Potential conflicts of interest

Speaker's name: MISCHIE Alexandru Nicolae

☐ **I do not have any potential conflict of interest**

Endothelial Dysfunction: Prognosis

Author / Method	Year of publication	Target Population	Number of patients	Median follow-up period	Conclusions
Coronary angiography					
Al Suwaidi et al (18)	2000	CAD	157	28 mo	Predictive of increased rates of myocardial events
Schachinger et al (19)	2000	Routine coronarography +/- PTCA for the evaluation of chest pain	147	7.7 y	Independent predictor of increased rates of myocardial events
Hollenberg et al (47)	2001	Post-cardiac transplant	73	a CAV or cardiac	Predictive of CV events
Halcox et al (20)	2002	With and without CAD	308	death	Independent predictor of CV events
Targonski et al (52)	2003	CAD	503	46+/3 months	Independent predictor of cerebrovascular events
von Mering et al (21)	2004	Clinical indication for coronarography	163	16 mo	Response to Ach was an indepent predictor of events
Kübrich et al (48)	2008	(females)	185	48 mo	Independent predictor of CV events
Sánchez et al (49)	2009	Post-cardiac transplant Coronary syndrome x	147	25+/-33 mo 7 y	Independent predictor of CV events, mainly hospital readmissions for worsening angina
Impedance Plethysmography					
Perticone et al (43)	2001	Untreated young (<54 y) hypertensives	225	31.5 mo	Predictive of increased rates of myocardial events
Heitzer et al (22)	2001	CAD	281	4.5 y	Independent predictor of CV events
Fichtlscherer et al (31)	2004	ACS	198	47.7+/-15.1 mo	Response to Ach predictive of events
Heitzer et al (45)	2005	Heart failure (early-stage)	289	4.8 y	Response to Ach was an indepent predictor of events
Flow-mediated dilatation					
Modena et al (44)	2002	Post-menopausal hypertensive females	400	67 mo	No improvement in ED with antihypertensives associated with CV events
Gokce et al (29)	2003	PAD before elective vascular surgery	187	1.2 y	FMD independently predictive of CV events
Brevetti et al (23)	2003	PAD	131	23+/-10 mo	FMD < 5.8% independent predictor of CV events
Chan et al (50)	2003	Patients in cardiac rehabilitation	152	34+/-10 mo	FMD associated with CV events
Patti et al (27)	2005	CAD after PTCA	136	6 mo	FMD < 7% predictive of restenosis
Karatzis et al (32)	2006	NSTEMI	98	24.8 +/- 5.9 mo	FMD < 1.9% independently predictive of CV events
Yoshida et al (24)	2006	Mixed cardiac heart disease	221	1st cardiac event	FMD predictive of CV events
Shimbo et al (36)	2007	Asymptomatic free of stroke or MI	842	36 mo	FMD < 7.5% predictive of increased risk (not in multivariate analysis)
Yeboah et al (34)	2007	Elderly (72-98 y)	2792	5 y	FMD predictive of CV events beyond traditional risk factors
Shechter et al (25)	2007	Consecutive healthy and cardiac patients	110	15+/-2 mo	FMD predictive of CV events beyond traditional risk factors
Rossi et al (38)	2008	Asymptomatic post-menopausal females	2264	45+/-13 mo	FMD predictive of CV events beyond traditional risk factors
Corrado et al (39)	2008	Asymptomatic	84	24 mo	FMD and IMT predictive of CV events
Suzuki et al (37)	2008	Asymptomatic free of stroke or MI	819	81+/-21 mo	FMD and metabolic syndrome predictive of higher CV events than those with either one of them alone
Takase (26)	2008	Clinically suspected CAD	103	50+/- 15 mo	FMD and exercise stress ECG predictive of CV events, whereas IMT less powerful in predicting CV events
Yeboah et al (35)	2009	Asymptomatic multi-ethnic (61.2+/-9.9 y)	6814	5 y	FMD predictive of CV events and increased accuracy when added to FRS
Kitta et al (33)	2009	CAD and FMD <5.5% after medical treatment	251	36 mo or 1st cardiac event	Persistent impairment of FMD despite optimized therapy to reduce RF-independent predictor of CV events
Corrado et al (28)	2009	CAD after PTCA	58	10 mo	IMT, glycemia, and a lower FMD predictive of stent restenosis
Takishima et al (46)	2011	Ischaemic heart failure and FMD <5.5% after medical treatment	245	36 mo or 1st cardiac event	Persistent impairment of FMD despite optimized therapy to reduce RF-independent predictor of CV events
Reactive hyperemia					
Mitchell et al (40)	2004	Asymptomatic with moderate RF (61 y)	2045	3 y	SS-RH related to CV RF, lesser correlation for SS-RH incorporated into FMD
Huang et al (30)	2007	PAD before elective vascular surgery	267	309 days	RH and FMD independent predictors of CV events beyond traditional RF
Philpott et al (43)	2009	Asymptomatic men without CV disease	1477	-	SS-RH and vti-RH better associated with CV RF than FMD
Anderson et al (13)	2011	Asymptomatic men without CV disease (49.4 y)	1574	5 y	vti-RH (but not FMT and CRP) and IMT predictive of CV events

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Halcox et al (20)	2002	With and without CAD	308		Independent predictor of CV events
Targonski et al (21)	2003	CAD	157	16 mo	Independent predictor of cerebrovascular events
von Mering et al (22)	2004	Clinical indication for coronarography (females)	139	48 mo	Response to Ach was an indepent predictor of events
Kübrich et al (23)	2005	Post-cardiac transplant	50	25+/-33 mo	Independent predictor of CV events
Sánchez et al (24)	2008	Coronary syndrome x	150	7 y	Independent predictor of CV events, mainly hospital readmissions for worsening angina
Impedance Plethysmography					
Flow-mediated dilatation					
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Endothelial Dysfunction: DES

Author	Year	Number of subjects	Median follow-up period	Stent type procedure	Testing method and dosage	Evaluated segment	Conclusions/Limitations
Corvaja et al.	1999	37	> 6 mo	BMS (n=14) BA (n=13) DCA (n=12)	Acetylcholine (10-5, 10-4, 10-4 mol/L)	Mean segment diameter at LAD	BMS-i-ED increased vs. BA/DCA
Aytemir et al.	2002	48	30 min after stenting	BMS (n=20) BMS+ Abciximab (n=20)	Acetylcholine (10-7, 10-6 mol/L) Nitroglycerin (200 mcg) Adenosine (24mcg)	5 and 10 mm distal to the stent	Superior Ach-i-DEP in Abciximab group
Hofma et al.	2004	15	At the intervention / 6 mo	Stent (n=7) Stent + irradiation (n=8)	Acetylcholine, LFA, IVUS.	Distal to the stent	Irradiation did not affect the EF acutely or at 6 mo. Irradiated segments had less negative remodeling but higher plaque burden than the controls did.
Togni et al.	2004	27	10+/-2 mo (BMS) 9+/-1 mo (Brachy T)	BMS (n=14) Brachy T (n=13)	Exercise	5 to 15 mm proximal and distal to the stent	Brachy-i-ED in the proximal and distal segments vs. BMS
Togni et al.	2005	25	6+/-1 mo	BMS (n=11) SES (n=14)	Exercise Nitrates	5 to 10 mm proximal and distal to stent	SES-i-ED in the proximal and distal segments vs. BMS
Hofma et al.	2005	12	6 mo	BMS (n=5) SES (n=7)	Acetylcholine (10-5, 10-4, 10-3 mol/L) Nitrates	2 to 17 mm distal to the stent	SES-i-ED in the proximal and distal segments vs. BMS
Togni et al.	2007	27	6+/-2 mo	BMS (n=12) PES (n=15)	Exercise Nitrates	5 to 10 mm proximal and distal to stent	PES-i-ED in the proximal and distal segments vs. BMS
Fuke et al.	2007	33	6 mo	BMS (n=12) SES (n=21)	Acetylcholine (10-5, 10-4 mol/L)	5 mm proximal and distal to the stent	SES-i-ED in the proximal and distal segments vs. BMS
Kim et al.	2007	22 77	6-9 mo	BMS (n=5) SES (n=9) PES (n=8)	Acetylcholine (10-5 mol/L) Nitrates	5, 10 and 20 mm proximal and distal to the stent	SES and PES-i-ED in the distal and far-distal segments vs. BMS
Kim et al.	2008	83	6 mo	BMS (n=10) SES (n=39) PES (n=36)	Acetylcholine (20, 30 and 100 mcg/min) Nitrate (200 mcg/min)	5 mm proximal and 5 mm distal to the stent	SES and PES-i-ED especially in the distal segments vs. BMS
Hamilos et al.	2008	93	9-12 mo	BMS (n=13) ZES (n=10) SES (n=21) PES (n=11) bAPES (n=28)	Atrial pacing	10 mm proximal and 10 mm distal to the stent	SES and PES-i-ED in the proximal and distal segments vs. BMS/ZES/bAPES
Hamilos et al.	2008	34	9 mo	BMS (n=19) SES (n=15)	Atrial pacing	5 to 15 mm proximal and distal to the stent	SES-i-ED in the proximal and distal segments vs. BMS
Kim et al.	2008	23	6-9 mo	ZES (n=11) SES (n=12)	Acetylcholine (10-5 mol/L) Nitrates	5, 10 and 20 mm proximal and distal to the stent	SES-i-ED in the distal and far distal segments vs. ZES.
Kim et al.	2009	90	6 mo	BMS (n=10) ZES (n=20) SES (n=20)	Acetylcholine (10, 20, 30 and 100 mcg/min) Nitrate (200 mcg/min)	5 mm proximal and 5 mm distal to the stent	Progressive ED in incremental doses of Acetylcholine for ZES and SES vs. BMS. Superior SES-i-ED in distal segments vs. ZES.
Ueda et al.	2009	39	2 weeks, 6 mo post-STEMI	BMS (n=19) SES (n=19)	Acetylcholine (10 mcg/min) Nitrates	10 to 20 mm distal to the stent	SES-i-ED in the distal segments vs. BMS. EF recovery of BMS at 6 mo vs. 2 weeks. Impaired anterior LV-RWM in SES vs. BMS at 6 mo, even though LVEF between the 2 groups was similar at any time points.
Iaccarino et al.	2010	40	12 mo post Non-STEMI	TES (n=20) PES (n=20)	Atrial pacing	-	Study in progress, performed in Non-STEMI setting. 3 stents per patient.
Neria et al.	2010	160	1 mo / 12 mo	BMS (n=86) DES (n=74)	Exercise stress test	Clinical evaluation and follow-up	At 1 mo, increased positive exercise stress test rate in DES vs. BMS probably due to DES-ED. At 12 mo, DES patients had lower rate of TVR but a higher rate of MI.
Lee et al.	2011	42	Angiography at follow-up after DES	DES (Cypher and Taxus)	Acetylcholine (20, 30 and 100 mcg/min) Nitrates (2-5 mg isosorbide dinitrate)	5 to 10 mm proximal and distal; 10 to 20 mm distal to the stent	DES-i-ED in distal segments. Stent length proportionally with ED degree.
Kitabata et al.	2011	14	6 mo	BMS (n=14) SES (n=14)	Acetylcholine (10-3 mcg/min) Nitrate (200 mcg/min)	10 and 5 mm proximal to the stent. 5, 10 and 20 mm distal to the stent. Proximal, distal and total mean segment diameter.	Stents implanted in pairs in each patient. SES-i-ED in the proximal and especially distal and far-distal segments vs. BMS. Severe ED in atherosclerotic SES distal arteries subgroup vs. the same BMS subgroup. ED correlated with SES length and disproportional with SES diameter. Mean segment diameters more adequate for ED studies involving stents.

Endothelial Dysfunction: DES

Author	Year	Number of subject	Median follow-up period	Stent type procedure	Testing method and dosage	Evaluated segment	Conclusions/Limitations
Carrozza i et al.	1999	37	> 6 mo	BMS (n=14) BA (n=13) DCA (n=12)	Acetylcholine (10-6, 10-5, 10-4 mol/L)	Mean segment diameter at LAD	BMS-i-ED increased vs. BA/DCA
Aytekin et al.	2002	48	30 min after stenting	BMS (n=20) BMS+ Abciximab (n=20)	Acetylcholine (10-7, 10-6 mol/L) Nitroglycerin (200 mcg) Adenosine (24mcg)	5 and 10 mm distal to the stent	Superior Ach-i-DEP in Abciximab group
Hofma et al.	2004	15	At the intervention / 6 mo	Stent (n=7) Stent + irradiation (n=8)	Acetylcholine, LFA, IVUS.	Distal to the stent	Irradiation did not affect the EF acutely or at 6 mo. Irradiated segments had less negative remodeling, but higher plaque burden than the controls did.
Togni et al.	2004	27	10+/-2 mo (BMS) 9+/-1 mo	BMS (n=14) Brachy T (n=13)	Ergotrate	5 to 15 mm proximal and distal to the stent	Brachy-i-ED in the proximal and distal segments vs. BMS
Togni et al.							
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Hamilos et al.	2008	34	9 mo	BMS (n=19) SES (n=15)	Atrial pacing	5 to 15 mm proximal and distal to the stent	SES-i-ED in the proximal and distal segments vs. BMS
Kim et al.	2008	23	6-9 mo	ZES (n=11) SES (n=12)	Acetylcholine (10-6 mol/L) Nitrates	5, 10 and 20 mm proximal and distal to the stent	SES-i-ED in the distal and far distal segments vs. ZES.
Kim et al.	2009	30	6 mo	BMS (n=10) ZES (n=20) SES (n=20)	Acetylcholine (10, 20, 30 and 100 mcg/min) Nitrate (200 mcg/min)	5 mm proximal and 5 mm distal to the stent	Progressive ED in incremental doses of Acetylcholine for ZES and SES vs. BMS. Superior SES-i-ED in distal segments vs. ZES.
Ubaid et al.	2009	39	2 weeks, 6 mo post-STEMI	BMS (n=19) SES (n=15)	Acetylcholine (10 mcg/min) Nitrates	15 to 20 mm distal to the stent	SES-i-ED in the distal segments vs. BMS. EF recovery of BMS at 6 mo vs. 2 weeks. Impaired anterior LV-RWM in SES vs. BMS at 6 mo, even though LVEF between the 2 groups was similar at any time points.
Iaccarino et al.	2010	40	12 mo post Non-STEMI	TES (n=20) PES (n=20)	Atrial pacing	-	Study in progress, performed in Non-STEMI setting. 2 stents per patient.
Neria et al.	2010	160	1 mo / 12 mo	BMS (n=86) DES (n=74)	Exercise stress test	Clinical evaluation and follow-up	At 1 mo, increased positive exercise stress test rate in DES vs. BMS, probably due to DES-ED. At 12 mo, DES patients had lower rate of TVR but a higher rate of MI.
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Alfonso et al.	2011	14	6 mo	BMS (n=14) SES (n=14)	Acetylcholine (10-3 mcg/min) Nitrate (200 mcg/min)	10 and 5 mm proximal to the stent. 5, 10 and 20 mm distal to the stent. Proximal, distal and total mean segment diameter.	Stents implanted in pairs in each patient. SES-i-ED in the proximal and especially distal and far-distal segments vs. BMS. Severe ED in atherosclerotic SES distal arteries subgroup vs. the same BMS subgroup. ED correlated with SES length and disproportional with SES diameter. Mean segment diameters more adequate for ED studies involving stents.

Most of these studies conclude that SES and PES induce ED proximal and especially distal to stent edges, but comparison was made in different persons with different risk factors.

Head-to-head *C*omparison of si*R*olimus eluting st*E*nt vs. bare metal stent evaluating the en*D*oth*E*lial dysfu*N*ction in the same pa*T*ient with mult*I*ple coronary *A*rtery *L*esions.

The ***CREDENTIAL*** study

Authors: Alexandru Nicolae Mischie, M.D., Marco Stefano Nazzaro, M.D., PhD, Rosario Fiorilli, M.D., Francesco De Felice, M.D., Carmine Musto, M.D., Carla Boschetti, M.D., Crina Sinescu, M.D., PhD, FESC, Roberto Violini, M.D., PhD, FESC.

The study was performed at the Interventional Cardiology Unit, Ospedale San Camillo (Roma, Italy), Direttore Prof. Roberto Violini, from from January to September 2009.

Head-to-head *C*omparison of si*R*olimus eluting st*E*nt vs. bare metal stent evaluating the en*D*oth*E*lial dysfu*N*ction in the same pa*T*ient with mult*I*ple coronary *A*rtery *L*esions.

The ***CREDENTIAL*** study

The aim of our randomized study was to provide the best accuracy regarding the effects of SES and BMS over ED in the same patient. To date, no study has investigated this issue in a prospective randomized fashion and by using a pair-stenting concept which overcomes the different risk factors of each patient.

Study Design:

In this monocentric study, we compared the ED of SES vs. BMS, both implanted in the same patient with multiple de novo coronary artery lesions undergoing elective percutaneous coronary intervention (PCI). Patients, data analyst and statistician were masked to treatment allocation.

Inclusion criteria:

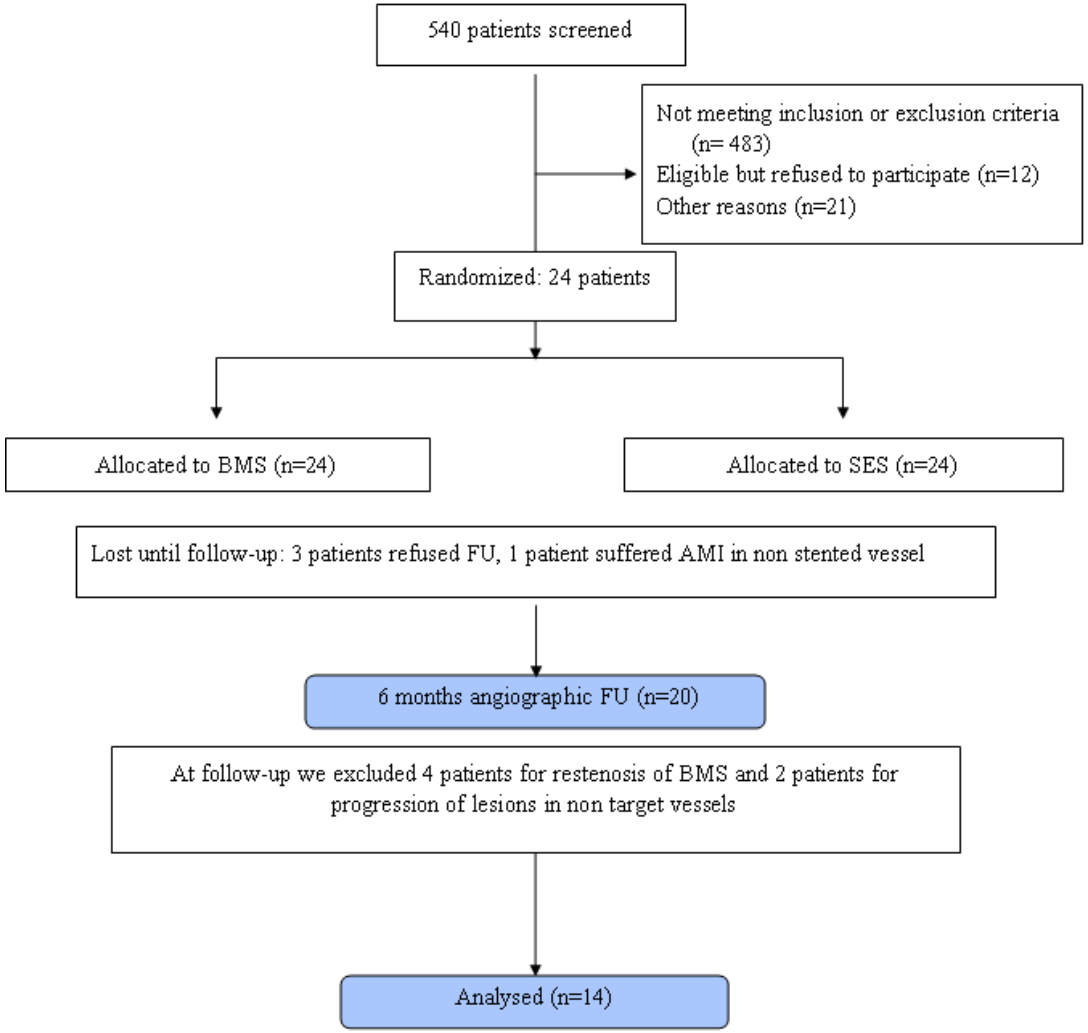
- **stable angina pectoris and/or a positive stress test**
- **presence of at least two de novo significant angiographic stenosis in different native coronary vessels or in the same vessel but in different ramifications with similar diameter.**

Exclusion criteria:

- acute coronary syndrome in the last 3 months
- coronary vasospasm, coronary angiographic findings of a fresh thrombus at the initial angiography (filling defect proximal to or involving the stenosis)
- coronary anatomy unsuitable for intracoronary Ach infusion (left main coronary artery disease >30%, surgical diffuse three vessel disease or other anatomical considerations that make it unsafe to perform intracoronary studies)
- target vessel diameter <2,50 mm and lesion length <10 and >30 mm
- target vessel diameter difference >0,5mm and difference of the length of the stenosis >50%
- severe LV dysfunction
- bifurcation/ostial lesions
- presence of a dissection
- any contraindication/nontolerance to the use of aspirin, heparin and/or clopidogrel
- chronic renal failure requiring dialysis
- lack of consent to participate
- survival expectancy < 1 year
- angiographic restenosis at follow-up
- patients with severe risk factors for ED: uncontrolled diabetes mellitus (DM), uncontrolled hypertension (systolic blood pressure >180mmHg), refuse to discontinue smoking, persistent hypercholesterolemia (total cholesterol >240mg/dl)

Head-to-head *C*omparison of si*R*olimus eluting st*E*nt vs. bare metal stent evaluating the en*D*oth*E*lial dysfu*N*ction in the same pa*T*ient with mult*I*ple coronary *A*rtery *L*esions.

The *CREDENTIAL* study



Study protocol

euro PCR

Head-to-head *C*omparison of si*R*olimus eluting st*E*nt vs. bare metal stent evaluating the en*D*oth*E*lial dysfu*N*ction in the same pa*T*ient with mult*I*ple coronary *A*rtery *L*esions.

The ***CREDENTIAL*** study

Table 1. Baseline characteristics.

Age (years)	70.8 ± 7.1
Body surface area (m^2)	1.879 ± 0.117
Male sex	9 (64.2%)
Current smoking	4 (28.5%)
Positive family history of HD*	8 (57.1%)
Hypertension	13 (92.8%)
Prior myocardial infarction	6 (42.8%)
Diabetes mellitus type II	5 (35.7%)
Stable angina (CCS† class)	2.857 ± 0.363
Heart Failure (NYHA‡ class)	1.50 ± 0.65

*HD= heart disease;
†CCS= Canadian Cardiovascular Society;
‡NYHA= New York Heart Association.

Table 2. Blood samples results at 6 moths follow-up.

C-Reactive Protein (mg/dl)	0.09 ± 0.04
Creatinin (mg/dl)	0.94 ± 0.27
HbA1C (%)	6.043 ± 0.696
Homocysteine (microm/l)	9.95 ± 2.59
Hemoglobin (gr/dL)	13.5 ± 1.3
Total Cholesterol (mg/dl)	155.9 ± 29.7
Low Density Lipoprotein (mg/dl)	78.8 ± 19.1
High Density Lipoprotein (mg/dl)	45.9 ± 13.8
Triglyceride (mg/dl)	112.1 ± 64.2
Fibrinogen (mg/dl)	302.6 ± 45.9

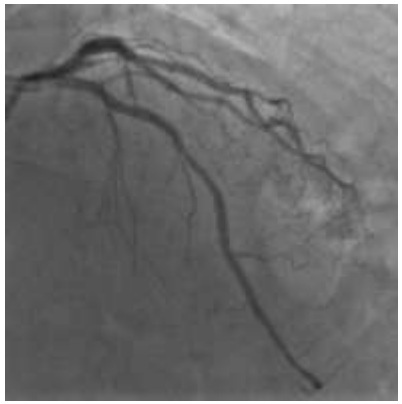
PCR EAPCI EUROPEAN SOCIETY OF CARDIOLOGY EACTS

Head-to-head *C*omparison of si*R*olimus eluting st*E*nt vs. bare metal stent evaluating the en*D*oth*E*lial dysfu*N*ction in the same pa*T*ient with mult*I*ple coronary *A*rtery *L*esions.

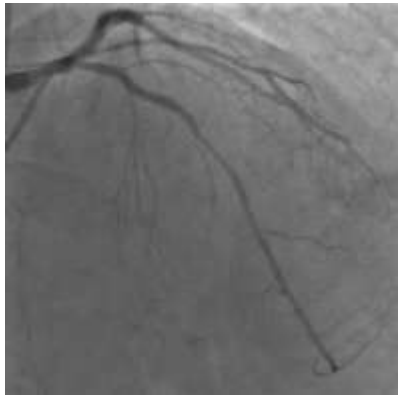
The *CREDENTIAL* study

Table 3. PCI Characteristics.

Mean BMS length (mm)/ (range)	16.1 ± 2.9	(12.00-19.00)
Mean BMS diameter (mm)/ (range)	3.2 ± 0.4	(2.50-4.00)
Mean SES stent length (mm)/ (range)	19.29 ± 7.28	(13.00-30.00)
Mean SES stent diameter (mm)/ (range)	2.86 ± 0.39	(2.50-4.00)
BMS Artery		
Right Coronary Artery	5(35.7%)	
Circonflex Artery	5 (35.7%)	
Left Anterior Descendent Artery	4(28.5%)	
SES Artery		
Left Anterior Descendent Artery	5 (35.7%)	
Right Coronary Artery	4 (28.5%)	
Circonflex Artery	3 (21.4%)	
Ramus Intermedius	2 (14.2%)	



Baseline



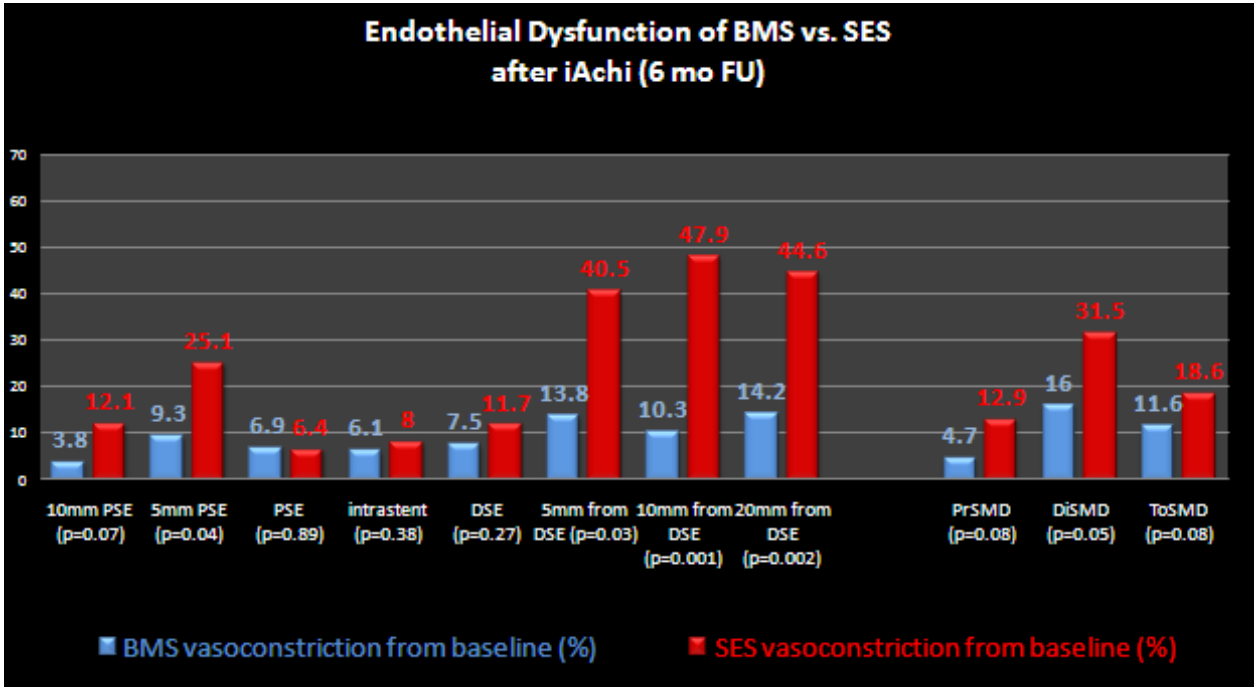
Ach infusion

Head-to-head *C*omparison of si*R*olimus eluting st*E*nt vs. bare metal stent evaluating the en*D*oth*E*lial dysfu*N*ction in the same pa*T*ient with mult*I*ple coronary *A*rtery *L*esions.

The ***CREDENTIAL*** study

Results (1):

For the overall population SES produce:
•a 3.5 fold vasoconstriction of SES vs. BMS calculated for distal diameters (mean value for the 3 distal diameters)
•a 1.9 fold vasoconstriction of SES vs. BMS calculated for DiSMD.



BMS = bare metal stents;
FU = follow-up;
SES = sirolimus eluting stents;
iAchi = intracoronary acetylcholine infusion;
mo = month;
PSE = proximal (to) stent edge;
DSE = distal (to) stent edge;
PrSMD = proximal segment mean diameter- mean diameter calculated from 10 mm PSE to PSE;
DiSMD = distal segment mean diameter- mean diameter calculated from DSE to 20 mm after DSE;
ToSMD = total segment mean diameter - mean diameter from 10 mm PSE to 20 mm from DSE

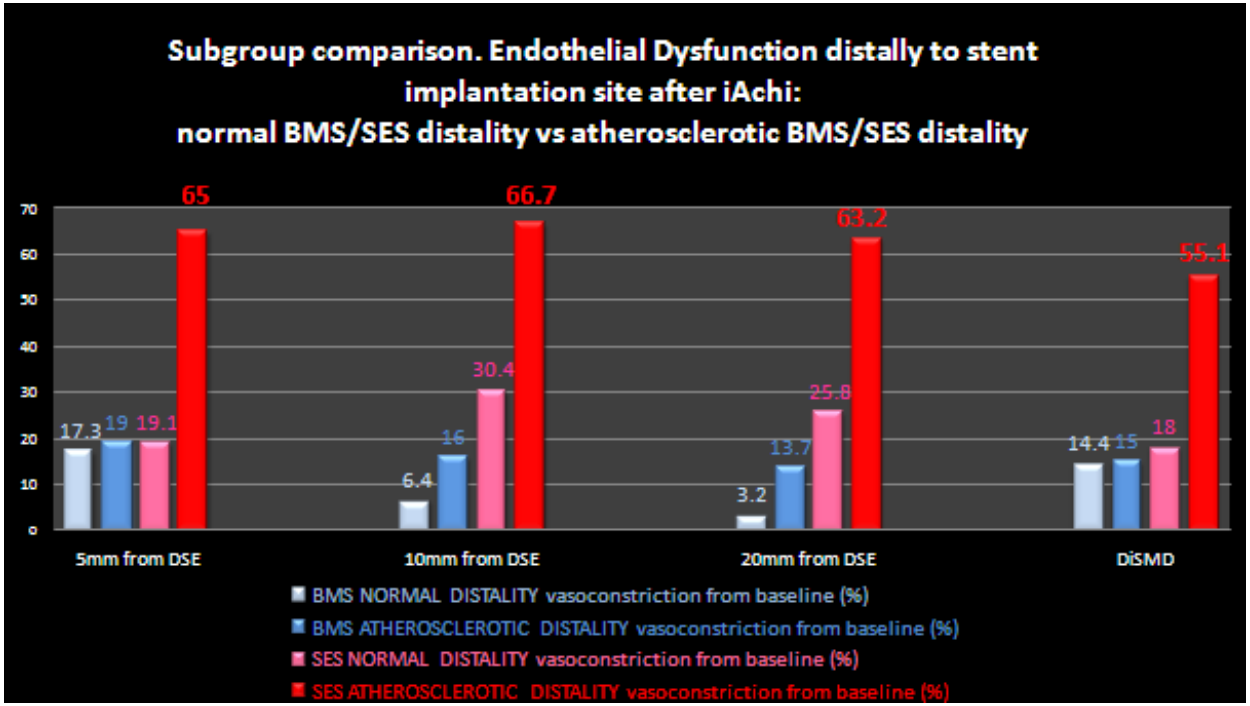
Head-to-head *C*omparison of si*R*olimus eluting st*E*nt vs. bare metal stent evaluating the en*D*oth*E*lial dysfu*N*ction in the same pa*T*ient with mult*I*ple coronary *A*rtery *L*esions.

The ***CREDENTIAL*** study

Results (2):

For the subgroup with diffuse distal atherosclerotic coronary segments, SES produce:

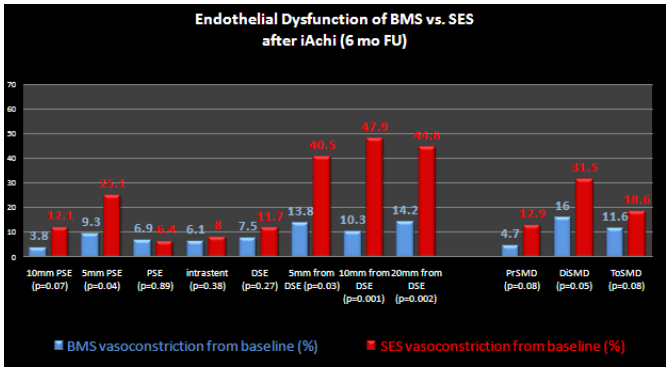
- **a 4.0 fold vasoconstriction vs. BMS calculated for distal diameters (mean value for the 3 distal diameters)**
- **a 3.6 fold vasoconstriction vs. BMS calculated for DiSMD.**

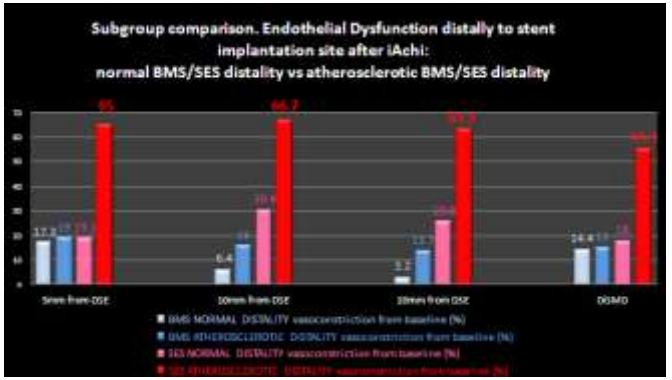


BMS = bare metal stents;
SES = sirolimus eluting stents;
iAchi = intracoronary acetylcholine infusion;
DSE = distal (to) stent edge;
DiSMD = distal segment mean diameter- mean diameter calculated from DSE to 20 mm after DSE

Possible mechanisms of SES-induced-ED:

- the drug (sirolimus normally eluted after 60 days)
- the polymer (decreased ED with 2nd-Gen-DES)
- vasa vasorum involvement
- mechanical injury during PCI…
- SES-i-ED could be time-limited (could dissapear after 1 or more years)





Limitations:

- small number of enrolled patients
- high rate of drop-out at the angiographic follow-up
- no Ach infusion for EF evaluation before stent implantation
- short period of follow-up (6 months)

Conclusions:

- **In comparison to BMS, SES implantation produce an increased vasoconstrictive response after Ach infusion. The effect is more severe in the subgroup with distal atherosclerotic coronary disease.**

- **These findings could have implications regarding the type of stent we choose (BMS, 1st-genDES or 2nd-genDES), the duration of double antiplatelet treatment and other medical interventions to improve EF.**

- **We suggest *a possible new gold-standard* in evaluating stent-induced ED by measuring mean segment diameters, which are more accurate than measuring predefined punctual diameters.**

- ***So, if a SES should be implanted in a vessel with diffuse distal atherosclerosis, aggressive medical treatment should be administered to decrease the ED and atherosclerosis.***

What stent to choose for best results?

euro PCR

Head-to-head *C*omparison of si*R*olimus eluting st*E*nt vs. bare metal stent evaluating the en*D*oth*E*lial dysfu*N*ction in the same pa*T*ient with mult*I*ple coronary *A*rtery *L*esions.

The ***CREDENTIAL*** study

What stent to choose for best results?

PCR EAPCI EUROPEAN SOCIETY OF CARDIOLOGY EACTS

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Head-to-head *C*omparison of si*R*olimus eluting st*E*nt vs. bare metal stent evaluating the en*D*oth*E*lial dysfu*N*ction in the same pa*T*ient with mult*I*ple coronary *A*rtery *L*esions.

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What stent to choose for best results?

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Thank you for your attention!

Additional slides

Head-to-head *C*omparison of si*R*olimus eluting st*E*nt vs. bare metal stent evaluating the en*D*oth*E*lial dysfu*N*ction in the same pa*T*ient with mult*I*ple coronary *A*rtery *L*esions.

The ***CREDENTIAL*** study

Additional slides: BASKET study

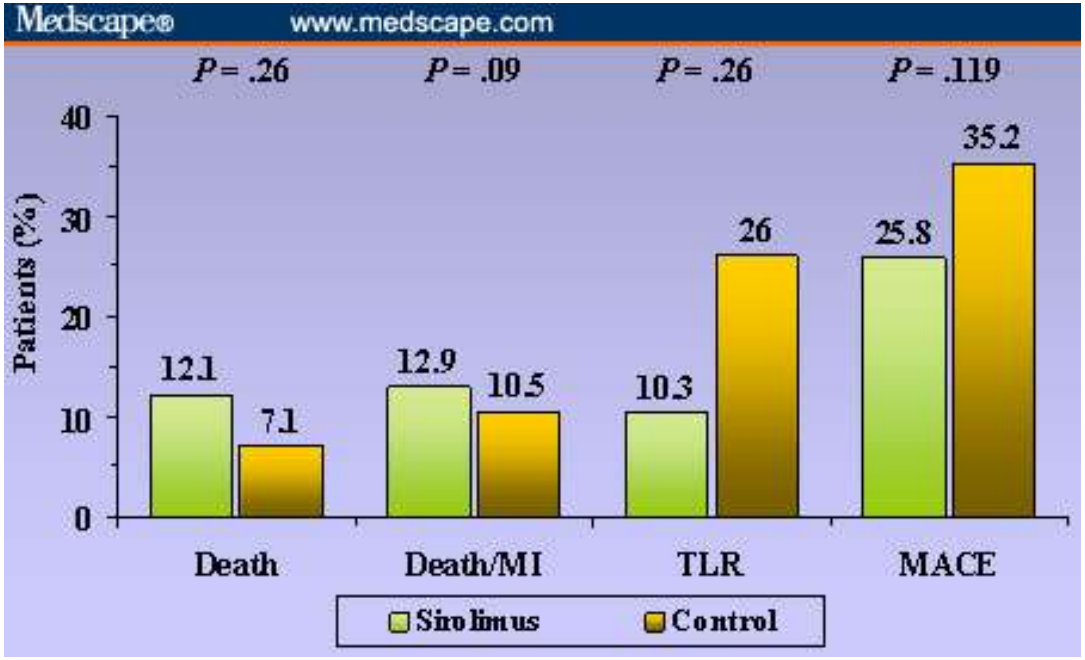
Table 2. Clinical Outcomes at 24 Months in the Intention-to-Treat Population.*

Outcome	Sirolimus-Eluting Stent (N=775)	Everolimus-Eluting Stent (N=774)	Bare-Metal Stent (N=765)	Sirolimus-Eluting Stent vs. Bare-Metal Stent		Everolimus-Eluting Stent vs. Bare-Metal Stent		Sirolimus-Eluting Stent vs. Everolimus-Eluting Stent	
				Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
	no. of patients (%)								
Death									
From any cause	28 (3.6)	25 (3.2)	34 (4.4)	0.82 (0.50–1.35)	0.71	0.73 (0.43–1.22)	0.46	1.13 (0.66–1.94)	0.85
From cardiac causes	13 (1.7)	13 (1.7)	22 (2.9)	0.59 (0.30–1.18)	0.38	0.58 (0.29–1.14)	0.37	1.03 (0.48–2.23)	0.93
Nonfatal myocardial infarction	7 (0.9)	13 (1.7)	20 (2.6)	0.37 (0.15–0.87)	0.13	0.67 (0.33–1.36)	0.51	0.54 (0.22–1.36)	0.43
Death from cardiac causes or nonfatal myocardial infarction									
Total	20 (2.6)	25 (3.2)	37 (4.8)	0.54 (0.31–0.93)	0.13	0.66 (0.40–1.10)	0.37	0.82 (0.45–1.47)	0.78
0–6 mo	11 (1.4)	10 (1.3)	21 (2.7)	0.52 (0.25–1.08)	0.31	0.47 (0.22–1.01)	0.22	1.10 (0.47–2.59)	0.92
7–24 mo	9 (1.2)	15 (1.9)	16 (2.1)	0.56 (0.25–1.27)	0.42	0.90 (0.44–1.82)	0.90	0.63 (0.27–1.43)	0.51
Target-vessel revascularization									
Any	33 (4.3)	29 (3.7)	79 (10.3)	0.47 (0.31–0.72)	0.005†	0.41 (0.27–0.65)	0.002†	1.13 (0.68–1.88)	0.85
Not related to myocardial infarction	29 (3.7)	24 (3.1)	68 (8.9)	0.46 (0.30–0.73)	0.007†	0.39 (0.24–0.63)	0.002†	1.18 (0.69–2.04)	0.82
Related to myocardial infarction	4 (0.5)	5 (0.6)	11 (1.4)	0.40 (0.13–1.28)	0.37	0.49 (0.17–1.44)	0.43	0.82 (0.22–3.04)	0.90
Death, myocardial infarction, or target-vessel revascularization	61 (7.9)	59 (7.6)	99 (12.9)	0.59 (0.43–0.82)	0.009†	0.56 (0.41–0.78)	0.005†	1.05 (0.74–1.51)	0.90
Stent thrombosis									
Definite	3 (0.4)	2 (0.3)	6 (0.8)	0.50 (0.13–2.02)	0.59	0.33 (0.07–1.62)	0.42	1.54 (0.26–9.23)	0.85
Definite or probable	6 (0.8)	5 (0.6)	9 (1.2)	0.75 (0.26–2.18)	0.85	0.62 (0.20–1.88)	0.67	1.23 (0.37–4.02)	0.90
Definite, probable, or possible	11 (1.4)	12 (1.6)	13 (1.7)	0.92 (0.41–2.10)	0.92	0.96 (0.43–2.15)	0.93	0.96 (0.42–2.18)	0.93

* Patients may have had more than one event. All P values have been adjusted for multiple comparisons.
† The difference between groups is significant after adjustment for multiple comparisons by means of the step-up procedure.

DRUG-ELUTING VS. BARE-METAL STENTS IN LARGE ARTERIES

Additional slides: RAVEL study



Additional slides: SIRIUS study

	SES	CS	P-value	# events prevented per 1,000 patients
Overall	9.4	24.3	<0.001	149
Male	10.1	24.9	<0.001	149
Female	7.5	22.8	<0.001	153
Diabetes	13.7	33.1	<0.001	194
No Diabetes	8.0	20.8	<0.001	129
LAD	11.5	28.4	<0.001	168
Non-LAD	7.7	21.4	<0.001	137
Small Vessel (<2.75)	13.3	26.0	<0.001	127
Large Vessel	5.6	22.6	<0.001	170
Short Vessel	9.3	21.8	<0.001	125
Long Lesion (>13.5)	9.7	26.8	<0.001	170
Overlap	11.0	30.1	<0.001	191
No Overlap	8.6	21.6	<0.001	130

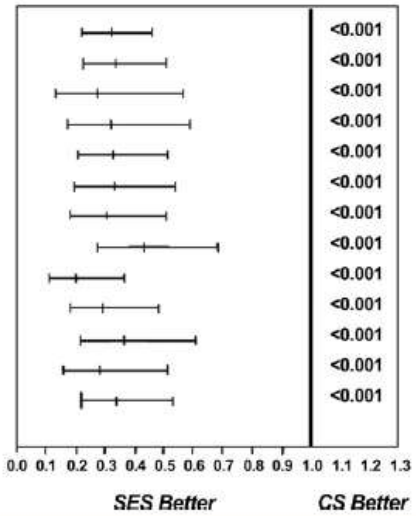


Figure 2 Odds Ratios for Target Lesion Revascularization at 5 Years for the Overall Population and by Subgroup

Values represent event rates (%) in each arm by subgroup. **Bars** represent odds ratio point estimates and 95% confidence intervals.
CI = confidence interval; CS = control stent; LAD = treatment of lesions in the left anterior descending artery; SES = sirolimus-eluting stent.

Additional slides: SIRIUS study

Table 1 Cumulative Clinical Events at 1- and 5-Year Clinical Follow-Up

	SES (n = 533)	BMS (n = 525)	Difference (95% CI)	p Value
All events at 1 yr				
Death	7 (1.3)	4 (0.8)	0.6% (−0.7% to 1.8%)	0.55
Cardiac	3 (0.6)	2 (0.4)	0.2% (−0.6% to 1.0%)	1.00
Noncardiac	4 (0.8)	2 (0.4)	0.4% (−0.5% to 1.3%)	0.69
MI (all)	16 (3.0)	22 (4.2)	−1.2% (−3.4% to 1.1%)	0.33
Q-wave	4 (0.8)	4 (0.8)	−0.0% (−1.1% to 1.0%)	1.00
Non-Q-wave	12 (2.3)	18 (3.4)	−1.2% (−3.2% to 0.8%)	0.27
Death or any MI	23 (4.3)	25 (4.8)	−0.4% (−3.0% to 2.1%)	0.77
Death or Q-wave MI	11 (2.1)	8 (1.5)	0.5% (−1.1% to 2.1%)	0.64
TLR	26 (4.9)	106 (20.2)	−15.3% (−19.2% to −11.4%)	<0.001
TL CABG	5 (0.9)	9 (1.7)	−0.8% (−2.2% to 0.6%)	0.30
TL PCI	23 (4.3)	102 (19.2)	−15.1% (−18.9% to −11.3%)	<0.001
All TVR	38 (7.1)	120 (22.9)	−15.7% (−19.9% to −11.5%)	<0.001
TVR (non-TL)	20 (3.8)	34 (6.5)	−2.7% (−5.4% to −0.1%)	0.05
MACE	44 (8.3)	122 (23.2)	−15.0% (−19.3% to −10.7%)	<0.001
TVF	52 (9.8)	130 (24.8)	−15.0% (−19.5% to −10.5%)	<0.001
All events at 5 yrs				
Death	45 (8.4)	44 (8.4)	0.1% (−3.3% to 3.4%)	1.00
Cardiac	22 (4.1)	19 (3.6)	0.5% (−1.8% to 2.8%)	0.75
Noncardiac	23 (4.3)	25 (4.8)	−0.4% (−3.0% to 2.1%)	0.77
MI (all)	33 (6.2)	34 (6.5)	−0.3% (−3.2% to 2.7%)	0.90
Q-wave	8 (1.5)	6 (1.1)	0.4% (−1.0% to 1.7%)	0.79
Non-Q-wave	26 (4.9)	28 (5.3)	−0.5% (−3.1% to 2.2%)	0.78
Death or any MI	74 (13.9)	70 (13.3)	0.6% (−3.6% to 4.7%)	0.86
Death or Q-wave MI	51 (9.6)	49 (9.3)	0.2% (−3.3% to 3.8%)	0.92
TLR	50 (9.4)	127 (24.2)	−14.8% (−19.2% to −10.4%)	<0.001
TL CABG	12 (2.3)	18 (3.4)	−1.2% (−3.2% to 0.8%)	0.27
TL PCI	43 (8.1)	121 (23.0)	−15.0% (−19.3% to −10.7%)	<0.001
All TVR	88 (16.5)	160 (30.5)	−14.0% (−19.0% to −8.9%)	<0.001
TVR (non-TL)	55 (10.3)	68 (13.0)	−2.6% (−6.5% to 1.2%)	0.21
MACE	108 (20.3)	176 (33.5)	−13.3% (−18.5% to −8.0%)	<0.001
TVF	120 (22.5)	182 (34.7)	−12.2% (−17.6% to −6.8%)	<0.001
All events between 1 and 5 yrs				
Death	38 (7.1)	40 (7.6)	−0.5% (−3.6% to 2.7%)	0.81
Cardiac	19 (3.6)	17 (3.2)	0.3% (−1.9% to 2.5%)	0.87
Noncardiac	19 (3.6)	23 (4.4)	−0.8% (−3.2% to 1.5%)	0.53
MI (all)	17 (3.2)	12 (2.3)	0.9% (−1.1% to 2.9%)	0.45
Q-wave	4 (0.8)	2 (0.4)	0.4% (−0.5% to 1.3%)	0.69
Non-Q-wave	14 (2.6)	10 (1.9)	0.7% (−1.1% to 2.5%)	0.54
Death or any MI	51 (9.6)	45 (8.6)	1.0% (−2.5% to 4.5%)	0.59
Death or Q-wave MI	40 (7.5)	41 (7.8)	−0.3% (−3.5% to 2.9%)	0.91
TLR	24 (4.5)	21 (4.0)	0.5% (−1.9% to 2.9%)	0.76
TL CABG	7 (1.3)	9 (1.7)	−0.4% (−1.9% to 1.1%)	0.62
TL PCI	20 (3.8)	19 (3.6)	0.1% (−2.1% to 2.4%)	1.00
All TVR	50 (9.4)	40 (7.6)	1.8% (−1.6% to 5.1%)	0.32
TVR (non-TL)	35 (6.6)	34 (6.5)	0.1% (−2.9% to 3.1%)	1.00
MACE	64 (12.0)	54 (10.3)	1.7% (−2.1% to 5.5%)	0.38
TVF	68 (12.8)	52 (9.9)	2.9% (−1.0% to 6.7%)	0.15

Values are number of cases (%). Events at 1 year were reported previously (4).
BMS = bare-metal stent(s); CABG = coronary artery bypass graft surgery; CI = confidence interval; MACE = major adverse cardiac event(s); MI = myocardial infarction; PCI = percutaneous coronary intervention; SES = sirolimus-eluting stent(s); TL = target lesion; TLR = target lesion revascularization; TVF = target vessel failure; TVR = target vessel revascularization.

Additional slides: RESOLUTE study

Clinical Evaluation of the Resolute Zotarolimus-Eluting Coronary Stent System in the Treatment of De Novo Lesions in Native Coronary Arteries

The RESOLUTE US Clinical Trial

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Palo Alto and Fremont, California; New York, New York; Tyler, Texas; Clearwater, Florida; Anderson, South Carolina; and Boston, Massachusetts

Objectives The RESOLUTE US (R-US) trial is a prospective, observational study designed to evaluate the clinical effectiveness of the Resolute zotarolimus-eluting stent (R-ZES) in a U.S. population.

Background The R-ZES releases zotarolimus over a 6-month period in order to achieve optimal clinical effectiveness and safety.

Methods The R-US trial recruited patients with de novo native coronary lesions suitable for 1- or 2-vessel treatment with stents from 2.25 to 4.0 mm in diameter. In the main analysis cohort (2.5- to 3.5-mm stents and single-lesion treatment), the primary endpoint was 12-month target lesion failure (TLF) defined as the composite of cardiac death, myocardial infarction (MI), and clinically-driven target lesion revascularization (TLR), compared with data from Endeavor zotarolimus-eluting stent (E-ZES) trials, adjusting for baseline covariates through propensity scores.

Results Overall, 1,402 patients were enrolled with a mean reference vessel diameter of 2.50 ± 0.47 mm and diabetes prevalence of 34.4%. In the main analysis cohort, TLF was 3.7% at 12 months compared with historical E-ZES results (TLF = 6.5%). The R-ZES met the 3.3% margin of noninferiority (rate difference = −2.8%, upper 1-sided 95% confidence interval: −1.3%, $p < 0.001$). The overall TLF rate was 4.7%, and rates of cardiac death, MI, and TLR were 0.7%, 1.4%, and 2.8%, respectively. The 12-month rate of stent thrombosis was 0.1%.

Conclusions The R-ZES achieved a very low rate of clinical restenosis while maintaining low rates of important clinical safety events such as death, MI, and stent thrombosis at 1-year follow-up. (The Medtronic RESOLUTE US Clinical Trial [R-US]; NCT00726453) (J Am Coll Cardiol 2011;57:1778–83) © 2011 by the American College of Cardiology Foundation

Head-to-head *C*omparison of si*R*olimus eluting st*E*nt vs. bare metal stent evaluating the en*D*oth*E*lial dysfu*N*ction in the same pa*T*ient with mult*I*ple coronary *A*rtery *L*esions.

The ***CREDENTIAL*** study