ALLogeneic Heart STem Cells To Achieve Myocardial Regeneration (ALLSTAR): The One Year Phase I Results

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Introduction

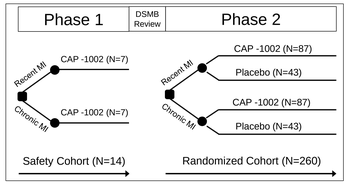
In the CADUCEUS study, autologous cardiosphere-derived cells decreased infarct size and increased viable tissue in post-MI subjects. The first-in-human Phase I ALLSTAR trial was designed to test the safety and feasibility of intracoronary infusion of allogeneic cardiosphere-derived cells (CAP-1002).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

Methods

Phase I enrolled 14 adult subjects with a recent (28-90 days) or chronic (91-365 days) anterior MI and ejection fraction (EF) less than 50% were consented, prospectively enrolled, and infused with CAP-1002 (n=4 at 12.5M cells; n=10 at 25M cells) via stop-flow intracoronary infusion.

Phase I/II study design

- Infarct size ≥15% on MRI, Stratified patient recruitment (recent/chronic)
- Phase I open label; Phase II double blind randomized placebo controlled (2:1)
- Baseline, 6, and 12 month cardiac MRI analysis performed at the core lab*.

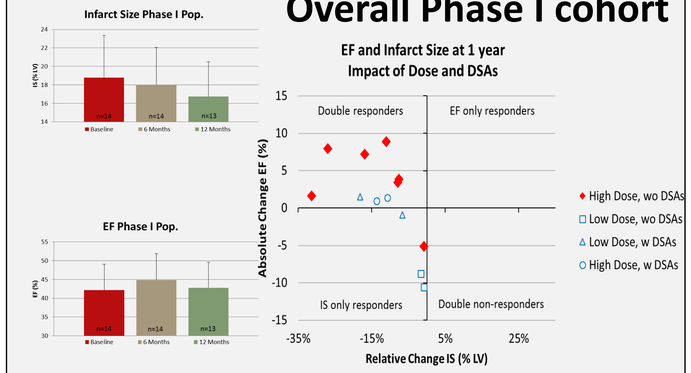


Results

All Phase I subjects have reached one year post-infusion. 13 of the 14 subjects completed one year MRI follow-up. One subject declined their one year follow-up visit.

Primary 1 Year Safety Endpoints	Immunology	MRI Infarct Scar Size/Heart Function
• NO Acute myocarditis • NO Death due to VT/VF • NO Sudden death • NO Major Adverse Cardiac Events ***NIH DSMB approved proceeding to ALLSTAR Phase II enrollment***	• Antibody response (DSA) revealed low level antibodies (MFI <5000) • 4 subjects with pre-existing DSAs: 1 resolved, 3 persisted • 4 subjects with de novo DSAs: 3 resolved, 1 persisted • No clinical sequelae seen (acute myocarditis, LV dysfunction) • Cellular response (ELISPOT) revealed no de novo responses	• Phase I subjects showed trend towards improvement in infarct scar size • Phase I subjects that received 25M cells to which they had no DSAs (Phase II equivalent population) showed a 15% reduction in scar size and a 4% improvement in EF at one year, despite one apparent non-responder. • A separate sub-study analysis^ of baseline and 6 month MRI wall thickening in infarcted segments showed significant improvement in the Phase II equivalent subjects. ***MRI Core Lab: Dr Joao Lima at Johns Hopkins / ^Substudy analysis: Dr Konstantinos Malliaras**

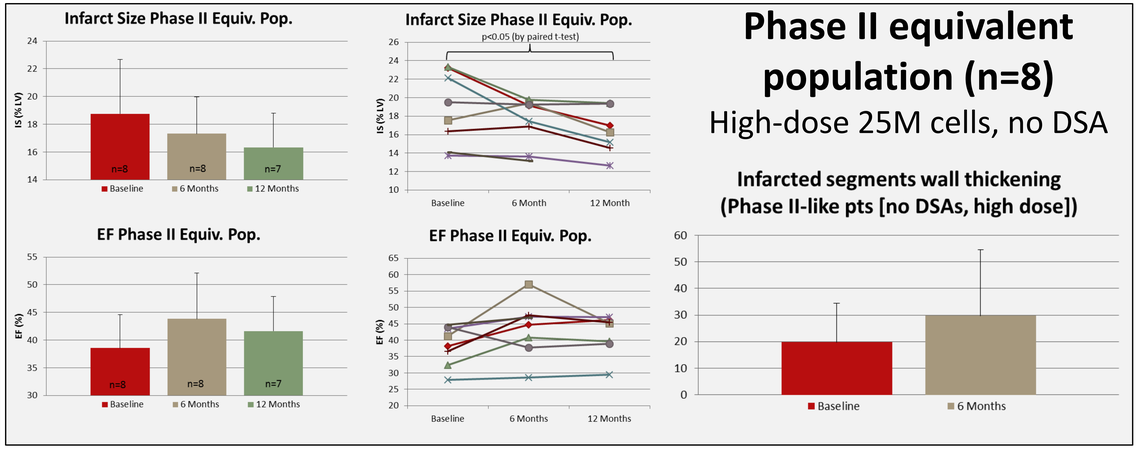
Overall Phase I cohort



Mean age 56 ± 8 years Mean EF 42.0 ± 7.0 %

Phase II equivalent population (n=8)

High-dose 25M cells, no DSA



Conclusions

- Intracoronary infusion of allogeneic cardiosphere-derived cells (CAP-1002) appears to be ***safe and feasible***.
- In Phase II equivalent subjects (high-dose 25 M cells and DSA negative), there is a
  - ***Significant improvement in infarct scar size*** at 1 year
  - ***Significant improvement in infarcted segments wall thickening*** at 6 months.1 year analysis awaited.
- Enrollment is currently underway in ALLSTAR Phase 2 study to confirm these findings in a larger cohort of patients.