2nd Generation DES for DES-ISR -RESTENT-ISR trial

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Reported TLR >10% of DES era

• Left Main	14.1% *
• Bifurcation	18.7-28% **
• SVG	>10% (SECURE)
• VBT Failure	>47.8% (SECURE)
• Multivessel TAXUS	>12% (TAXUS V-TRUE)
• Multivessel Cypher	>11% (RECIPE Registry)
• >4 Cypher /pt	14% ***
• DES-ISR	6~18%

* Chieffo A, Circulation, 2005
** Colombo A, Circulation 2004
*** Iakovou I, et al CCI 2004

DES for DES-ISR vs. BMS-ISR

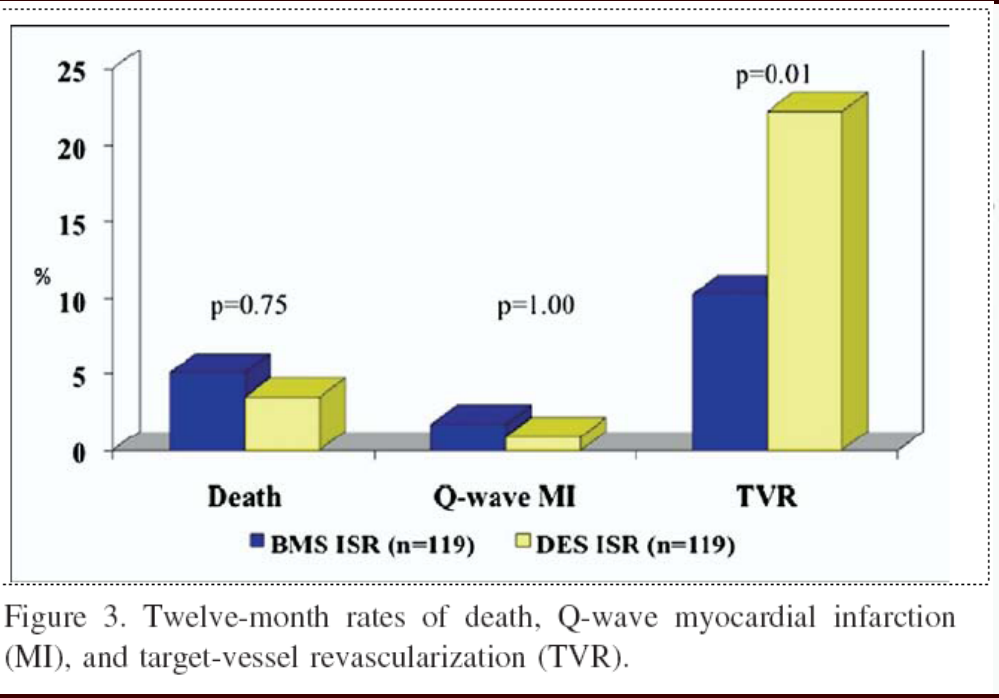
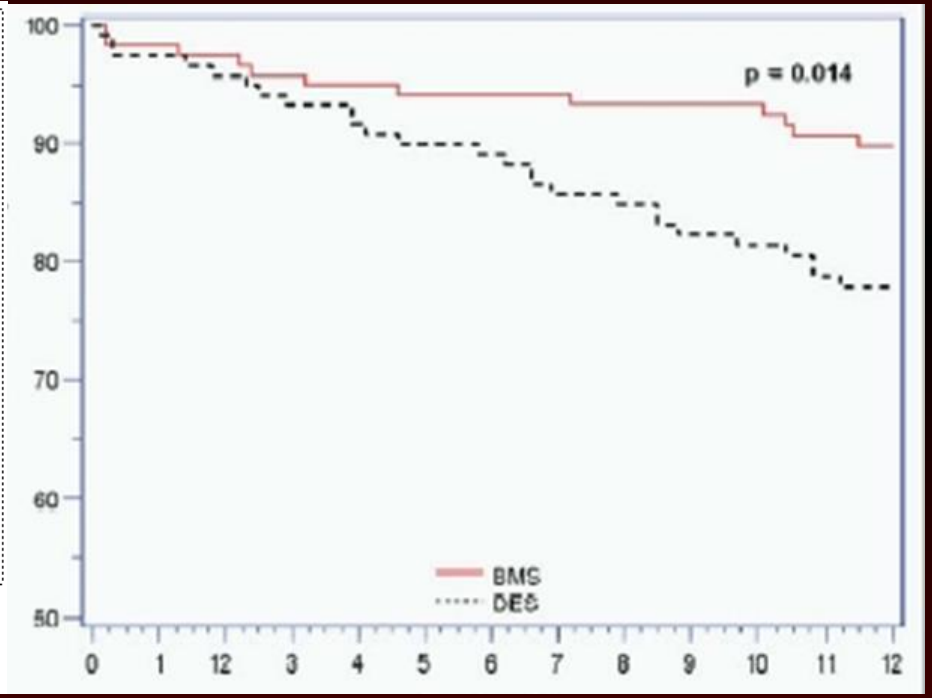


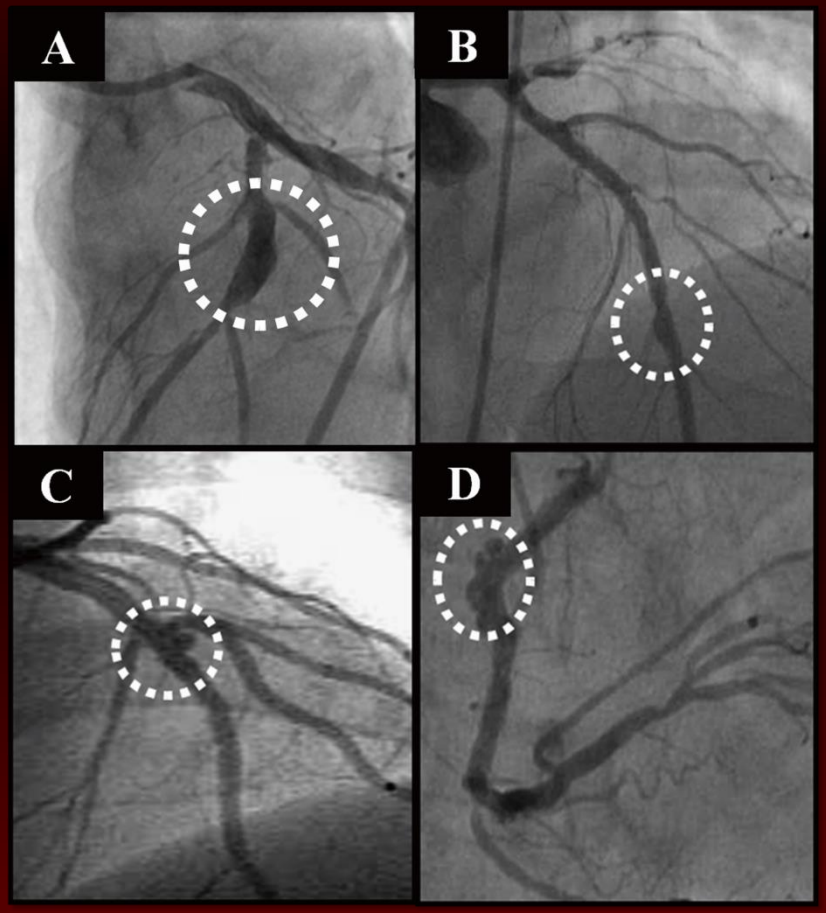
Figure 3. Twelve-month rates of death, Q-wave myocardial infarction (MI), and target-vessel revascularization (TVR).



TVR more frequent in DES ISR group than BMS ISR group
→ DES ISR is more challenging scenario

Am J Cardiol 2009;103:491– 495

Challenging scenario in 1st G DES-ISR



Coronary artery aneurysm with DES

Ahn, Chul-Min, Bum-Kee Hong et al, AHJ 2010

- Off-label lesion revascularization
- DES-ISR
- Late catch-up
- Coronary anuerysm
- Stent fracture
- Stent thrombosis
- Endothelial dysfunction
- Dual antiplatelet maintenance

High MACE after stent DES sandwich for DES ISR

1. Enhanced allergic or inflammatory response to drug or polymer
2. Excessive intimal hyperplasia
3. Insufficient stent expansion

Mishkel. JACC 2007;49:181-4

In-Stent Restenosis in the Drug-Eluting Stent Era

Predictors of ISR or TLR After DES Implantation

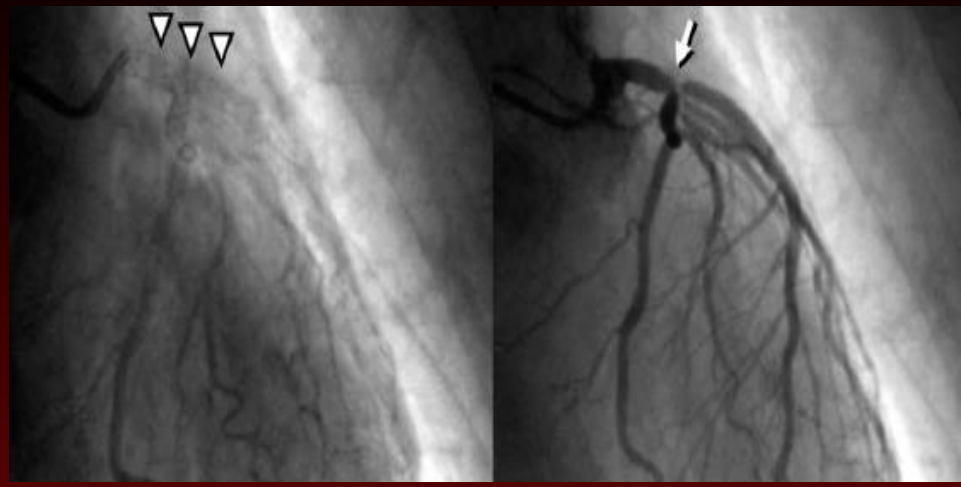
Patient Characteristics	Lesion Characteristics	Procedural Characteristics
Age	ISR	Treatment of multiple lesions
Female sex	Bypass graft	Type of DES
Diabetes mellitus	Chronic total occlusion	Final diameter stenosis
Multivessel coronary artery disease	Small vessels	
	Calcified lesion	
	Ostial lesion	
	Left anterior descending coronary artery lesion	

DES = drug-eluting stent(s); ISR = in-stent restenosis; TLR = target lesion revascularization.

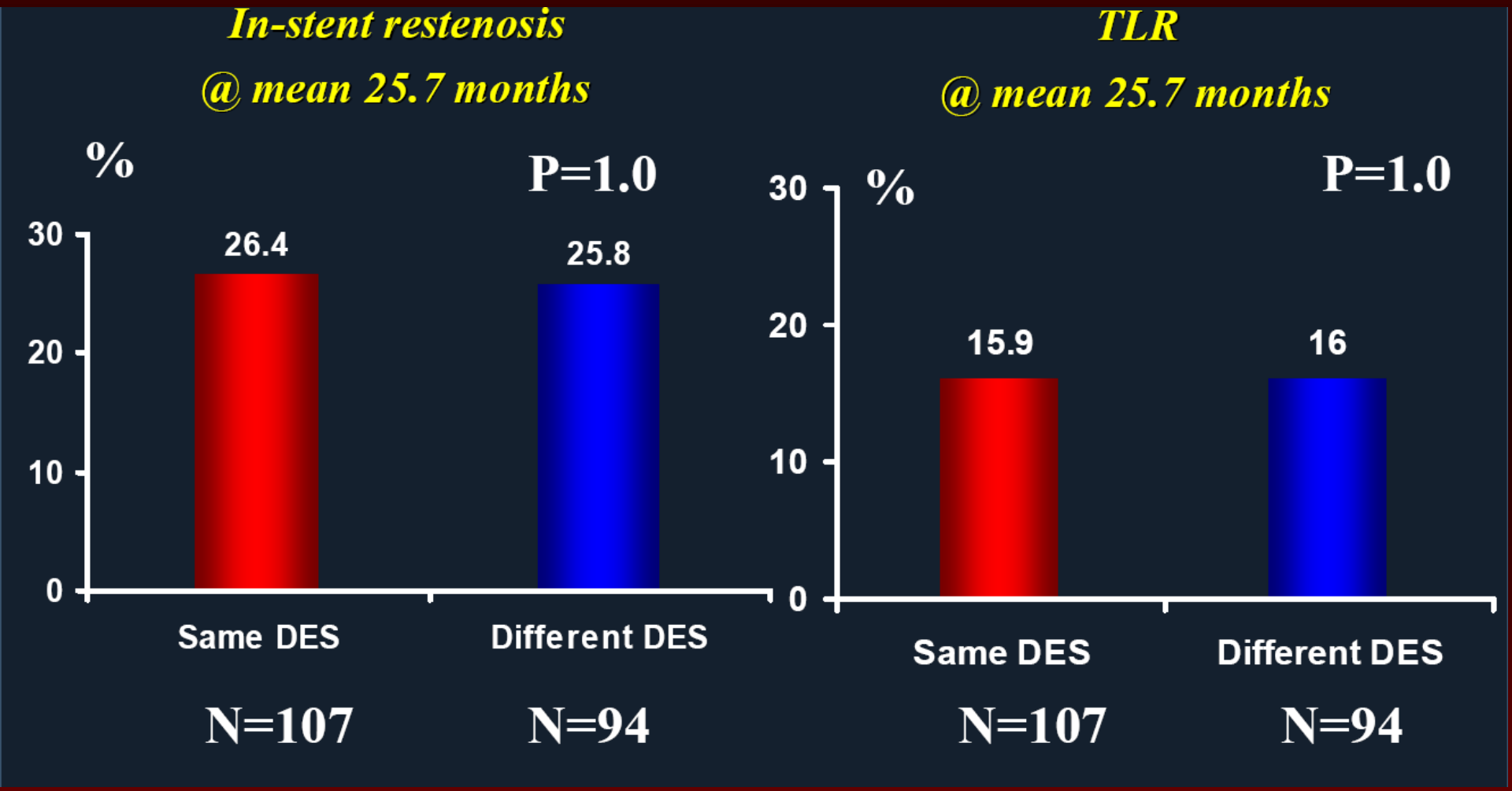
JACC 2010 Nov 30;56(23):1897-907

Treatment Option for DES failure

- Maximal medical therapy
- Repeated PCI
  - Balloon
  - Cutting balloon
  - Another stenting
  - Brachytherapy
  - DEB
- Bypass surgery
  - With or without endarterectomy

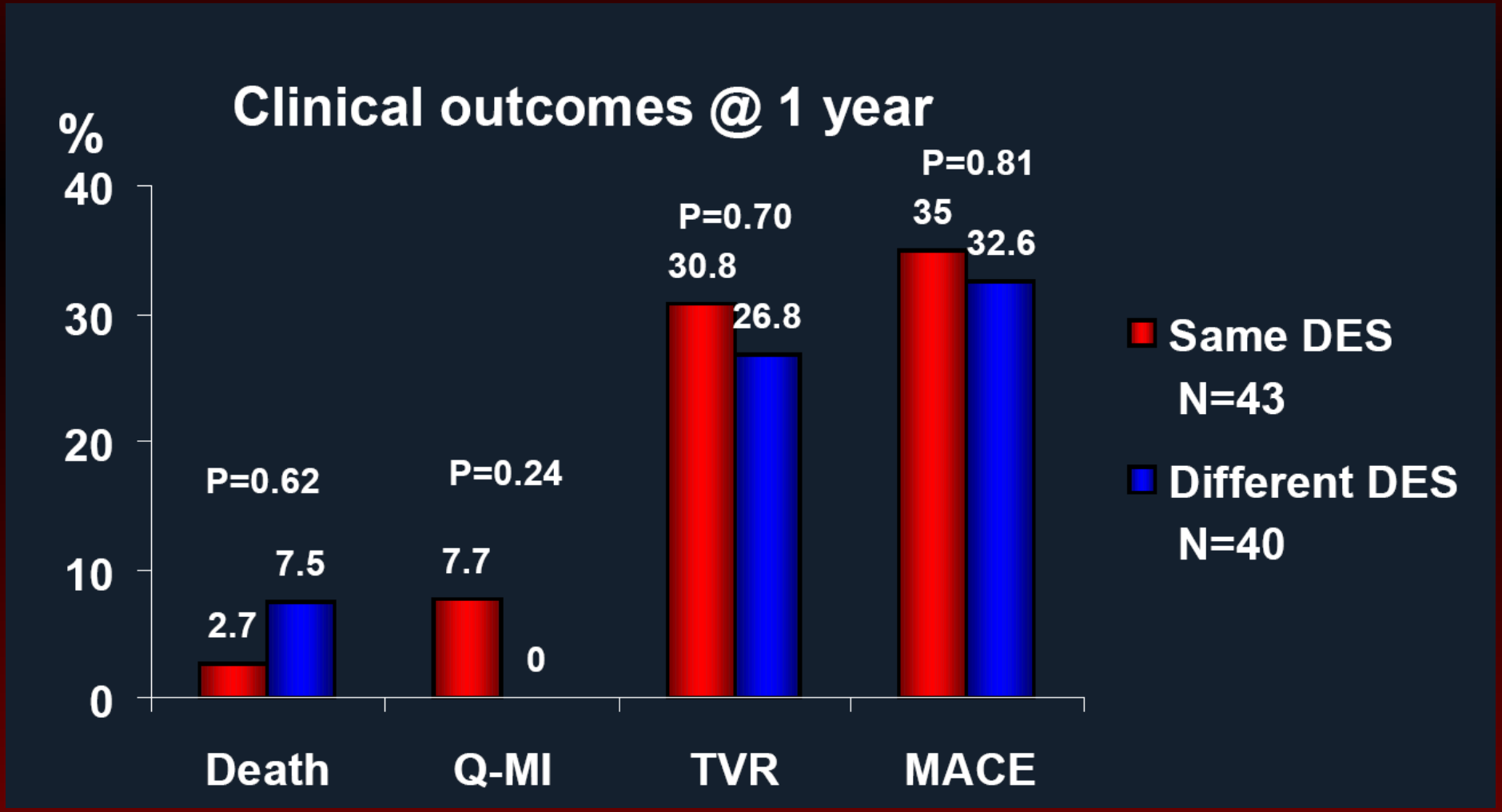


Same DES vs. other DES vs. other treatment for DES failure - Does the switch therapy work?



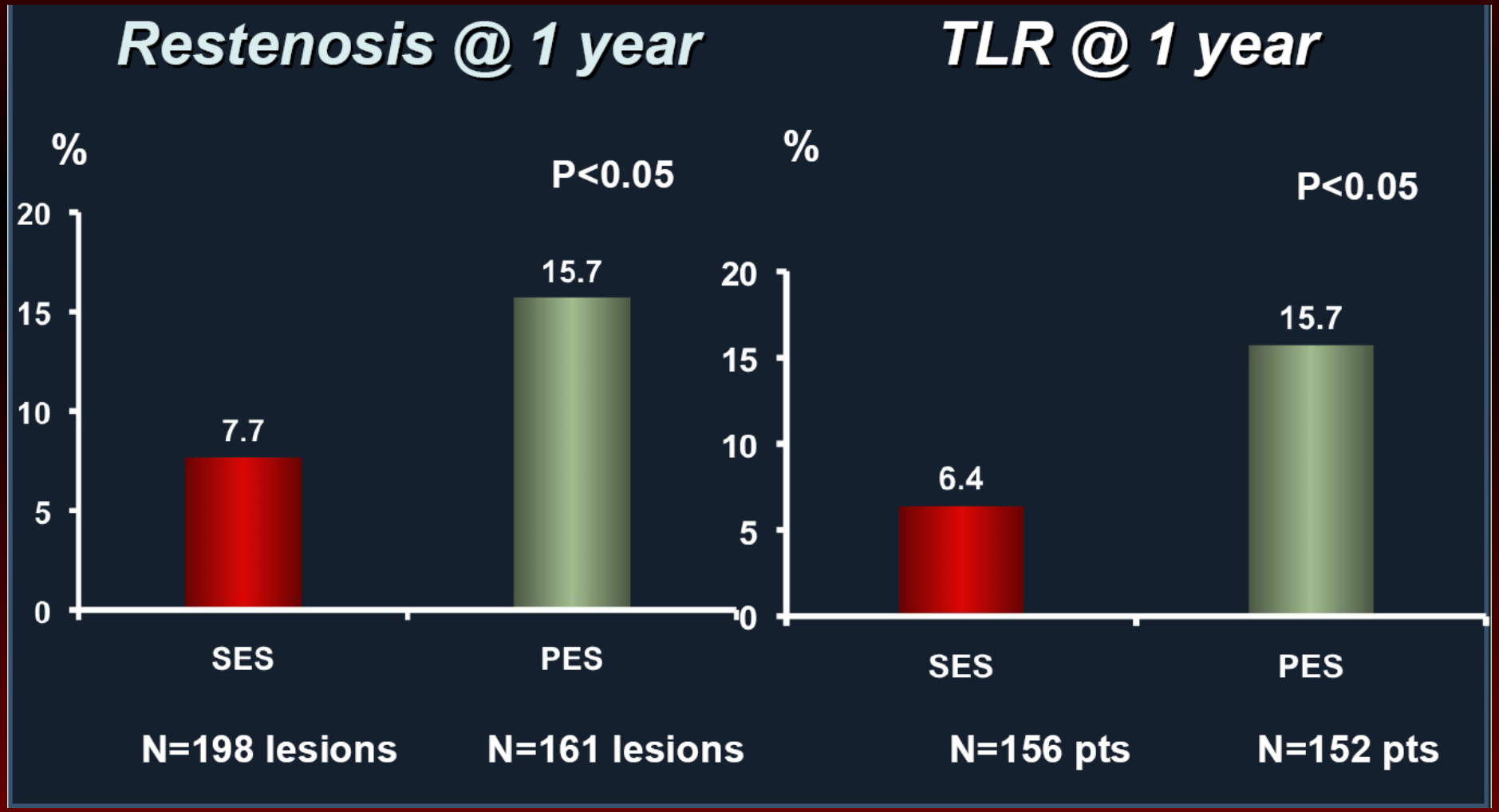
Cosgrave, Colombo AHJ 2007;153:354-9

Same DES vs. other DES for DES ISR- Does the switch therapy work?



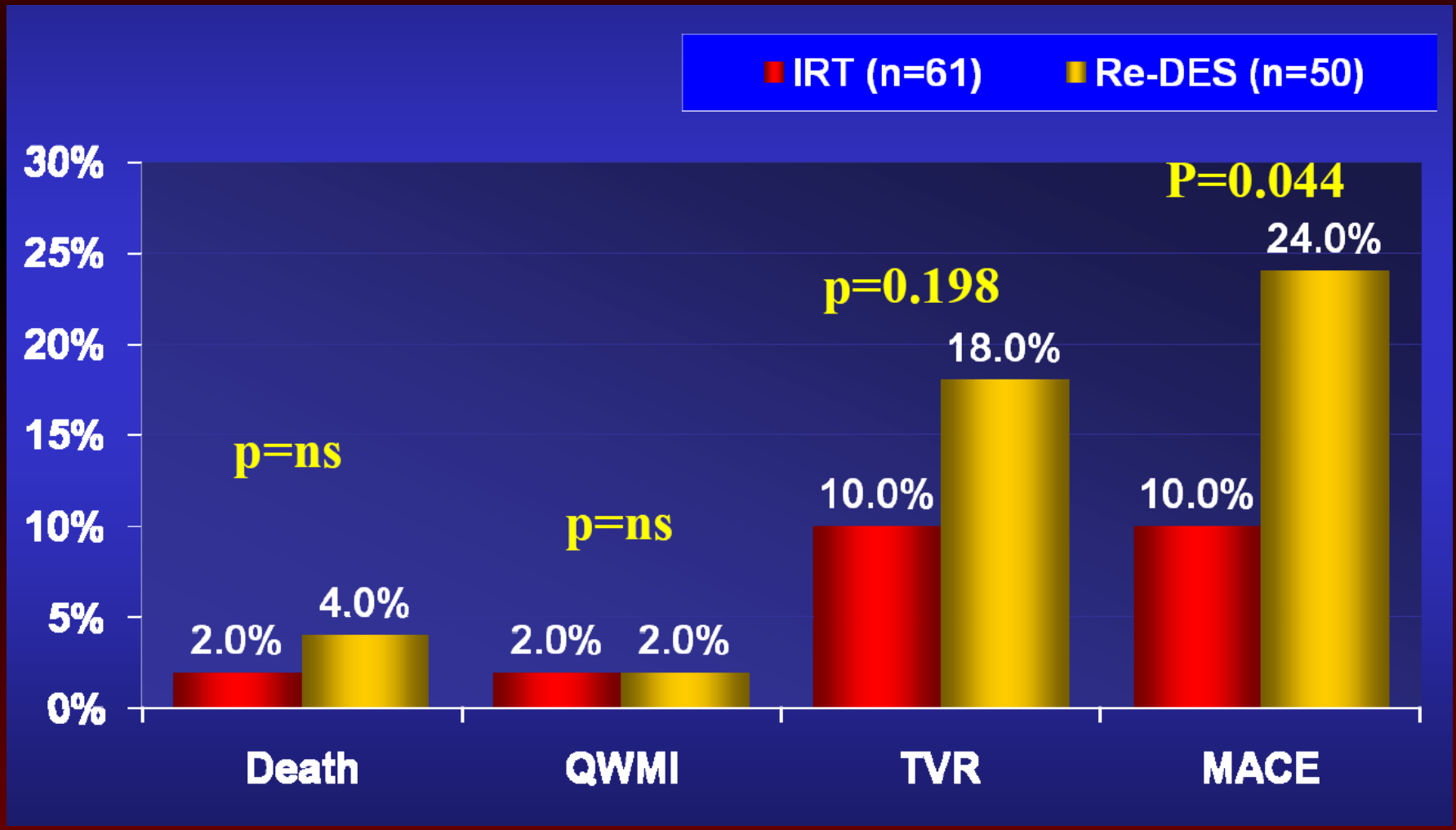
Garg S et al. Cathet Cardiovasc Interv 2007;70:9

SES vs. PES for SES failure - Multicenter Registry in Asia



Nakamura S. et al. ACC 2007

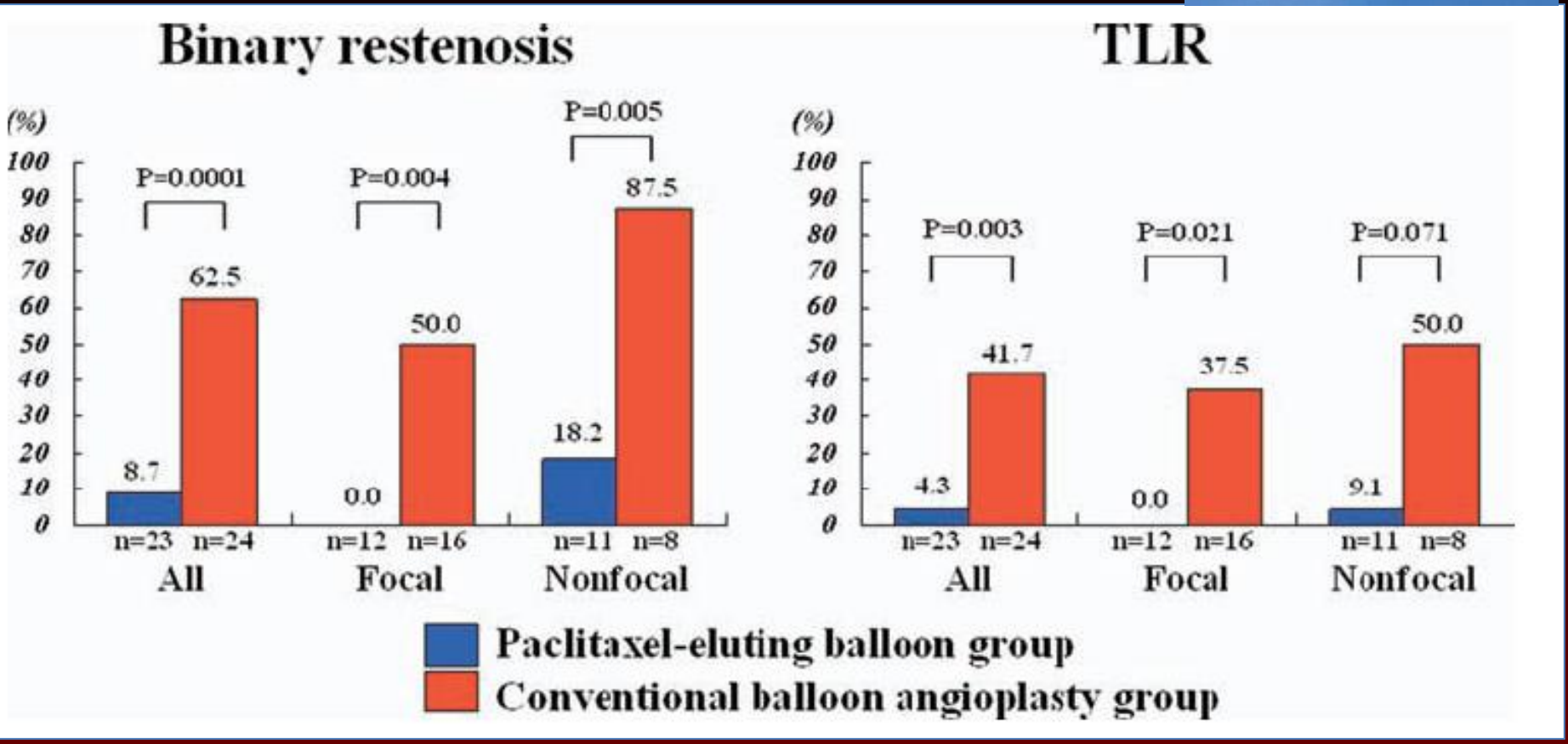
Brachytherapy vs. Re-DES



Torguson, AJC 2006;98:1340-1344

Drug eluting balloon in SES-ISR

- Angiographic restenosis and TLR (n=50)



Habara S et al. J Am Coll Cardiol Intv 2011;4:149

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, atherectomy
	Heterogeneous drug distribution	DES, BA, atherectomy
Focal at stent edge	Geographic miss	DES
	Plaque progression	DES
Diffuse in-stent	Vessel biology / Drug resistance	Different DES, CABG
Proliferative	Vessel biology / Drug resistance	Different DES, CABG

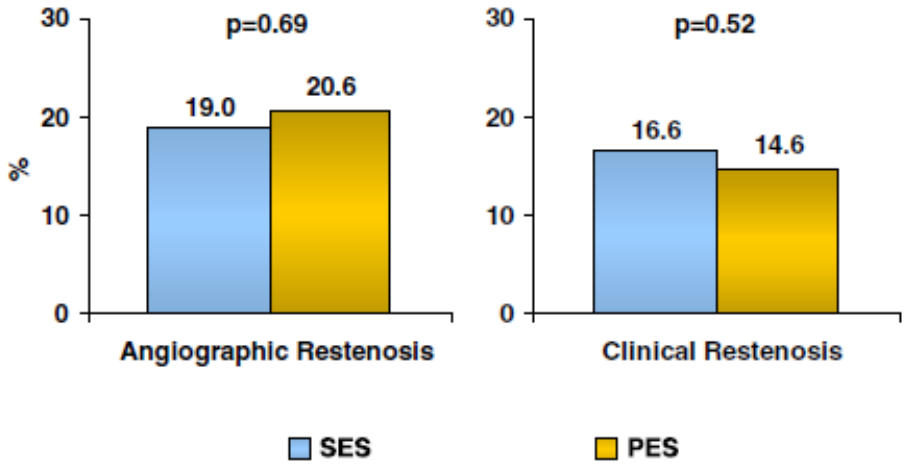
Costa MA. et al. *AHJ.2007;153: 447-9*

Angiographic outcome at 1 year of ISAR-DESIRE II

Angiographic Outcomes at 6 to 8 Months

	SES (n = 205)	PES (n = 204)	p Value
Minimal luminal diameter, in-stent, mm	2.14 ± 0.78	2.16 ± 0.72	0.78
Minimal luminal diameter, in-segment, mm	1.93 ± 0.73	1.94 ± 0.67	0.98
Stenosis, in-stent, %	26.6 ± 23.6	25.4 ± 21.5	0.53
Stenosis, in-segment, %	34.0 ± 21.1	33.3 ± 18.7	0.73
Late loss, in-stent, mm	0.40 ± 0.65	0.38 ± 0.59	0.85
Late loss, in-segment, mm	0.26 ± 0.61	0.25 ± 0.58	0.86
Recurrent binary restenosis	39 (19.0)	42 (20.6)	0.69
Restenosis morphology			0.42
Type I (focal)			
Focal marginal	9 (23.0)	14 (33.2)	
Focal body	18 (46.1)	11 (26.3)	
Multifocal	4 (10.3)	6 (14.3)	
Type II (diffuse)	4 (10.3)	7 (16.7)	
Type III (proliferative)	0 (0.0)	0 (0.0)	
Type IV (occlusive)	4 (10.3)	4 (9.5)	

Data shown as mean ± SD or n (%).
Abbreviations as in Table 1.

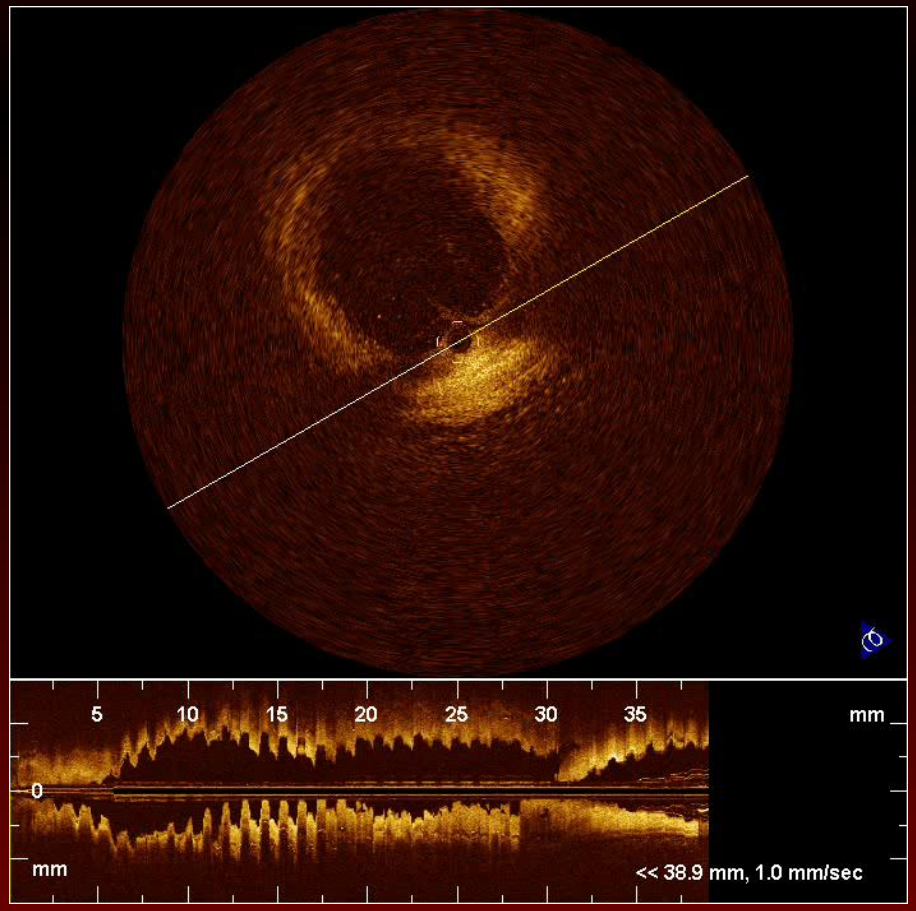


Angiographic Restenosis at 6 to 8 Months and Clinical Restenosis at 1 Year

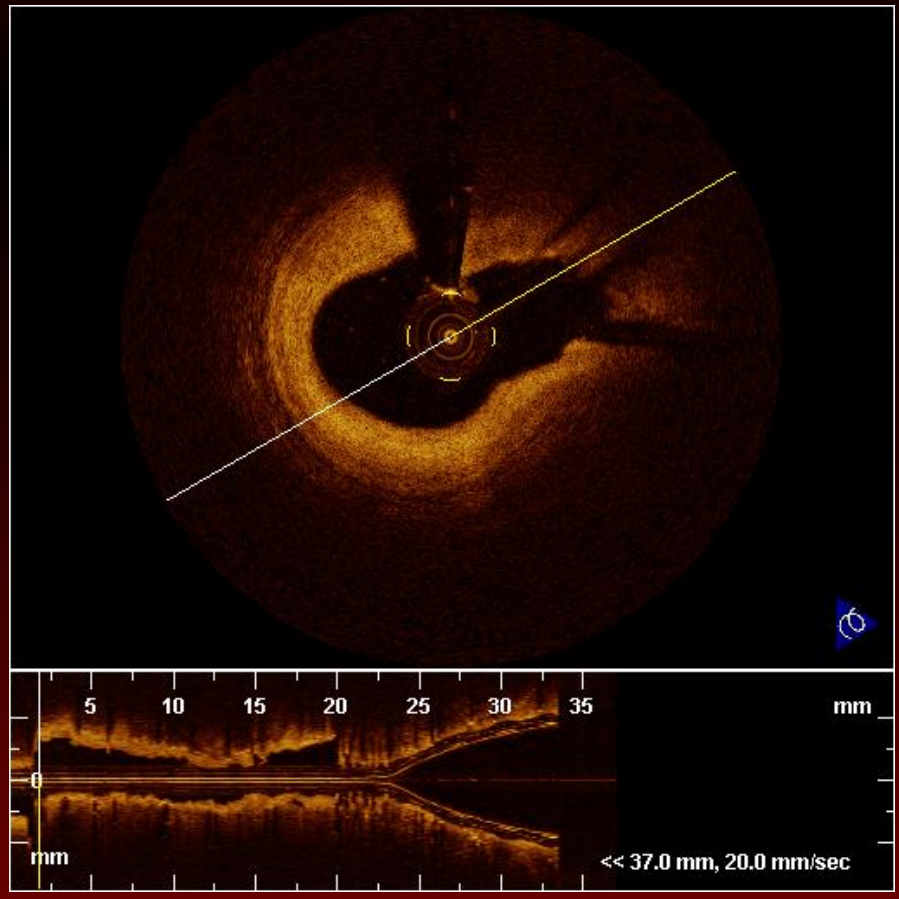
The **blue bars** indicate sirolimus-eluting stents; the **gold bars** indicate paclitaxel-eluting stents. Clinical restenosis refers to target lesion revascularization.

Cutting balloon, DEB

Cutting Balloon



DEB



Courtesy of JS KIM

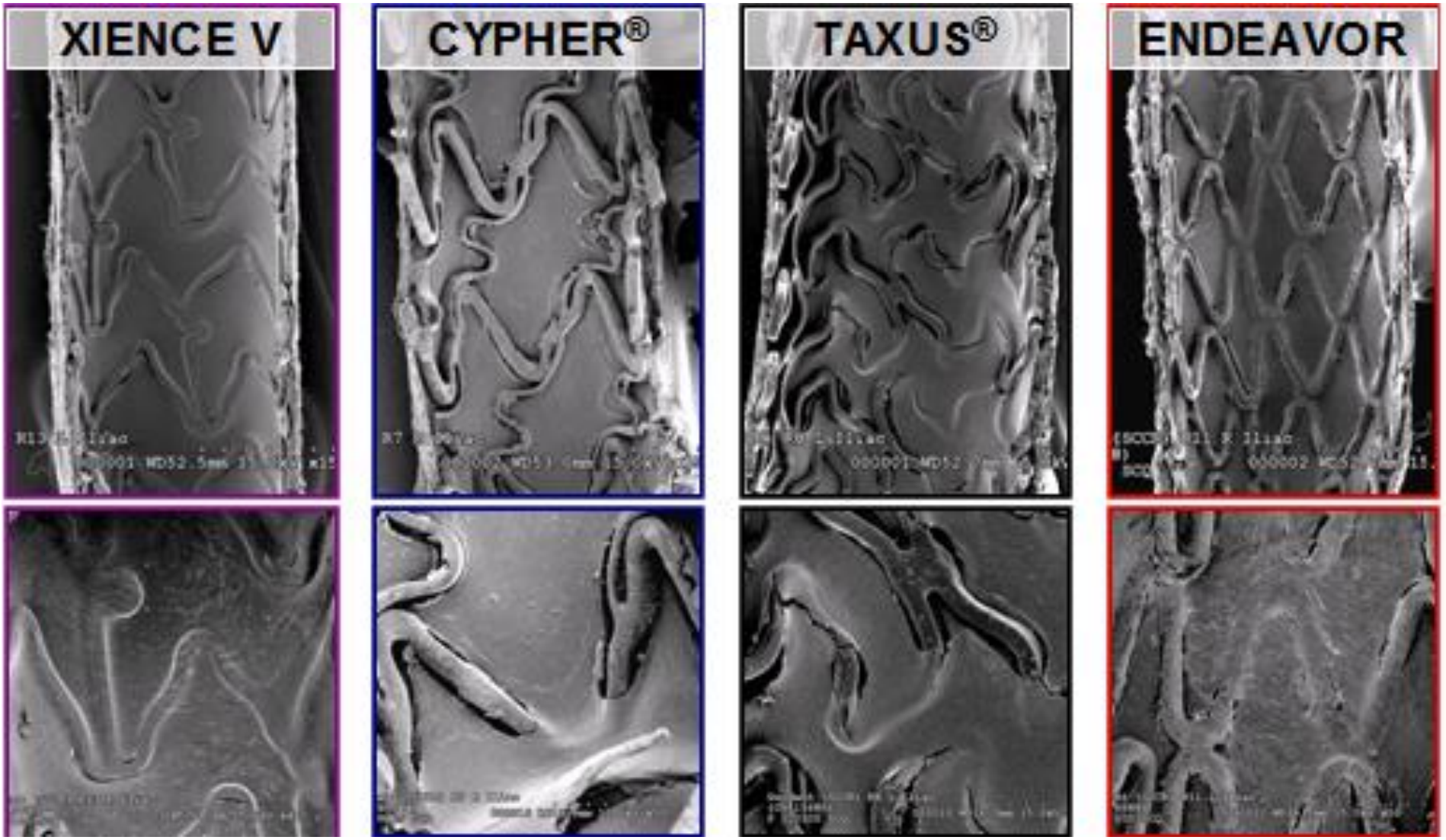
Preferred Treatment for DES-ISR

- Multiple strategy for different type of ISR
- Poor controlled randomized study

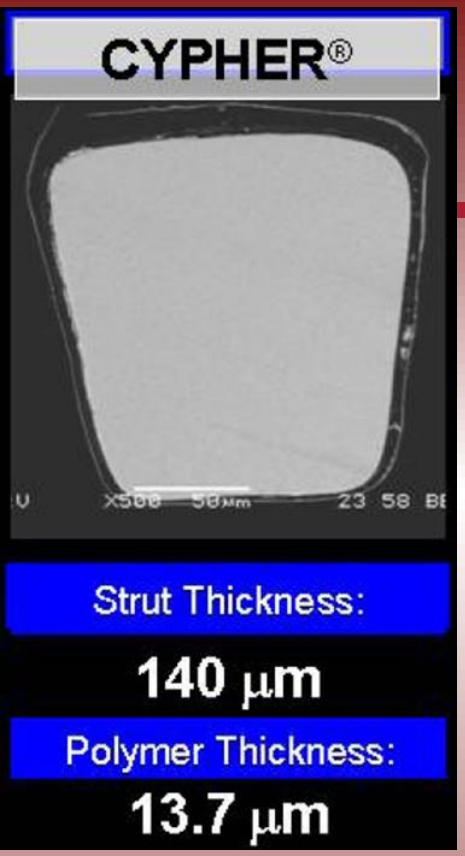
No DATA

We need general method for DES ISR

Re-endothelialization
14-Day Rabbit Iliac Study



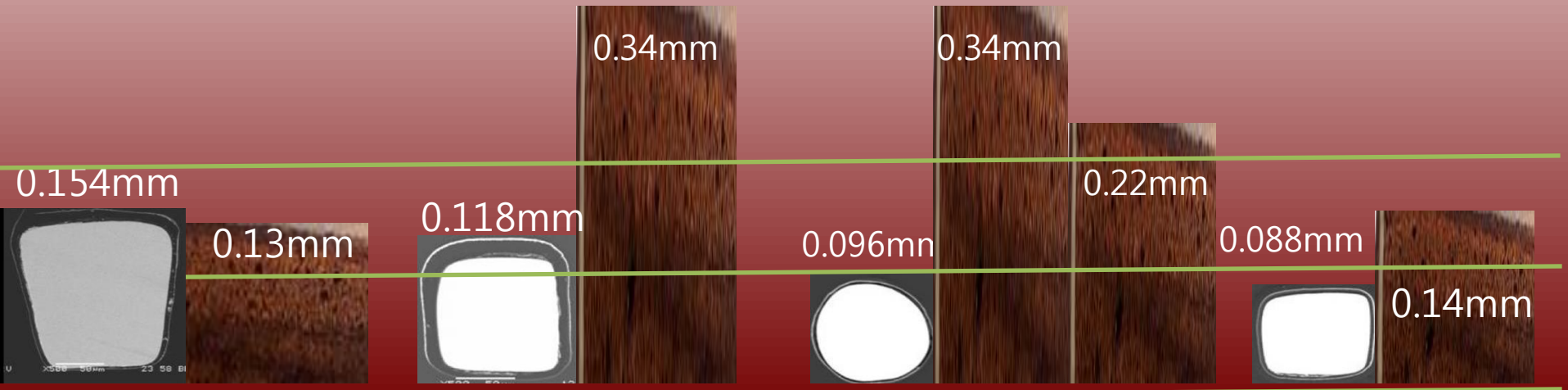
Courtesy of Dr. R Virmani


CYPHER®
Strut Thickness:
140 µm
Polymer Thickness:
13.7 µm


TAXUS® Liberté
Strut Thickness:
97 µm
Polymer Thickness:
17.8 µm


ENDEAVOR™
Strut Thickness:
91 µm
Polymer Thickness:
4.8 µm


XIENCE™ V
Promus
Strut Thickness:
81 µm
Polymer Thickness:
7.8 µm


0.154mm
0.13mm
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0.34mm
0.22mm
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0.14mm

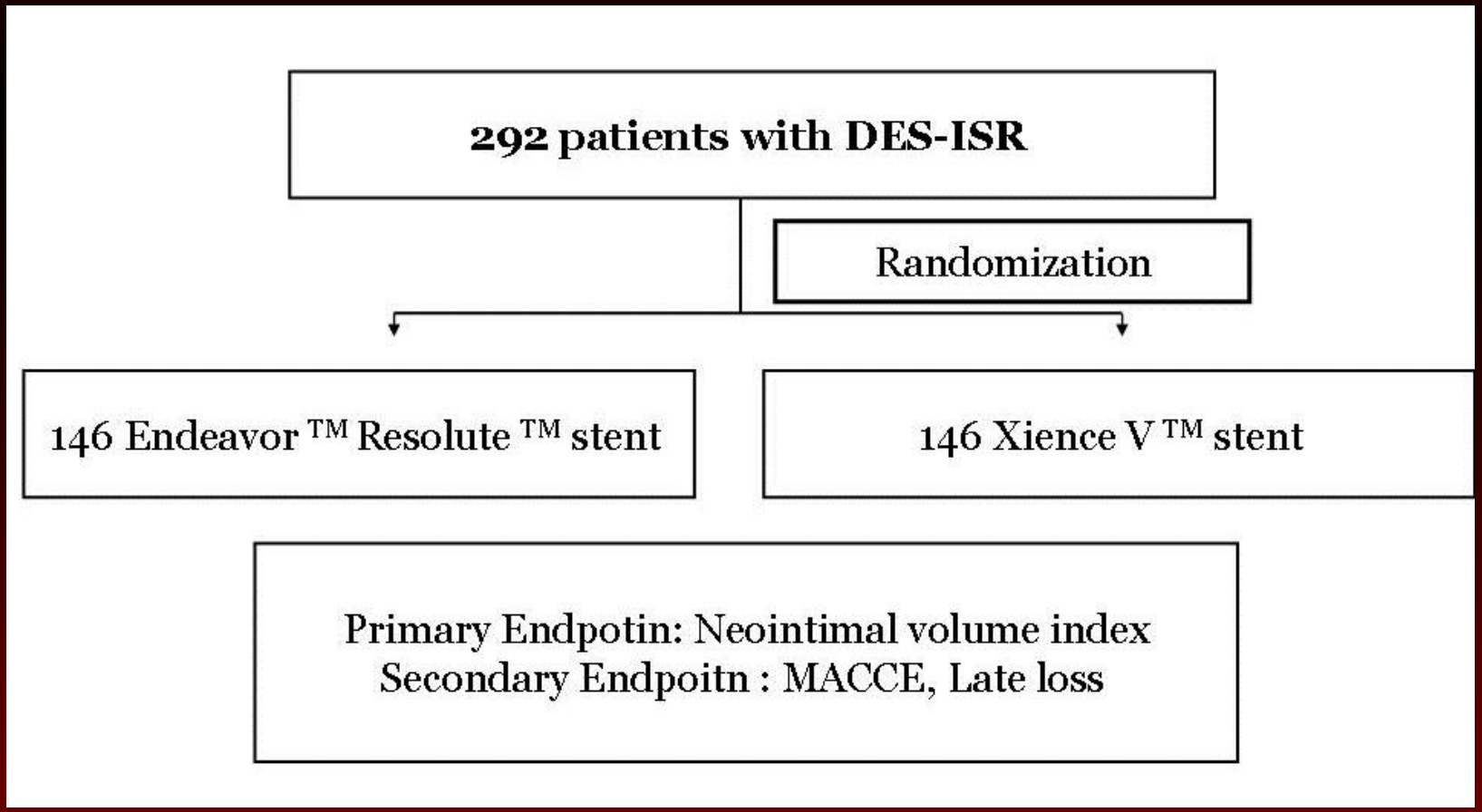
Prospective, single-blinded, Randomized comparison of the clinical and angiographic results with intravascular analysis of EverolimuS-Eluting versus ZoTarolimus-Eluting steNTs for In-Stent Restenosis(ISR) lesions: Volumetric Analysis with Intravascular ultrasound (IVUS) : (RESTENT-ISR trial)

- Prospective, randomization of Xience V™ vs. Endeavor resolute™ at DES-ISR leson
- Volumetric analaysis of neointimal hyperplasia and Major cardiovascular event

ClinicalTrials.gov **NCT01365572**

Restent-ISR trial

Comparison of 2nd Generation DES efficacy for DES-ISR
- Primary end point : Neointimal Volume index



ClinicalTrials.gov NCT01365572

Statistical calculation
primary endpoint– neointimal volume index (NVI)

	Pts	NVI (Mean)	SD	Follow-up
Xience V	49	0.21 mm^3/mm	0.19	6 months
Endeavor resolute	81	0.3 mm^3/mm	0.3	9 months

(1) Non-inferiority design, level of significance, α=5%
(2) β =0.1 & power of the test =90%
(3) maximum allowable difference, δ= 0.1

	Xience V	Endeavor R	Total	FU loss
Patients, n	146	146	292	15%

2008 Yoshihiro Tsuchia et al. *Am J Cardiol.* 2006;98(4):464-469.
2008 AHA abstract Katsuhisa Waseda

New Generation Drug Eluting Stent for In-stent Restenosis of Drug Eluting Stent(RESTENT-ISR Trial)

This study is currently recruiting participants.
Verified on March 2011 by Korea University Anam Hospital

Study NCT01365572 Information provided by Korea University Anam Hospital

Inclusion criteria

- In-stent restenosis (≥50% by quantitative angiographic analysis) following all types of DES; only in-segment restenotic lesions without ISR are not included
- Evidence of myocardial ischemia due to restenosis (e.g., stable, unstable angina, recent infarction, silent ischemia, positive functional study or a reversible changes in the ECG c/w ischemia) or ≥ 70% by quantitative angiographic analysis
- Repeat revascularization, needed with another stent (single stent implanted lesion : lesion length 28mm)
- IVUS available lesions
- Non-emergent conditions
- Patients confirmed about study enrollment and 9-month follow-up angiogram & IVUS

Exclusion criteria

General exclusion criteria

- Contraindication to anti-platelet agents & Bleeding history within prior 3 months
- Prior history or current presentation of DES thrombosis
- Age > 80 years
- Known hypersensitivity or contraindication to any of the following medications: Heparin, Aspirin, Clopidogrel, Zotarolimus, Everolimus
- Severe hepatic dysfunction (≥ 3 times normal reference values)
- Serum creatinine level ≥ 2.0 mg/dL or end-stage renal diseases on dialysis
- LVEF < 30%
- Pregnant women or women with potential childbearing
- An elective surgical procedure is planned that would necessitate interruption of clopidogrel during the first 9 months
- Life expectancy ≤ 1 year

Exclusion criteria

Lesion & Procedural exclusion criteria

- IVUS-unavailable lesion
- Restenotic lesions following PCI of de novo lesion like as below;
- . left main lesions
- . BMS restenotic lesion
- . vein graft lesion
- Restenotic lesions following 2.25mm DES implantation
- Prior history of repeat DES implantation for DES restenosis (only conventional or cutting ballooning treatment for DES restenosis is included in this study)
- Simultaneous implantation of different types of DES on restenotic or another de novo lesions (Only same DES implantation is allowed on the restenotic or another de novo lesions)
- Patients with little possibility of performing follow-up angiogram and IVUS

Endpoint

- **Primary Endpoint**

➔total neointimal volume, neointimal volume index by intravascular ultrasound

- **Secondary Endpoint**

➔MACE, stent thrombosis, late loss , binary restenosis

➔IVUS parameter-remodeling index etc.

Procedure & CRF

- Pre-TLR IVUS (possible lesion)
- Stent randomization (Xience V/Endeavor R)
- Post-TLR IVUS (mandatory)
- In-hospital/1/3/9/12 m clinical outcome
- Stress test for confirmation of ischemic-driven TLR
- 9 month FU IVUS (mandatory)

RESTENT-ISR trial: Baseline characteristics

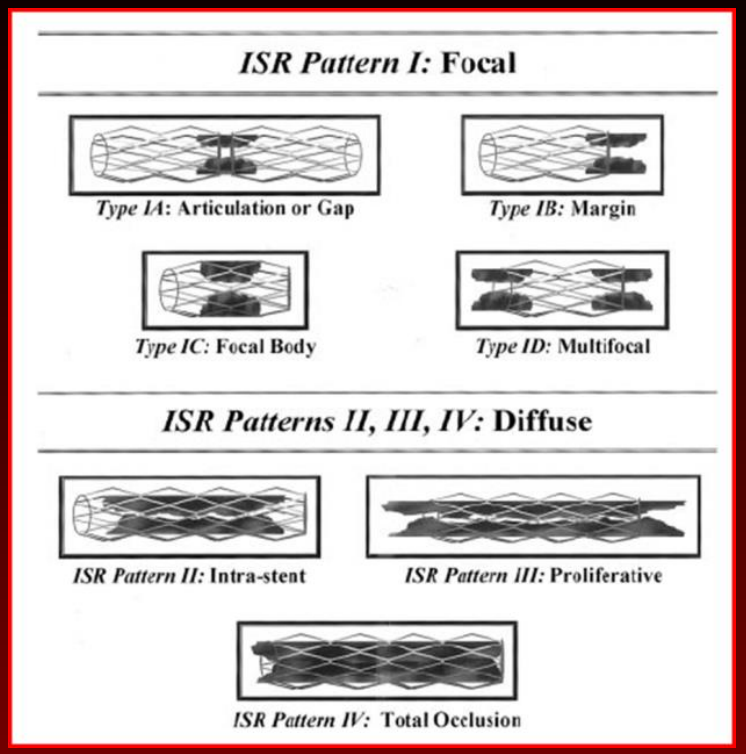
	빈도	퍼센트
고려대학 안암병원	45	14.8
연세의대 심장혈관병원	38	12.5
계명대학 동산의료원	32	10.5
부천세종병원	29	9.5
성균관의대 삼성서울병원	19	6.2
순천향대학 천안병원	17	5.6
연세의대 원주기독병원	15	4.9
고려대학 구로병원	15	4.9
전남대학병원	15	4.9
노원을지대학병원	14	4.6
경북대학병원	9	3.0
원광대학병원	8	2.6
강원대학교병원	8	2.6
단국대학 천안병원	8	2.6
중앙대학병원	7	2.3
서울대학병원	5	1.6
관동의대 일산명지병원	5	1.6
연세의대 강남세브란스병원	4	1.3
영남대학병원	4	1.3
성균관의대 강북삼성병원	2	.7
광주보훈병원	2	.7
충북대학병원	2	.7
한림대 강동성심병원	2	.7
합계	305	100.0

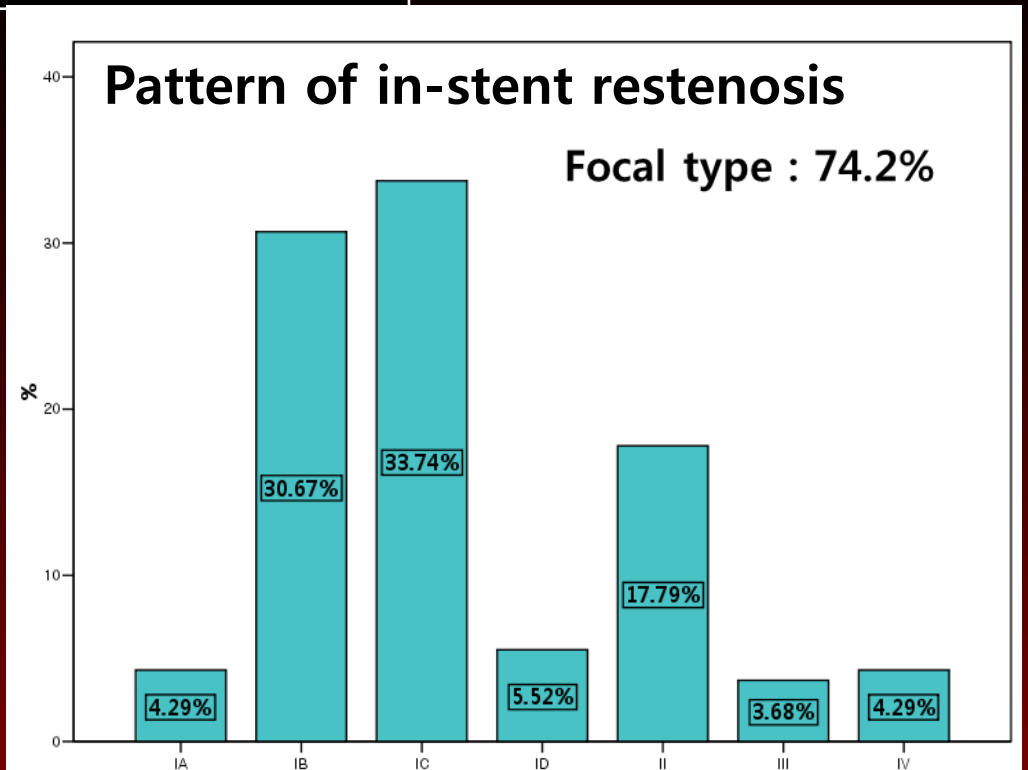
- 22 centers/ 305 pts (10 center>10 cases)
- Age : 63.2± 9.6 (31 -82)
- M:F = 202: 103 (1.96:1)
- Diagnosis at presentation
  - Unstable angina : 124 pts (40.7%)
  - Stable angina : 137 pts (44.9%)
- Previous MI : 77 pts (25.2%)
- HTN : 151 pts (49.5%)
- DM : 100 pts (32.8%)
- Smoking Hx : 117 pts (38.3%)
- Hypercholesterolemia : 186 (61.0%)
- **Exclusion 11 pts (Xience 150/Endeavor 144)**

RESTENT-ISR investigator group

RESTENT-ISR : baseline characteristics

Clinical Diagnosis on presentation		Frequency(pts)	%
Silent ischemia		21	6.9
Stable angina		137	44.9
Acute coronary syndrome	Unstable angina	124	40.7
	NSTEMI	13	4.3
	STEMI	4	1.3
unknown		6	2.0

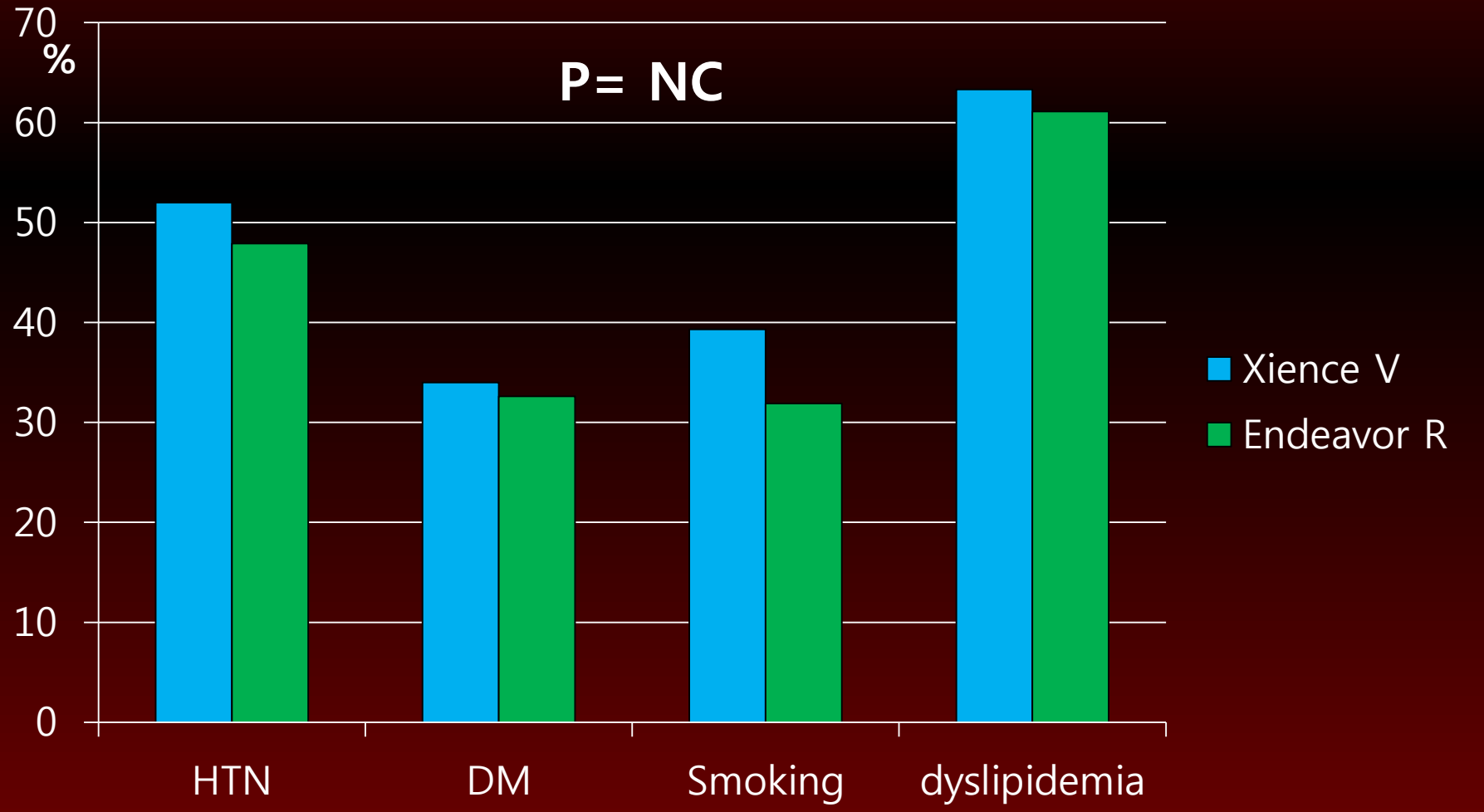




Baseline characteristics

	Xience VI (150)	Endeavor resolute(144)	P value
Age, yr	64.1±8.9	62.2±10.2	0.09
Male, n(%)	100 (66.6%)	93 (64.6%)	0.70
Previous MI, n(%)	32 (21.3%)	43 (29.8%)	0.11
HTN Hx, n(%)	78 (52.0%)	69 (47.9%)	0.68
DM Hx, n(%)	51 (34.0%)	47 (32.6%)	0.93
Smoking Hx, n(%)	59 (39.3%)	46 (31.9%)	0.37
Dyslipidemia, n(%)	95 (63.3%)	88 (61.1%)	0.82
Total Cholesterol, mg/dl	139.8±32.9	144.5±32.9	0.32
LDL Cholesterol, mg/dl	78.4±27.3	78.7±25.1	0.93
Triglyceride, mg/dl	115.9±66.3	126.4±106.3	0.76
Fasting glucose, mg/dl	129.4±52.9	128.1±46.1	0.86
hsCRP, mg/dl	1.48±4.7	3.42±10.6	0.14
Ejection fraction, %	61.3±9.2	58.9±10.1	0.16
Previous stent diameter, mm	3.10±0.38	3.05±0.40	0.27
Previous stent length, mm	**23.3±7.1**	**25.0±6.4**	**0.06**

Baseline characteristics



RESTENT-ISR investigator group

RESTENT-ISR trial – QCA

	Xience V(150)	Endeavor resolute(144)	P value
Stent diameter, mm	3.15±0.44	3.07±0.38	0.13
Stent length, mm	20.6±5.92	20.7±6.54	0.97
P-Reference Diameter(pre),mm	3.03±0.58	3.13±0.53	0.66
D-Reference Diameter(pre),mm	2.90±0.84	2.86±0.50	0.47
P-Reference Diameter(post),mm	3.19±0.49	3.25±0.49	0.71
D-Reference Diameter(post),mm	3.05±0.80	2.96±0.52	0.31
Diameter stenosis(pre), %	73.4±14.9	77.2±14.3	0.16
Diameter stenosis(post), %	10.9±10.2	11.6±13.1	0.81
Lesion Length, mm	17.3±7.73	17.8±10.5	0.67
Minimal lumen diameter(pre)	0.75±0.46	0.82±0.59	0.55
Minimal lumen diameter(post)	2.71±0.51	2.71±0.58	0.99
Acute gain, mm	1.95±0.68	1.89±0.81	0.67
P-Inseg. MLD(post), mm	2.73±0.52	2.93± 0.41	0.05
D-Inseg. MLD(post), mm	2.42±0.59	2.32± 0.59	0.39

RESTENT-ISR investigator group

RESTENT-ISR trial –181 FU CAG- analysis 91

	Xience V(47)	Endeavor resolute(44)	P value
P-Reference Diameter(post),mm	3.19±0.49	3.25±0.49	0.71
D-Reference Diameter(post),mm	3.05±0.80	2.96±0.52	0.31
Minimal lumen diameter(pre)	0.75±0.46	0.82±0.59	0.55
Minimal lumen diameter(post)	2.71±0.51	2.71±0.58	0.99
Acute gain, mm	**1.95±0.68**	**1.89±0.81**	**0.67**
P-Inseg. MLD(post), mm	2.93±0.52	2.93± 0.41	0.76
D-Inseg. MLD(post), mm	2.42 ± 0.59	2.32± 0.59	0.39
P-Reference Diameter(fu), mm	3.04 ± 0.52	3.11 ± 0.51	0.51
D-Reference Diameter(fu), mm	2.81 ± 0.55	2.69 ± 0.44	0.22
Minimal Lumen diameter(fu)	2.25 ± 0.66	2.32 ± 0.75	0.63
Late loss	**0.39± 0.52**	**0.50± 0.65**	**0.43**
P-Inseg. MLD (fu), mm	2.97 ± 0.51	2.95 ± 0.66	0.88
P-Inseg. MLD (fu), mm	2.61 ± 0.55	2.57 ± 0.51	0.74

Acute Gain & Late Lumen Loss

Major adverse clinical outcome in 9 months (185/294, 62.9% clinical follow-up)

	MACE (9months)	Mortality	Ischemic TLR	TLR	Non-TLR	Stroke
Total (185 pts)	24 (12.9%)	3	8 (4.3%)	16(8.6%)	3	2
Xience V (98 pts)	11 (11.2%)	1 cancer	3 (3.1%)	7(7.1%)	1	2
Endeavor resolute (87 pts)	13 (14.9%)	1 ST 1 cancer	5 (5.7%)	9(10.3%)	2	0

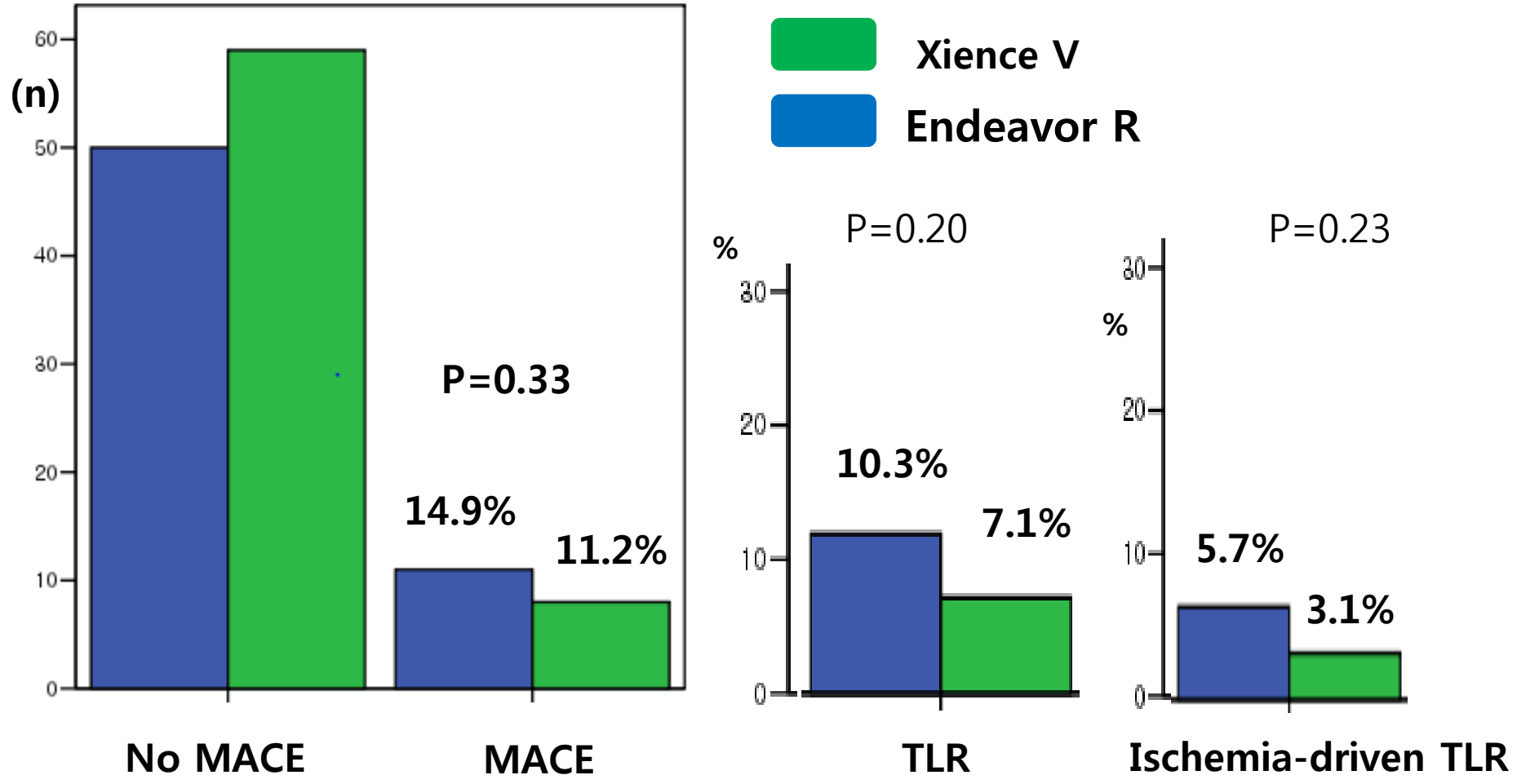
ISAR-DESIRE II 1Y MACE	SES (n = 225)	PES (n = 225)	p Value
Death	7 (3.4)	9 (4.5)	0.60
Myocardial infarction	6 (2.7)	4 (1.8)	0.53
Death or myocardial infarction	13 (6.1)	12 (5.8)	0.86
Definite stent thrombosis	1 (0.4)	1 (0.4)	0.67
Death, myocardial infarction, or stent thrombosis	13 (6.1)	13 (6.3)	0.98
Death, myocardial infarction, or target lesion revascularization	44 (20.4)	41 (19.6)	0.71

9 month TLR : 16
- Xience : 7
  - unstable 1 asymptomatic 4, stable 1, silent 1
- Endeavor : 9
  - unstable 3, asymptomatic 4, stable 1, silent 1

Ischemic driven TLR : 9 months
- Clinical presentation
  - Unstable angina 4 pts
  - Stable angina /silent 4 pts

ISAR-DESIRE II, JACC 2010

Major adverse clinical outcome in 9 months (185/294, 62.9% clinical follow-up)



Comparison of ISAR-DESIRE II- Angiographic Restenosis in DES-ISR

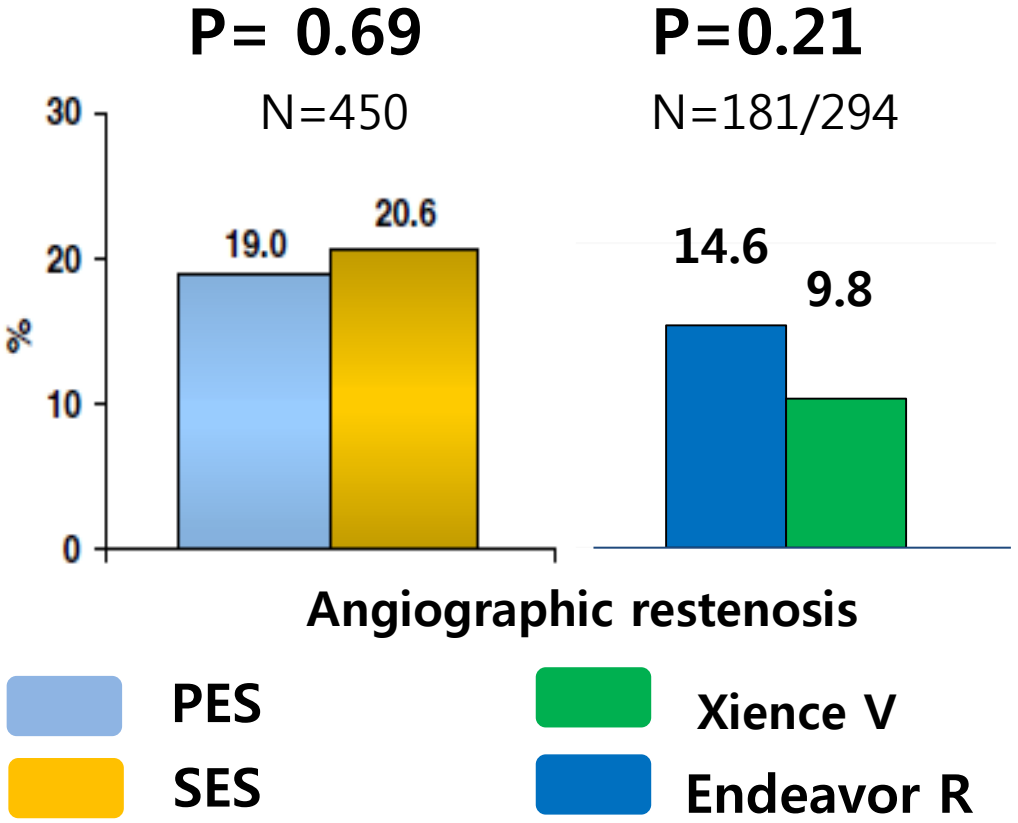
Randomized Trial of Paclitaxel- Versus Sirolimus-Eluting Stents for Treatment of Coronary Restenosis in Sirolimus-Eluting Stents

The ISAR-DESIRE 2 (Intracoronary Stenting and Angiographic Results: Drug Eluting Stents for In-Stent Restenosis 2) Study

Table 3 Angiographic Outcomes at 6 to 8 Months

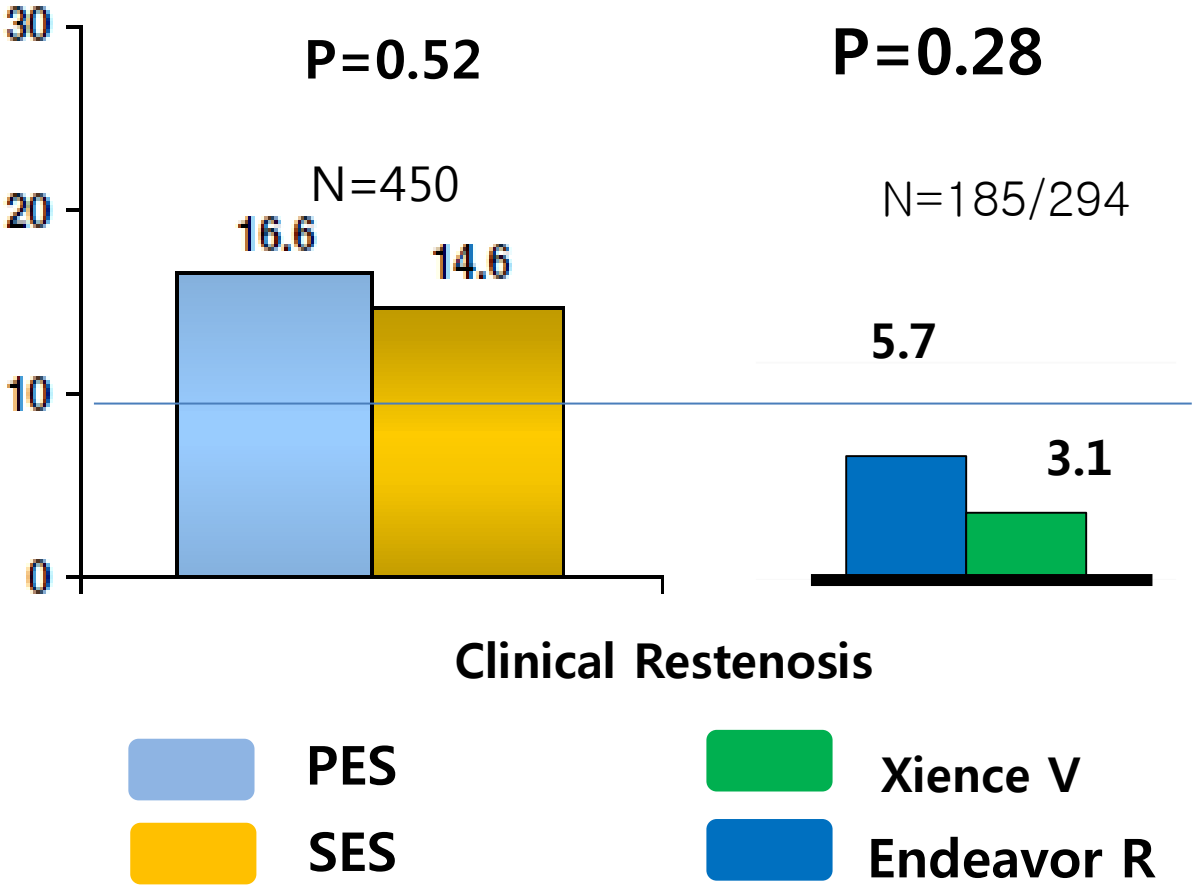
	SES (n = 205)	PES (n = 204)	p Value
Minimal luminal diameter, in-stent, mm	2.14 ± 0.78	2.16 ± 0.72	0.78
Minimal luminal diameter, in-segment, mm	1.93 ± 0.73	1.94 ± 0.67	0.98
Stenosis, in-stent, %	26.6 ± 23.6	25.4 ± 21.5	0.53
Stenosis, in-segment, %	34.0 ± 21.1	33.3 ± 18.7	0.73
Late loss, in-stent, mm	0.40 ± 0.65	0.38 ± 0.59	0.85
Late loss, in-segment, mm	0.26 ± 0.61	0.25 ± 0.58	0.86
Recurrent binary restenosis	39 (19.0)	42 (20.6)	0.69
Restenosis morphology			0.42
Type I (focal)			
Focal marginal	9 (23.0)	14 (33.2)	
Focal body	18 (46.1)	11 (26.3)	
Multifocal	4 (10.3)	6 (14.3)	
Type II (diffuse)	4 (10.3)	7 (16.7)	
Type III (proliferative)	0 (0.0)	0 (0.0)	
Type IV (occlusive)	4 (10.3)	4 (9.5)	

Data shown as mean ± SD or n (%).
Abbreviations as in Table 1.



ISAR-DESIRE II, JACC 2010 VS. RESTENT-ISR trial

Comparison of ISAR-DESIRE II- Clinical Restenosis in DES-ISR (9 mon)



ISAR-DESIRE II, JACC 2010

Major adverse clinical outcome in 1 year (119/294, 40.4% follow-up)

	MACE (1months)	MACE (3months)	MACE (9months)	MACE (12months)	Ischemic TLR	TLR	nonTLR	Stroke	MACE (9months)	MACE (12months)
Total (185/305 pts)	2	2	18	6	11	22	3	2	24	30
Xience V (98 pts)	2	1	8	2	4	9	1	2	11	13
Endeavor resolute (87 pts)	0	1	12	4	7	13	2	0	13	17

◆**1 yr MACE = Ischemic TLR** / TLR

- **Stent thrombosis/MI : 12 months : Endeavor resolute**
- **Unstable angina/TLR : 12 months : Endeavor resolute**
- **Stable angina/TLR : 12 months ; Xience V**
- Asymptomatic/ TLR 12month ; Endeavor resolute
- Asymptomatic/TLR 12months : Endeavor resolute
- Asymptomatic/ TLR 12months : Xience V

Summary

- Underlying mechanism of DES restenosis involve a complex interplay of biological, mechanical, and technical factors compared to BMS era
- The treatment of DES restenosis is based on appreciation of underlying mechanisms and can vary from simple POBA, to DES, DEB when appropriate, to CABG in the most extreme cases.
- 2nd generation DES for DES-ISR would be safe and effacious compared to 1st generation DES

Thank you for your kind attention

Special Thank for RESTENT-ISR investigator group

Backup slide

Clinical outcome of percutaneous treatment of in-stent restenosis with drug-eluting stents: results from the first phase of the prospective multicentre German DES.DE registry

Mohamed Abdel-Wahab[1]*, MD; Christoph A. Nienaber[2], MD; Ahmad E. Mostafa[1], MD; Georg Sabin[3], MD; Ulrich Tebbe[4], MD; Matthias Hochadel[5], PhD; Jochen Senges[5], MD; Ibrahim Akin[2], MD; Karl-Heinz Kuck[6], MD; Christian Hamm[7], MD; Gert Richardt[1], MD; for the German Drug-Eluting Stent (DES.DE) registry

Table 1. Baseline clinical characteristics of the study population.

	In-stent restenosis (n=872)	*De novo* stenosis (n=4272)	*p*-value	OR (95% CI)
Men	75.9%	74.4%	0.35	1.08 (0.91-1.28)
Age (years)	66.2±10.4	65±10.5	<0.01	
BMI	27.4 (25-30.1)	27.4 (25-30.2)	0.89	
Diabetes mellitus	28.8%	32.2%	<0.05	0.85 (0.72-0.99)
Hypertension	86.9%	83.3%	<0.01	1.33 (1.07-1.64)
Smoking	16.2%	23.5%	<0.0001	0.63 (0.51-0.78)
Hyperlipidaemia	84.5%	79.6%	<0.01	1.4 (1.14-1.7)
Positive family history	39.5%	35.5%	0.07	1.18 (0.99-1.42)
Previous MI	49.8%	26.2%	<0.0001	2.8 (2.41-3.26)
Previous CABG	15%	14.2%	0.54	1.07 (0.87-1.31)
Renal insufficiency	13.2%	12.2%	0.41	1.1 (0.88-1.36)
Heart failure	15%	15.7%	0.59	0.94 (0.76-1.17)
Atrial fibrillation	6.5%	8.2%	0.08	0.77 (0.58-1.03)

Values are in percentage, mean±standard deviation or median and interquartile range; BMI: body mass index; MI: myocardial infarction; CABG: coronary artery bypass grafting

Table 5. Clinical outcome at one year (unadjusted).

	In-stent restenosis (n=817)	*De novo* stenosis (n=3973)	*p*-value	OR (95% CI)
MACCE	8.7%	8.2%	0.63	1.07 (0.82-1.4)
Mortality	3.5%	4.2%	0.39	0.84 (0.56-1.25)
Myocardial infarction	4.7%	3.1%	<0.05	1.56 (1.07-2.27)
Cerebrovascular stroke	0.8%	1.2%	0.26	0.61 (0.26-1.44)
TVR	12.7%	10.5%	0.07	1.24 (0.98-1.56)
Definite stent thrombosis	1.3%	0.7%	0.13	1.75 (0.84-3.61)
Medications				
Aspirin	95.4%	94.1%	0.14	1.32 (0.91-1.91)
Clopidogrel	56.3%	55.6%	0.76	1.03 (0.87-1.21)
Statin	85.7%	82.7%	<0.05	1.25 (1-1.56)
ACE-inhibitor	66.1%	60.2%	<0.01	1.29 (1.09-1.52)
Beta-blocker	87.7%	83.3%	<0.01	1.42 (1.13-1.79)

MACCE: major adverse cardiac and cerebrovascular events (composite of death, myocardial infarction and stroke); TVR: target vessel revascularisation; ACE: angiotensin converting enzyme

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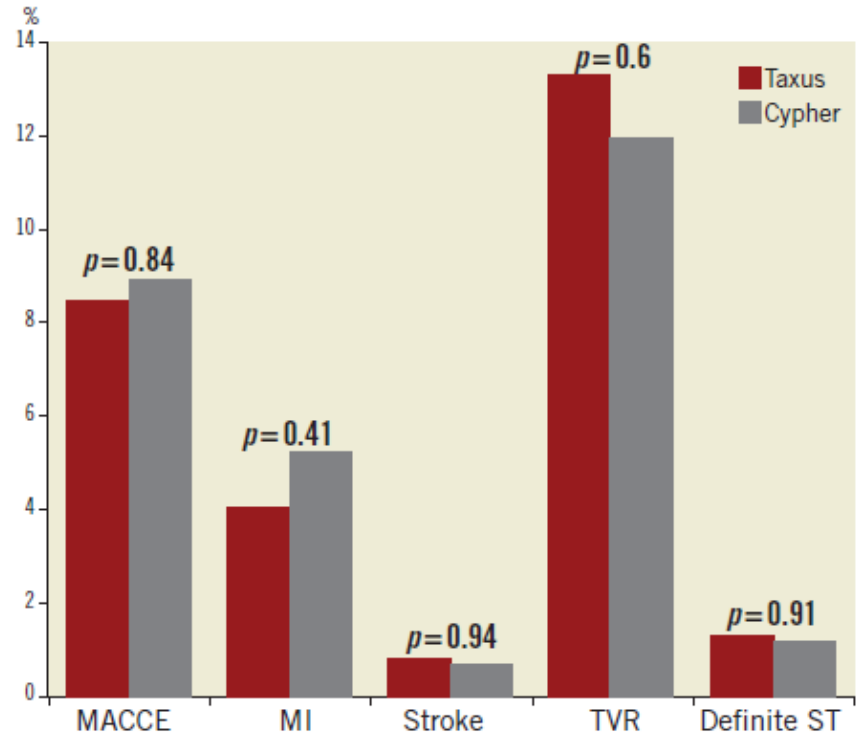

Figure 2. *Clinical outcome at 12 months for patients treated with Cypher versus Taxus stents for in-stent restenosis. MACCE: major adverse cardiac and cerebrovascular events; MI: myocardial infarction; TVR: target vessel revascularisation; ST: stent thrombosis*

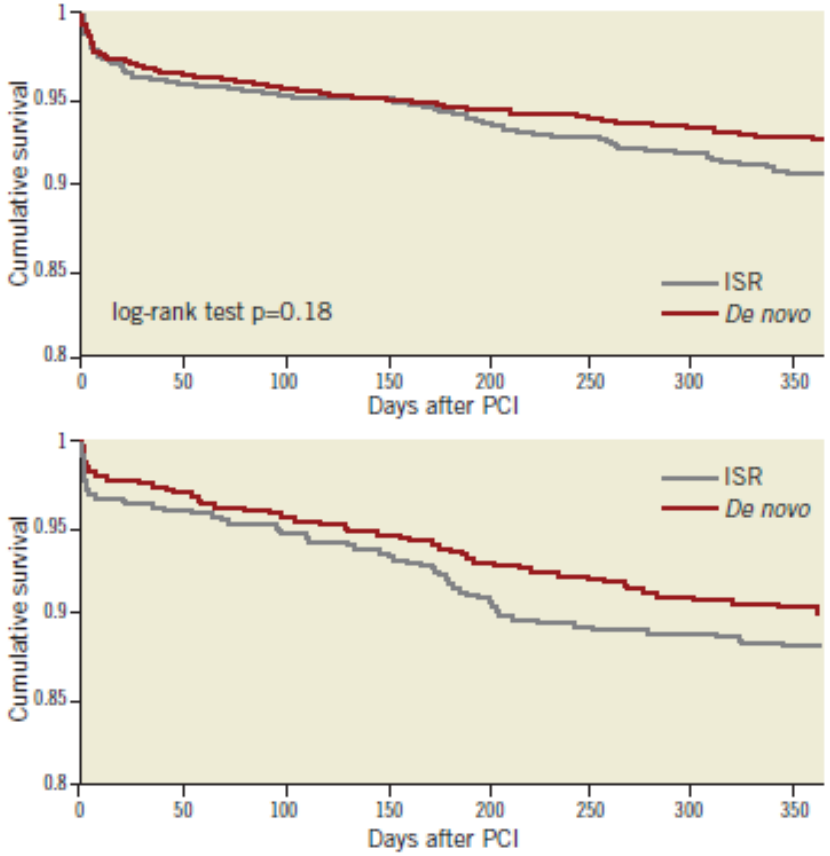

Figure 1. *Kaplan-Meier curves for survival free of myocardial infarction/stroke and target vessel revascularisation up until one year of follow-up among patients with in-stent restenosis and de novo lesions.*

Abstract

Aims: Treatment of in-stent restenosis (ISR) was historically considered the Achilles heel of percutaneous coronary intervention (PCI) and has been associated with worse clinical outcome than PCI of *de novo* lesions. However, comparative data on ISR and *de novo* lesions using drug-eluting stents (DES) are scarce. Therefore, we aimed to assess the impact of ISR on procedural and long-term outcome in patients treated with DES.

Methods and results: We analysed data from 5,144 patients enrolled in the prospective multicentre German Drug-Eluting Stent Registry (DES.DE). The registry included 872 patients (17%) treated for ISR with follow-up data (median 12.4 months) available for 817 patients (94%). Of the ISR patients, 37.1% (n=323) presented with acute coronary syndromes. In total, 1,027 DES were used (528 sirolimus-eluting stents and 499 paclitaxel-eluting stents), with successful implantation in 97.7% of patients. In the ISR cohort, myocardial infarction (MI) during hospitalisation was observed in 1.6% of patients (n=14) and in-hospital mortality was only 0.3% (n=3). Major adverse cardiac and cerebrovascular events (MACCE) rate at follow-up (defined as a composite of death, MI and stroke) was 8.7% (n=71) versus 8.2% (n=325) in patients treated for *de novo* lesions (p=0.63). Target vessel revascularisation (TVR) rate was 12.7% (n=100), numerically higher than in patients with *de novo* lesions (10.5%, p=0.07). Ten patients (1.3%) suffered from ARC definite stent thrombosis versus 0.7% observed in patients with *de novo* lesions (p=0.13). After adjustment for differences in baseline characteristics, TVR rates were statistically higher in the ISR cohort (OR 1.27, 95%CI 1.01-1.61, p=0.04), while MACCE rates remained comparable (OR 1.10, 95%CI 0.83-1.44, p=0.51). The type of stent used (sirolimus vs. paclitaxel-eluting stent) did not impact the rate of MACCE, TVR or definite stent thrombosis at one year.

Conclusions: Results from this large prospective multicentre registry confirm that treatment of ISR with DES is effective and safe, with similar procedural outcome but slightly higher revascularisation rates at one year compared to patients treated for *de novo* lesions, with no differences in outcome between sirolimus- and paclitaxel-eluting stents.

In-stent restenosis: the gold standard has changed

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Abstract

In-stent restenosis remains an important issue even in the drug-eluting stent (DES) era today. In recent years, drug-eluting balloons (DEB) have emerged as a potential alternative to the treatment of in-stent restenosis. Paclitaxel was identified as the primary drug for DEB because of its rapid uptake and prolonged retention. Non-stent-based local drug delivery using DEB maintains the antiproliferation properties of DES, but without the limitations of DES such as subacute stent thrombosis, stent fractures, prolonged antiplatelet therapy and more importantly, avoiding a "stent-in-a-stent" approach. The first major impact of drug-eluting balloon (DEB) in the management of bare metal instent restenosis was the "PACCOCATH ISR I" randomised trial, comparing the efficacy of drug-eluting balloon versus uncoated balloon. The six months angiographic results showed a binary restenosis of 5% and 4% MACE in the drug-eluting balloon group, compared with 43% binary restenosis and 31% MACE, in the uncoated balloon group (p=0.002 and 0.02). The second major DEB trial is the "PEPCAD II Trial", comparing the efficacy of the SeQuent Please DEB with the Taxus drug-eluting stent in the treatment of bare-metal stent instent restenosis. At 6-month follow-up, in-segment late lumen loss was 0.38±0.61 mm in the DES group versus 0.17±0.42mm (p=0.03) in the DEB group, resulting in a binary restenosis rate of 12/59 (20%) versus 4/57 (7%; p=0.06). At 12 months, MACE rates were 22% in the Taxus group and 9% in the DEB group (P=0.08). The TLR at 12 months was 15% in the Taxus group and 6% in the DEB group (p=0.15). Based on these two pivotal trials, the European Society of Cardiology Guidelines for Percutaneous Coronary Intervention (2010) recommended that DEB should be considered for the treatment of in-stent restenosis after prior bare-metal stent. This was accorded a class 2 IIa indication, with a level B evidence.

EuroIntervention 7 Suppl K: K43-46.