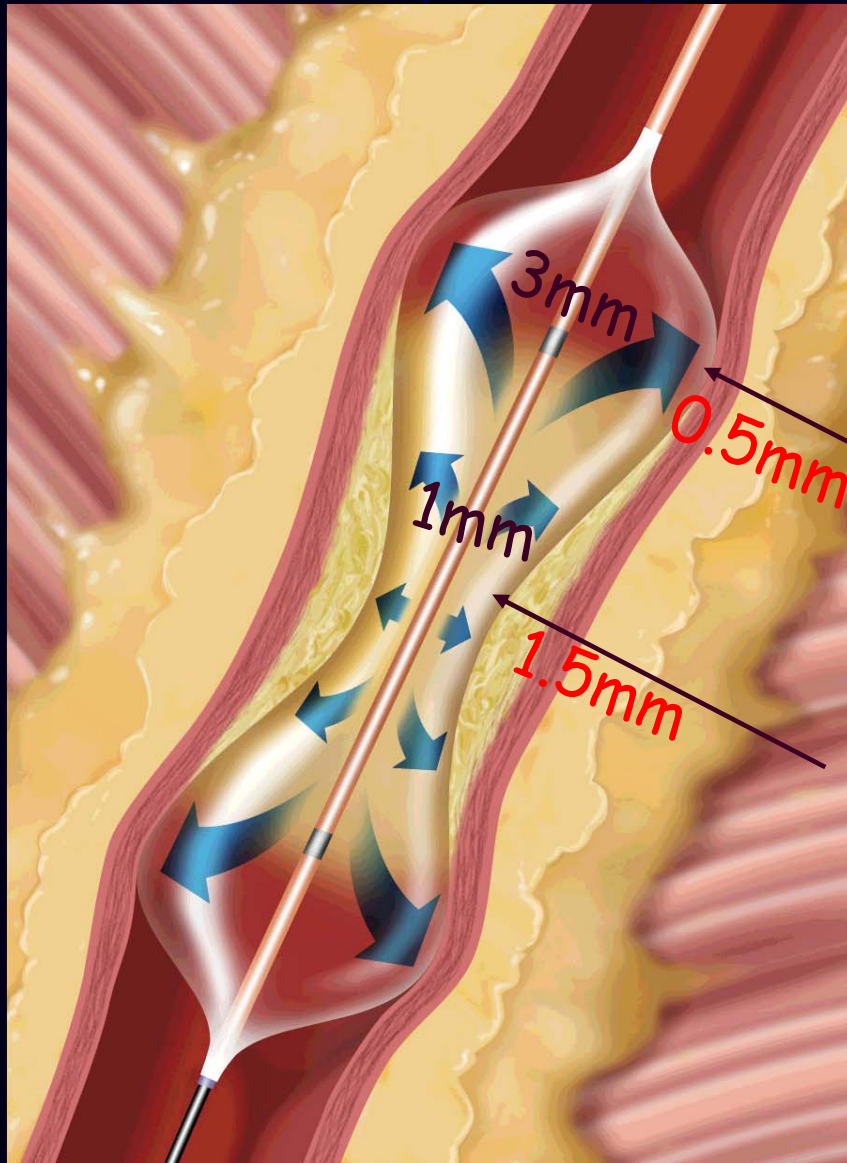


Primary End point

Cardiovascular Death + MI + Stroke 14 months

	Prasugrel	Clopidogrel	Risk reduction
BMS (6,461 pts)	10%	12.2%	20%
DES(6,383 pts)	9.4%	11.6%	18%

Inflation pressure and dilatation force



Inflation pressure = 10 atm

Dilation force varies from

$$10 \times 3 / 2 \times 0.5 = 30 \text{ atm}$$

to

X 10 Dilatation Force

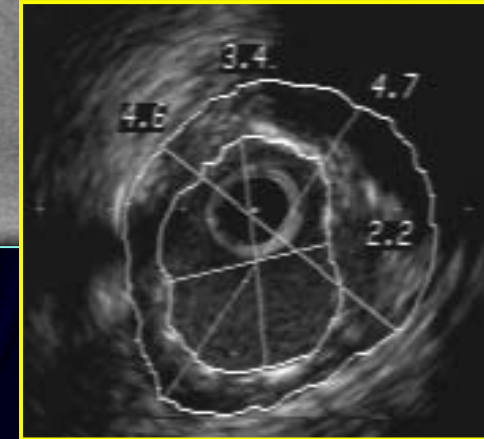
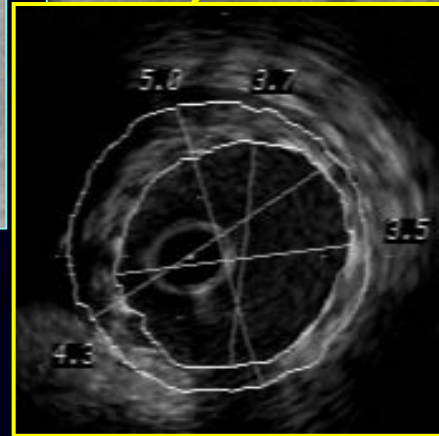
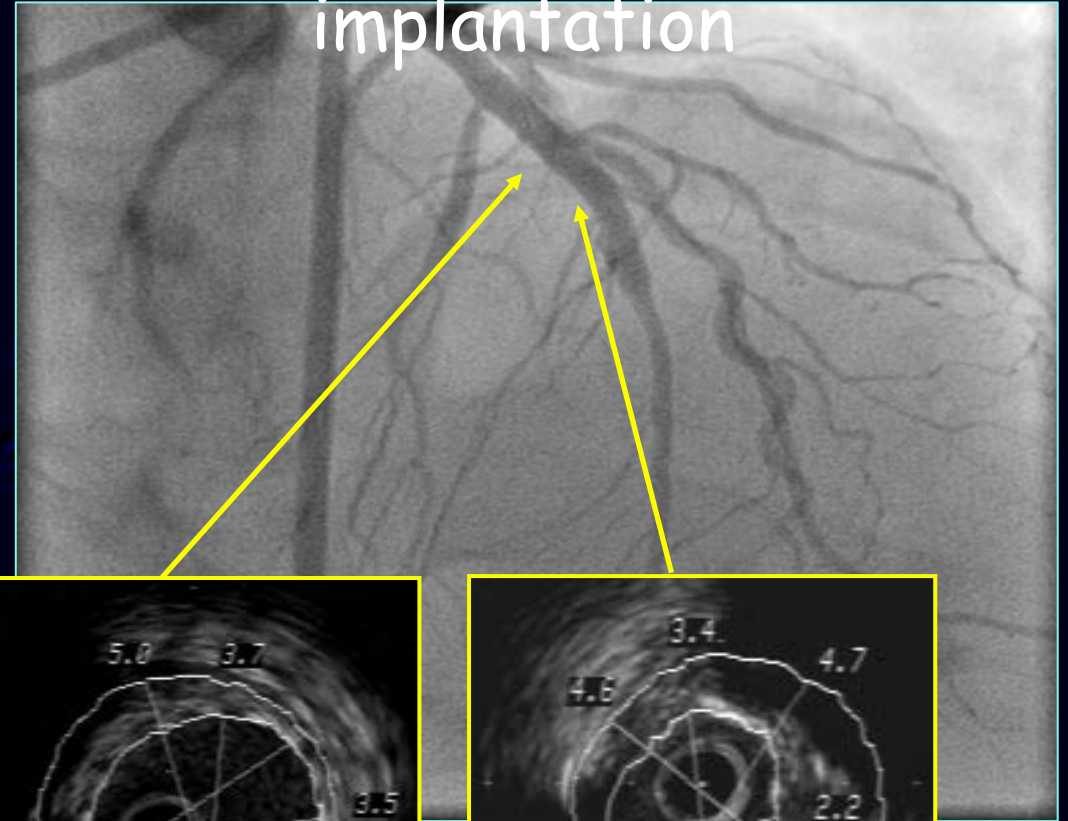
$$10 \times 1 / 2 \times 1.5 = 3.3 \text{ atm}$$

$$F = \frac{\text{Pressure} \times \text{Diameter}}{2 \times \text{Wall Thickness}}$$

Baseline



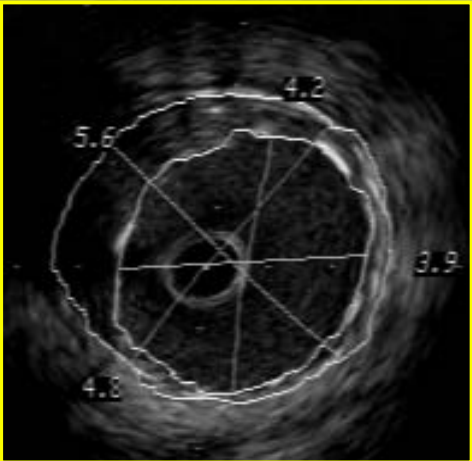
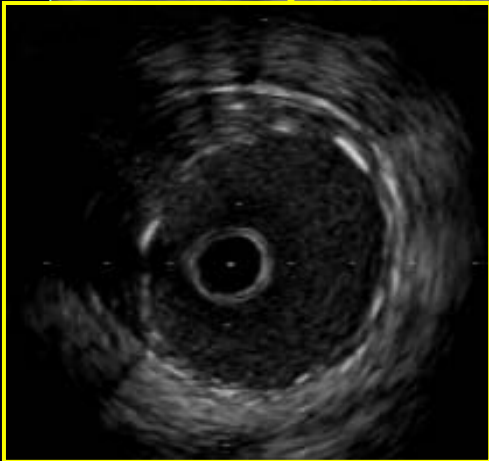
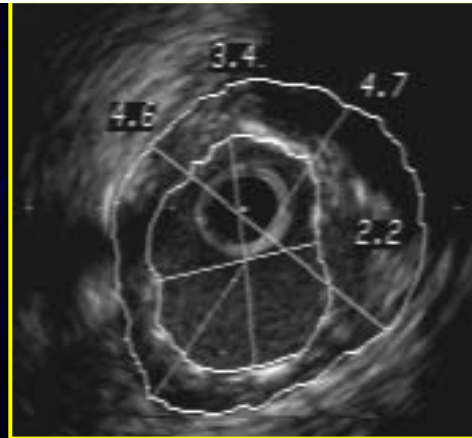
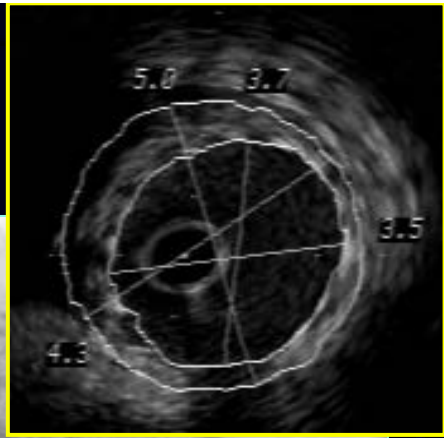
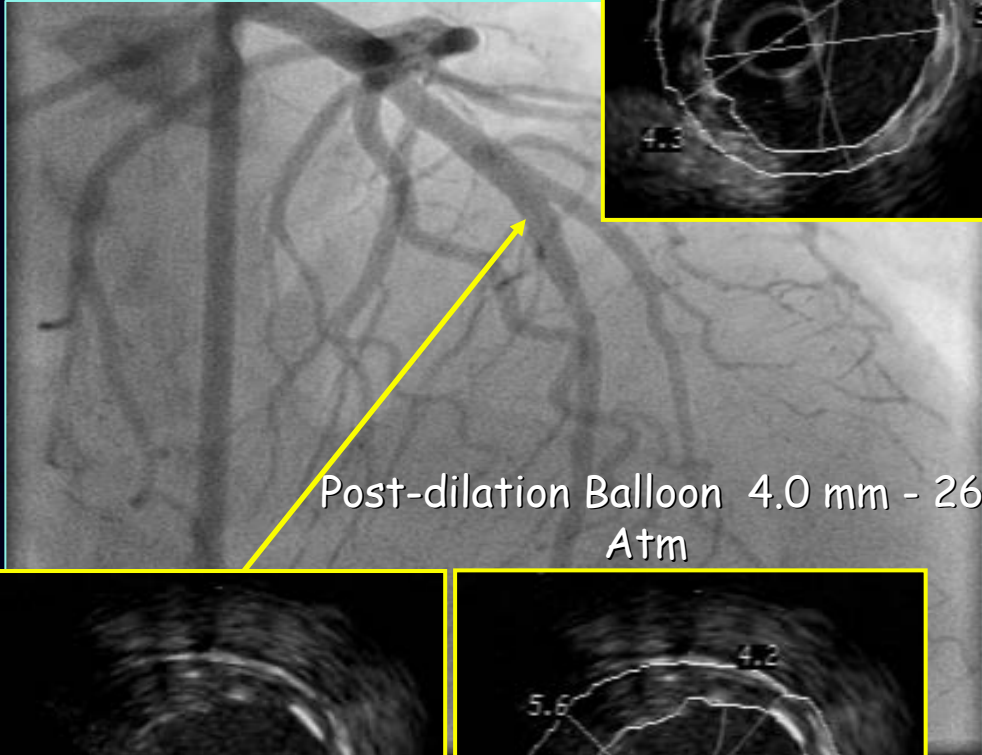
After stent
implantation



We should post-dilate with 4 mm NC b



After stent
implantation



Final Result



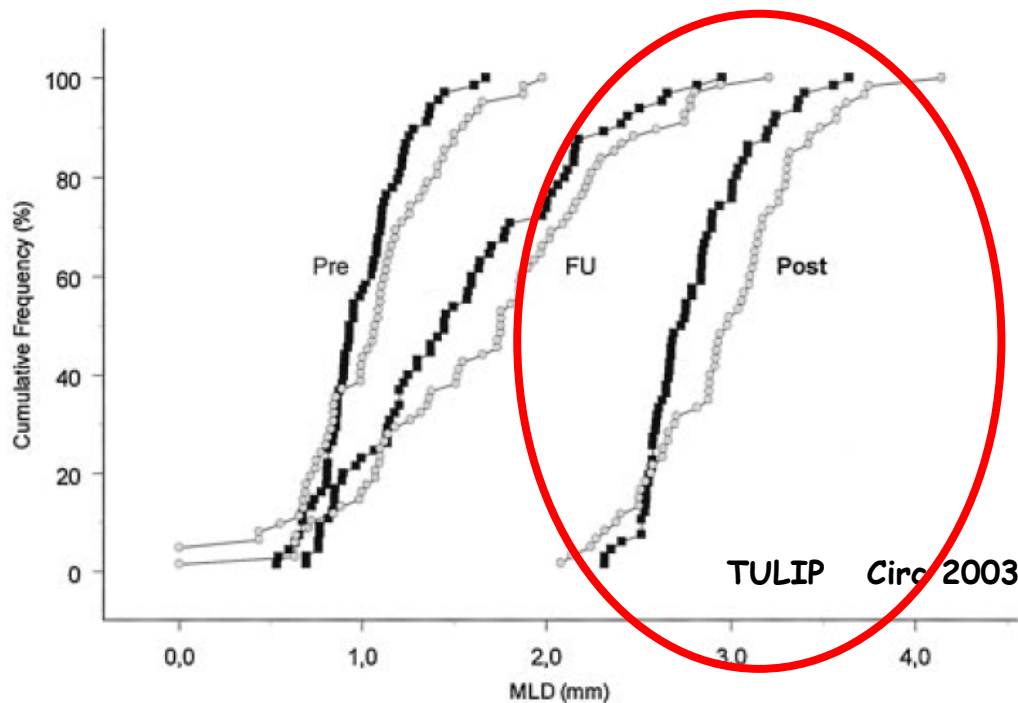
9-mo Follow-Up



Matched comparison of Angio vs. IVUS guided DES implantation

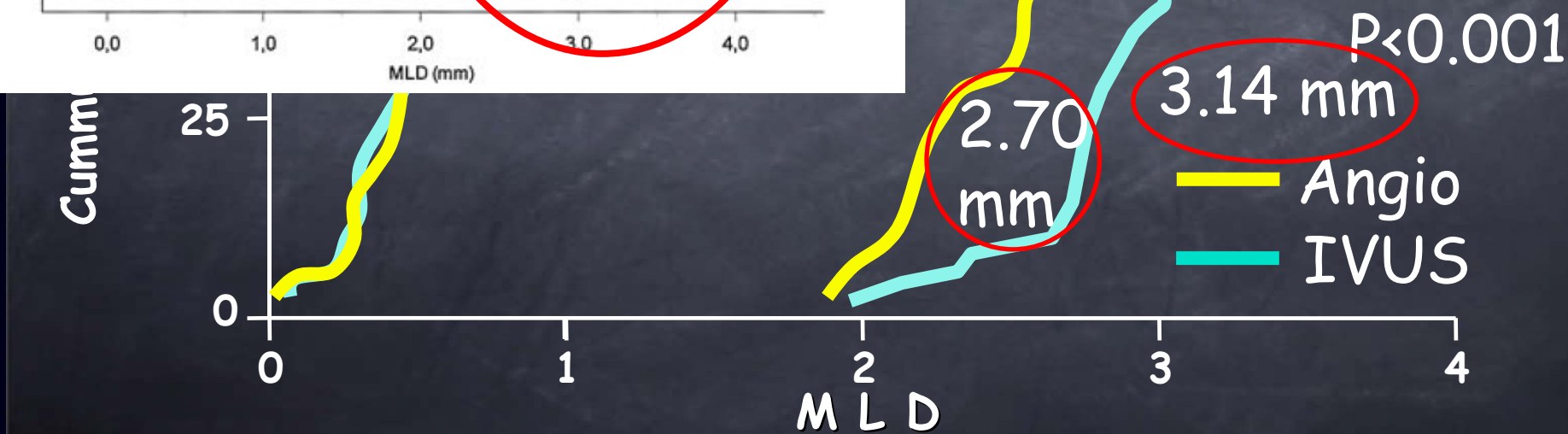
- 49 pts. with 49 lesions treated with Angio guided DES implantation (San Raffaele Hosp) and 49 pts. with 49 lesions treated with IVUS guidance (AVIO criteria, Columbus Hospital) blinded matched according to: diabetes, vessel type, reference vessel size, baseline MLD and lesion length

Preliminary Study of IVUS Guided DES Implantation According to AVIO



Balloon 2.97 ± 0.5
 18 ± 6 atm

Balloon 3.3 ± 0.5
 23 ± 4 atm



49 (1:1) Matched Lesions Using Following Criteria:

1. DM
2. Vessel
3. RVD ± 0.5 mm
4. MLD ± 0.1 mm
5. Lesion Length



Conclusions

Preventing restenosis and re-interventions are appropriate objectives.

The use of DES vs. BMS in unselected patients shows that this goal can be obtained without an increase in the risk of death or myocardial infarction.

We can still improve on these very positive results!