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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.