



DES In-Stent Restenosis: Mechanisms, Frequency, Clinical Outcomes, and Treatment Alternatives

Ron Waksman, MD
Washington Hospital Center

CRT2011

FEBRUARY 27-MARCH 1, 2011

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SCIENCE

Ron Waksman, MD

Consulting Fees

- Abbott Vascular, Biotronik, Medtronic CardioVascular, Inc, Boston Scientific Corporation

Grants/Contracted Research

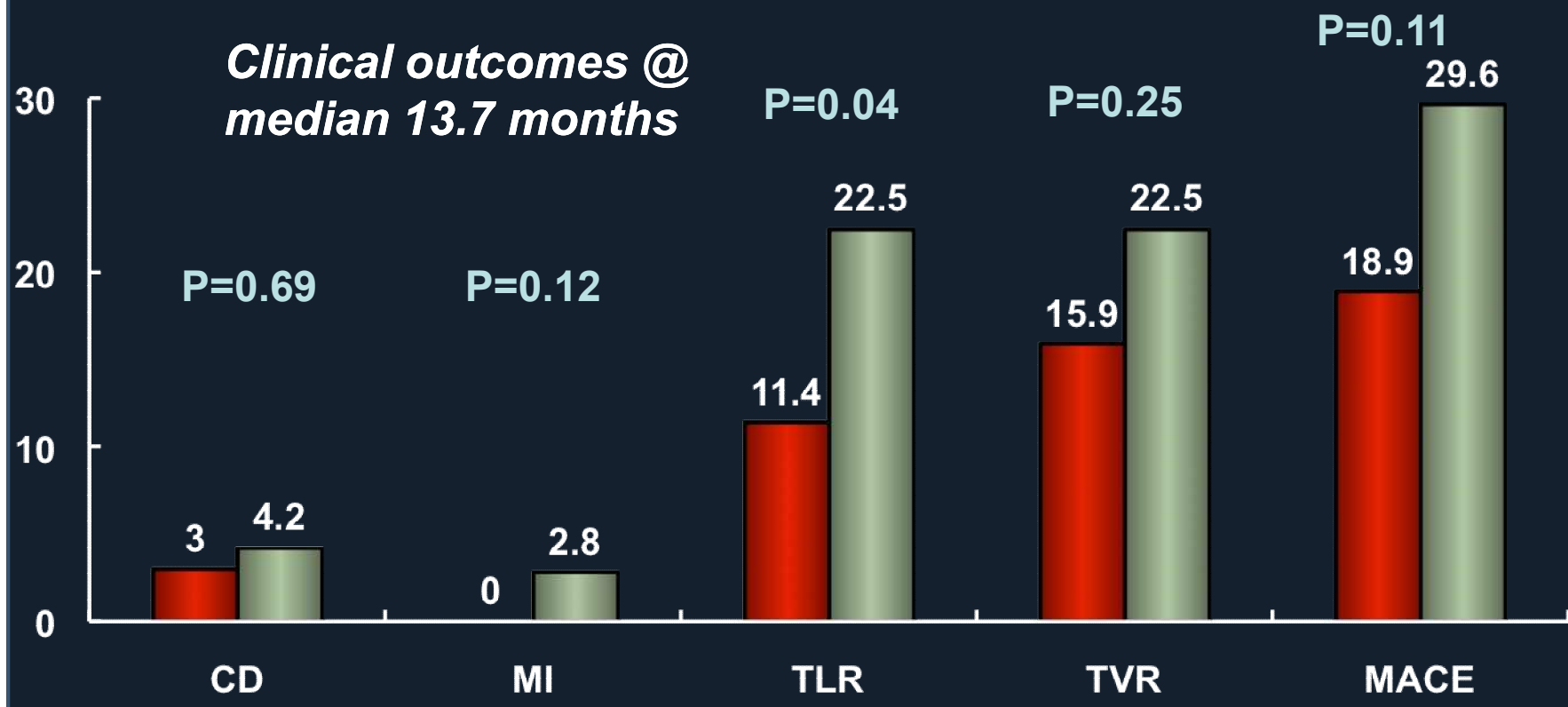
- Abbott Vascular, Biotronik, Boston Scientific Corporation, The Medicines Company, GlaxoSmithKline, Schering-Plough, sanofi-aventis U.S. LLC

Mechanism of DES Restenosis

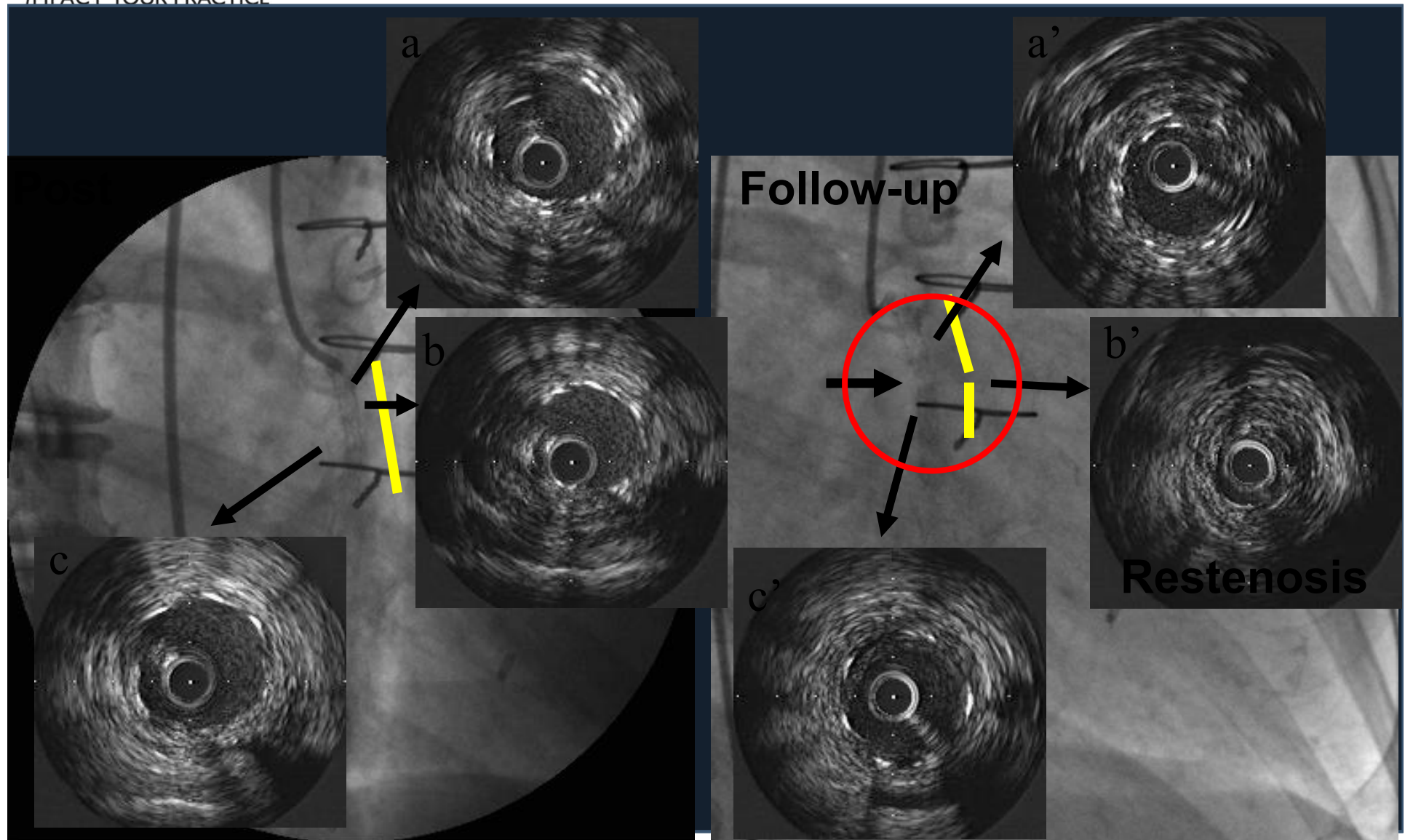
- ***Biological factors***
 - Drug resistance
 - Hypersensitivity
- ***Mechanical factors***
 - Non uniform stent strut distribution
 - Stent fractures
 - Polymer peeling
 - Non uniform drug deposition
- ***Technical factors***
 - Incomplete stent expansion
 - Stent gaps or “misses” (uncovered lesion segments)
 - Barotrauma to unstented segments

Patterns of in-stent restenosis predict outcomes in the DES era?

- **Focal (N = 132) Repeat DES 57.1%, POBA 42.9%**
- **Non focal (N = 71) Repeat DES 69%, POBA 31%**

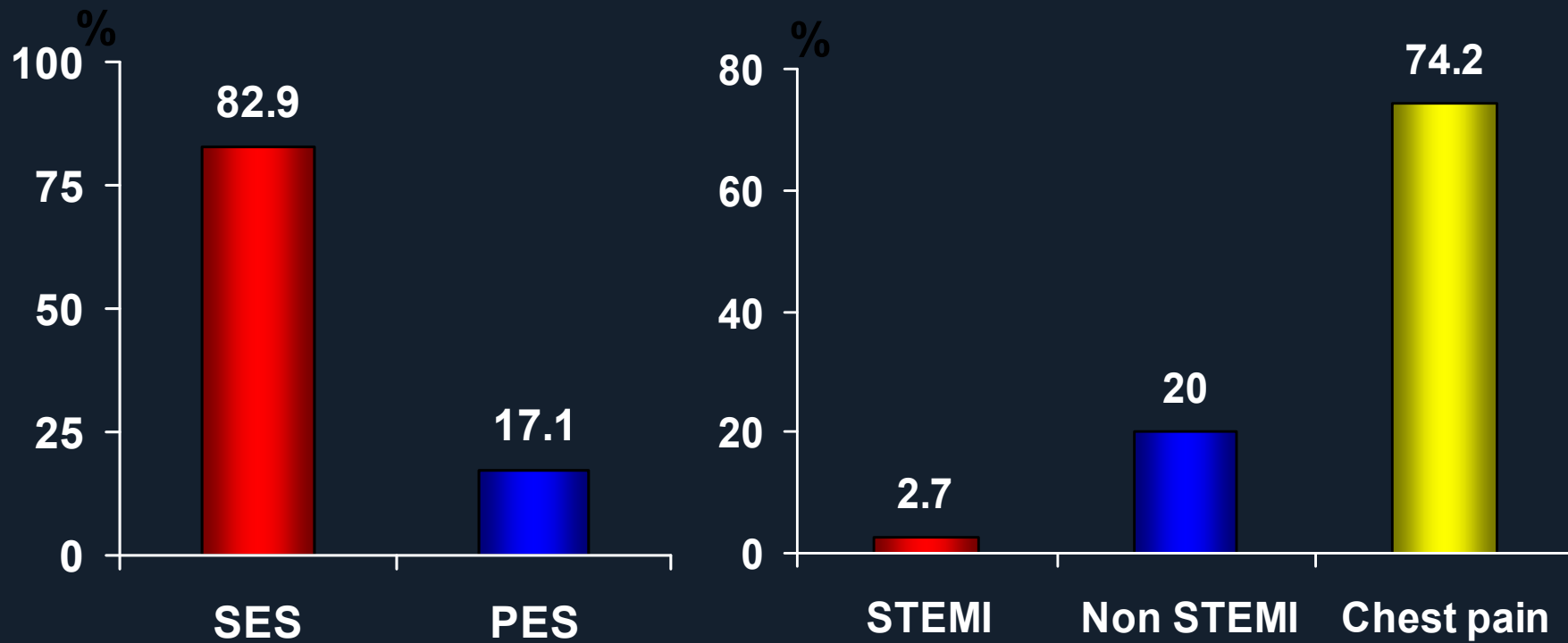


DES fractures



Incidence and clinical presentation of stent fractures

Among 188 pts with DES restenosis, stent fracture was identified in 35 (18.5%) cases.



Lack of Traditional Correlates for recurrence of ISR

- From 2003 to 2007, 535 patients presenting with angiographic ISR after DES implantation were included. Of these, 396 patients completed 1-year follow-up
- **The primary endpoint** was defined as clinically driven target lesion revascularization (TLR) at 1-year follow up
- Stepwise manner multivariable analysis (retention criteria $p < 0.2$) was used to determine predictors of recurrent ISR at 1-year follow-up

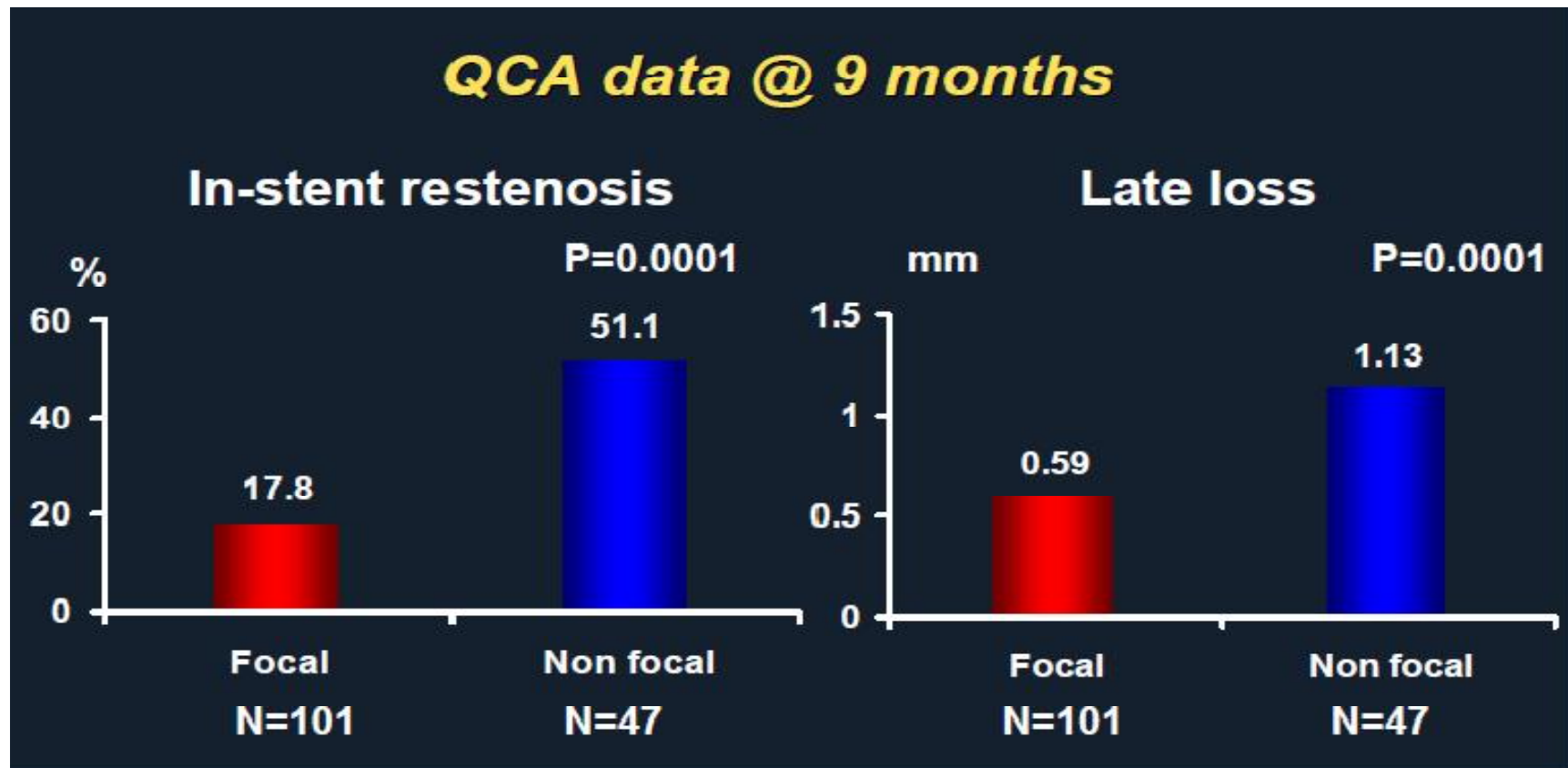
Non-adjusted predictors of recurrent ISR at 1-year follow-up

	HR	95% CI	Valor P
Age	1.0	0.99-1.05	0.9
Presentation with AMI	3.1	1.1-8.6	0.03
Diabetes	0.9	0.5-1.5	0.6
Chronic renal failure	1.1	0.5-2.3	0.7
Baseline Us-CRP	1.0	0.99-1.05	0.003
Prior VBT failure	1.3	0.3-5.2	0.7
Ostial location	1.4	0.3-6.1	0.7
Type C lesion, AHA/ACC	0.5	0.1-2.2	0.3
Therapy option	0.9	0.4-2.0	0.9
VBT	0.8	0.3-2.5	0.4
c-PCI	0.7	0.4-1.4	0.3
Diffuse ISR (> 10 mm)	1.7	0.2-13	0.6
Focal ISR (< 10 mm)	1.9	0.3-14	0.5
Stent diameter	1.7	0.8-4.1	0.5

DES Restenosis Therapeutic approaches

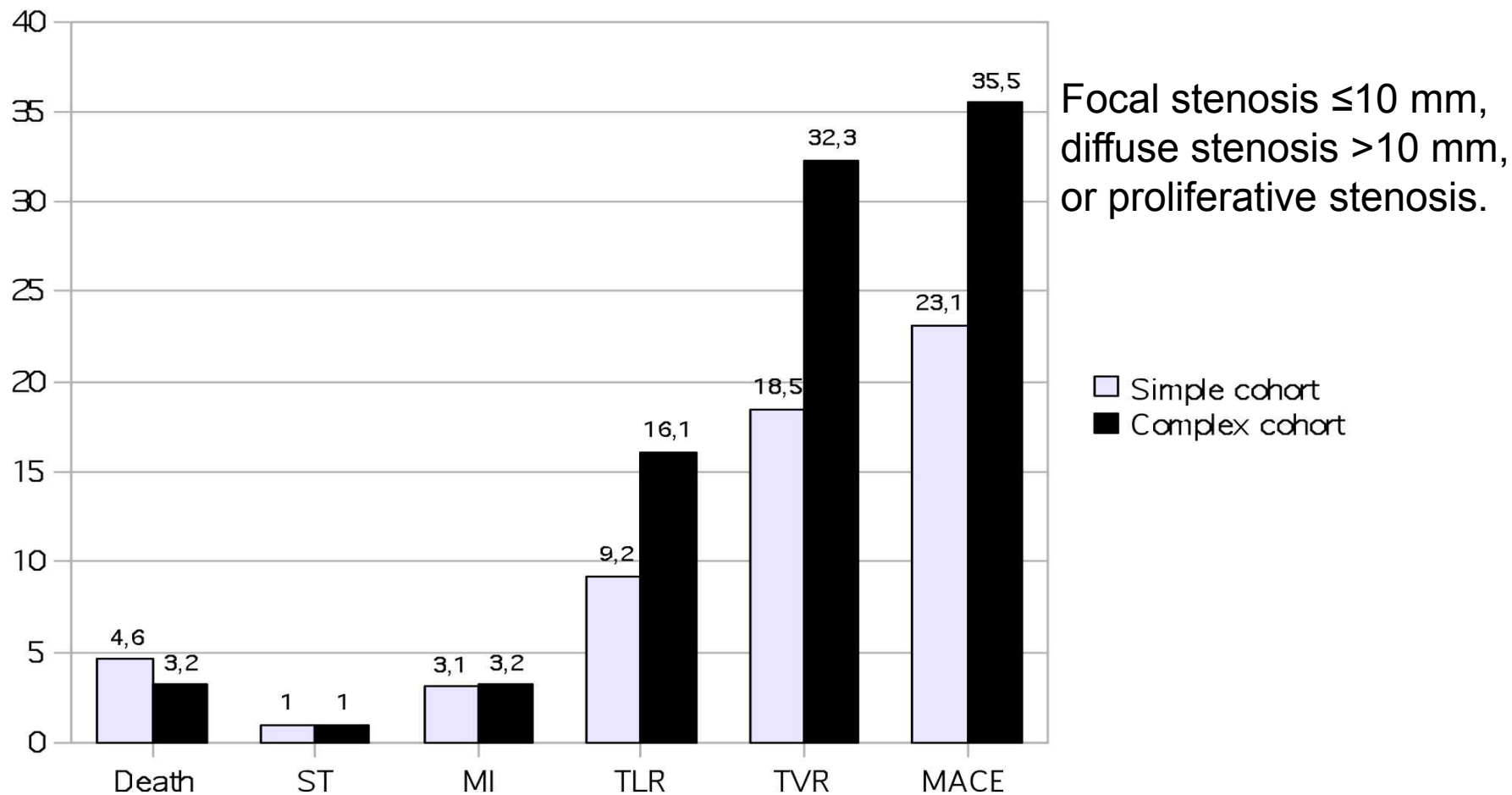
- Conventional POBA, Cutting Balloon**
- Same versus Different DES**
- Vascular Brachytherapy***
- Drug Eluting Balloon***
- CABG**

Do patterns of in-stent restenosis predict outcomes in the DES era?



Cosgrave J. et al. *JACC* 2006;47: 2399-404

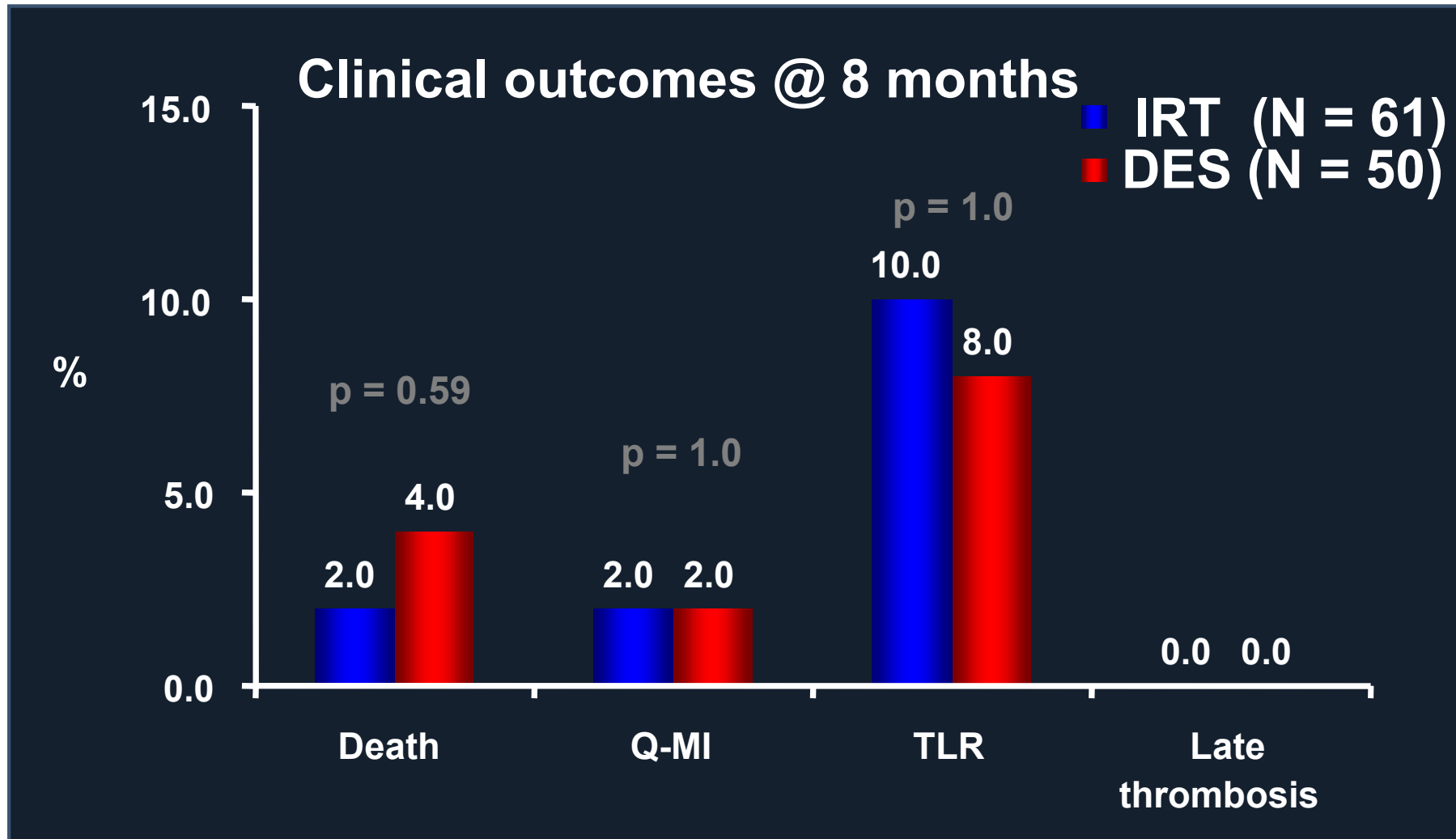
Vascular Brachytherapy: Effective Treatment for Patients with Drug-eluting Stent Restenosis



Bonelloo, Waksman et al. J Interv Cardiol. 2008

Radiation (IRT) vs DES for DES Failures

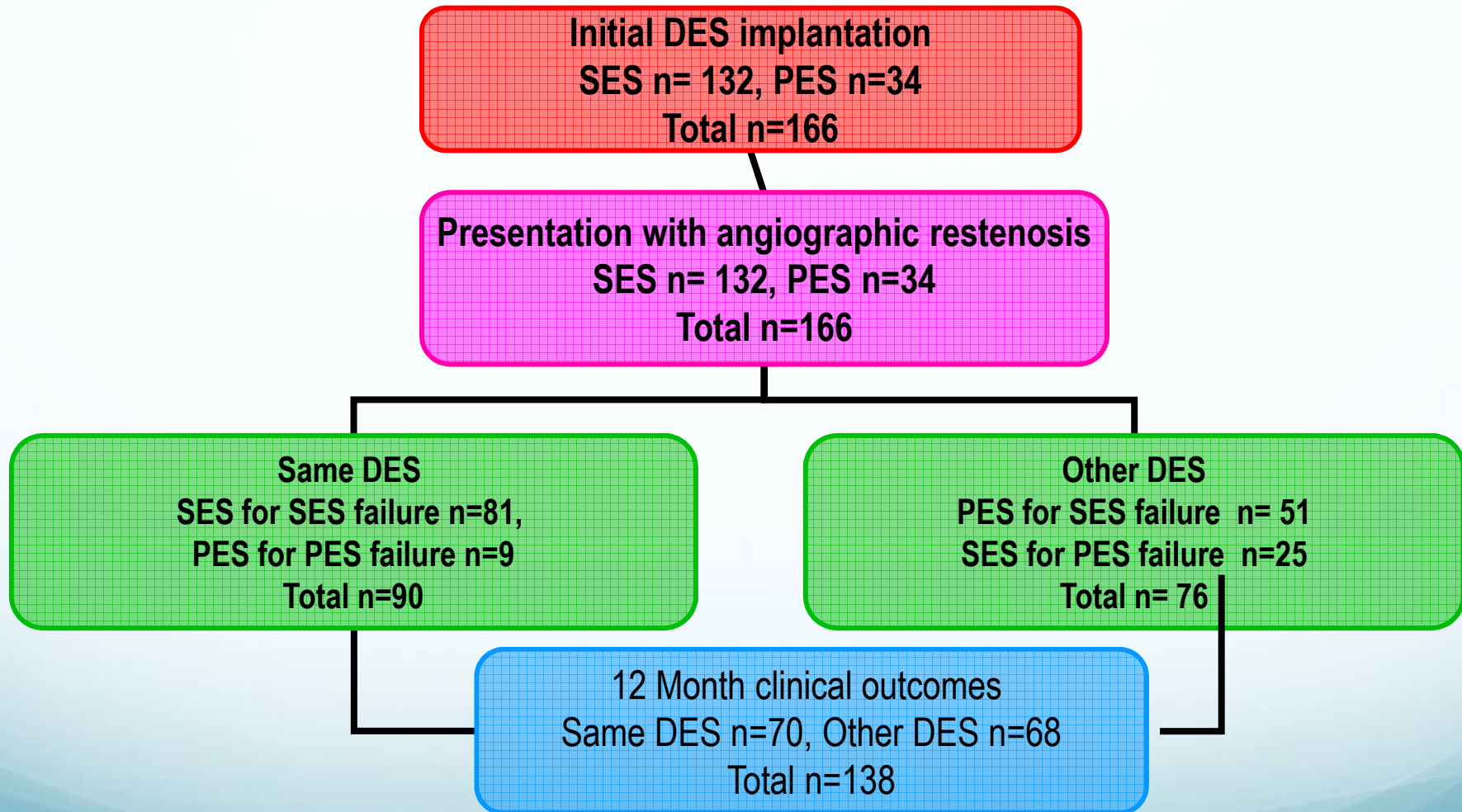
Results form the RESCUE Trial



Treatment of Drug-Eluting Stent Restenosis with the Same or Different Drug-Eluting Stent: To Switch or not to Switch

Kimberly Smith Kaneshige, Rebecca Torguson, Zhenyi Xue, Daniel H. Steinberg, Tina L. Pinto Slottow, Probal K. Roy, Saquib Samee, Joseph Lindsay, Augusto D. Pichard, Lowell Satler, William O. Suddath, Kenneth Kent, Ron Waksman
Washington Hospital Center, Washington, DC

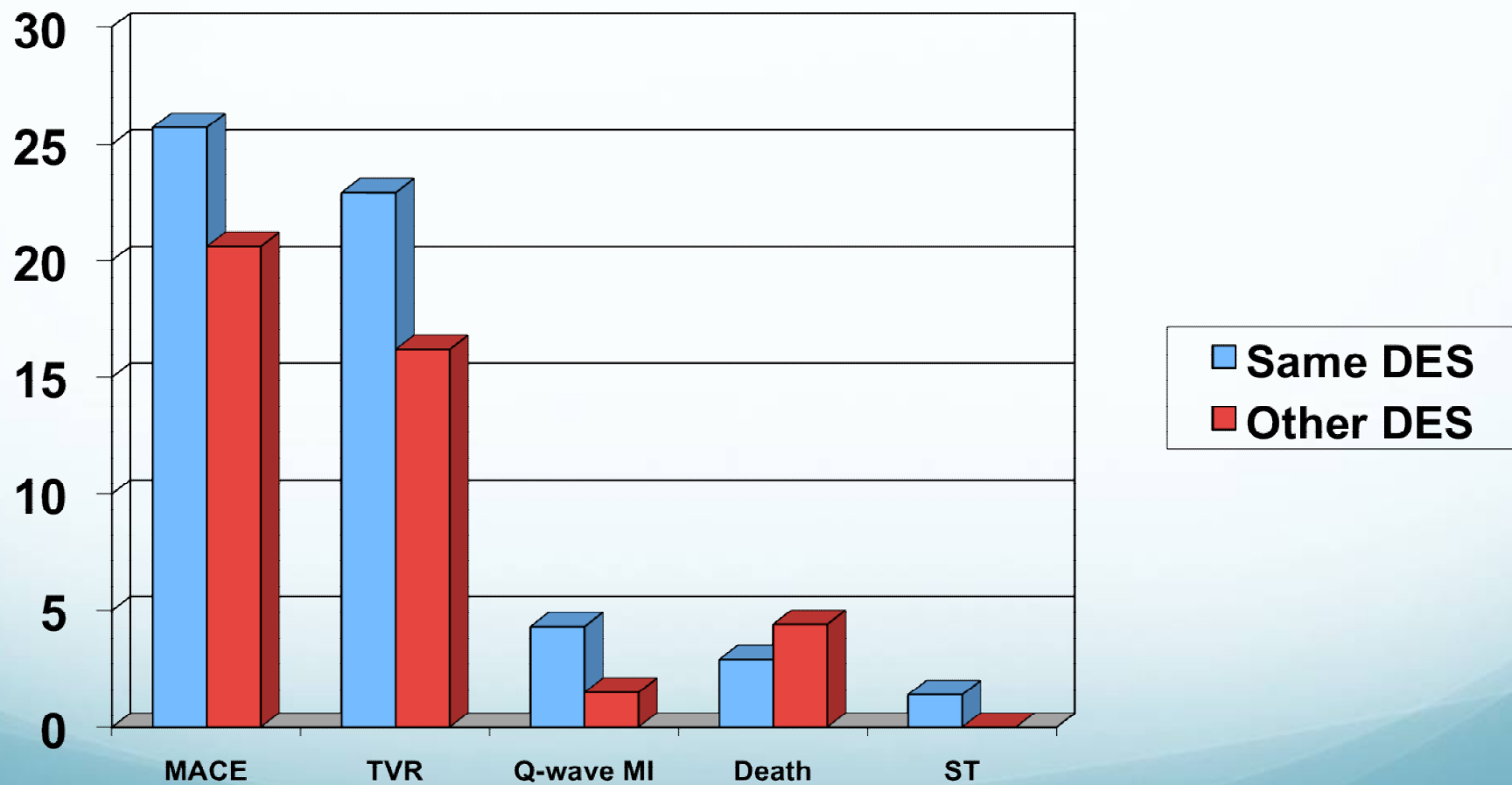
Study Design



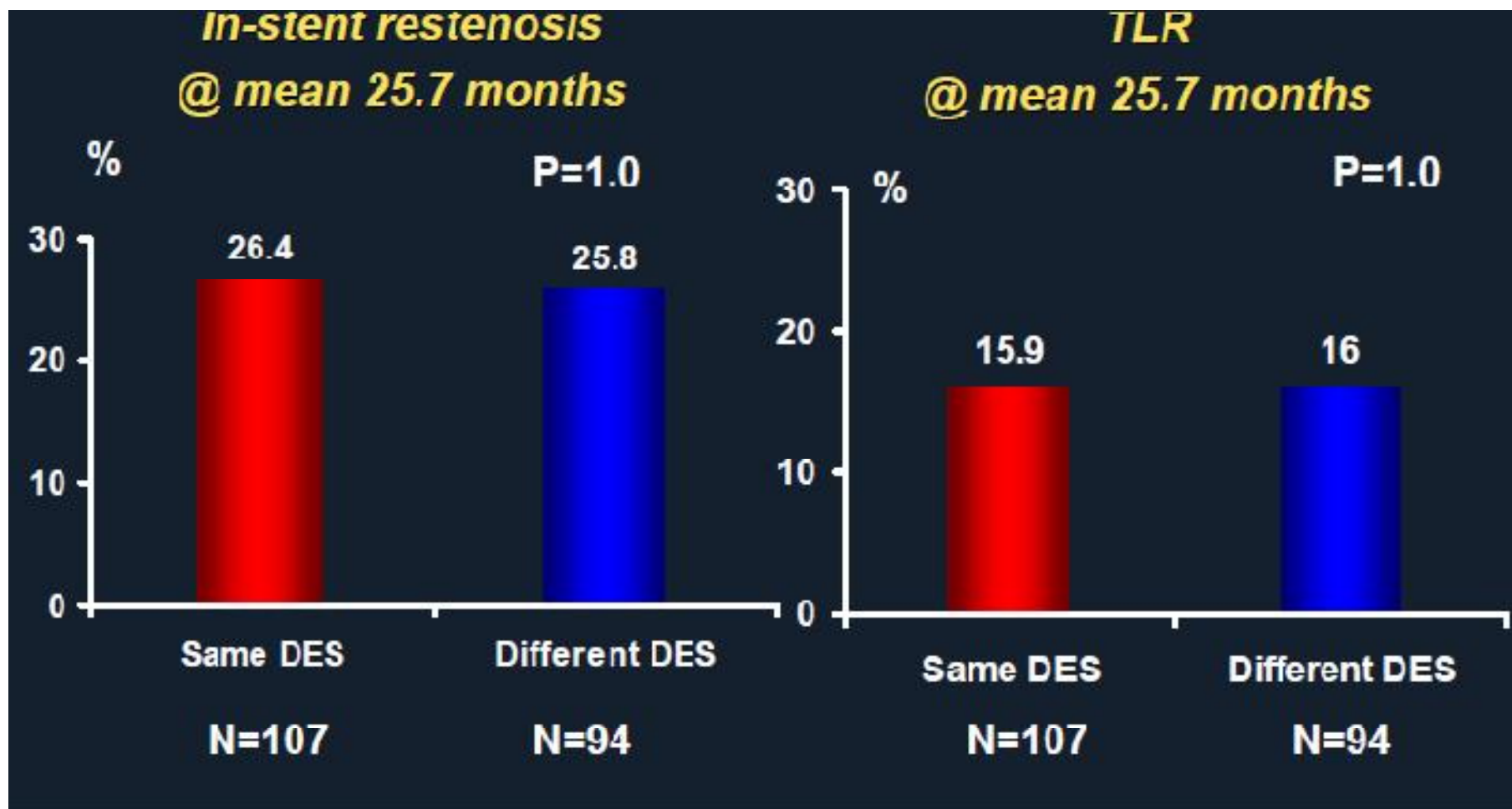
Indication for Implantation of Failed DES

Clinical Indications (%)	Same DES n=90	Other DES n=76	p Value
Stable Angina	35.6	32.9	0.719
Unstable Angina	40.0	39.5	0.945
Silent Ischemia	6.7	9.2	0.543
ST-elevation Myocardial Infarction	11.1	7.9	0.484

12 Month Similar Between Same versus Other DES



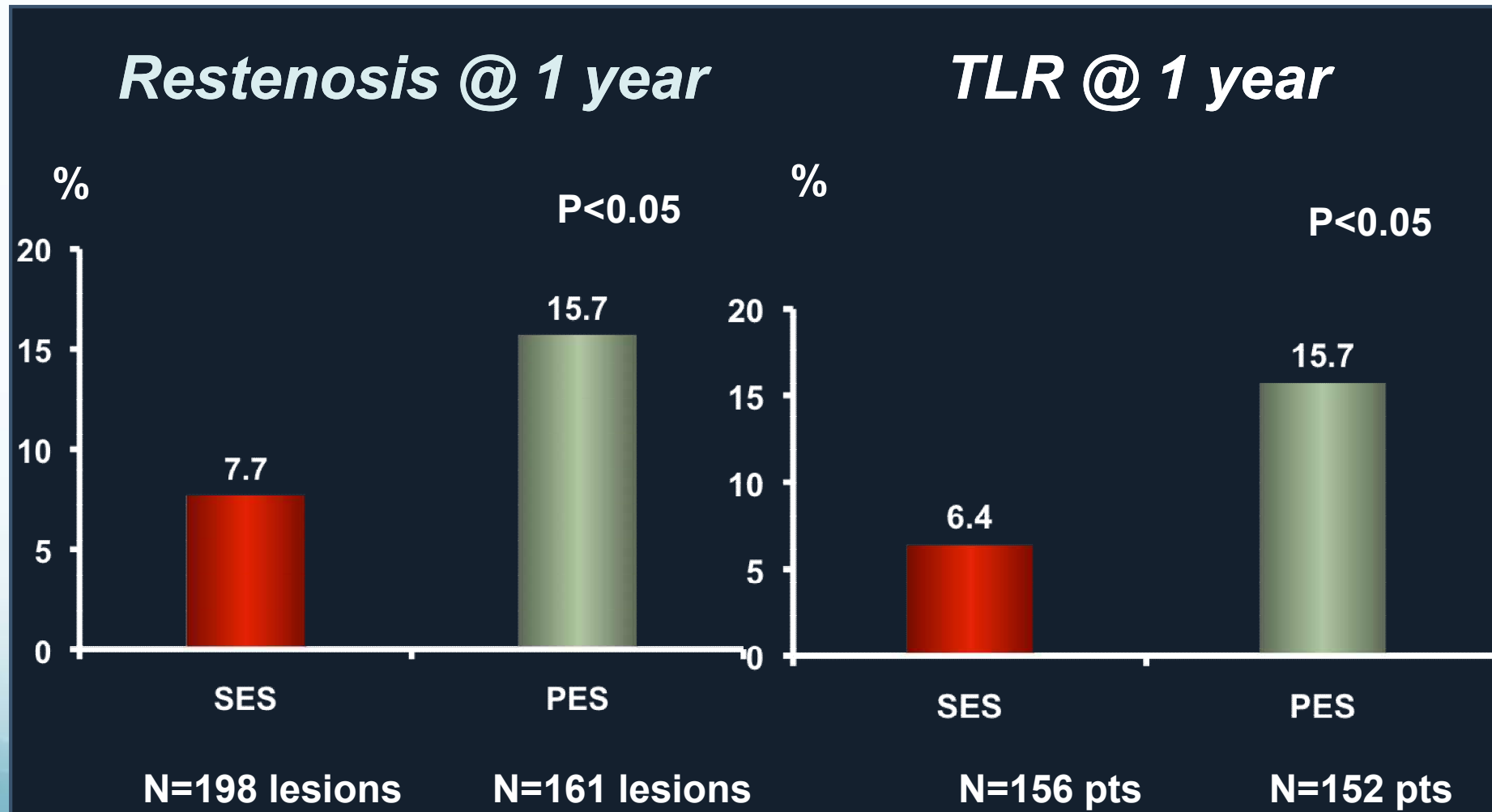
Same DES vs other DES vs other treatment for DES Failures



Cosgrave J. et al. *AHJ*.2007;153: 354-9

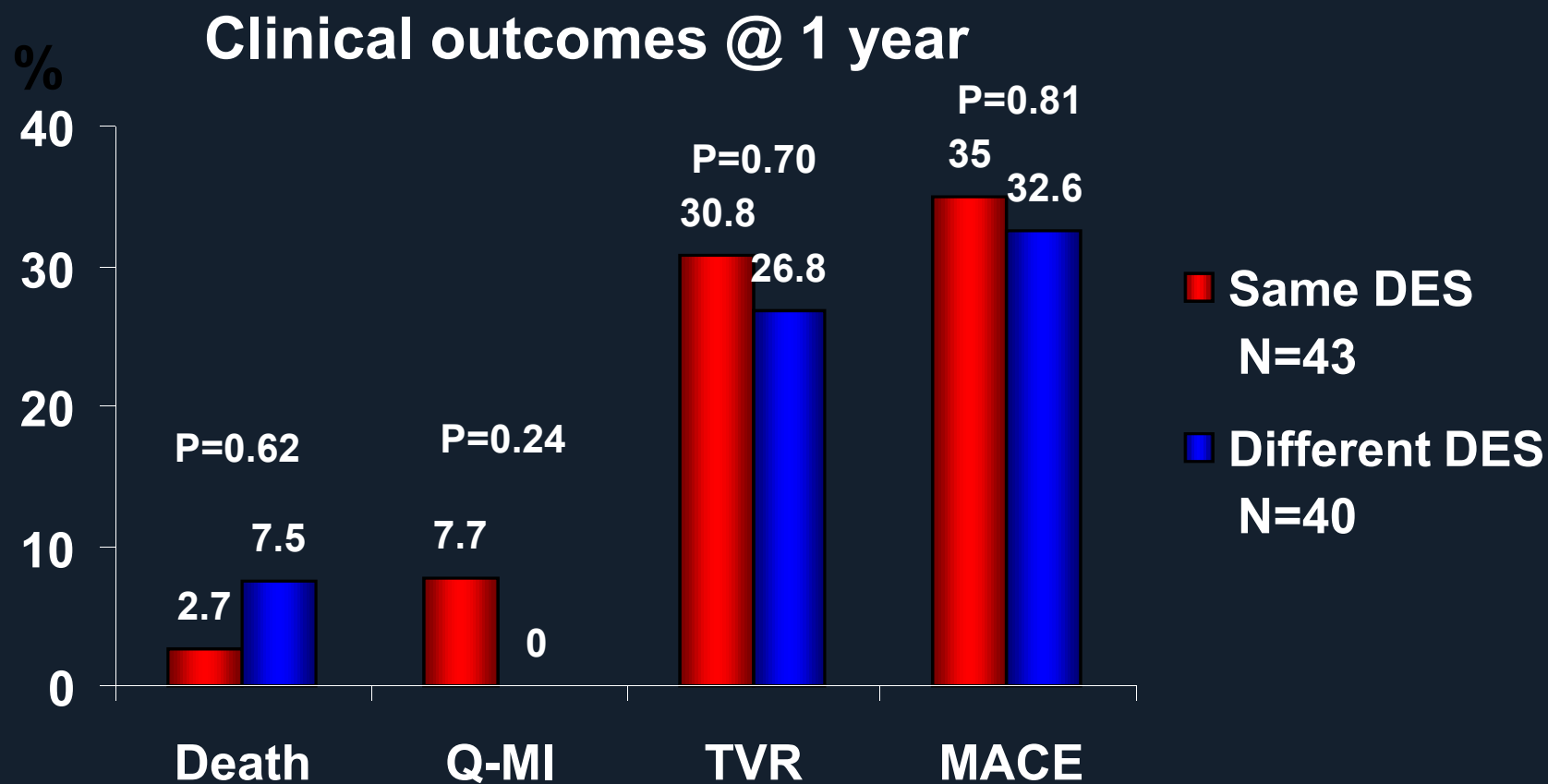
SES vs PES for SES Failures

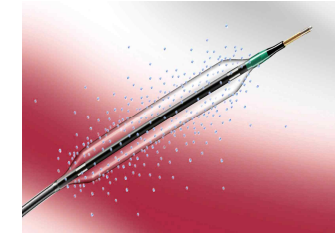
Multicenter Registry in Asia



Same DES vs other DES vs. other treatment for DES Failures

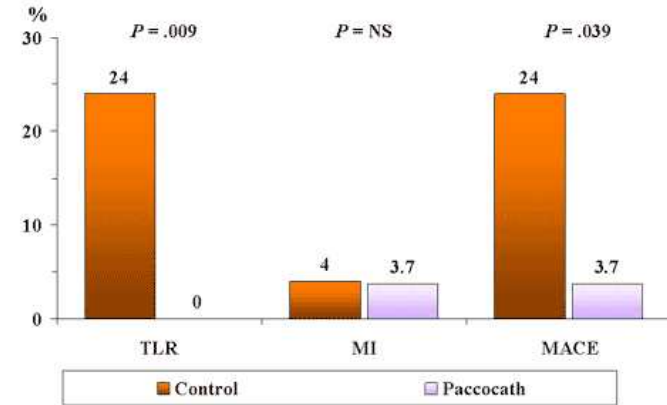
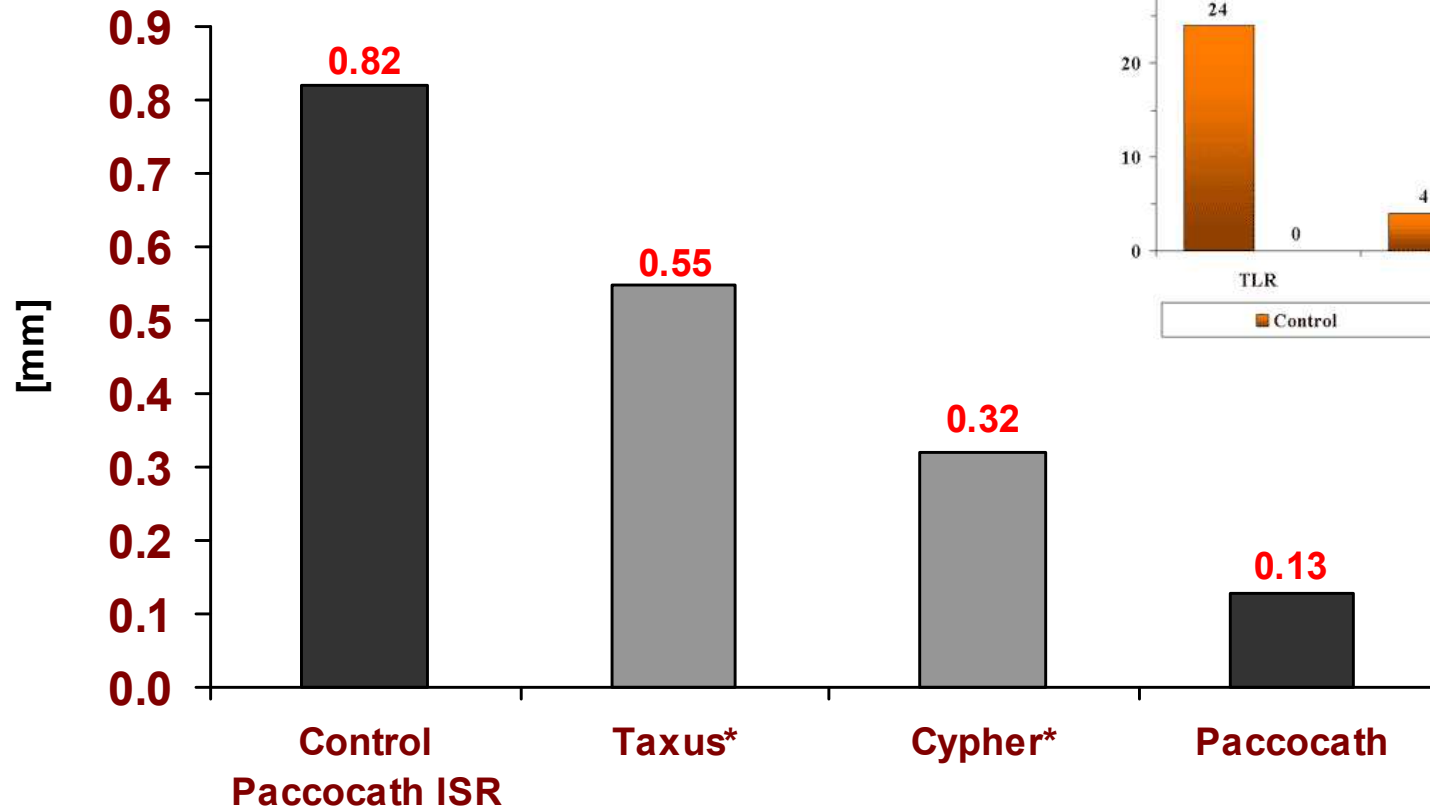
Does the Switch Therapy work?





Late loss in-segment - comparison Paccocath ISR I with ISAR DESIRE

Medscape® www.medscape.com

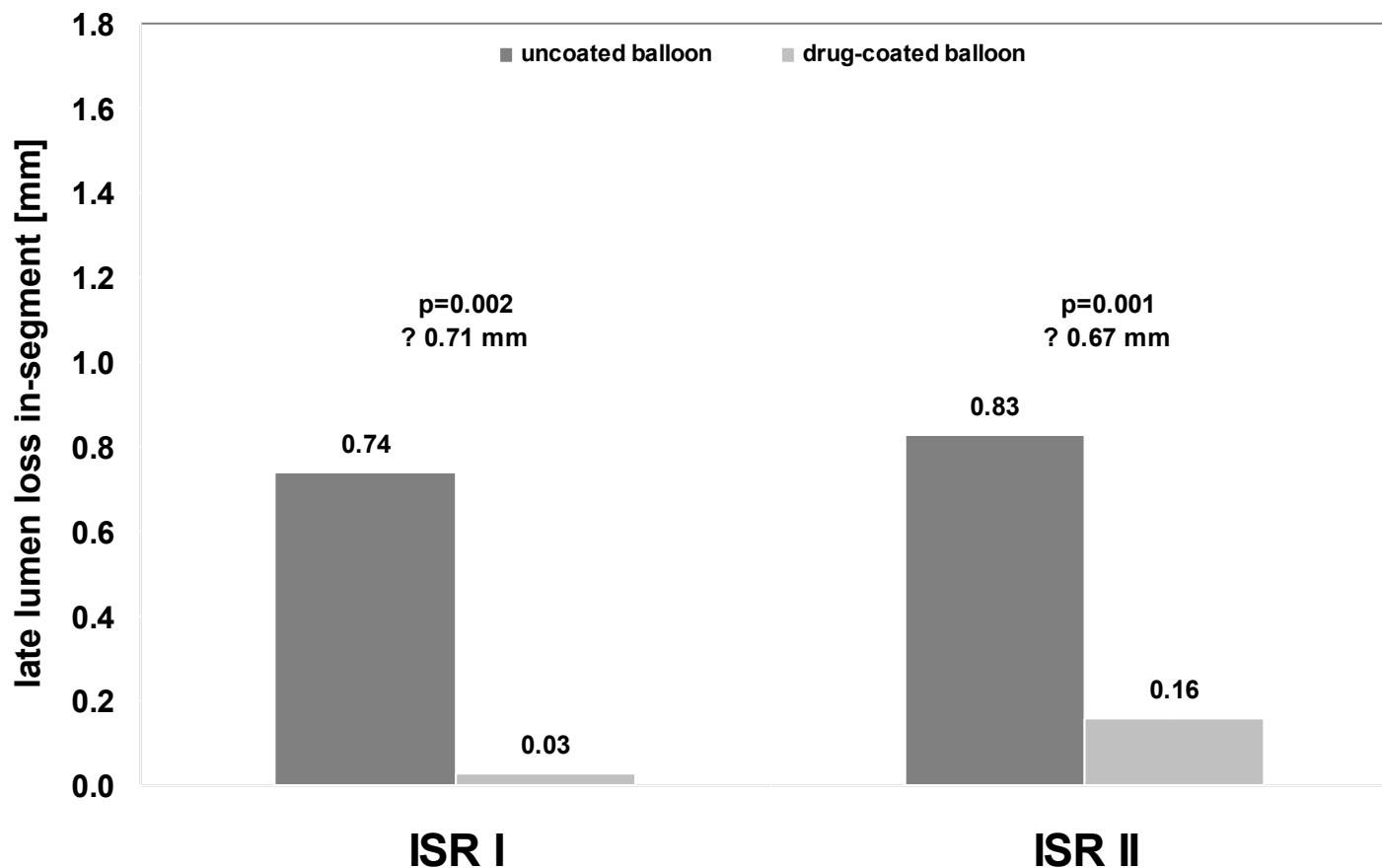


*data from ISAR DESIRE; Kastrati, JAMA 2005; 293: 165 - 71

Drug Eluting Balloon

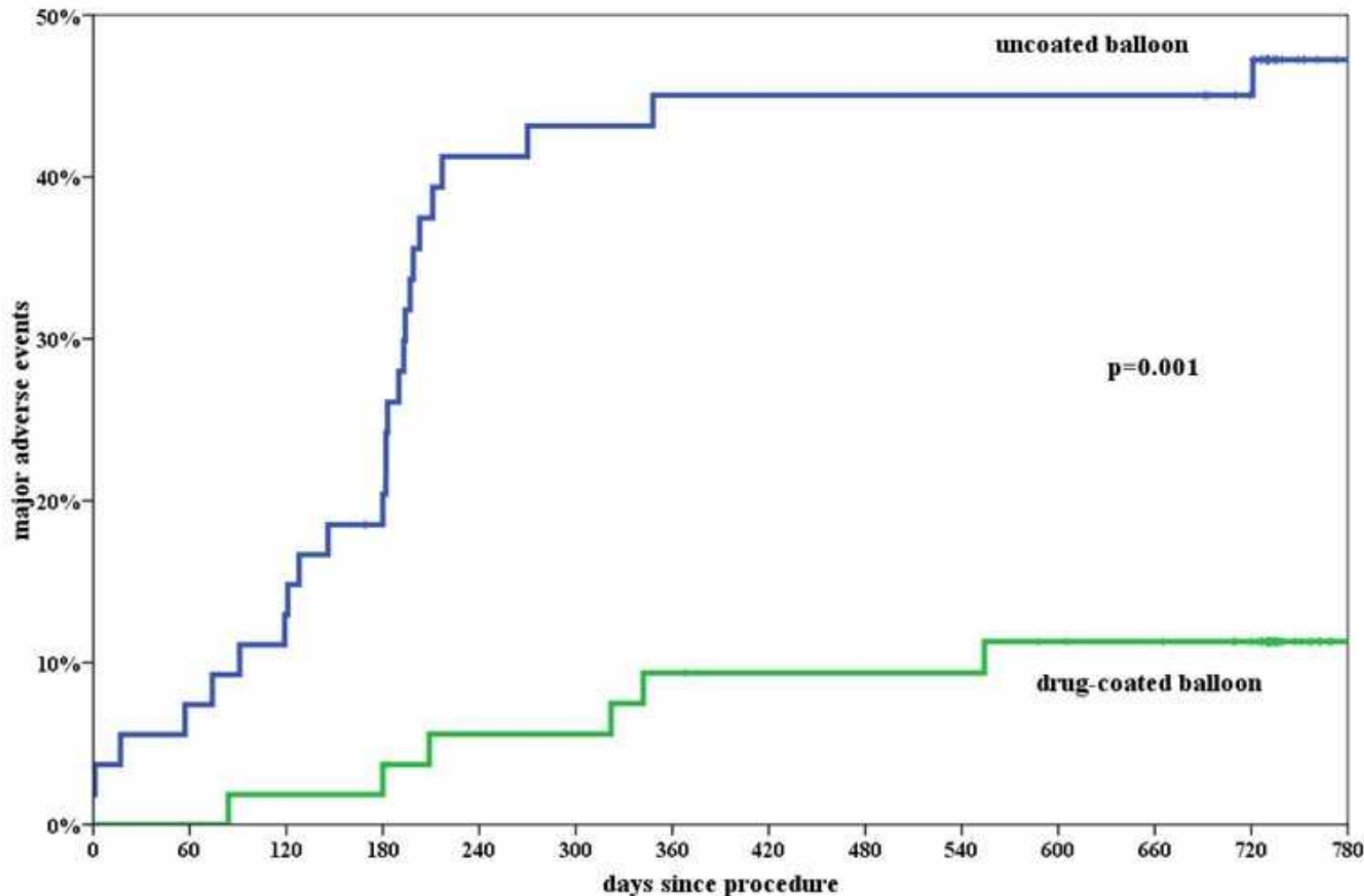
Paccocath ISR I vs. II

Late lumen loss in-segment



Paccocath ISR I/II - MACE

TLR, MI,
acute/subacute
closure, stroke, or
death



No. at risk

Drug-coated balloon	54	53	51	49	49	48	48
Uncoated balloon	54	47	32	30	30	30	29

The Valentine Trial

A CRT 2010 - DIOR Worldwide Trial

DEB for ISR of BMS and DES

The Valentines trial is a unique first of it's kind registry.

From Valentines day (14. Feb. 2010) till the end of the CRT congress
in Washington (23. Feb. 2010) it will enrol as many ISR cases
of a previous placed stent as possible



Current therapeutic options according to potential mechanisms of DES restenosis

Type of restenosis	Potential mechanisms	Treatment options
Focal in-stent	Underexpansion	BA
	Fracture	DES, BA
	Local vessel biology	DES, BA, DEB
	Heterogeneous drug distribution	DES, BA, DEB VBT
Focal at stent edge	Geographic miss	DES
	Plaque progression	DES
Diffuse in-stent	Vessel biology / Drug resistance	Different DES, CABG VBT DEB
Proliferative	Vessel biology / Drug resistance	Different DES, VBT CABG DEB

DES Restenosis

Summary

- ❑ Restenosis after DES still occurs and at a disturbing frequency in the highest risk lesion/patient subsets.**
- ❑ Underlying mechanism of DES restenosis involve a complex interplay of biological, mechanical, and technical (operator-dependent) factors.**
- ❑ Strut fractures are more frequent than previously suspected, occurring most commonly at the edge of an overlap segment and they have been implicated in many clinical events, including restenosis, thrombosis, and aneurysm formation.**

Summary

- The treatment of DES restenosis is based on appreciation of underlying mechanisms and can vary from simple POBA, to DES.**
- Drug Eluting Balloon is currently tested for this applicattion**
- When appropriate, VBT or CABG remains an effective therapeutic option**
- The absence of the traditional predictors for ISR in this population invokes the presence of unrecognized predisposed conditions**