BACKGROUND Ixmyelocel-T is an investigational multicellular therapy produced from a patient's own bone marrow by selectively expanding two key types of bone marrow mononuclear cells: CD90+ mesenchymal stem cells and CD35+ CD14+ autoflourescent+ alternatively activated macrophages. IxCELL-DCM (N=109) was a double blind, placebo controlled trial that randomized NYHA class III or IV patients with LVEF<35%, and either 6 minute walk <400 meters, NT pro BNP ≥2000, or BNP ≥400 pg/ml or HF related hospitalization within the last 6 months 1:1 to Ixmyelocel-T:placebo. Treatment with Ixmyelocel-T resulted in a 37% reduction in the primary endpoint of all-cause mortality, cardiac hospitalizations, and outpatient treatment of acute decompensated HF at 1 year (p=0.03). Multiple mechanisms have been proposed for how Ixmyelocel-T reduces cardiac events, but the exact mechanism(s) remains unclear.

METHODS A pre-specified secondary endpoint of the IxCELL-DCM trial included intermittent assessment of AICD interrogation for events defined as ventricular arrhythmia lasting > 30 sec, ventricular tachycardia resulting in shock, and any ventricular arrhythmia resulting in anti-tachycardia pacing. 58/58 IXT patients and 50/51 placebo patients had AICD interrogation during the 12 month follow-up. A Poisson regression of the events per 100 patient years was performed (Wald Chi-Square).

RESULTS Patients randomized to Ixmyelocel-T had an average of 236.42 ventricular arrhythmia events/ 100 patient years compared to 310.99 in the placebo group (p=0.05), rate ratio of 0.76 (0.58-1.00, 95% CI). Moreover, 8 patients who received placebo had ventricular fibrillation severe adverse events compared to none in the patients who received Ixmyelocel-T.

CONCLUSION These data suggest that reduction in ventricular arrhythmias may play a role in the clinical benefit observed with Ixmyelocel-T multicellular therapy. These results need to be confirmed with subsequent trials.

CATEGORIES STRUCTURAL: Heart Failure

PRE-CLINICAL/FIRST IN-HUMAN STUDIES

Abstract nos: 825 - 844

TCT-825

Simplicity Denervation System for Pulmonary Artery Denervation in Patients with Chronic Thrombembolic Pulmonary Hypertension (first-in-man study)

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BACKGROUND The goal of our study was to evaluate the safety and effectiveness of Simplicity denervation system in lowering pulmonary artery pressure in patients with chronic thromboembolic pulmonary hypertension.

METHODS Patients with the chronic thromboembolic pulmonary hypertension (defined as mean pulmonary artery pressure > 25) were eligible for the study. A total of 12 patients were included. All patients were on the multidrug theraphy, including sildenafil. Functional capacity was determined by the 6MWT performed 1 week prior and 3 months following the PADN procedure. The right heart catheterization, hemodynamic measurements and blood oxygen saturation data from the RA, RV, and PA were done before the PADN procedure. The PVR [PVR = (mean PAP — PAOP)/CO] was calculated. The PADN procedure was made by Simplicity 6 Fr-compatible radiofrequency ablation catheter inserted through the coronary guiding catheter. Ablation was perfored at the bifurcation level of the main PA and at the ostium of the left and right PA. Procedural success was defined as a reduction in the mean PAP >10 mm Hg (as measured by guiding catheter at the end of ablation), and there were no complications. The primary endpoints were improvement of functional capacity by the 6MWT and mean PAP at 3 months.

RESULTS During and immediately following the PADN procedure, no complications (death, arrhythmias, PA perforation, acute thrombus formation in the PA or in the femoral vein, bleeding) were recorded. During 3-months of follow-up no rehospitalization was required. All patients reported no deterioration of the symptoms and no complications were registered. 9 patients noticed significant improvements in dyspnea and fatigue, in all patients sildenafil was discontinued. After 3 months all patients underwent right heart catheterization and functional capacity measurements. At 3 months follow-up the reduction of mean pulmonary artery pressure was 25 mm Hg (from 58 ± 6 to 33 ± 4 mm Hg) ($p < 0.01$) and improvement of the 6 minutes walking test from 321 ± 19 m to 487 ± 29 m ($p < 0.01$) was observed.

CONCLUSION The Simplicity denervation system is proven to be safe and effective for pulmonary artery denervation. Further randomized study is needed to confirm the clinical benefit of this procedures in patients with pulmonary hypertension.

CATEGORIES OTHER: Pre-Clinical/First In-Human Studies

TCT-826

Prospective single center First In Human (FIH) clinical trial to evaluate the safety and effectiveness of a septal occluder with bioresorbable framework in patients with clinically significant atrial septum defect (ASD) or patent foramen ovale (PFO)

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BACKGROUND The objective of this trial is to investigate the effectiveness and safety of a new septal occluder with bioresorbable framework (Carag Bioresorbable Septal Occluder CBSO, CARAG AG, Switzerland) in the treatment of secundum ASD or PFO. Device closure of ASD/PFO is standard of care in most countries. Current devices use a metal framework and occlusive patch material. Metal frameworks are reported to cause serious complications (eg erosion, perforation, arrhythmia) as late as 10 years following implantation. A septal occluder with bioresorbable framework has long been desired. Until now, development of a clinically effective bioresorbable framework has been elusive. We report on the initial 14 subjects implanted at the CardiovascularCenter, Frankfurt.

METHODS The CBSO employs a poly lactic-co-glycolic acid (PLGA) framework with polyester patches. Available in 3 sizes, it treats defects ≤25mm balloon diameter. It is delivered over a guidewire via a 12F transseptal sheath under fluoro/TEE guidance. Follow-up is at 1, 6, 12 and 24 months & includes clinical examination echo, ECG & blood panel. Closure effectiveness is determined by TEE at 6 months. In this FIH trial, only ASD with atrial rims ≥5mm or PFO tunnels ≤4mm are treated.

RESULTS 14 patients (age 50.5±11.4 years) have been treated: ASD (n=8) ranged from 12.9-21mm in diameter, PFO (n=6) ranged from 5.4-10.8mm in diameter. All devices were successfully implanted without complication. Mean time for loading and placement was 30±25.0 minutes. At 6 months, echo exam showed complete closure in 4/6 PFO patients and complete closure in 6/7 ASD and one small residual shunt (2mm). TTE at long term follow-up (2 at 24 months; 8 at 12 months) confirmed flat septum and showed no re-canalization. There have been no procedure or device related serious adverse events, no thrombus formation and no new occurring arrhythmias during follow-up.

CONCLUSION CBSO is the first clinically effective septal occluder with a bioresorbable framework. It can be easily and safely implanted in humans with excellent closure results at procedure and long term. A learning curve may be required. Additional patients and longer follow-up is needed to further assess outcome.

CATEGORIES OTHER: Pre-Clinical/First In-Human Studies

TCT-827

Abstract Withdrawn

TCT-828

Very Late Vasomotor Responses and Gene Expression Profiles of Porcine Coronary Arteries at 4 Years after Deployment of the Everolimus-eluting Bioresorbable Vascular Scaffold and the Everolimus-eluting Metallic Xience V stent

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