**TCT-596**

Pantera Lux Drug Coated Balloon: Twelve-Month Results On The Diabetics Subgroup Of The International DELUX Registry

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**Background:** In recent years, drug coated balloons have emerged as treatment option for PCI. The present registry aims to evaluate the safety and efficacy of the Pantera Lux Paclitaxel Coated Balloon in a real world setting.

**Methods:** Between April 2010 and April 2011, 363 diabetic patients were enrolled at 50 sites in 12 countries. Clinical follow-up was performed at 1, 6 and 12 months. The primary endpoint was MACE, a composite of all death, non-fatal MI and clinically driven TVR, at 6 months. Secondary endpoints include MACE at 1 and 12 months. All reported MACE were adjudicated by an independent clinical events committee.

**Results:** Two hundred fifty-nine men (71.3%) and 104 female (28.7%) with a mean age of 67.4 ± 10.2 years have been enrolled. One hundred forty-twent-four patients (59.4%) were insulin dependent. Eighty-six patients (23.7%) presented with congestive heart failure and 195 patients (53.7%) had a history of previous MI. The majority of patients presented with stable angina (n=184, 50.7%) followed by unstable angina (n=107, 29.5%). A total of 388 lesions were treated, mainly located in LAD (n=144, 37.1%) and RCA (n=136, 35.1%). The mean reference vessel diameter was 2.9 mm and the mean target lesion length was 15.6 mm. Three hundred forty lesions (87.6%) were in-stent restenosis (ISR) lesions. Thereof 165 lesions were in a BMS (48.5%) and 172 lesions in a DES (50.6%). The majority of ISR lesions were diffuse (n=159, 43.8%), Mehran class III or focal (n=104, 31.6%, Mehran class II). Follow-up compliance at 6 month follow up is 93.9%. The MACE rate (hierarchical) at 6 months is 11.2% including 11 all death (3.2%, 6 n=76) and 40 slides in the long term study (14 days, 11; 30 days, n=29). Fibin deposits when present, were found to be deposited on the luminal surface of the vessel and covering crystalline material. At 7 days following PCB inflation, fibrin scores significantly increased according to the number of inflations. Single PCB inflation showed the lowest fibrin score (0.2±0.5) followed by double PCB inflation (0.43±0.55). Six inflations showed a significantly increase in fibrin score (1.88±0.71, p<0.001). In the analysis of PCB over time, a peak in fibrin deposition was seen at 14 days (2.45±1.04) before it decreases at 30 days (1.66±0.90).

**Conclusions:** Our study suggests that fibrin gets deposited on the surface of the vessel in a dose dependent fashion following PCB delivery and may play a major role in the creation of drug reservoirs and long term intra-vessel drug delivery. The course of the luminal fibrin deposition overtime suggests that this process peaks at 14 days and starts to resorb thereafter.

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**TCT-598**

Luminal Fibrin as a Key Component in Mechanism of Action in Drug Coated Balloon Technologies

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**Background:** The mechanism of action of Drug Coated Balloons (DCB) is not fully understood. It’s suggested that following balloon dilatation, Paclitaxel is deposited on the vascular luminal surface and serves as a natural drug delivery system. We hypothesize that fibrin acts as a biological glue covering Paclitaxel deposits following balloon delivery.

In this study, we aimed to evaluate the effect of the number of balloon inflations on luminal fibrin deposits over time.

**Methods:** A total of 22 porcine femoral arterial segments were randomized to tx (n=4), 2x (n=7) and 6x (n=11) PCB inflations (Covatane, Medrad, Inc. Indianola, PA) and followed for 7 days. Additional 7 arterial segments received 6x PCB inflations and were followed for 14 (n=2) and 30 days (n=5). Vessels were harvested for the evaluation of luminal fibrin deposition using a semi-quantitative score.

**Results:** A total of 148 vessels segments were analyzed in the 7 day study (tx, n=35; 2x, n=37; 6x, n=76) and 40 slides in the long term study (14 days, n=11; 30 days, n=29). Fibin deposits when present, were found to be deposited on the luminal surface of the vessel and covering crystalline material. At 7 days following PCB inflation, fibrin scores significantly increased according to the number of inflations. Single PCB inflation showed the lowest fibrin score (0.2±0.5) followed by double PCB inflation (0.43±0.55). Six inflations showed a significantly increase in fibrin score (1.88±0.71, p<0.001). In the analysis of PCB over time, a peak in fibrin deposition was seen at 14 days (2.45±1.04) before it decreases at 30 days (1.66±0.90).

**Conclusions:** Our study suggests that fibrin gets deposited on the surface of the vessel in a dose dependent fashion following PCB delivery and may play a major role in the creation of drug reservoirs and long term intra-vessel drug delivery. The course of the luminal fibrin deposition overtime suggests that this process peaks at 14 days and starts to resorb thereafter.

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**TCT-597**

Acute Delivery and Long Term Retention of Sirolimus Nanoparticles Using A Novel Porous Angioplasty Balloon in the Porcine Coronary Model

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**Background:** Drug coated balloons using Paclitaxel have demonstrated to be clinically effective in selected clinical settings. In contrast, Sirolimus is not easily transferred to the vessel wall using current coating Methods and tissue levels cannot be maintained long enough to control restenosis. In this study, we aimed to evaluate the feasibility of delivery and long term retention of Sirolimus nanoparticles delivered through a novel porous angioplasty balloon in normal porcine coronary arteries.

**Methods:** A total of 155 coronary arterial segments were treated with a porous angioplasty balloon delivering Sirolimus nanoparticles (Caliber Therapeutics, New Hope, PA) at a 20% overlap stretch ratio. Coronary angiography was performed at baseline and after delivery to assess safety. Treated coronary segments were harvested immediately after Sirolimus delivery (n=25) and at 4 (n=30), 7 (n=84), 21 (n=7) and 28 days (n=9) and analyzed to detect tissue Sirolimus levels. Distal tissue samples (distal myocardium, lung, liver and kidney) were also collected to determine Sirolimus systemic distribution following local drug delivery.

**Results:** The Sirolimus levels found immediately after balloon delivery were 422.6 ± 110 ng/mg. Subsequently tissue levels decreased to 4 (200.1 ± 80.4) ng/mg and 7 (49.8 ± 17.1) ng/mg at 21 (32.7 ± 13.6) mg/ml. At last follow up (30 days), Sirolimus tissue levels were still above the target therapeutic levels (18.5 ± 9.6 ng/mg). At any given time point, Sirolimus concentrations were ≥3-fold higher in coronary segments than in distal tissue samples. Drug levels in remote tissues were unstable after 7 days.

**Conclusions:** The local arterial delivery of Sirolimus nanoparticles using a novel porous balloon delivery system was safe and capable of achieving long term intra-arterial drug levels without significant systemic residual exposure in a porcine model.