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Drug-Eluting Stent Failure: Why & How?
Drug Eluting Balloon for In-Stent Restenosis: The New Standard of Care

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Disclosure Statement of Financial Interest

I DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Advantages of DEB Angioplasty for In-Stent Restenosis

Efficacy

Predominantly firm fibrous nature of neointimal hyperplastic tissue makes acute vessel wall recoil and abrupt vessel closure after PTCA less likely, obviating need for stent placement

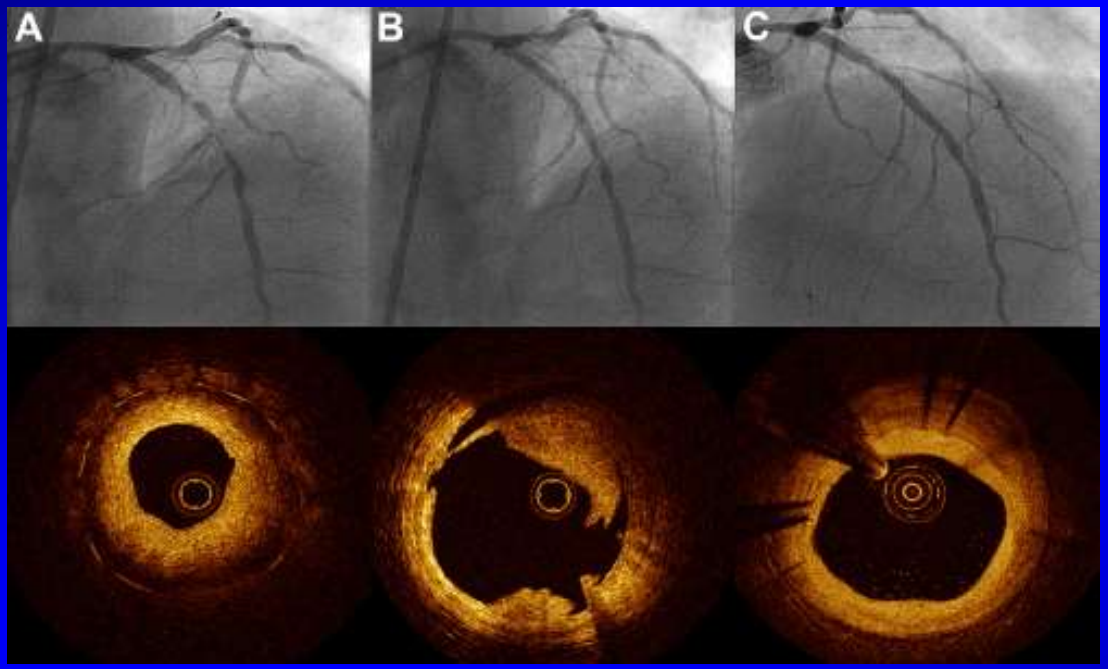
Safety

- Shorter duration of drug release and lack of second durable polymer/stent platform favours earlier vascular healing, reduced hypersensitivity, and lower likelihood of stent thrombosis

- Shorter duration of DAPT results in lower bleeding risk and medical cost

Understanding Mechanism of Action of DEB With Angiography & OCT

25 pts with ISR treated with DEB had serial angiographic, OCT and FFR measurements performed before, after procedure and at 6 months



- **Acutely,** DEB mechanically increase lumen and stent volumes by compression of neointimal hyperplasia, with intra-stent dissection; dilatation of old stent
- **At 6 months,** further increase in lumen volume and decrease in neointimal volume, and complete sealing of neointimal dissections ensure vessel patency
- **Mechanism**: Mechanical expansion + local drug release effect

PR Stella et al J Am Coll Cardiol Intv 2013; 6: 569-76

What Are the Evidence for DEB in ISR?

- RCT Comparison of DEB vs POBA
- Worldwide Registries of DEB
- RCT Comparison of DEB vs DES

What Are the Evidence for DEB in ISR?

- **RCT Comparison of DEB vs POBA**
- Worldwide Registries of DEB
- RCT Comparison of DEB vs DES

Treatment of Coronary In-Stent Restenosis with a Paclitaxel-Coated Balloon Catheter (PACCOCATH ISR 1)

- 52 pts with ISR randomised to DEB and uncoated balloon
- Primary endpoint: 6 mth late luminal loss on angiography

Primary endpoint (late lumen loss in-segment)

Uncoated balloon	PACCOCATH
0.74 ± 0.86 mm	0.03 ± 0.48 mm

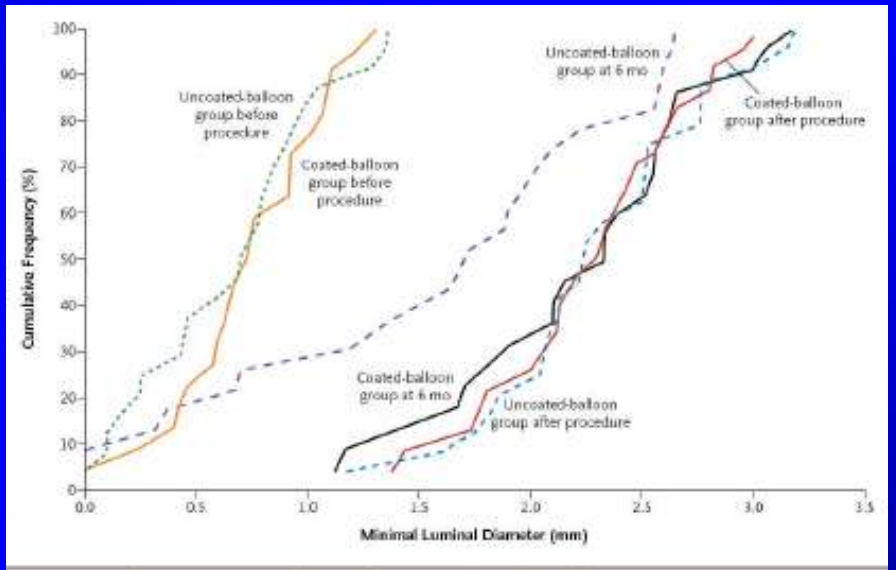


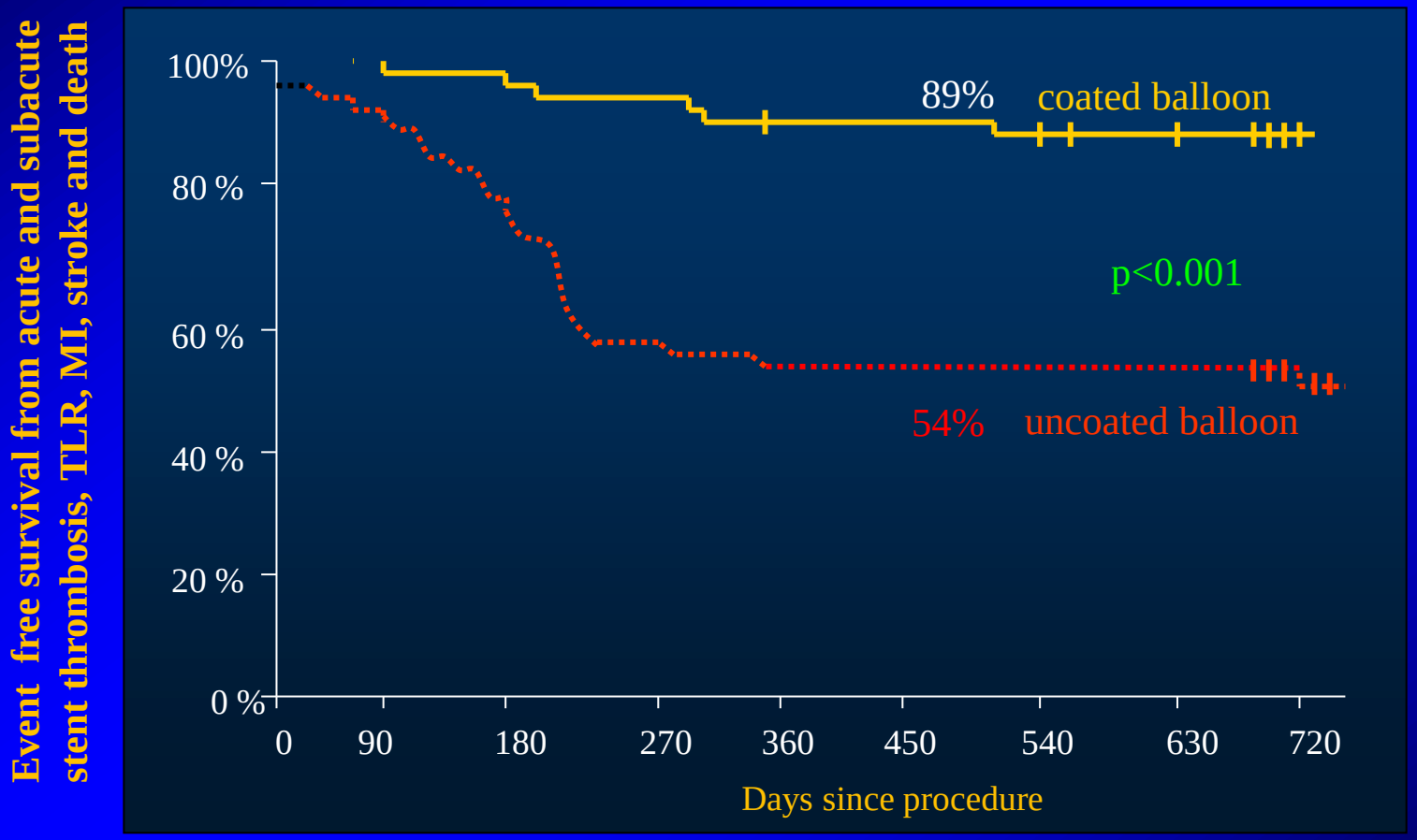
Figure 1. Cumulative Frequency Distribution of In-Segment Minimal Luminal Diameter on Quantitative Coronary Angiography (Intention-to-Treat Analysis).

Data are shown for the uncoated-balloon group and the coated-balloon group before the procedure, after the procedure, and at 6 months.

Conclusions: Treatment of coronary ISR with paclitaxel-coated balloon catheters significantly reduced the incidence of restenosis. Inhibition of restenosis by local drug delivery may not require stent implantation & sustained drug release at the site of injury

Scheller B et al New J of Medicine 2006; 355: 2113-2124

PACCOCATH ISR I/II: Two-Year Follow-up after Treatment of Coronary In-stent Restenosis with Paclitaxel-Coated Balloon Catheter (n=108)



Scheller B et al Clin Res Cardiol 2008; 97: 779-81

PEDCAD-DES

Multicentre randomised comparison of 110 pts with DES ISR to paclitaxel-coated balloon angioplasty or uncoated balloon angioplasty

Clinical Outcomes at 6 Months			
	Drug-Coated Balloon (n=72)	**Uncoated Balloon (n=38)**	***P* Value**
Target lesion revascularization	**11 (15.3%)**	**14 (36.8%)**	**0.005**
Myocardial infarction	0 (0.0%)	1 (2.6%)	0.35
Cardiac death	1 (1.4%)	4 (10.5%)	0.048
MACE	12 (16.7%)	19 (50.0%)	<0.001
Stent Thrombosis			
Definite	0	0	
Possible	1 (1.4%)	4 (10.5%)	0.048

Angiographic Outcomes at 6 Months According to Type of Restenotic Stent			
	Drug-Coated Balloon	**Uncoated Balloon**	***P* Value**
Non-PES	56	31	
Late lumen loss, mm	0.41 ± 0.65	0.90 ± 0.65	0.004
PES	16	7	
Late lumen loss, mm	0.46 ± 0.50	1.58 ± 1.03	0.021

Rittger H et al J Am Coll Cardiol 2012; 59: 1377-82

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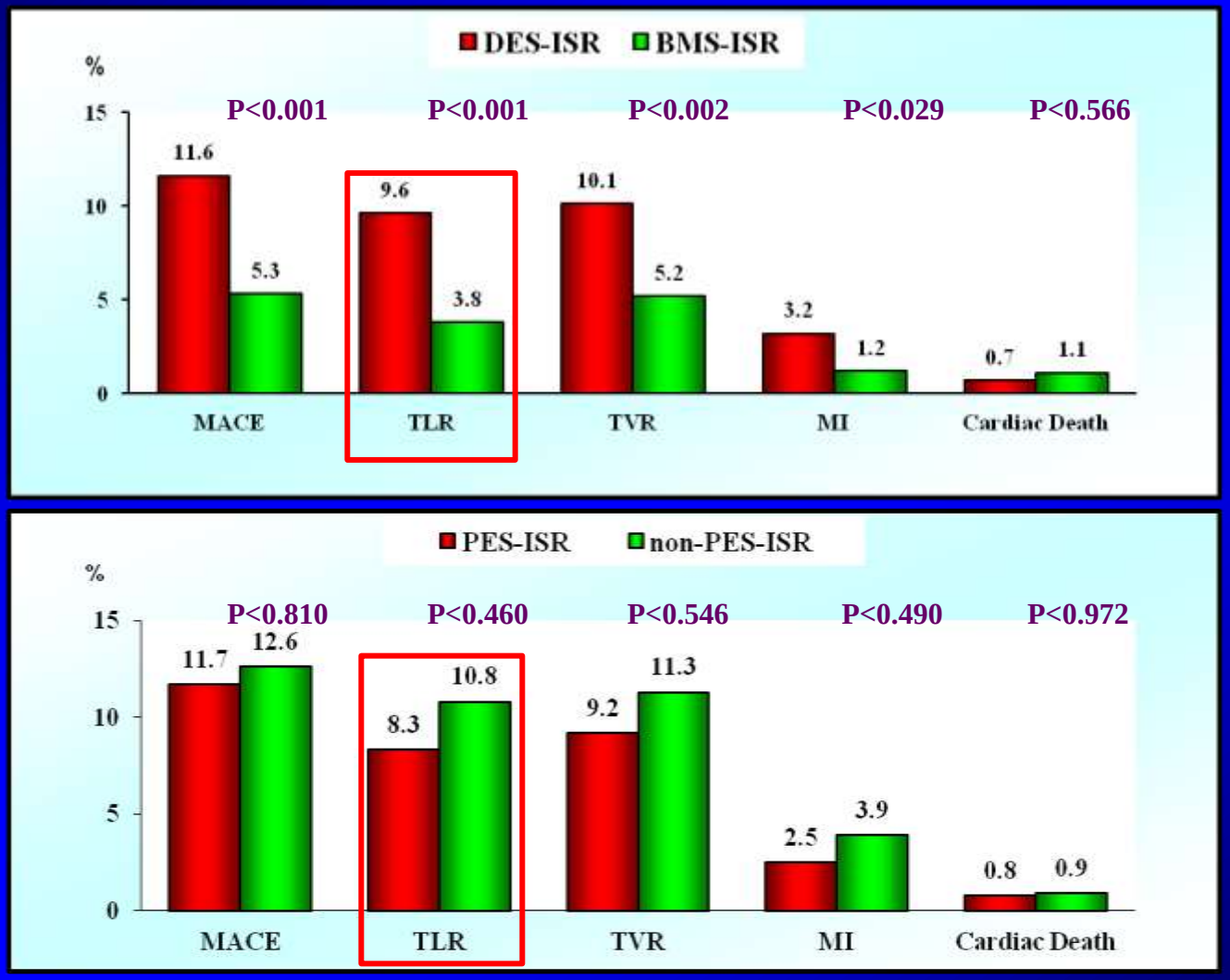
Sequent Please World Wide Registry: DEB in DES & BMS-Restenosis

1523 patients with DES & BMS-restenosis- 9-Month Outcome after paclitaxel-eluting balloon

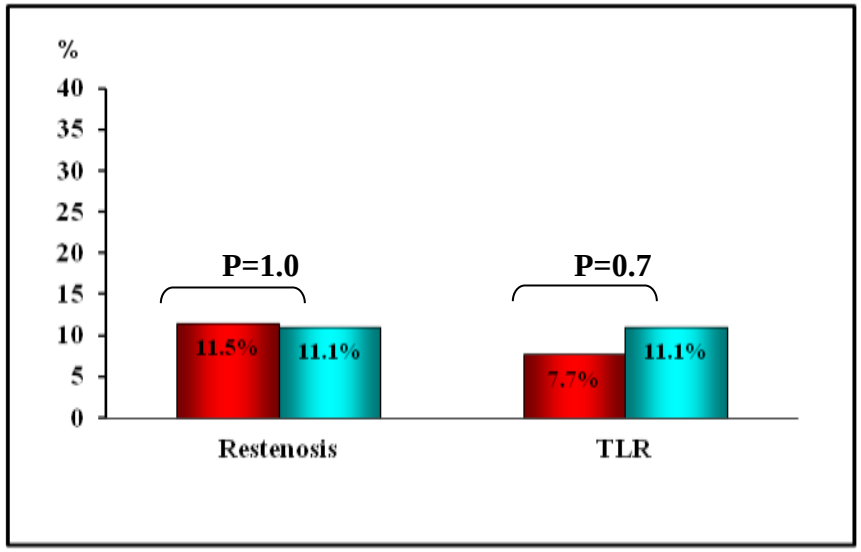


Wöhrle J et al J Am Coll Cardiol 2012; 60: 1733-8

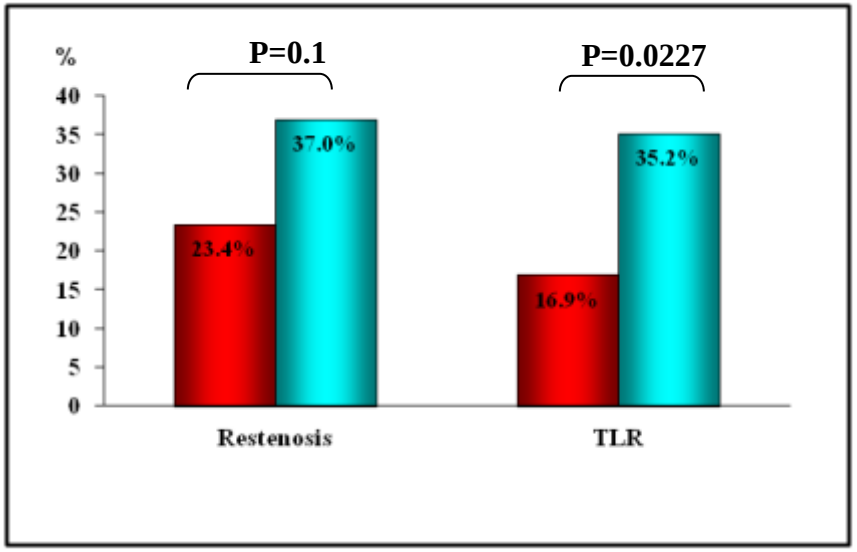
JAPAN DEB vs SES for Sirolimus-DES *Focal vs Proliferative* ISR: Binary Restenosis & Target Lesion Revascularisation

- 218 pts with 254 lesions between June 2004 to Mar 2011 with SES restenosis were enrolled in analysis
- Nonrandomised comparison of paclitaxel-eluting balloon vs repeat
- Follow-up rate: 70.6% (291/412 Lesions) DEB: 49, DES: 242

Focal lesion: n=115
(I b, I c)



Non-focal lesion: n=139
(I d, II, III, IV)



DEB
DES

Habara S et al Kurashiki General Hospital, Japan

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Interventional Cardiology

Paclitaxel-Coated Balloon Catheter Versus Paclitaxel-Coated Stent for the Treatment of Coronary In-Stent Restenosis

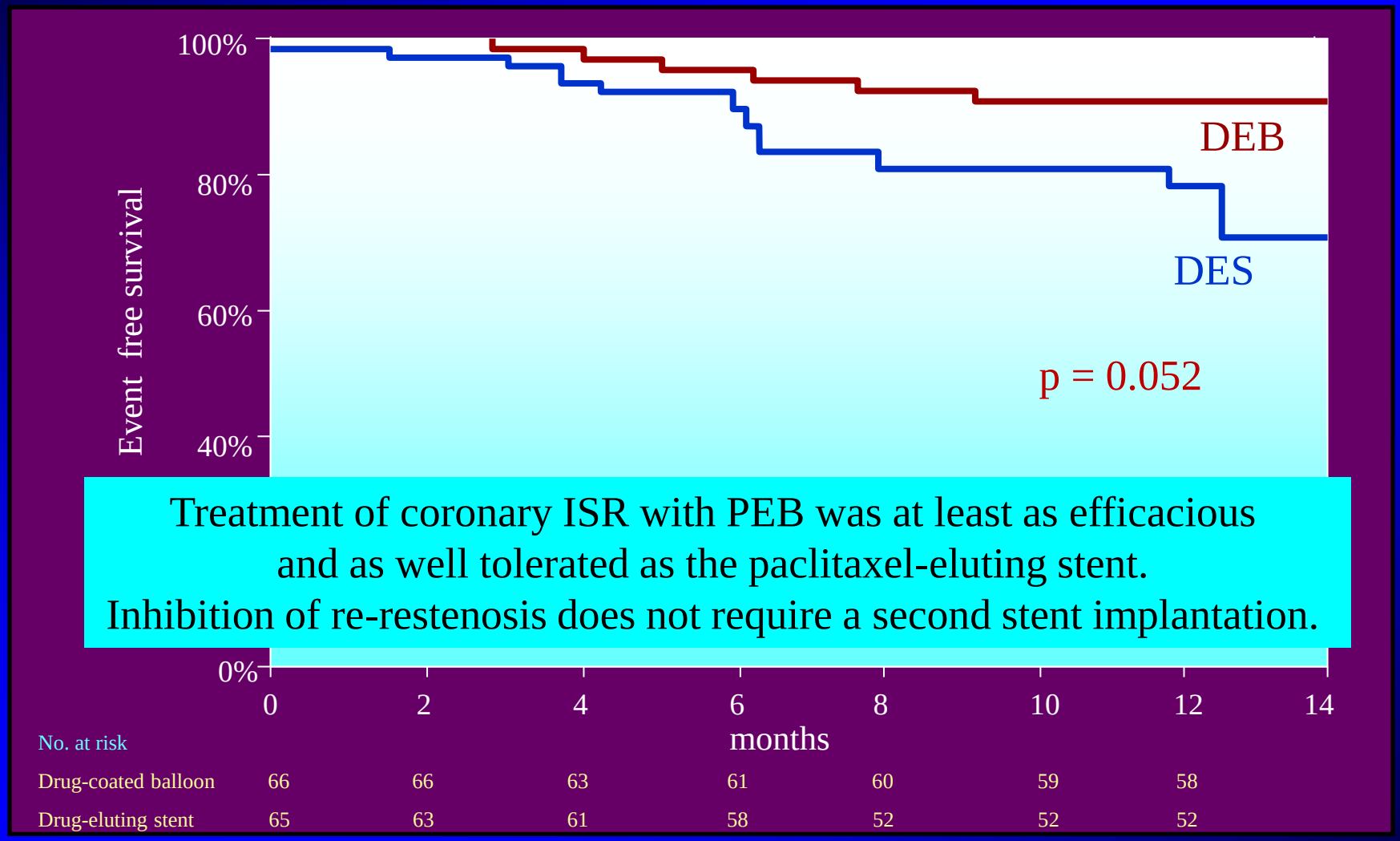
- Inclusion criteria: Diameter stenosis of ≥70% and ≤22 mm in length, with a vessel diameter of 2.5 to 3.5mm
- Primary endpoint was angiographic in-segment late lumen loss

PEPCAD II: Angiographic follow-up			
	DEB	**Taxus DES**	**p**
n	66	65	
Late lumen loss In-segment	0.17 ± 0.42 mm	0.38 ± 0.61 mm	0.03
Binary restenosis rate (In-segment)	7%	20%	0.04

Unverdorben M et al Circulation 2009; 119: 2986-2994

PEPCAD II: Clinical Follow-Up at 12 Mths

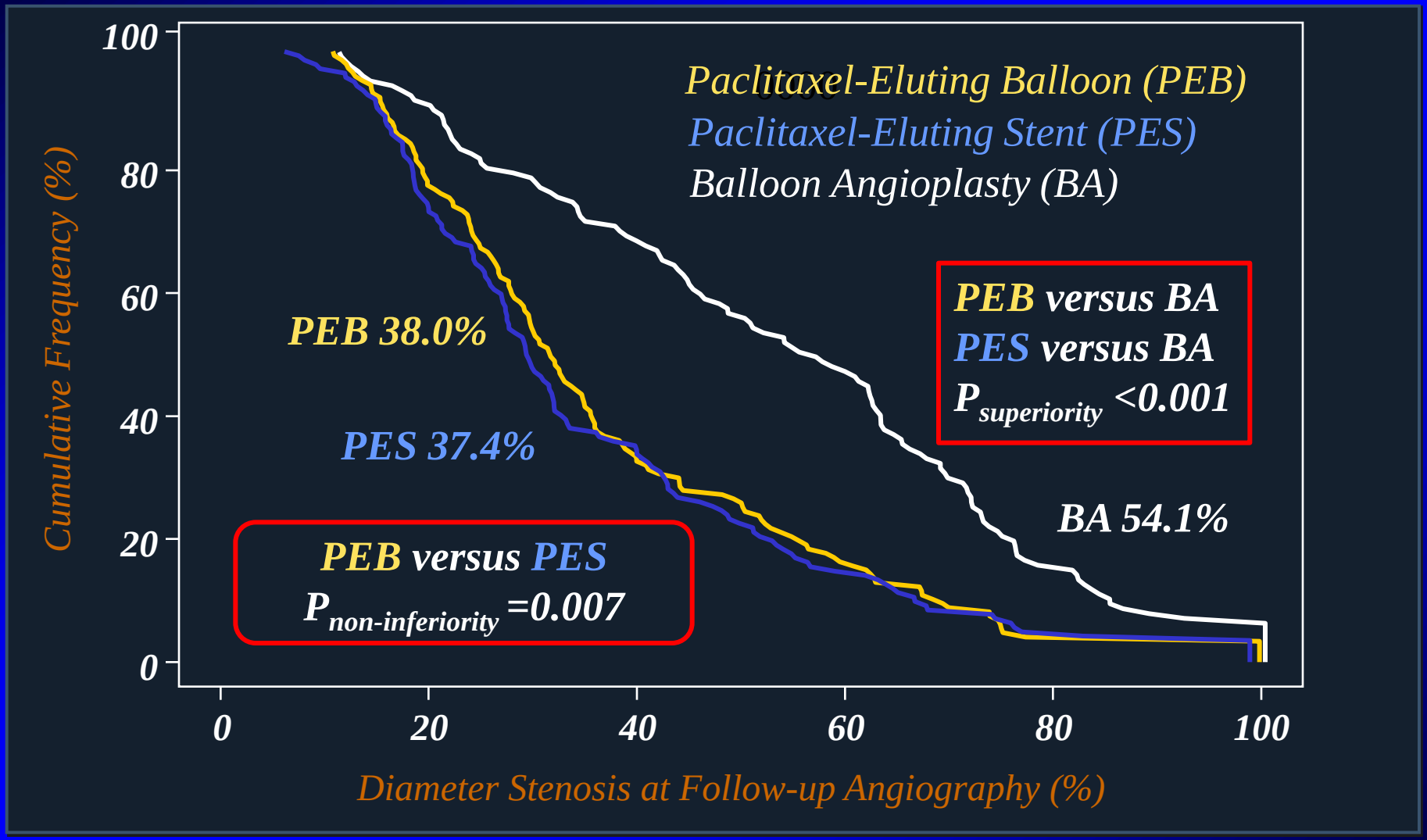
(Freedom from stent thrombosis, target lesion revascularization, myocardial infarction, and death – intention to treat)



Treatment of coronary ISR with PEB was at least as efficacious and as well tolerated as the paclitaxel-eluting stent.
Inhibition of re-restenosis does not require a second stent implantation.

Unverdorben M et al Circulation 2009; 119: 2986-2994

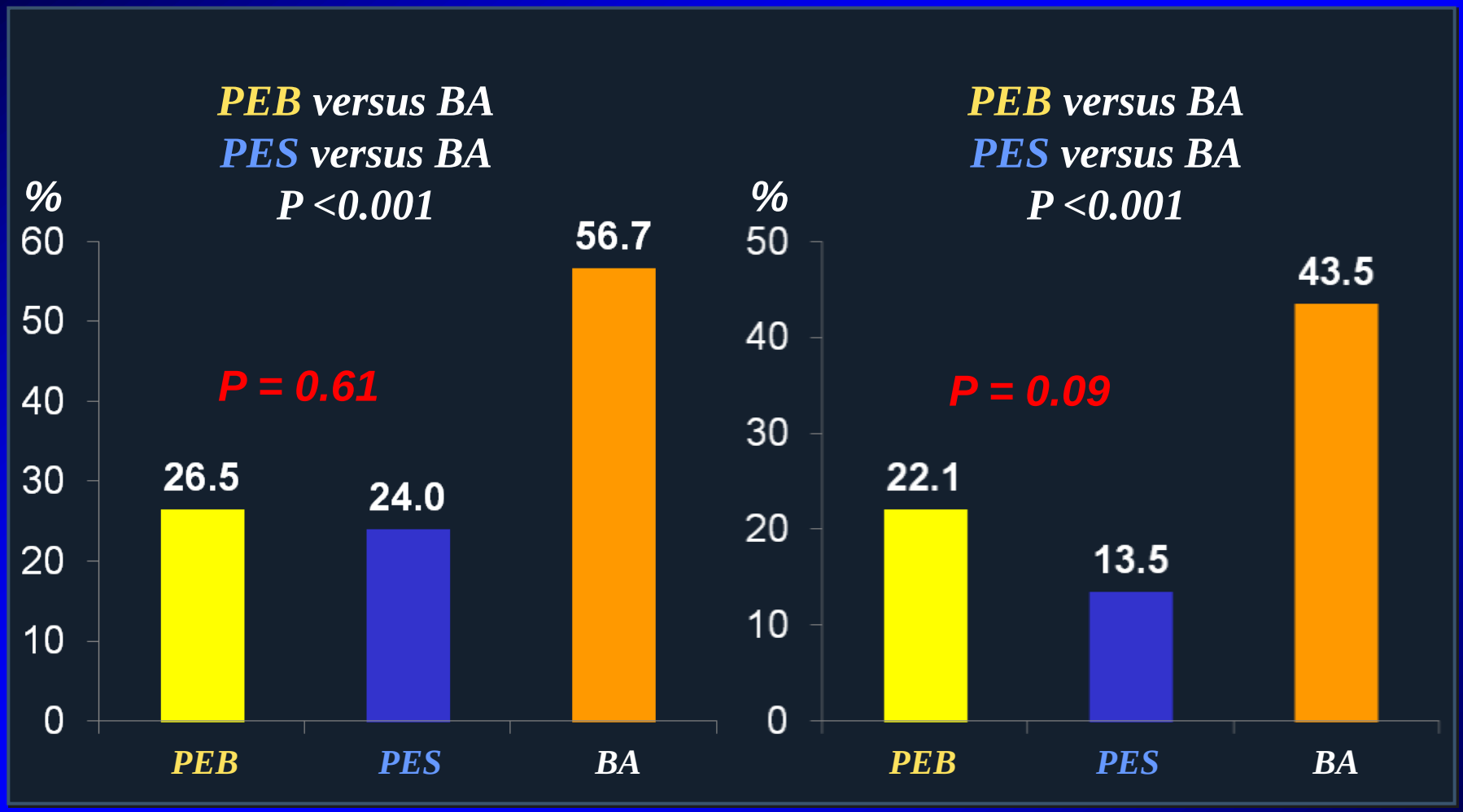
ISAR-DESIRE 3 (DES ISR): Primary Endpoint
Diameter Stenosis at Follow-up Angiography



RA Byrne et al TCT 2012

National University Health System

ISAR-DESIRE 3: Secondary Endpoint

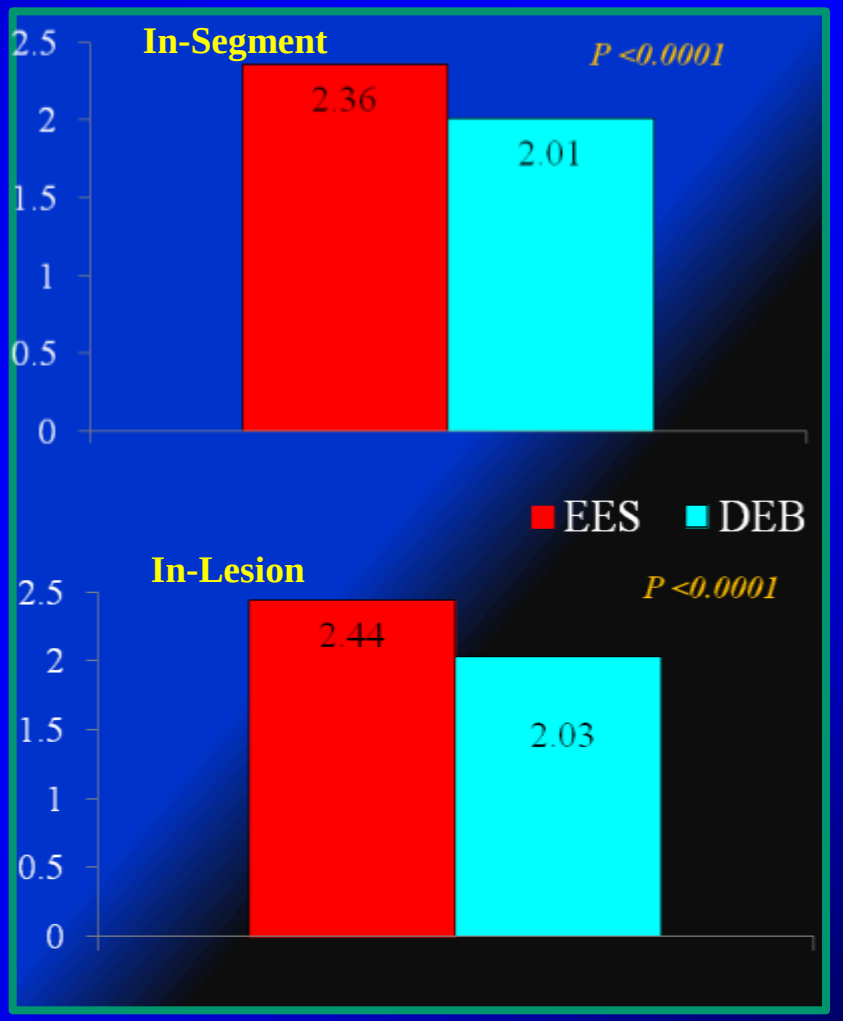


RA Byrne et al TCT 2012

RIBS V: Primary Endpoint MLD at FU

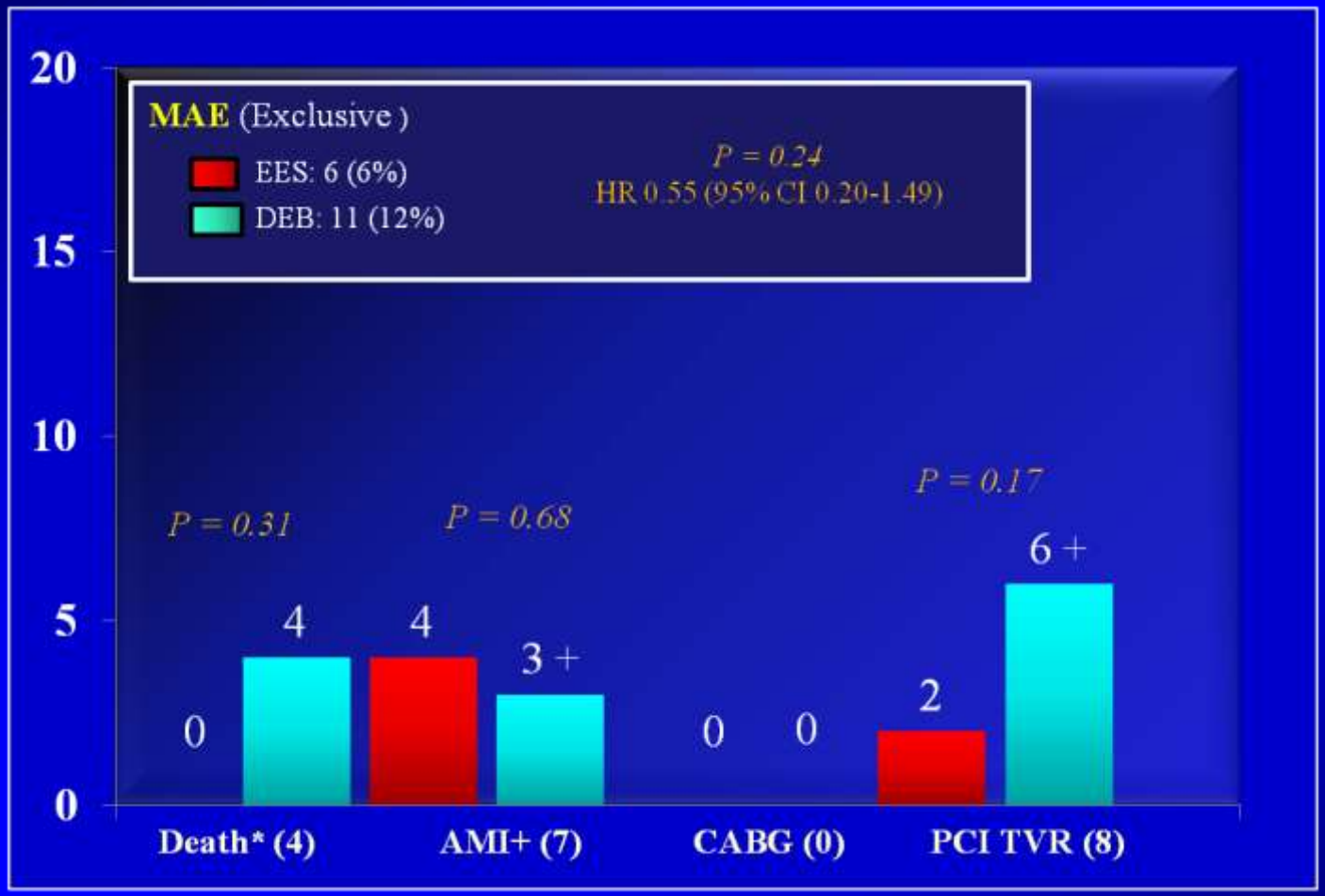
189 pts BMS ISR randomized to Xience Prime® vs Sequent Please®

Adjusted (age, smoker, diabetes) p=0.001



RIBS V: Events at Final Follow-Up (1 Year)

(100%) FU, time 361 ±28 days



*3 Non Cardiac Deaths +1 Definitive ST Thrombosis Intention to Treat

Meta-Analysis of DEB Angioplasty for In-Stent Restenosis

5 studies (PACCOCATH, PEPCAD II, PEPCAD DES, ISAR-DESIRE, Habara et al) with 801 pts analysed. Follow-up duration 12 to 60 mths.

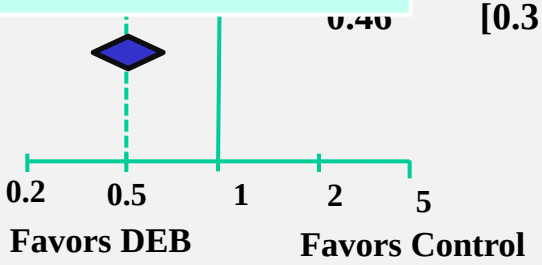
	DEB		Control		Risk Ratio	
	Total	MACE	Total	MACE	RR	95%-CI
PEPCAD-II ISR 2009	66	6	65	14	0.42	[0.17; 1.03]
Habara et a						[0.01; 0.72]
PACCOCA						[0.29; 0.76]
PEPCAD-						[0.18; 0.61]
ISAR-DES						[0.51; 1.02]
Random e					**0.46**	**[0.31; 0.70]**
Heterogene						

DEB reduces:

- MACE 54%
- TLR 66%
- In-seg restenosis 72%
- Mortality 52%

No difference in:

- MI
- Stent thrombosis



Indermuehle A et al Heart 2013; 99: 327-33

Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

For PCI of unstable lesions, i.v. abciximab should be considered for pharmacological treatment of no-reflow.	IIa	B
Drug-eluting balloons[d] should be considered for the treatment of in-stent restenosis after prior BMS.	IIa	B
Proximal embolic protection may be considered for preparation before PCI of SVG disease.	IIb	B

ESC Guidelines Eur Heart J 2010; 31: 2501-55

Conclusions

- Paclitaxel drug-coated balloon technology has shown safety and efficacy in the treatment of coronary in-stent restenosis

- Bare-metal stent in-stent restenosis is the only approved indication for use of drug-coated balloon on the European guidelines

- However, it is reasonable also to employ drug-eluting balloon as first option for patients with DES restenosis with current evidence

- Successful use of drug-coated balloon is predicated on operator experience and technical expertise (predilation to achieve ‘stent-like’ results, avoid ‘geographic miss’)