

TCT-152

Allogeneic Heart Stem Cells To Achieve Myocardial Regeneration (ALLSTAR): The Six Month Phase I Safety Results

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Background: In CADUCEUS, autologous cardiosphere-derived cells decreased infarct size and increased viable tissue in post-MI patients. The first-in-human Phase I ALLSTAR trial was designed to test the safety and feasibility of intracoronary infusion of allogeneic cardiosphere-derived cells (CAP-1002) in patients with a previous anterior myocardial infarction (MI), within the prior 12 months with scar size >15% by MRI.

Methods: A total of 14 adult subjects (mean age = 55.6 yr; range 40-66 years) with a recent (28-90 days; n=9) or chronic (91-365 days; n=5) anterior wall MI (mean infarct size 25.4%; range 15.3% - 32.7%) and LV dysfunction (mean LVEF 42%; range 26.7% - 55.1%) were prospectively enrolled and infused with CAP-1002 (n=4 at 12.5M dose; n=10 at 25M dose) via stop-flow intracoronary infusion. Primary safety endpoints were: MACE events (recurrent MI, hospitalization or ER treatment for heart failure, LVAD placement or heart transplantation), acute myocarditis, death due to arrhythmias or unwitnessed death in persons otherwise well. Humoral and cellular immunologic responses were assessed via single antigen bead and ELISpot assays.

Results: No pre-specified safety endpoint occurred. Only two adverse events were treatment-related, both transient hypotension related to nitroglycerin. There were no clinically significant rises in peri-procedural cardiac enzymes. Donor specific antibodies (DSAs) were present in four subjects prior to infusion; one resolved and three persisted during 6 months of follow up. De novo DSA's developed in four subjects, three resolved during follow up and one persisted at 6 months of follow up. All DSA levels observed were low (MFI < 5000). ELISpot revealed no de novo cellular immune responses.

Conclusions: Intracoronary infusion of allogeneic cardiosphere-derived cells (CAP-1002) appears to be safe and feasible. On the basis of the present findings, the ALLSTAR trial has proceeded to a Phase II randomized, double-blind component, powered to assess reduction of scar size by MRI.

TCT-153

Safety and efficacy of transendocardial injection of mesenchymal and induced pluripotent stem cells in a swine subacute model of myocardial ischemia

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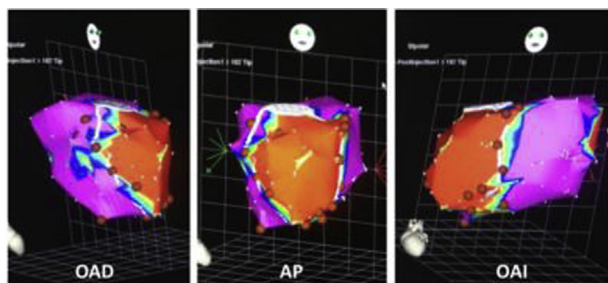
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Background: Mesenchymal stem cells (MSC) are the most promising cells for ischemic myocardial repair. Nowadays we can obtain them from induced pluripotent stem cells (iPS). Our objective is to compare the safety and efficacy of "conventional" MSC and iPS-derived MSC in a large animal model of myocardial ischemia.

Methods: Phase I/II preclinical randomized, placebo-controlled trial, with 30 large white pigs included. Acute myocardial infarction (AMI) will be created after 90-min occlusion of the LAD. The 3 groups are: injection of 20x106 MSC from human adipose tissue (n=10); injection of 20x106 MSC from human iPS (n=10); injection of saline (n=10). Injections will be performed in the scar border with the NOGA XP platform, 7 days after AMI. Safety endpoints include MACE, malignant arrhythmias and lab parameters (intra-procedural and for 5 weeks). Efficacy endpoints include scar size and LV parameters (MRI) and myocardial repair by histology (fibrosis and capillary density, staining with human nuclear antibodies) at 5 weeks.



Results: So far 10 pigs have been included, weight 34.8±6.2 kg. Troponin and CPK values (µg/L) were preinjection 0.41±0.61 and 4.7±3.0, and postinjection 0.44±0.33 and 8.6±5.1, respectively. Cell injection was successful in all cases, with 1 episode of ventricular fibrillation successfully cardioverted and no other events during the procedures or in the follow-up.

Conclusions: This is the first stem cell study designed to assess the cardiac repair ability of iPS-derived MSC. NOGA-guided injections 7 days after AMI were safe. No efficacy data are available, but will be during the conference.

TCT-154

Impact of Intracoronary Injection of CD133+ Bone Marrow Stem Cells on Coronary Atherosclerotic Progression in Patients with STEMI: A COMPARE-AMI IVUS Substudy

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Background: COMPARE-AMI was a randomized, prospective, double-blind, single-center trial to investigate the effect of an intracoronary injection of CD133+ bone marrow stem cells (SC) vs placebo (Placebo) on infarcted myocardium in pts with ST-segment elevation myocardial infarction (STEMI) who underwent primary percutaneous coronary intervention. This IVUS substudy sought to evaluate the adverse effect of CD133+ bone marrow stem cells onto the progression of coronary artery disease in the stented, non-stented segment of culprit vessel, and non-culprit vessels.

Methods: Baseline and 4-month follow-up IVUS images were obtained in 17 SC and 20 Placebo pts. In culprit vessels stented and 5mm proximal and distal reference segments, and proximal and distal non-stented segments were analyzed every 1mm; in non-culprit vessels the entire segments were analyzed every 1mm.

Results: In the culprit vessel analysis, in-stent median % neointimal hyperplasia (NIH) (=NIH/stent volume) (12.1% vs 7.6%, p=0.95), reduction of minimal lumen area (MLA) (-1.2 mm² vs -1.5 mm², p=0.97), and MLA at follow-up (4.3mm² vs 5.3mm², p=0.22) were similar between SC and Placebo. Changes in proximal and distal non-stented segment lumen areas and %plaque volume (=plaque/vessel volume) were also similar between SC and Placebo pts. However, there was a decrease in the maximum arc of attenuated plaque behind the stent from baseline to follow-up in Placebo, but not in SC pts (-12.4° vs 1.0°, p=0.004). In the non-culprit vessel analysis, there were no differences in changes of MLA, %plaque volume, or attenuated plaque between SC and Placebo pts. **Conclusions:** CD133+ bone marrow stem cells (SC) injection through the coronary artery has no effect on disease progression in both culprit and non-culprit vessels.

Segment	Variable	SC	Placebo	p value
Culprit stented segment	Δ MLA (mm ²)	-1.2 [-3.0, 0.2]	-1.5 [-3.2, -0.1]	0.97
	% NIH volume (%)	12.1 [3.7, 29.8]	7.6 [3.5, 30.6]	0.95
	Δ Maximum arc of attenuated plaque (°)	1.0 [-3.6, 9.0]	-12.4 [-25.0, -3.7]	0.004
Culprit proximal 5mm reference segment	Δ MLA (mm ²)	-1.2 [-2.7, -0.7]	-0.7 [-1.2, -0.5]	0.19
	Δ% plaque volume (%)	3.3 [0.6, 8.3]	3.1 [-2.7, 7.0]	0.41
Culprit distal 5mm reference segment	Δ MLA (mm ²)	0.0 [-1.5, 0.2]	-0.1 [-0.2, 0.4]	0.72
	Δ% plaque volume (%)	3.9 [0.3, 8.3]	0.6 [-2.1, 5.2]	0.19
Proximal non-culprit segment in culprit vessel	Δ MLA (mm ²)	-0.4 [-0.8, 0.1]	-0.6 [-1.2, 0.5]	0.69
	Δ% plaque volume (%)	0.8 [-1.9, 2.7]	-0.5 [-3.5, 2.9]	0.53
Distal non-culprit segment in culprit vessel	Δ MLA (mm ²)	-0.2 [-0.7, 0.4]	-0.1 [-0.7, 0.6]	0.97
	Δ% plaque volume (%)	-1.1 [-2.7, 0.0]	-0.8 [-2.5, 2.4]	0.50
Non-culprit segment in non-culprit vessel	Δ MLA (mm ²)	-0.2 [-0.7, 0.1]	-0.2 [-0.1, 0.6]	0.10
	Δ% plaque volume (%)	0.6 [-1.9, 2.1]	-1.4 [-2.0, 1.3]	0.50

TCT-155

A Novel Multi Lumen Compliant Balloon Catheter (ND® Infusion Catheter) Preserves Stem Cell Viability and Improves Dispersion When Compared to a Standard Single Lumen Balloon Angioplasty Catheter

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Background: Intracoronary infusion of stem cells (SC) is typically administered through a single lumen balloon angioplasty catheter (SLC). These catheters are not optimized for SC delivery and potentially compromise SC viability and effectiveness. A multi-lumen catheter (MLC), (ND® Infusion Catheter, Translational Research Institute Gilbert, AZ) may preserve cell viability (CV) and improve dispersion.

Methods: A standard .014" over the wire SLC was compared to a novel MLC 3 Fr. 014" rapid exchange catheter with 6 micro-lumens that act as cell separators.