Evidence-Based Medicine Analysis of Current DES Clinical Use Guidelines: A Roadmap for Clinicians

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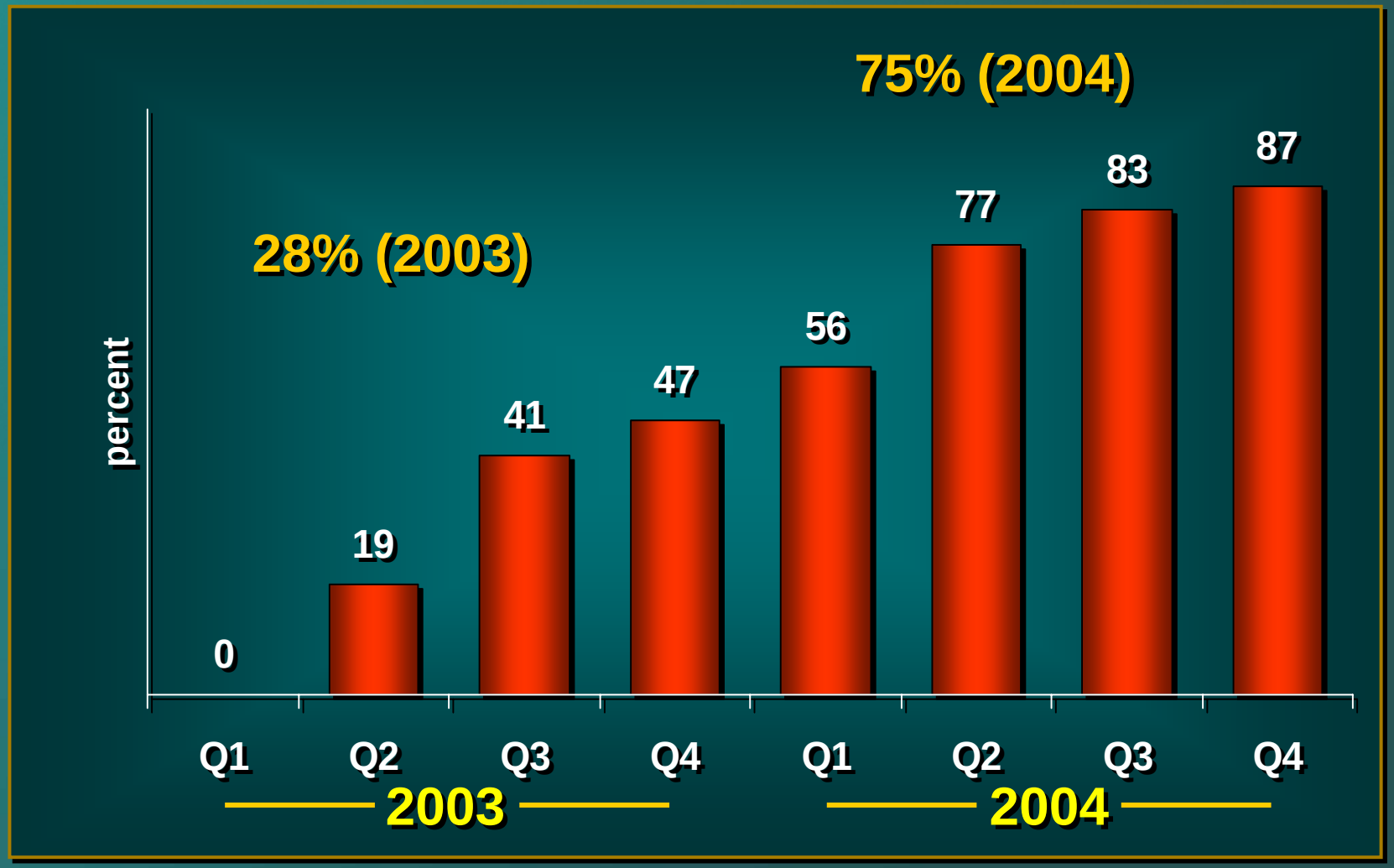
U.S. Penetration of DES



Cypher approved April 2003 and Taxus approved March 2004

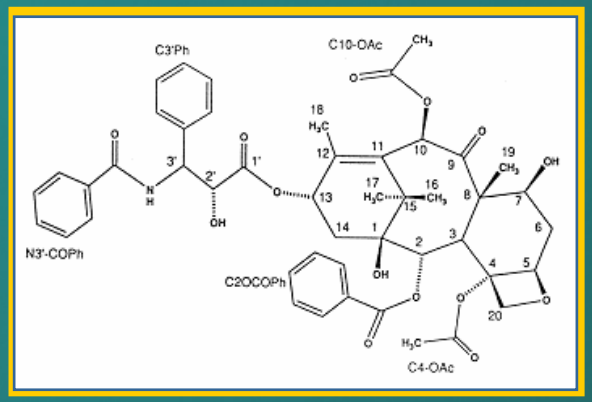
Evidence-based Medicine

- **Randomized Clinical Trials** – the gold standard
  - **CAVEATS**
    - Multicenter and adequately powered
      - Beware of alpha and beta error
    - Blinded core labs & clinical events committees
    - Apply only to the patient and lesion subgroups and the specific device studied
- **Registry data**
  - Must be large-scale, multicenter, monitored
  - Utility: Use patterns & low freq safety events

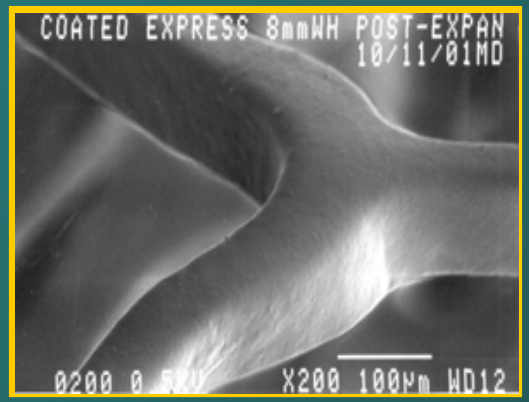
Drug-eluting Stents in 2005

Safety and Efficacy Proven

TAXUS



Paclitaxel

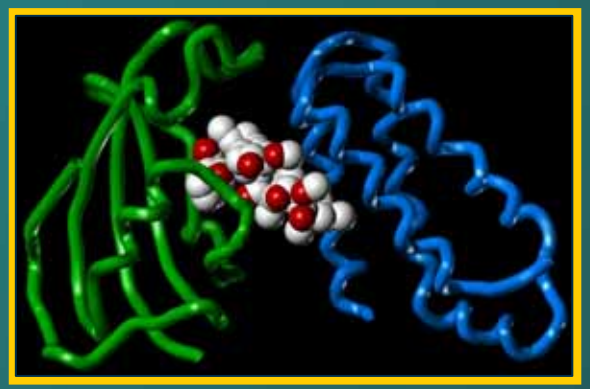


Polyolefin derivative

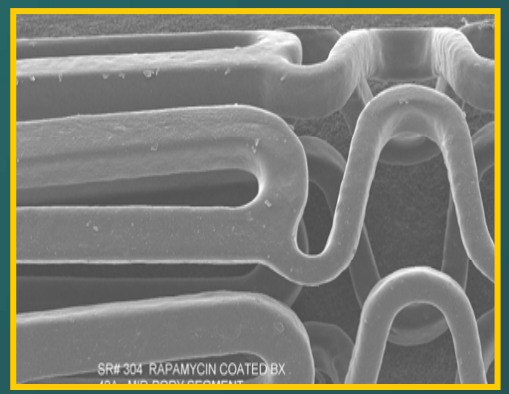
Express^2

Drug **Polymer** **Stent**

Cypher



Sirolimus

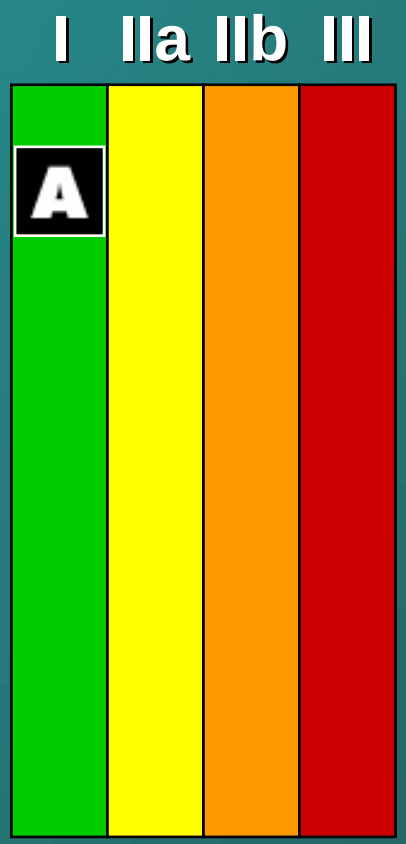


PEVA + PBMA blend

BX Velocity

DES Evidence-based Medicine Guidelines Summary 2005

De Novo Lesions



RVD 2.25 – 3.5 mm Length ≤30 mm	RVD 2.25 – 4.0 mm Length ≤46 mm
Polymer-based Sirolimus-eluting Cypher™ stents	**Polymer-based Paclitaxel-eluting TAXUS™ stents**
RAVEL	TAXUS-I
SIRIUS	TAXUS-II
E-SIRIUS	TAXUS-IV
C-SIRIUS	TAXUS-V
SES-SMART	TAXUS-VI
DIABETES	

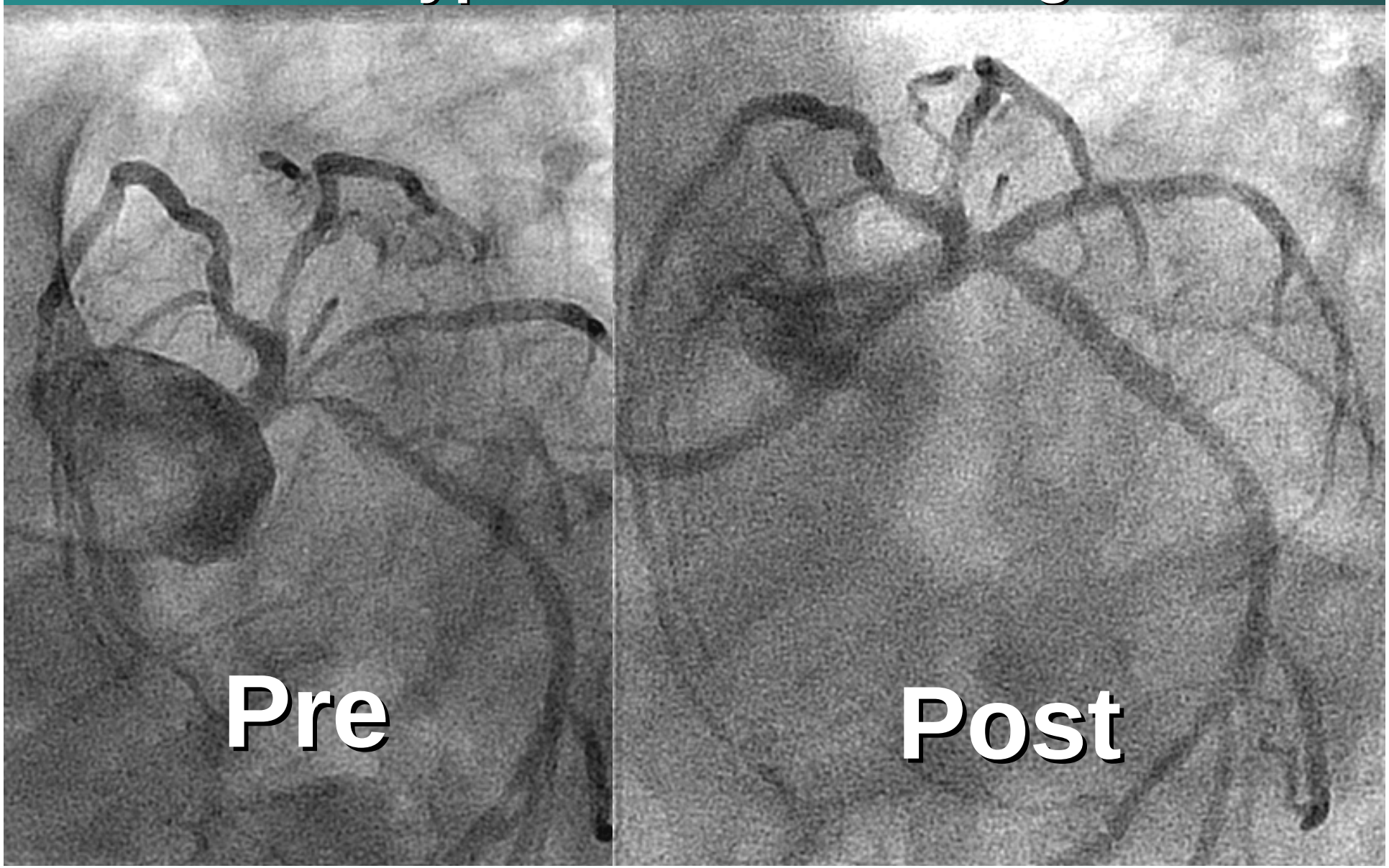
Unsettled Issues with Class 1A Lesions

- Non Q-wave MI with Multiple Stents
- Late Stent Thrombosis

Drug – Eluting Stents

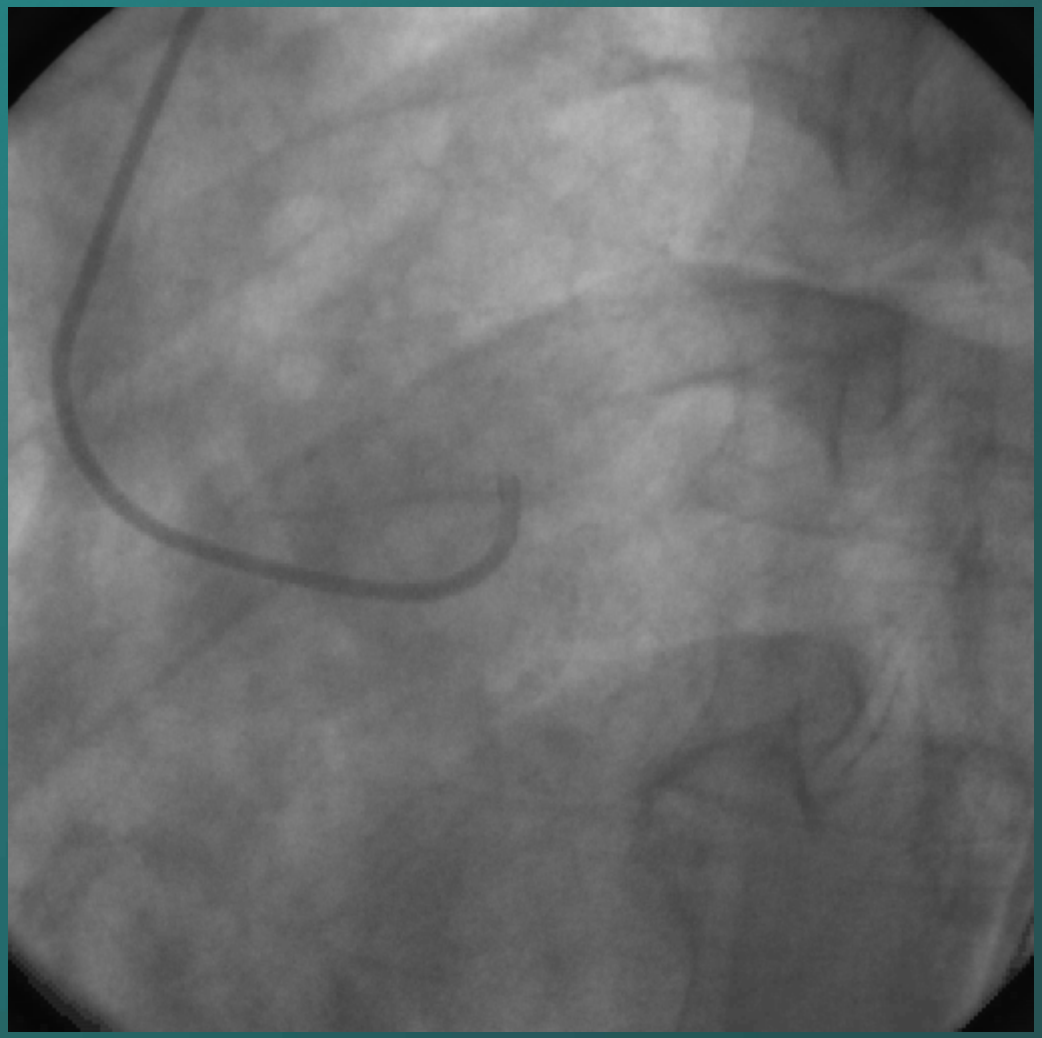
- Unapproved (and under-studied) indications
  - Very small or large vessels
  - Ultra long lesions
  - Chronic total occlusions
  - Bifurcations
  - Left main disease
  - In-stent restenosis
  - Multivessel disease
  - Acute myocardial infarction

Distal left main, PLCX, Ramus bifurcation
3 Cyphers with crushing

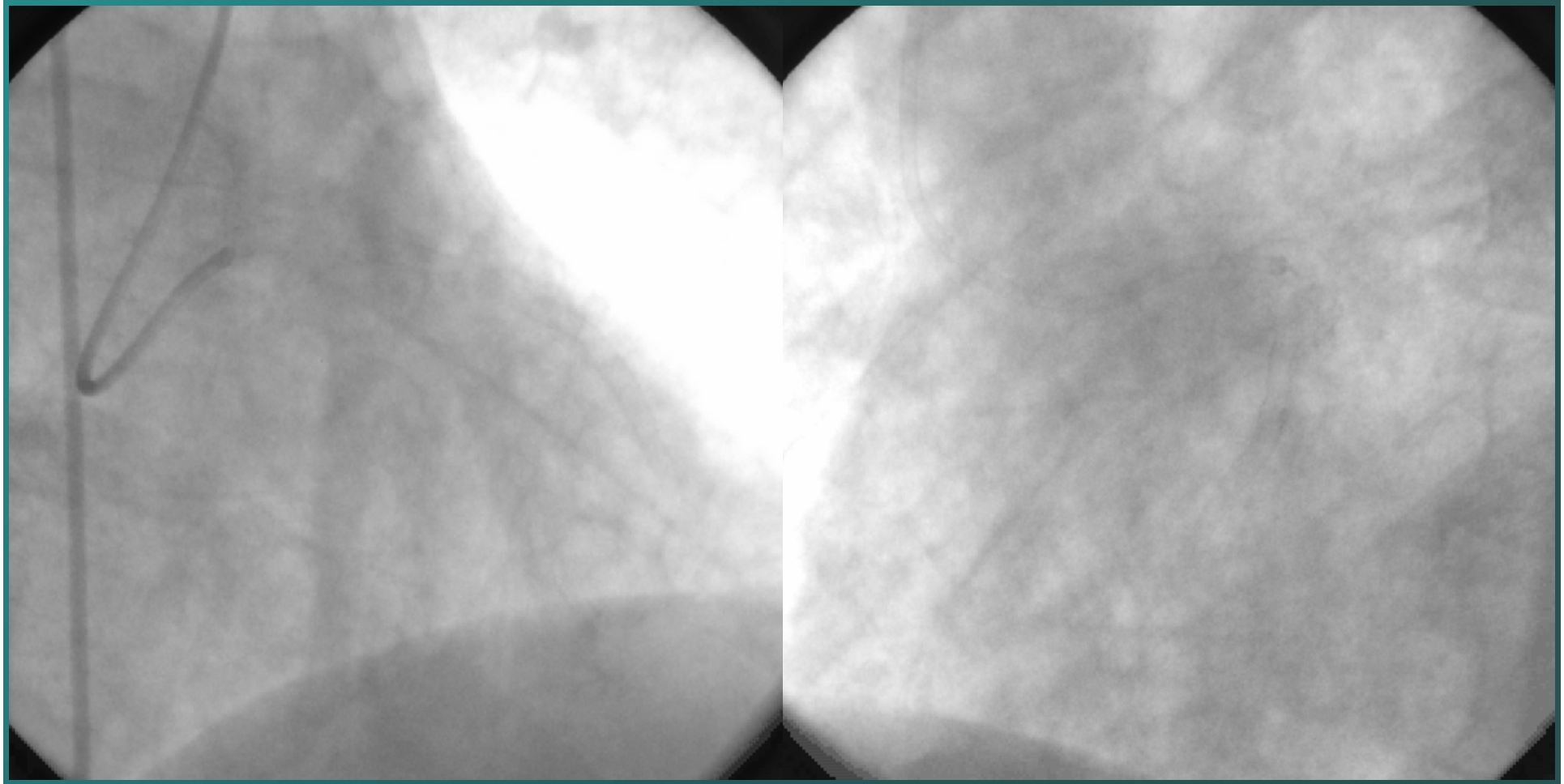


2 Months Later

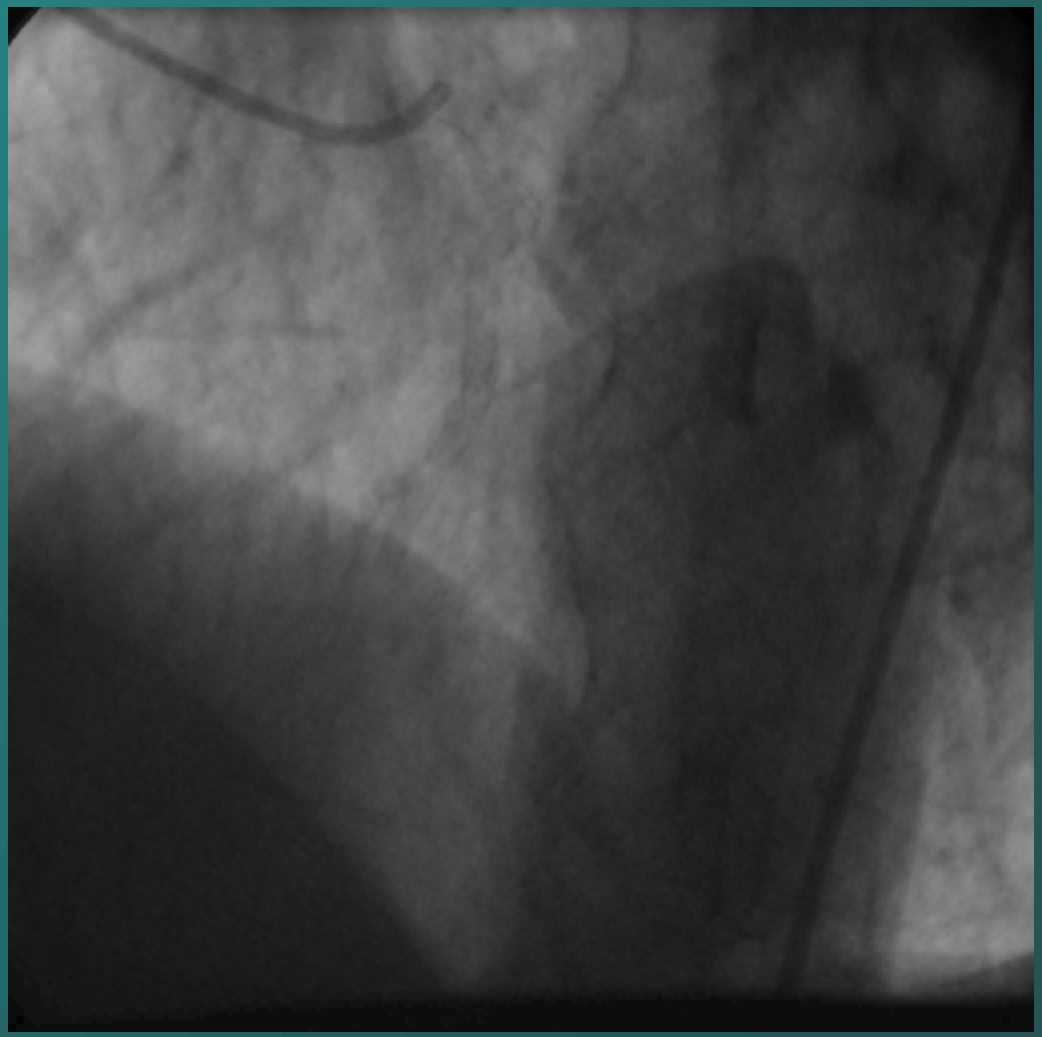
Complex DES Implantation



S/P 4 Cypher stents in LM, LAD and RI

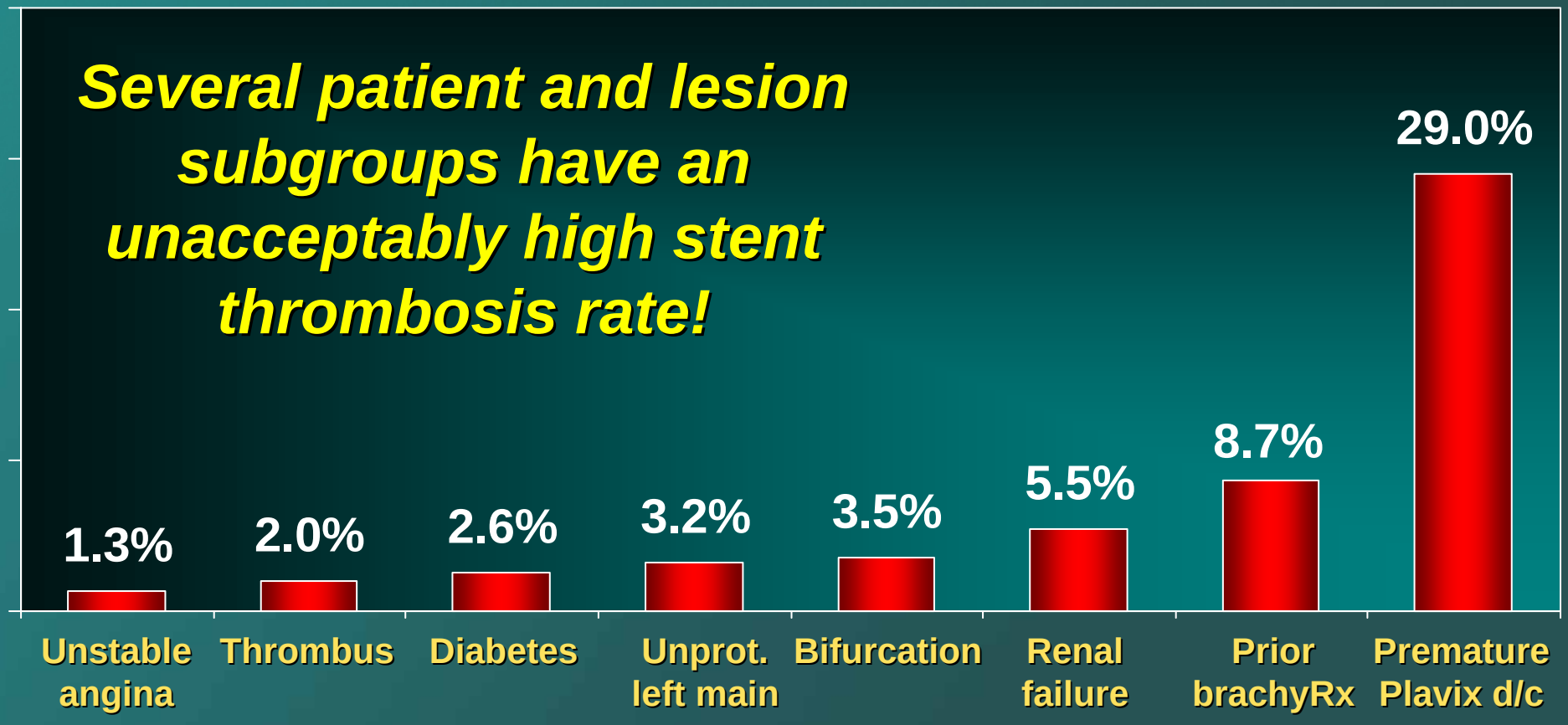


8 Days Later



Milan/Siegburg Experience

Stent thrombosis after DES (SES or PES) occurred in 29/2229 pts (1.3%) at 9.3±5.6 mos



DES Evidence-based Medicine
Guidelines Summary
2005

Bifurcation Disease

SIRIUS Bifurcation Study
MACE at 6 months

	ITT		AT	
	(n=43)	(n=42)	(n=63)	(n=22)
Death, n (%)	1 (2.3)	-	1 (1.6)	-
Q MI, n (%)	1 (2.3)	1 (2.3)	1 (1.6)	1 (4.5)
Non-Q MI, n (%)	4 (9.3)	4 (9.5)	6 (9.5)	1 (4.5)
TLR, n (%)	3 (7.0)	3 (7.1)	6 (9.5)	1 (4.5)
CABG, n (%)	-	1 (2.3)	1 (1.6)	-
Total, n (%)	8 (18.6)	7 (16.6)	12 (19.0)	3 (13.6)

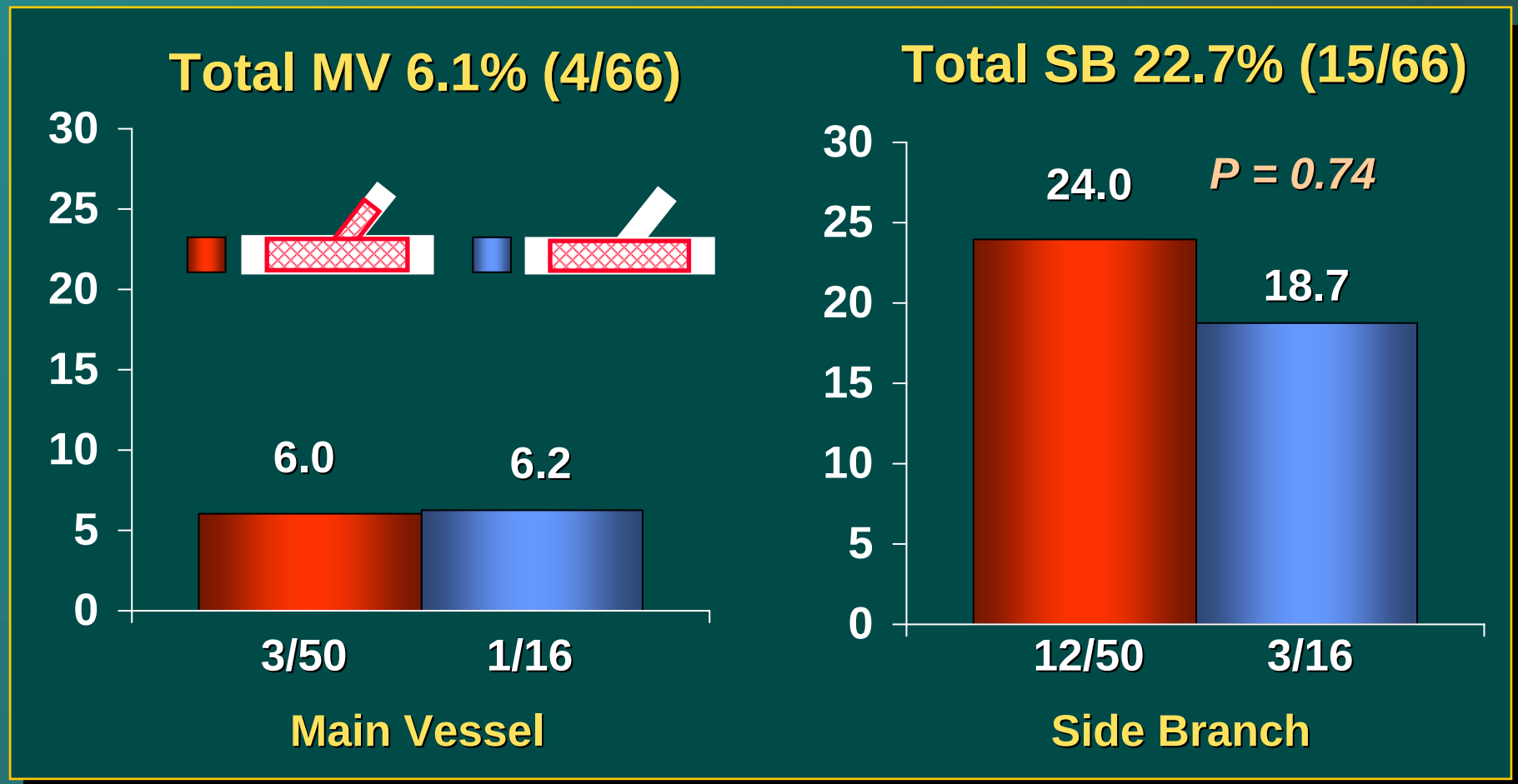
Stent thrombosis 3 (3.5%)

ITT: intention to treat, AT: actual treatment

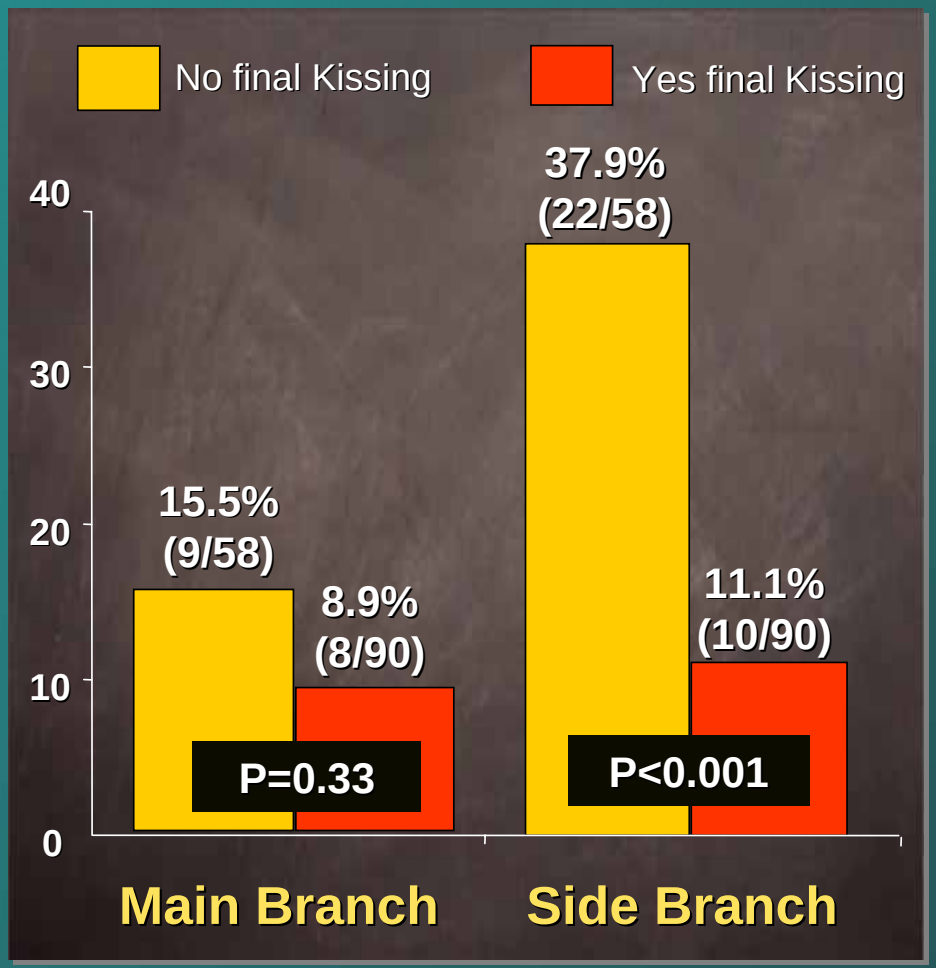
SIRIUS Bifurcation Study

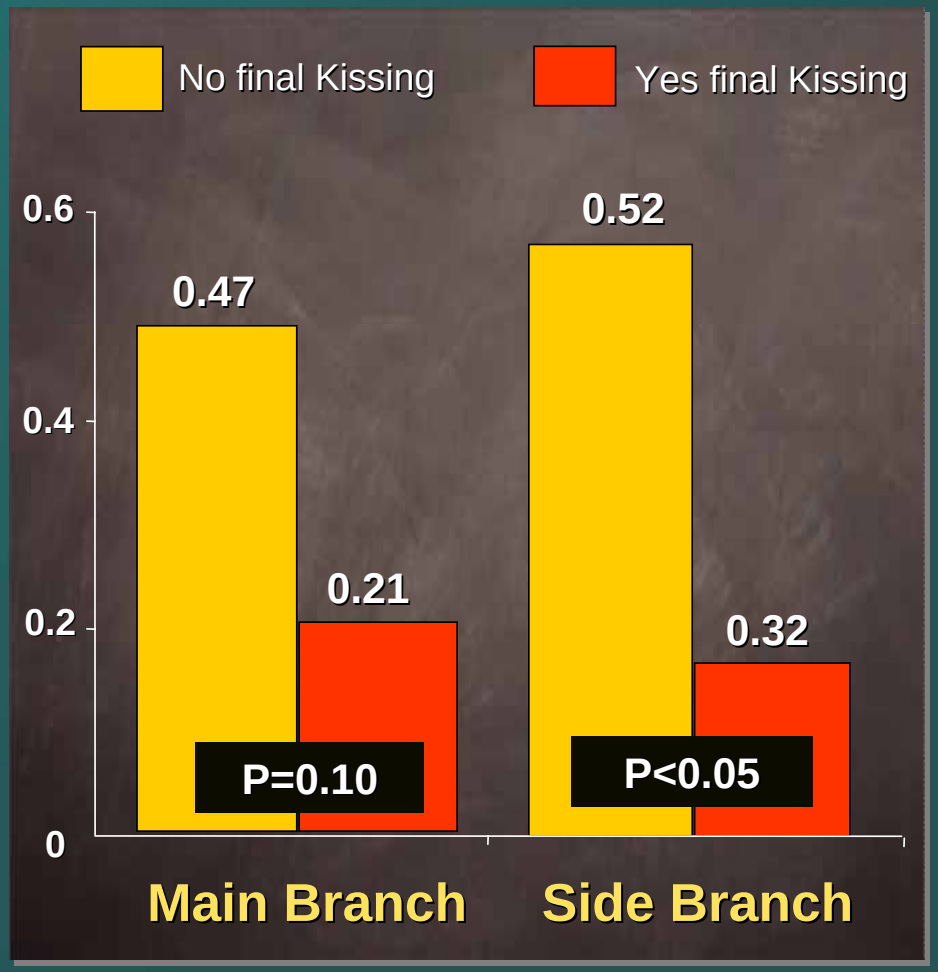
In-lesion Restenosis (treatment received)

Total Restenosis (MV and/or SB) 25.7% (17/66)



Results with Crush stenting according to performance of final kiss (n=148)

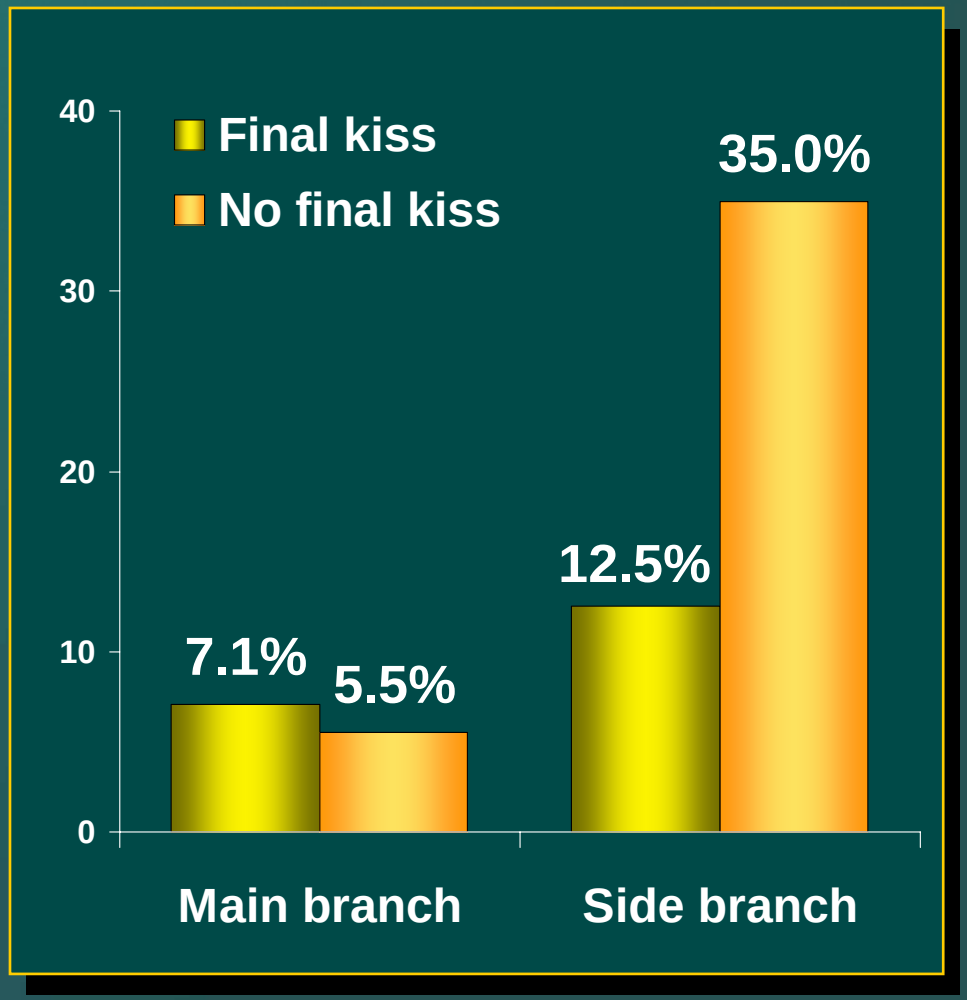




Centro Cuore Columbus

Crush stenting
6 Month Restenosis

Pts	59
Lesions	67
Final kiss	30%
Angiog FU	79%
TLR (pts)	18.6%



DES Evidence-based Medicine
Guidelines Summary
2005

IIa

B - Bifurcation (DES main branch, side branch PTCA w/provisional DES)

IIb

B - Bifurcation (routine T-stent or crush of side branch with final kiss)

C - Bifurcation (V-stent)

DES Evidence-based Medicine

Guidelines Summary

2005

Unprotected Left Main Disease

Unprotected Left Main Stenting (n=73)

SJ Park et al.

Post discharge 6 mo events	Prox/mid LM (n=17)	Distal LM (n=56)
Death	0	0
Q MI	0	0
Non Q MI	0	0
Stent thrombosis	0	0
Emergent CABG	0	0
Repeat PCI	0	1 (1.8%)

**TLR due to edge restenosis

Unprotected Left Main Stenting (n=73)

SJ Park et al.

6-Month QCA	Prox/mid LM (n=17)	Distal LM (n=56)
Angiographic F/U	13 (76%)	48 (86%)
Reference vessel (mm)	3.56±0.44	3.58±0.65
MLD (mm)	3.59±0.32	3.26±0.59
Diameter stenosis (%)	-1.8±8.1	7.5±17.0
Late loss (mm)	0.17±0.21	0.23±0.50
Restenosis	0 %	3 (6.3%)

Left main stenting: Scripps

Angiographic FU in 99% @ 3 months (n=49)

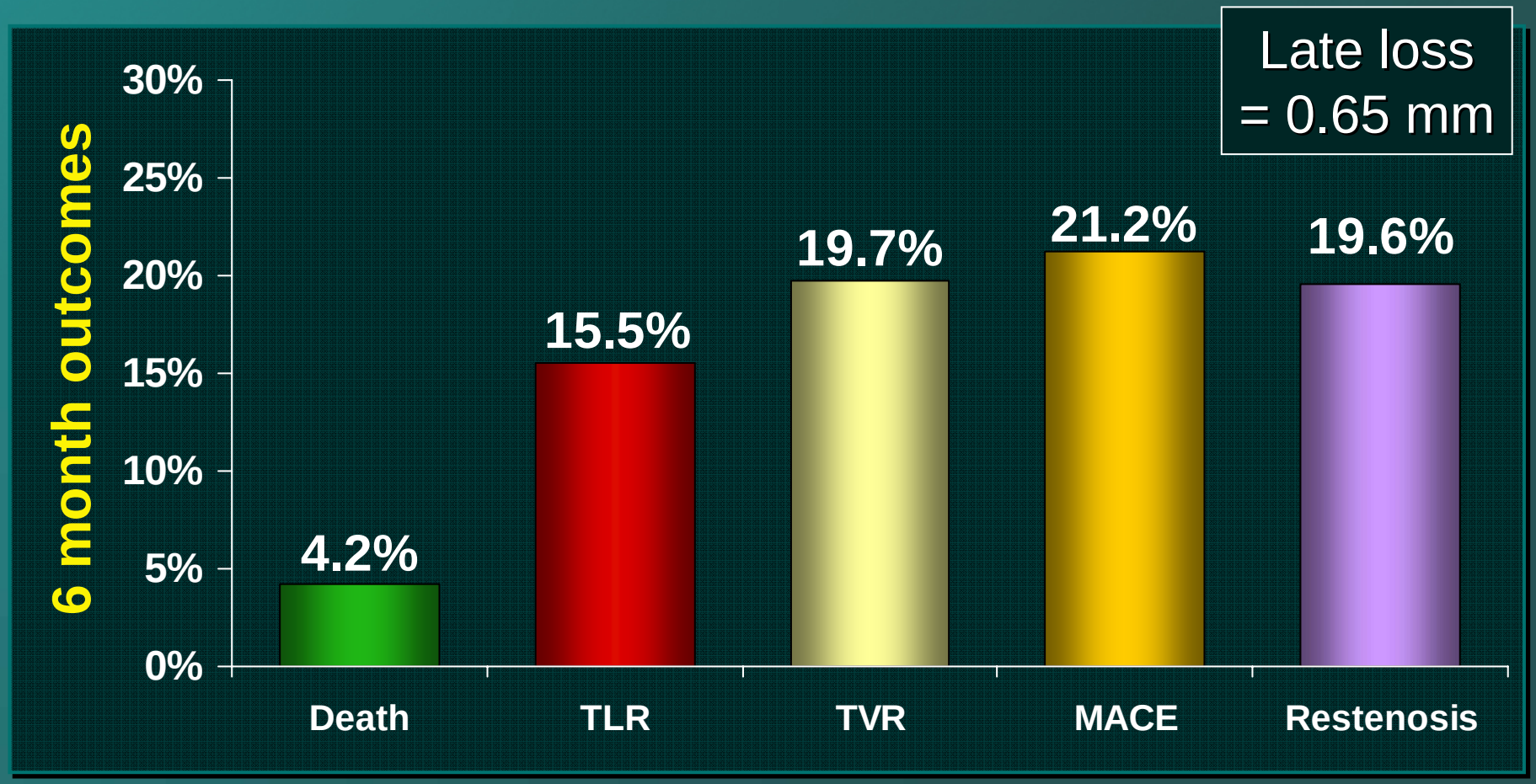
Death*	2 (4%)
MI	0 (0%)
Restenosis	15 (31%)
TLR**	14 (29%)
TLR-PCI	12 (25%)
TLR-CABG	2 (4%)
Late thrombosis	0 (0%)
Death, MI, TLR, or thrombosis	16 (33%)

* 1 cardiac, 1 non-cardiac

**Asymptomatic TLR = 10 (71%)

Unprotected Left Main Milan DES Experience (n=86)

Distal bifurcation 82%; 48% Cypher, 52% TAXUS; 59% crush, 24% V=stent



DES Evidence-based Medicine
Guidelines Summary
2005

IIb

B - Unprotected left main

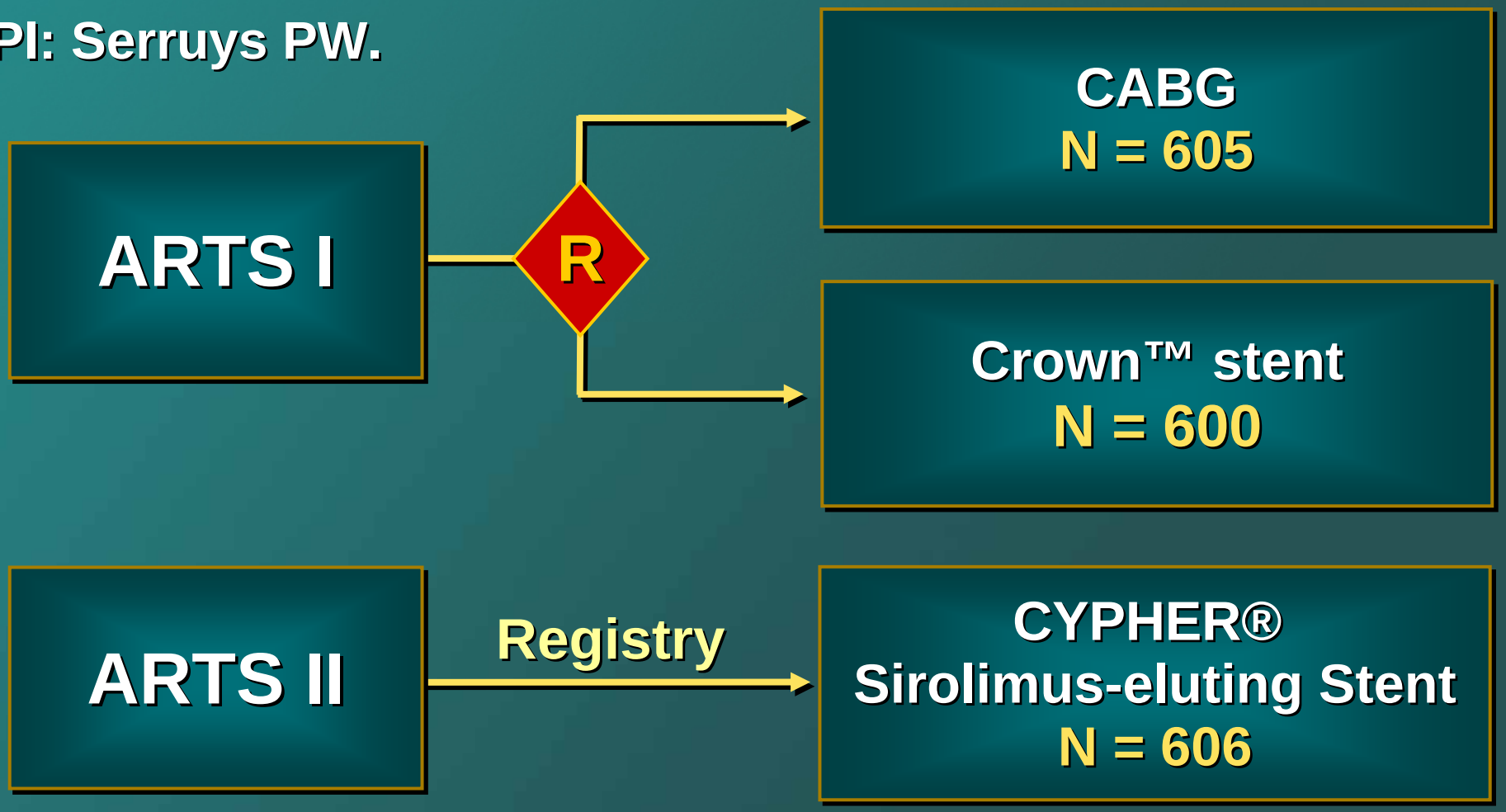
DES Evidence-based Medicine
Guidelines Summary
2005

Multivessel Disease

Arterial Revascularization Therapy Study

ARTS II – Study Design

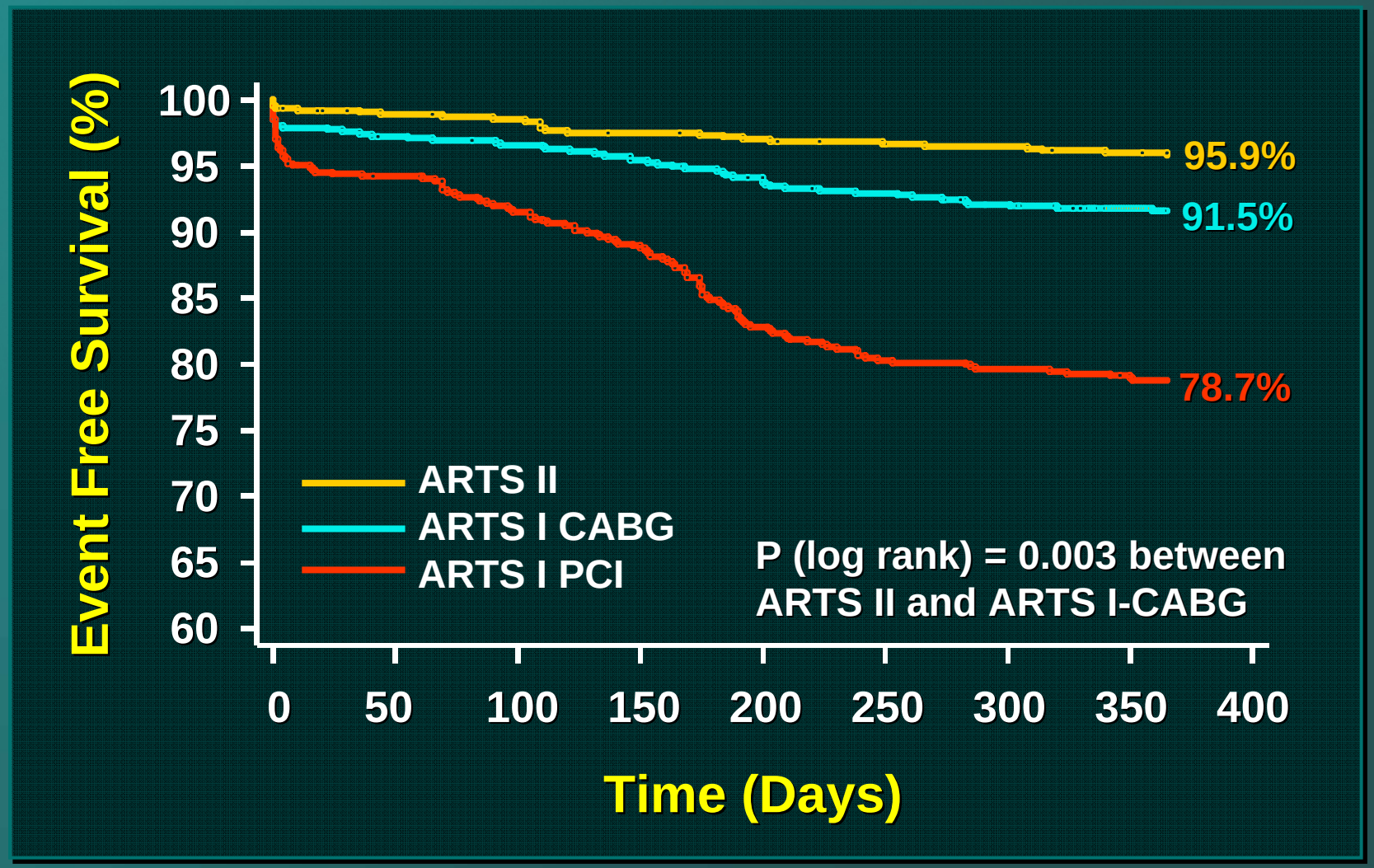
PI: Serruys PW.



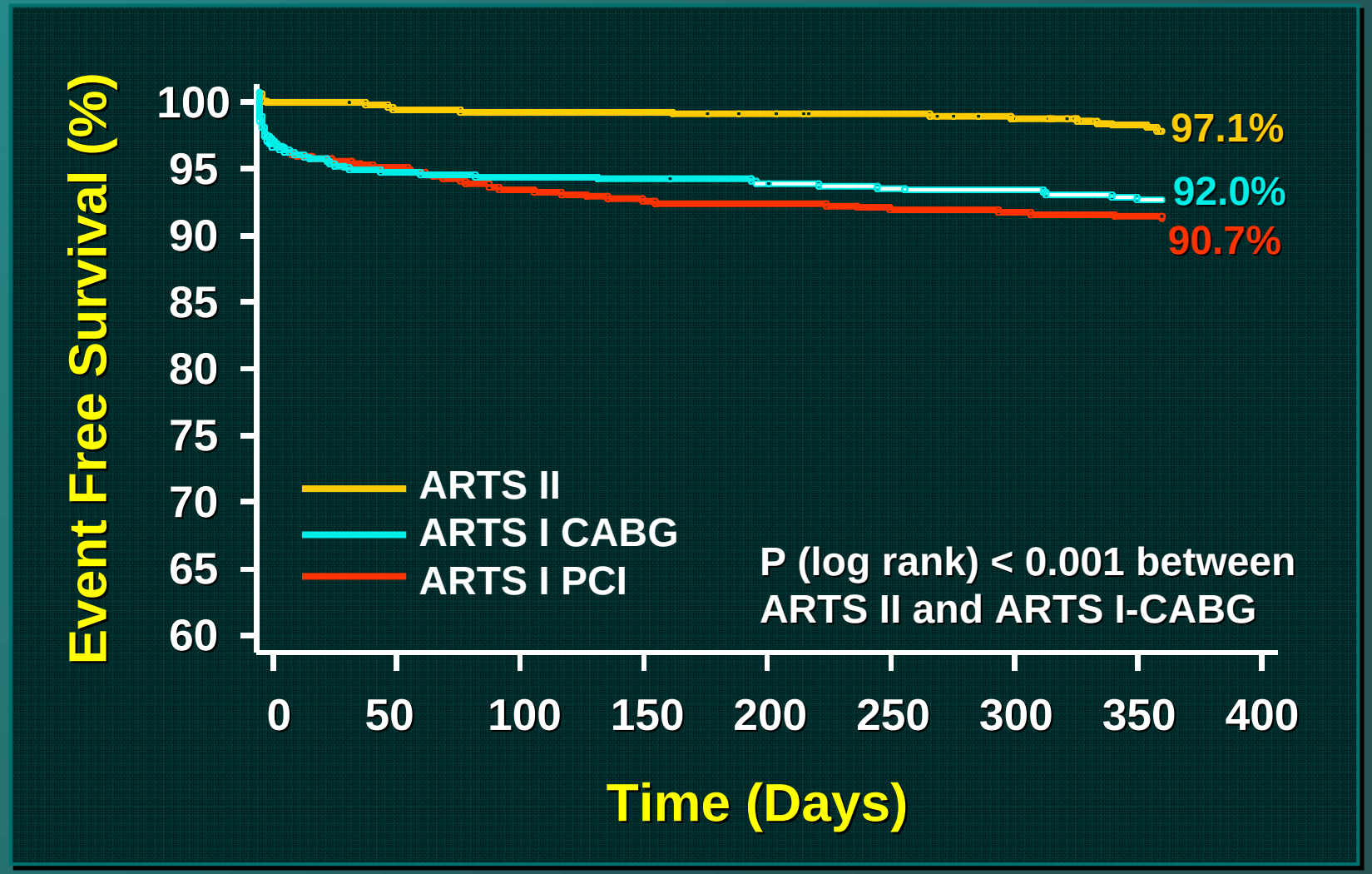
ARTS II: Procedural Data

	ARTS I – CABG arm (n = 605)	ARTS I – PCI arm (n=600)	ARTS II (n = 606)
# Diseased Vessels / Patient	2.3	2.2	2.5
# of Lesions / Patient	2.8	2.8	3.6
# Stents / Patient	-	2.8	3.6
Total Stent Length	-	48	73
Duration of Procedure (Min)	193	99	85
Hospital Stay (days)	9.6	3.9	3.4
Elevated CKs Post-procedure			
>1x ULN	89.6	25.3	18.5
3-5x ULN	23.1	3.4	1.7
>5x ULN	26.6	4.0	0.5
Clinical Success	–	83.8	84.6
Use of GPIIb/IIIa Inhibitors	–	–	35.8
Lipid Lowering Drug @d/c	31.8	38.8	89.8

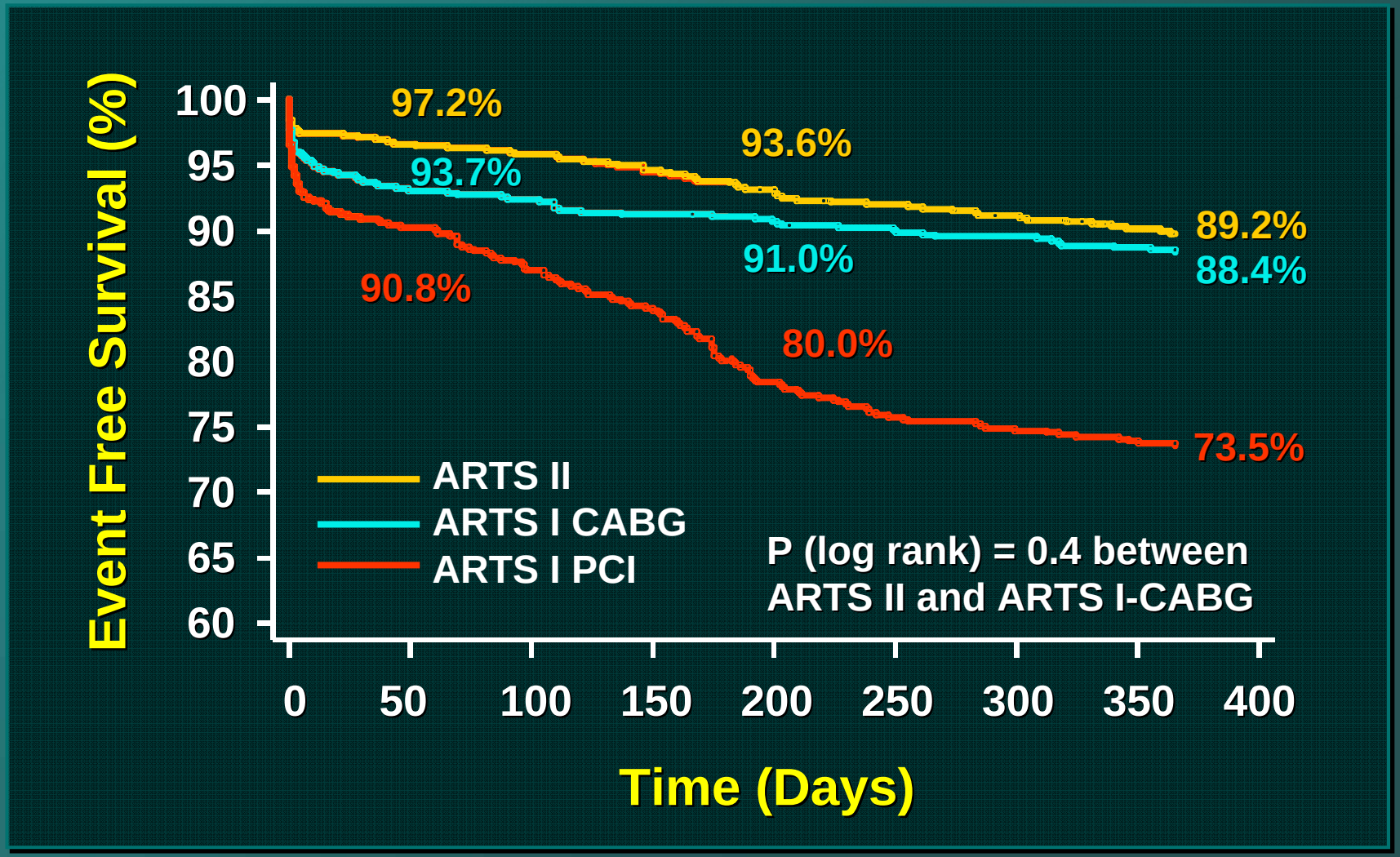
ARTS II: Re-Intervention



ARTS II: Death, Stroke, MI



ARTS II: MACCE



CYPHER® Milan Multivessel Disease Mid-Term Results

Orlic et al
JACC
In press

Baseline Clinical Characteristics

N = 155 patients

Prior CABG, %	31 (20.0%)
Prior MI, %	74 (47.7%)
Unstable angina, %	32 (20.6%)
2-vessel disease, %	67 (43.2%)
3-vessel disease, %	88 (56.8%)
3-vessel stenting, %	27 (17.4%)
Pts bifurc les %	71 (45.8%)
Pts with CTO %	28 (18.1)

CYPHER® Milan Multivessel Disease Mid-Term Results

Six Month Clinical Outcome (112 pts – 359 lesions)

Death, (% pts)	3 (2.7%)
Q-Wave MI, (% pts)	4 (3.6%)
CVA , (% pts)	0
TLR, (% lesions)	24 (6.7%)
PCI (% lesions)	20 (5.6%)
CABG (% lesions)	4 (1.1%)
TLR, (% pts)	16 (14.3%)
TVR, (% pts)	18 (16.1%)
Cumulative MACE (% pts)	25 (22.3%)

Orlic et al
JACC
In press

DES Evidence-based Medicine
Guidelines Summary
2005

IIa

B - Multivessel disease (vs. CABG)

? Non complex lesions only
? Long-term mortality in diabetics

DES Evidence-based Medicine

Guidelines Summary

2005

I

B

- ISR of BMS (vs. PTCA)

IIa

B

- ISR of BMS (vs. brachytherapy)
- Bifurcation (DES main branch, PTCA of side branch w/provisional DES)
- Aorto-ostial lesions
- Chronic total occlusions
- Multivessel disease (? diabetics)
- Saphenous vein grafts

DES Evidence-based Medicine
Guidelines Summary
2005

IIb

B
- Bifurcation – T stent or crushing of side branch
- Ultra-long lesions (full metal jacket)
- Unprotected left main
- Acute myocardial infarction
- ISR after failed brachy (if no surgical option!)

C
- Bifurcation – V stent
- ISR after failed DES

"We desperately need more data regarding the safety and efficacy of DES in unapproved and high risk indications before their use should be considered routine."