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Table 1

(@270 days)	SES (N=533)	Control (N=525)	P-value
Death	0.9%	0.6%	ns
MI (all)	2.8%	3.2%	ns
Stent thrombosis (all)	0.4%	0.8%	ns
TLR	4.1%	16.6%	<0.001
TVR (non-TL)	3.2%	4.8%	ns
MACE	7.1%	18.9%	<0.001
TVF	8.6%	21.0%	<0.001

TLR = target lesion revascularization, TVR = target vessel revascularization, MACE = major adverse cardiac events, TVF = target vessel failure

10:00 a.m.

805-4 **Late Incomplete Stent Apposition Following Sirolimus-Eluting Stent: Serial Quantitative Intravascular Ultrasound Analysis From the SIRIUS Trial**

Junya Ako, Yoshihiro Morino, Yasuhiro Honda, Shinjo Sonoda, Mitsuyasu Terashima, Ali Hassan, Martin B. Leon, Jeffrey W. Moses, Steve Osterle, Charles L. Brown, Donald S. Baim, Paul G. Yock, Peter J. Fitzgerald, the SIRIUS Investigators, Stanford University, Stanford, CA, Lenox Hill Hospital, New York, NY

Background: Stent incomplete apposition (IA) at follow-up is reported in drug-eluting stents. The aim of this study was to clarify the morphometric IVUS characteristics of late IA as compared with persistent IA following sirolimus-eluting stents (SES) vs bare metal stents (BMS).
Methods: IVUS data were obtained from SIRIUS, a prospective, randomized, multicenter trial. IA was defined as >1 struts separated from vessel wall with evidence of blood speckle behind the struts. The maximal stent/lumen gap, maximal axial length, and arc degrees of incompletely apposed struts were quantified. IA index was defined as total lumen area divided by lumen area within the stent. Persistent IA was considered present when IA was observed at both baseline and 8-month follow-up. Late IA was defined as new IA detected only at follow-up.
Results: Of 130 serial cases, there were 19 follow-up IA segments in 17 patients (BMS 6, SES 11) available for quantitative analysis. While persistent IA was observed in both groups (BMS 6, SES 4), late IA was seen only in SES. ΔVessel area was significantly larger in late IA than persistent IA ($p<0.05$), and 3 late IAs showed pathologic positive remodeling (>20% increase in vessel area compared to baseline). All persistent IAs were located at stent edges, whereas 77% of late IAs occurred at single or multiple mid-stent segments ($p<0.05$).
Conclusions: The characteristic morphometric findings of late IA following SES may suggest different vessel wall biology of this phenomenon compared to persistent IA.

	persistent IA BMS (n=6)	persistent IA SES (n=4)	late IA SES (n=9)
Gap, mm^2	0.36±0.17	0.40±0.12	0.69±0.33
Arc, °	107±22.5	97±14.0	145±53.1
Length, mm	1.9±0.65	2.8±1.7	4.2±3.4
Follow-up lumen area, mm^2	8.3±2.5	9.8±1.4	11.0±2.8
Follow-up vessel area, mm^2	19.0±7.3	17.0±2.5	18.9±3.6
Δvessel area, mm^2	-0.007±0.61	0.34±0.88	2.6±1.0
IA index	1.1±0.07	1.1±0.02	1.3±0.36

10:15 a.m.

805-5 **Do Overlapping Multiple Sirolimus-Eluting Stents Impact Angiographic and Clinical Outcomes? Insights From the SIRIUS Trial**

Giora Weisz, Jeffrey W. Moses, Jeffrey J. Popma, Greg Mishkel, Robert L. Wilensky, Barry Cohen, Hooman Madyoon, David Roberts, Martin B. Leon, Lenox Hill Hospital Heart and Vascular Institute of New York and Cardiovascular Research Foundation, New York, NY

Background: Although previous clinical studies have demonstrated a dramatic reduction in subsequent restenosis (Res) after sirolimus-eluting stent (SES) implantation, little is known about the impact of overlapping multiple stents on angiographic and clinical outcomes. **Methods**: In the randomized, double-blind SIRIUS trial, in longer lesions or to treat edge dissections, multiple overlapping stents were implanted in 33% of the SES pts (n=176) and in 32% of the control bare stent (CS) pts (n=168). Clinical and angiographic findings, including the contribution of the overlap region to Res, were assessed. **Results:** Overlap SES and CS pts had similar reference vessel diameter (2.77 vs 2.80 mm), lesion length (18.2 vs 18.1 mm), pre-treatment minimal luminal diameter (0.93 vs 0.94 mm), stent length (28.3 vs 27.8 mm), and stent overlap-segment length (4.6 vs 4.1 mm). There were no differences in safety outcomes including in-hospital MACE (4.5% vs 4.2%), subacute stent thrombosis (1 pt in each group, 0.6%), late stent thrombosis (none), and aneurysms (none). Angiographic and clinical efficacy were significantly better ($p<0.001$) in the SES vs. CS pts: in-lesion late loss (0.20 vs 0.93 mm), in-lesion binary restenosis (8.8% vs 42.7%), target lesion revascularization (4.7% vs 8.3%), and MACE (8.6% vs 23.1%). Eight pts in the overlap SES group had Res within the stent margins; one case was subacute stent thrombosis, one case was focal and not at the overlap region, one had diffuse Res (3 undersized stents after severe dissection), and the five remaining cases had focal Res within the overlap region. **Conclusions**: Overlapping SES vs. CS in the SIRIUS trial was associated with (1) infrequent adverse clinical outcomes (death, MI, stent thrombosis, or aneurysms), (2) maintained striking improvement for SES in all efficacy measures, and (3) the site of SES Res was usually within the stent at the overlap region. Factors such as vessel tortuosity, local flow disturbances, drug dosing effects or stent-edge incomplete apposition may contribute to this apparent increased overlap zone Res, which may be partially resolved with the use of longer single SES and IVUS guidance.

ORAL CONTRIBUTIONS

808 Restenosis: Basic Mechanisms

Monday, March 31, 2003, 9:15 a.m.-10:30 a.m.
McCormick Place, Room S403

9:15 a.m.

808-1 **Mobilized Bone Marrow Stem Cells Accelerate Reendothelialization, Reduce Vascular Inflammation, and Prevent Restenosis After Intravascular Radiation**

Hyun-Jai Cho, Hyo-Soo Kim, Dae-Hee Kim, Seil Oh, In-Ho Chae, Byung-Hee Oh, Myoung-Mook Lee, Young-Bae Park, Yun-Shik Choi, Seoul National University College of Medicine, Seoul, South Korea, Clinical Research Institute, Seoul National University Hospital, Seoul, South Korea

Background: Stem cell therapy may provide new possibilities for the treatment of vascular disorders. We investigated a role of mobilized stem cell in the healing process after intravascular radiation, the condition of few replicating endothelial cells in adjacent area. **Methods:** 1% cholesterol diet fed male New Zealand White rabbits with injured iliac artery were divided into two groups. The GM-CSF group (n=15) received rhGM-CSF (60μg/day) daily for 1 week, beginning 7 day before injury. Control group (n=18) received human albumin. One iliac artery was subjected to intravascular radiation via ^{188}Re-balloon and the contralateral iliac artery to balloon angioplasty control. Morphometry and immunohistochemistry were done. Peripheral blood mononuclear cells (MNCs) were isolated from blood just before vessel harvest, analyzed FACS and cultured for 4 weeks. **Results:** In control group, intravascular radiation therapy reduced neointimal hyperplasia (0.09±0.03 vs 0.26±0.11 mm^2, $P<0.01$) but delayed reendothalialization and promoted inflammatory cell infiltration. After GM-CSF pretreatment, reendothelialization index (defined as CD31 stained endoluminal perimeter) recovered to 81±13 % (n=7), whereas 30±11 % in the control radiation group (n=9) ($P<0.01$) and RAM11-positive cell (macrophage) infiltration reduced in media at 14 days. (12±7 vs 29±10 %, $P<0.01$) Also, additional significant reduction in neointimal thickening was observed. (0.04±0.01 vs 0.09±0.03 mm^2, $P<0.01$) FACS analysis showed that 24% of MNCs were positive for CD31 and 13% positive for CD34 in the GM-CSF group but all negative in the control group. Cultured cells were assayed with costaining with DiI/acLDL and FITC-conjugated BS Lectin as endothelial progenitor cells, also double positive stained cell count was significant higher in GM-CSF group. (33±15 vs 6±4 /mm^2, 2 weeks; 446±101 vs 58±29 / mm^2, 4 weeks after culture, $P<0.01$) **Conclusions:** GM-CSF pretreatment mobilizes stem cells, accelerates reendothelialization and reduces inflammatory cells infiltration after intravascular radiation therapy, which suggests that stem cell therapy is a promising strategy for enhancing vascular healing process after angioplasty.

9:30 a.m.

808-2 **Activation of Peroxisome Proliferator-Activated Receptor and Gamma Inhibits Neointimal Formation in a Diabetic Rat Carotid Artery Injury Model**

Kai Wang Liming Fan, Zhongmin Zhou, Farhad Forudi, Xiaorong Zhou, A. Michael Lincoff, Eric J. Topol, Marc S. Penn, The Cleveland Clinic Foundation, Cleveland, OH

Background: Peroxisome Proliferator-Activated Receptor γ (PPARγ) is member of the nuclear receptor superfamily of ligand-dependent transcription factors. Thiazolidinediones, which are anti-diabetic agents and high-affinity ligands for PPARγ, have been shown to inhibit the growth of vascular smooth muscle cells. In this study, the role of PPARγ on neointimal formation was studied in a diabetic rat carotid artery injury model. **Methods and Results:** Balloon injury of carotid artery was performed in the Zucker fat rats (diabetic) and lean rats (non-diabetic) using the standard method. In treatment groups, rosiglitazone (20mg/kg/day), PPARγ agonist, was given orally 1 week before injury through the 21 days follow-up. The animals were sacrificed after 21 days, and morphometric analysis was performed. Lipids and glucose assay was performed at baseline and 21 days. Neointimal formation was significantly decreased by the administration of rosiglitazone, but only in the diabetic rat cohort (Table). There was no difference of lipids and glucose levels between baseline and 21 days in the diabetic rats. **Conclusion:** The activation of PPARγ inhibits neointimal hyperplasia in a diabetic rat carotid artery injury