sirolimus-eluting stents (SES) with durable polymer within the randomized multi-center all-comers LEADERS trial through 5 years.
Methods: A stratified analysis of clinical outcomes out to 5 years was performed in 1707 patients randomized to BES and SES within the LEADERS all-comers trial with regards to the presence or absence of diabetes (one of three pre-specified subgroup analyses). Among diabetics, clinical outcomes were further stratified by insulin dependency.
Results: 414 patients out of 1707 were diabetics (24.3%) with 223 patients in the BES group and 191 in the SES group. Patients with diabetes were older, more likely to have hypertension, hypercholesterolemia, history of previous PCI or CABG (all p-values <0.01). Of 414 Diabetic patients, 158 (38%) were insulin-dependent (81 patients in the BES and 77 in the SES group). At 1 year, the composite endpoint of MACE (cardiac death (CD), myocardial infarction (MI) or clinically indicated TVR (ci-TVR)) was similar for DM patients in the BES and SES arms (15.7% vs. 14.7%, p=0.75) and for non-DM patients (8.8% vs 11.2%, p = 0.28), with a non-significant interaction. One year outcomes for CD, MI and ci-TVR were similar in patients with and without DM between the two groups. As expected, IDDM patients had higher rates of ci-TVR and MACE compared to NIDDM patients (13.3% vs. 7.0% and 18.4% vs. 13.3%) at 1 year. In the group of NIDDM patients, no difference in clinical outcomes was observed between two stents. Within IDDM patients, the use of BES compared to SES resulted in a lower CD rate (0% vs.6.5%). There was no difference in other clinical endpoints between two stents. The long-term analysis is currently ongoing.
Conclusions: Patients with IDDM continue to be a challenging population. The 5-year follow-up will be reported for the 1st time during this meeting.

TCT-570

Stents With Absorbable Tissue-Deployable Coatings Can Distribute Drug More Uniformly Between Struts

Abraham Tzafriri[1], Lynn Bailey[1], James Stanley[1], Brett Zani[1], Peter Markham[1], Wenda Carlyle[2], James McClain[2], Elazer Edelman[3]
[1]CBSET, Inc., Lexington, MA, [2]Micell Technologies, Inc., Durham, NC, [3]Harvard-MIT Biomedical Engineering Center, Cambridge, Massachusetts

Background: We examined whether deployment of coating from drug-eluting stents (DES) into surrounding neointima could protect a crystalline drug load from luminal washout and distribute drug more efficiently and uniformly compared to conventional DES.
Methods: Sirolimus eluting stents (AC-SES: MiStent® Sirolimus-Eluting Stent, Micell Technologies, Inc., Durham, NC) with an absorbable coating containing PLGA and crystalline sirolimus were implanted in the coronary arteries of Yucatan mini-swine (1 stent per artery, 1.13:1 B:A). Arteries were harvested after 30d and processed by histopathology to identify the location, shape and size of tissue-deployed coating. Computational modeling assessed drug release and distribution surrounding a tissue-embedded strut comparing fully adherent and 30% deployable coatings.
Results: 30d post implantation into porcine coronary arteries, AC-SES were embedded within a 4-strut thick neointima and had deployed coating segments as much as 200 μm away from struts (Fig 1). Modeling (Fig 1) predicted highly localized drug distribution around conformably coated struts. Coating deployment away from the strut increases the surface area for drug release and distributes drug more uniformly with lower peak values near each strut and higher levels between struts; peak-trough levels 150 μm below the IEL decline at a near constant rate of 1.7 ng/mg per 100 μm coating migration.

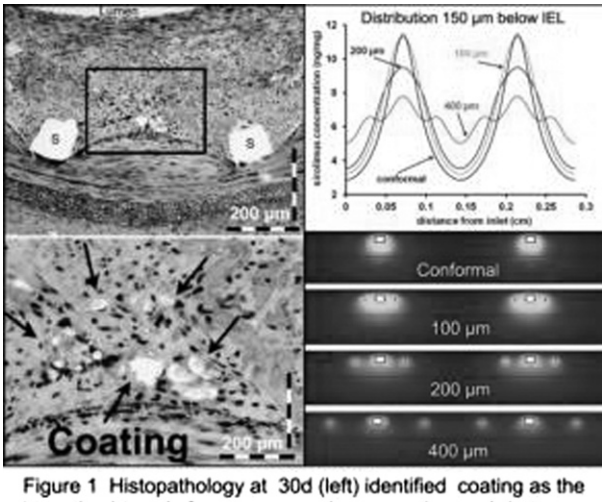

Figure 1 Histopathology at 30d (left) identified coating as the 'negative image' of space occupying mass (arrows) between struts (S) and motivated 2D computational modeling to predict drug distribution patterns around a strut pair (right) fully coated (conformal) or where the bottom coating deployed 100, 200 or 400 µm into intrastrut zones.

Conclusions: Deployment of sustained elution coatings flattens vicissitudes in drug tissue levels, promotes efficient drug delivery, and may reduce potential toxicity.

TCT-571

A Preliminary Study of Biodegradable Iron Stent in Mini-Swine Coronary Artery

Chao Wu[1], Xiaoying Hu[1], Hong Qiu[1], Yignmao Ruan[1], Yue Tang[1], Aili Wu[1], Yi Tian[1], Peng Peng[1], Yan Chu[1], Xinlin Xu[1], Qingzhi Wang[1], Liang Xu[1], Bo Xu[1], Deyuan Zhang[2], Run-Lin Gao[1]
[1]Fu Wai Hospital, National Center for Cardiovascular Diseases, China, Beijing, China, [2]Lifetech Scientic (Shenzhen) Co., Ltd., Shenzhen, China

Background: In order to develop a biodegradable iron stent, a feasibility study of biodegradable nitriding iron stent in coronary artery of mini-swine was undergone.
Methods: Eight iron stents (Lifetech Scientific, Shenzhen, China) and eight Vision stents (Abbott Vascular, CA, USA) as control were randomly implanted into LAD and RCA of 8 healthy mini-swine, respectively. Two stents with same brand were implanted into one mini-swine. At 4 weeks animals were sacrificed after Optical Coherence Tomography (OCT) examination; histopathologic examinations were performed.
Results: The mean neointimal thickness (0.46±0.17mm vs. 0.45±0.18mm, p=0.878), neointimal area (2.55±0.91mm2 vs. 3.04±1.15mm2, p=0.360), and percentage of area restenosis (44.50±11.40% vs. 46.00±17.95%, p=0.845) were not significantly different between iron stent and Vision stent. There were no inflammation, thrombosis and necrosis in both groups. The SEM scores(0.75±1.04 vs. 0.88±0.99, p=0.809) and rate of proliferating cell nuclear antigen (PCNA) positive staining (19.43±11.36% vs. 16.85±11.77%, p=0.392) had no significant difference between iron and Vision stents. The percentage of neointimal coverage by SEM (84.38±14.50% vs. 65.00±22.04%, p=0.057) had a increasing tendency in iron stent group. The minimal lumen diameter (1.81±0.18mm vs. 1.76±0.36mm, p=0.785), minimal lumen area (3.34±0.56mm2 vs. 2.96±0.82mm2, p=0.436) and percentage of stent strut coverage (99.63±0.38% vs. 99.66±0.68%, p=0.927) by OCT had also no significant difference. Iron stent corrosion was observed and iron staining in the adjacent tissue of iron stent was positive. Iron staining was positive in spleens of both groups. No iron overload and abnormal histopathologic changes were detected in heart, lung, liver, kidney and brain.
Conclusions: The biodegradable iron stent had good biocompatibility. The neointimal proliferation of iron stent was similar to that of Vision Stent. There were no thrombosis, inflammation and necrosis in both groups. Percentage of neointimal coverage by SEM was of 84% and the stent strut coverage by OCT was of 99% in iron stent. Corrosion of iron stent was observed and there were no signs of iron related organ toxicity.

TCT-572

One-Year Preclinical Data on a Novel Drug-Eluting Stent with Amino Acid-Based Bioabsorbable Drug Carrier Mounted on an Integrated Delivery System (IDS)

Jose Costa Jr[1], Gregory Kopia[2], James Stanley[3], Lynn Bailey[3], Paul Soskey[4], Alexandre Abizaid[5]
[1]Instituto Dante Pazzanese de Cardiologia, São Paulo, Brazil, [2]Kopia Consulting, Hillsborough, NJ, [3]CBSET, Inc., Lexington, MA, [4]Svelte Medical Systems, Inc., New Providence, NJ, [5]Visiting Professor Columbia University, São Paulo, Brazil

Background: The Svelte Drug-Eluting Stent (DES) with Integrated Delivery System (IDS) is specifically designed for direct stenting, consisting of an ultra low-profile, thin (81 μg) CoCr (L-605) stent and fully bioabsorbable, amino acid-based drug carrier eluting 220 μg/cm2 of sirolimus mounted on a fixed-wire IDS with a 0.012″ shapeable integrated guidewire tip. The low-compliant delivery balloon is fitted with proximal and distal elastic balloon control bands (BCBs) to restrict longitudinal balloon growth and allow for multiple, controlled inflations with minimal vessel contact.
Methods: Svelte DES, all 3.0 x 18mm in size, were implanted in porcine coronary and internal mammary arteries. Animals were euthanized at various times up to 60 days following implantation, with vessels and stents examined for sirolimus content. To assess in-vivo local tissue response, 3.0 x 18mm Svelte DES (n=20), drug carrier-only coated stents (n=16), Svelte BMS (n=22) and Xience V (n=8) were implanted in porcine coronary arteries for up to 1 year.
Results: Pre-clinical data demonstrate that 80% of the drug was released by 30 days, with remaining drug eluting by 60 days. Sirolimus levels in the arterial tissue reached peak levels of 5-6 ng/mg over the first 1-3 days, with levels decreasing to less than 1 ng/mg at 60 days. At 30-days, complete re-endothelialization with Svelte DES was confirmed. At 90-days, a small reduction in inflammatory response (as assessed by mean inflammation score) with Svelte DES (0.58) compared with Xience V (0.67), drug carrier-only (0.65) and Svelte BMS (0.72) was observed (p=NS). Svelte DES inflammation was characterized as lymphohistiocytic with few eosinophils and giant cells with micro-granuloma formation around the stent struts. SEM analysis showed no evidence of thrombus formation. The bio-erodible amino acid based carrier appears to possess high mechanical integrity and low-inflammatory properties.
Conclusions: In-vivo drug elution kinetics and tissue and blood levels of sirolimus are reported, as are histopathology and carrier erosion kinetics through 1-year, demonstrating low inflammatory response to the drug carrier and suppressed hyperplastic response through 390-days.

POSTERS