ratio) may contribute to edge stenosis. The greater reference residual plaque area by IVUS in this group also suggests that inadequate stent coverage contributes to edge stenosis. Optimal deployment techniques, including both inside and outside the stent, may further improve efficacy of SES.

	Edge Stenosis	No Edge Stenosis	P-Value
Reference MLA (mm^2)	4.7±2.3	6.5±2.3	0.06
Reference Residual Plaque (%)	60.5±9.0	49.1±11.5	0.03
Maximum SA / Reference MLA	1.8±0.2	1.5±0.5	0.03
Edge SA / Reference MLA	1.5±0.3	1.2±0.3	0.03
Maximum Pressure (atm)	15.4±3.2	16.9±2.7	NS
Balloon / Artery Ratio	0.9±0.1	1.0±0.1	NS
MLA: Minimum Lumen Area			
SA: Stent Area			
NS: Not Significant			

1101-66 **Intimal Hyperplasia Thickness Is Independent of Stent Size in Paclitaxel-Coated Stents: A Serial Intravascular Ultrasound Analysis From the Asian Paclitaxel-Eluting Stent Clinical Trial**

Esteban Escolar, Gary S. Mintz, Myeong-Ki Hong, Cheol Whan Lee, Jae-Joong Kim, Neal E. Fearnot, Seong-Wook Park, Seung-Jung Park, Neil J. Weissman, Washington Hospital Center, Washington, DC, Asan Medical Center, Seoul, Democratic People's Republic of Korea

Background. Intravascular ultrasound (IVUS) studies have shown that IH thickness is independent of bare metal stent size. This study determined whether intimal hyperplasia (IH) thickness within nonpolymeric paclitaxel-coated stents is dependent on stent size.
Methods. IVUS was performed post-stent implantation and at 6-months follow-up in 81 patients, 55 of which were randomized to the nonpolymeric paclitaxel-coated stent: 27 to 3.1 mcg/mm^2 (High dose) and 28 to 1.28 mcg/mm^2 (low dose). Stent, lumen, and IH cross-sectional area (CSA) and IH thickness were measured every 1mm over the length of the stent for a total of 810 slices. Maximum IH CSA and thickness and mean IH CSA and thickness over the length of the stent were calculated.
Results. Overall, maximum IH CSA measured 2.15±1.58mm^2, mean IH CSA measured 0.99±0.91mm^2, maximum IH thickness measured 0.49±0.33mm, and mean IH thickness measured 0.33±0.21mm. There was a weak correlation between IH CSA vs stent CSA (r=0.196, p<0.0001), but no correlation between IH thickness vs stent CSA (r=0.052, p=0.138) on a per slice basis or between maximum IH CSA vs stent CSA (r=0.259, p=0.056) or maximum IH thickness vs stent CSA (r=0.07, p=0.6) on a per stent basis. The results were similar when high and low dose patients were analyzed separately on a per slice basis: (1) IH CSA vs Stent CSA (r=0.252, p<0.0001, and r=0.153, p=0.0013) and (2) IH thickness vs Stent CSA (r=0.126, p=0.015, and r=0.002, p=0.96).
Conclusions. IH thickness is independent of stent size in drug-eluting stents, similar to bare metal stents.

POSTER SESSION

1102

Restenosis: Basic Research I

Monday, March 08, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1102-47 **Important Species Differences of Sirolimus, Paclitaxel, and Tacrolimus on Porcine and Human Coronary Smooth Muscle and Endothelial Cells**

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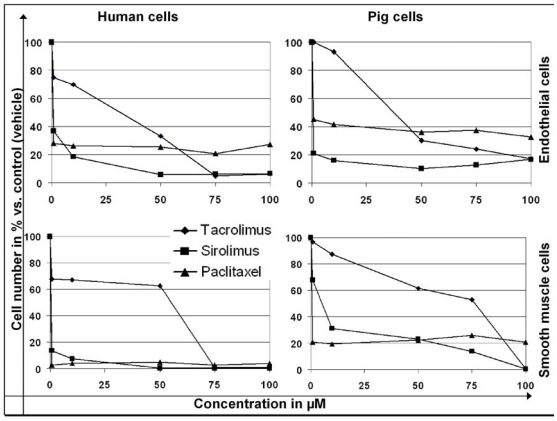
Background: Implantation of drug coated stents shows clinical efficacy for the prevention of restenosis, but large animal studies have not shown any long term benefit with the use of Sirolimus (SIR) and Paclitaxel (PAC). Despite this the possible interspecies differences have not been investigated. **Methods:** Porcine (p) and human (h) smooth muscle (SMC) and endothelial cells (EC) were serum deprived for 48h until addition of drugs. Cells were counted after 72h of exposure to SIR, PAC or Tacrolimus (TAC) by means of a CASY cell counter on the basis of the resistance measurement principle. Cell viability and size was determined simultaneously. **Results:** hSMC and hEC were generally more susceptible to growth inhibition than porcine cells (maximum differences seen with SMC). More than a 90% reduction in cell due to cytotoxicity could be seen for hSMC at 10µM for SIR and PAC compared to 75µM TAC. pSMC showed only a 80% reduction at 75µM for SIR and PAC and a 40% reduction with TAC. SIR showed the most pronounced effect with 99% reduction in cell count starting at 50µM compared to 100µM for pSMC. **Conclusion:** Toxicity and cell growth inhibition shows remarkable species differences at concentrations which are easily exceeded in the stent vicinity *in vivo* (100 µM). This partially explains the different results of re-endothelialization and reduction of in-stent restenosis with drug coated stents in swine and humans and shows the problems regarding the prediction of outcomes in human trials on the basis of animal data.



1102-48 **Inhibitory Effect of E5555, an Orally Active Thrombin Receptor Antagonist, on Intimal Hyperplasia Following Balloon Injury**

Toshiyuki Matsuoka, Motoji Kogushi, Tsutomu Kawata, Akifumi Kimura, Ken-ichi Chiba, Takashi Musha, Hiroko Kobayashi, Tetsuya Kawahara, Shuichi Suzuki, Akiharu Kajiwara, Ieharu Hishinuma, Clinical Research Center, Eisai Co., Ltd., Tokyo, Japan, Tsukuba Research Laboratories, Eisai Co., Ltd., Tsukuba, Japan

Background: Thrombin plays an important role in the development of restenosis and atherosclerosis after percutaneous coronary intervention via protease-activated receptors (PARs). Thrombin receptor (PAR-1), one of the PARs, mediates a variety of cellular actions of thrombin such as smooth muscle cell (SMC) proliferation and platelet aggregation. We succeeded in developing an orally active PAR-1 antagonist, E5555. The aims of this study is to clarify the in vitro profile of E5555 and to evaluate the effect of E5555 on intimal hyperplasia after balloon injury of the rat carotid artery.
Methods: 1) Human platelet membranes were incubated with [^{3}H]-high-affinity thrombin receptor activating peptide (TRAP) in the presence of E5555. 2) Effects of E5555 on rat SMC proliferation induced by thrombin (0.1 units/mL), basic fibroblast growth factor (3 ng/mL) or platelet-derived growth factor (30 ng/mL) was evaluated by colorimetric assay using MTT. 3) E5555 (10 and 30 mg/kg) or vehicle was given orally to male rats once a day for 16 days. On day 3, carotid artery lesion was induced by balloon denudation. Fourteen days after the surgery, the injured vessels were harvested and elastia-van Gieson's staining was performed.
Results: 1) E5555 inhibited binding of [^{3}H]-high-affinity TRAP to PAR-1 in human platelet membranes in a concentration-dependent manner with an IC_{50} value of 0.019 µM (n=6). 2) E5555 inhibited rat SMC proliferation induced by thrombin with an IC_{50} value of 0.16 µM (n=4), but did not inhibit that induced by basic fibroblast growth factor or platelet-derived growth factor. 3) The area of neointima in the vehicle-treated group (n=23) was 0.132±0.010 mm^2 (mean±SEM), while that in the group treated with E5555 at 10 mg/kg (n=24) and 30 mg/kg (n=24) were 0.116±0.007 mm^2 (ns vs. vehicle) and 0.078±0.009 mm^2 (p<0.001), respectively. The ratio of neointimal to medial area was significantly decreased in the group treated with E5555 at 30 mg/kg (0.866±0.092 vs. 1.404±0.091 in vehicle, p<0.001) without affecting the medial area.
Conclusion: E5555, a potent and orally active PAR-1 antagonist, may be beneficial for the treatment of restenosis after percutaneous coronary intervention.

1102-49 **A New Peptide to Block Interaction of Leukocyte Integrin MAC-1 With Fibrinogen Reduces Intimal Thickening in Mice**

Zhongmin Zhou, Marc S. Penn, Tatiana P. Ugarova, Kai Wang, Cleveland Clinic Foundation, Cleveland, OH

Background: The interaction between fibrinogen and leukocyte integrin MAC-1 mediates a range of adhesive reactions during vascular response to injury, and plays a key role in pathogenesis of restenosis. We developed a new peptide which duplicates the sequence in fibrinogen and which binds MAC-1 integrin, and investigated its effect on intimal thickening after vascular injury in mice. **Methods:** Carotid artery wire injuries were induced in ten CD57 mice of age 8 to 12 weeks, 0.2 mg/mouse of peptide or saline were given intraperitoneally at 0, 2, 4, and 6 days, mice were sacrificed at 21 days after injury, and morphometric analysis was carried out. **Results:** Neointimal area was significantly reduced by over 60% in peptide treated mice compared with saline control (0.009 ±0.006 mm^2 vs 0.022 ± 0.012 mm^2, $p < 0.05$), reduction of intima/media ratio was also observed in peptide versus saline group (0.374 ± 0.206 vs 0.795 ± 0.368, p <0.05) (table). **conclusion:** blockade of interaction between fibrinogen and leukocyte mac-1 by a new peptide suppresses neointimal thickening in mice.
table. morphometric data