Concerning PAD, gene expression in atherosclerotic lesions shows significant differences. Understanding of the local differences of atherosclerosis may aid to improve prevention and lead to targeted treatment of atherosclerosis and its complications.

TCT-819
Healing of a Combination Sirolimus-Eluting, Endothelial Progenitor Cell Capture Stent Compared to an Everolimus-Eluting Stent in an Atherosclerotic Rabbit Model
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Background: The Combo Dual Therapy stent (OrbusNeich Medical, Ft. Lauderdale, FL) combines anti-proliferative abluminal sirolimus elution from a bioresorbable matrix with luminal CD34 antibody endothelial progenitor cell capture. This study compares the healing of the Combo stent to an everolimus-eluting stent [EES] (Xience Prime; Abbott Vascular, Santa Clara, CA), along with the Genous stent (OrbusNeich) as control.

Methods: 31 atherosclerotic rabbits were implanted with bilateral iliac stents and survived for 28 days or 45 days. Select animals underwent assessment by OCT after stent implant and again prior to sacrifice. To assess cellular proliferation, animals were given BrdU before sacrifice. The stented arterial segments were designated for either light microscopy evaluation or en face assessment by both SEM for endothelial coverage and immune confocal microscopy for expression of endothelial markers CD31/PECAM and eNOS.

Results: At 28 days, morphometric comparison of areas measurements showed statistically comparable EEL, IEL, lumen, stent, media, and plaque areas and thicknesses between groups. Uncovered struts were seen in all groups with the highest and statistically significant frequency in EES > Combo > Genous. At 45 days, morphometric values remained relatively similar to day 28 with a slight increase of stenosis seen with Genous. Endothelial coverage at 28 days above struts by SEM was highest in Genous (98.3%), followed by Combo (83.3%), and lowest in EES (52.7%) (p=0.025). Endothelial coverage between struts was nearly identical (Combo 93.3%, Genous 87.5%, EES 92.0%, p=0.714). By OCT, 28-day animals showed less area stenosis and less neointimal thickness in Combo and EES as compared to Genous. There were no significant differences between Combo and EES in terms of area stenosis, neointimal thickness, and uncovered struts. No stents showed thrombosis or restenosis at both 28-day and 45-day time points. The OCT analysis correlated significantly with histologic findings.

Conclusions: Compared to the EES stent, the Combo stent was found to have a similar reduction in neointimal proliferation, while exhibiting fewer uncovered struts and significantly greater endothelial coverage over struts.

TCT-820
First Approach to Stimulate Arteriogenesis using Monoclonal Antibodies: Blocking the Interferon-Alpha/beta Receptor Subunit 1 Stimulates Restoration of Perfusion in a Murine Hindlimb-ischemia Model Without Affecting Atherosclerosis
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Background: Increased expression of interferon (IFN)-beta was shown in patients with insufficient coronary collaterals. Furthermore, mice treated with IFN-beta demonstrate inhibition of collateral artery growth (arteriogenesis). Importantly, type 1 interferons (IFN-alpha and IFN-beta) have been identified as proatherosclerotic cytokines and in mouse models of atherosclerosis, IFN-beta treatment accelerated lesion formation and increased accumulation of macrophages in plaques. We hypothesized that arteriogenesis can be stimulated using monoclonal antibodies inhibiting IFN-beta signaling without accelerating atherosclerosis.

Methods: In an atherosclerotic murine hindlimb-ischemia model, LDLR-/- mice were treated during a 4-week period with monoclonal antibodies specific for mouse Interferon-Alpha/beta Receptor subunit 1 (IFNAR-1) or a murine IgG isotype as control. After 28 days, hindlimb perfusion was measured using laser Doppler perfusion imaging (LDF) directly after arterial ligation as well as at 2, 7, 14 and 28 days following ligation. We used a disease model to investigate effects of anti-IFNAR-1 on arteriogenesis, which was evaluated with histology to determine plaque area and composition.

Results: Hindlimb perfusion restoration after femoral artery ligation was improved in mice treated with anti-IFNAR-1 compared to controls as assessed by LDFI after 7, 14 and 28 days (treatment vs. control; 7 days: 35.6 ± 16.5% vs. 23.6 ± 8.7%, p=0.027; 14 days: 51.4 ± 17.2% vs. 35.0 ± 12.3%, p=0.010; 28 days 71.5 ± 13.8% vs. 54.0 ± 16.3%, p=0.005). Total plaque area (treatment vs. control: 118.8 ± 46.1x103 μm² vs. 139.3 ± 46.5 x103 μm², p=0.275) as well as composition were unaltered.

Conclusions: Blocking IFNAR-1 using monoclonal antibodies stimulates collateral artery growth in mice and has a neutral effect on atherosclerosis.

TCT-821
Stem Cell Mobilization by Granulocyte-Colony Stimulating Factor in Patients With Acute Myocardial Infarction: Five-year results of the REVIVAL-2 trial
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Background: The REVIVAL-2 study showed that stem cell mobilization by G-CSF does not influence infarct size, left ventricular function and coronary restenosis in patients with AMI that underwent successful percutaneous coronary intervention (PCI). The objective of the present analysis was to assess the impact of G-CSF treatment on 5-year clinical outcomes from the REVIVAL-2 trial.

Methods: In the randomized, double-blind, placebo-controlled REVIVAL-2 study, 114 patients with the diagnosis of acute myocardial infarction were enrolled 5 days after successful perfluor percutaneous coronary interventional. Patients were assigned to receive 10 μg/kg G-CSF (56 patients) or placebo (58 patients) for 5 days. The primary outcome for this analysis was the composite of death, myocardial infarction or stroke 5 years after randomization.

Results: The endpoint occurred in 7.1% of patients in the G-CSF group versus 15.5% assigned to placebo (relative risk [RR], 0.4; 95% confidence interval [CI], 0.1-1.4; p=0.14). The major driver was mortality which was reduced from 10.3% in the placebo group to 3.6% in the G-CSF group (p=0.16).

Conclusions: These long term follow-up data show that G-CSF may reduce adverse events especially mortality in patients with acute myocardial infarction. ClinicalTrials.gov Identifier: NCT00126100

TCT-822
Effective Antegrade Cardiac Gene Therapy with VEGF-B167 for Pacing-induced Dilated Cardiomyopathy in a Pre-clinical Large Animal Model of Heart Failure
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Background: The selective VEGFR-1 activator VEGF-B has been shown to be antiapoptotic and cytoprotective in absence of angiogenic side effects. Thus...