



Autologous Mononuclear Cell Injections for Refractory Angina CardiAMP Chronic Myocardial Ischemia Roll-in Cohort Results

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Myocardial Ischemia Trial Investigators



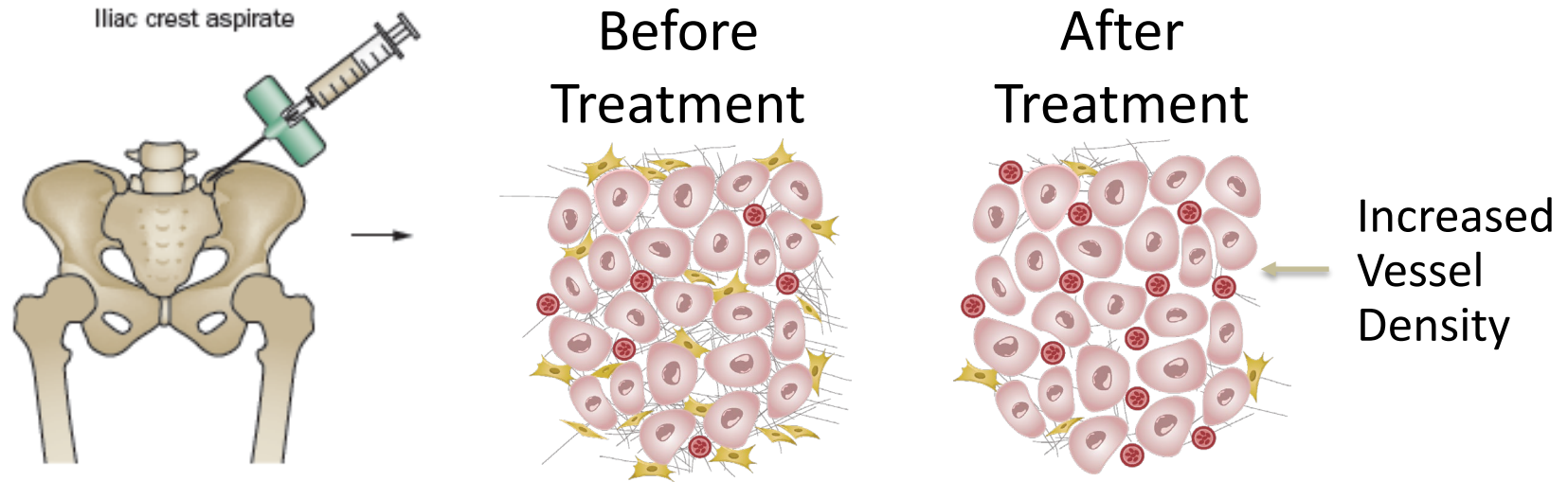
Potential conflicts of interest

Speaker's name: Amish Raval

- I have the following potential conflicts of interest to report
 - Receipt of grants / research supports - Other
 - Receipt of grants / research supports - Shockwave Medical
 - Stock shareholder - Other

Pre-Clinical Background

- Direct intra-muscular injections of bone marrow mononuclear cells that include CD34+ & CD133+ are associated with increased vascular density in cardiovascular ischemia models



Asahara et al. (1997) *Science* 275,5302:964-966

Silva et al. *Tex Heart Inst J* (2011);38(3):219-24.

Takahashi, M. et al. (2006) *Am J Physiol Heart Circ* 291:H886-H893.

Clinical Motivation

- Intramyocardial injections of autologous mononuclear cells (MNCs) was safe and beneficial in early chronic myocardial ischemia trials¹⁻³
- Clinical responders were identified, particularly for patients receiving higher doses of certain enriched cell populations, such as CD34+ and CD133+^{4,5,6}
- MNCs may be beneficial for microvascular dysfunction
 - immunosuppression not required
 - low potential for arrhythmias
 - all other therapeutic options remain available to patients

1. Beeres 2006 American Heart Journal
2. REACT 2009 Cell Transplantation
3. Leiden Predictor 2014 Int J of Cardiology

4. ACT-34 2011 Circ Res
5. RENEW 2016 JACC Interv
6. Bhatnagar 2016 Am Heart J (CCTRN)

Patient-Centered, Point of Care Approach

Objective:

Determine feasibility and best practices for high dose auto-MNC treatment in patients with chronic refractory angina due to obstructive CAD and whose cells met prespecified cell population analysis thresholds.

Pre-procedure Screening

Small amount of bone marrow collected from hipbone and sent to lab for testing

1 Cell Collection

Small amount of bone marrow obtained from hipbone
~ 20 minutes

2 Cell Processing

Bone marrow cells prepared for transfer at point of care
~ 25 minutes

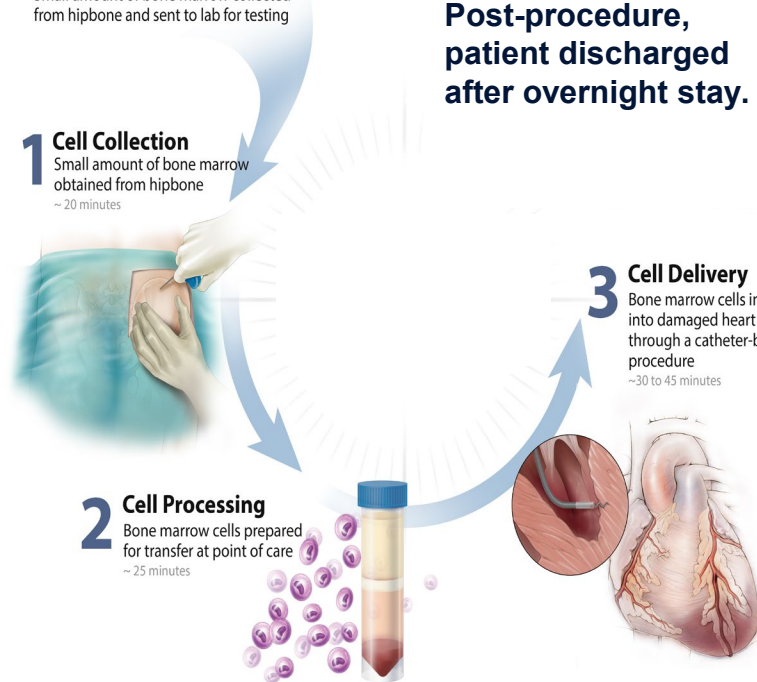
Post-procedure, patient discharged after overnight stay.

3 Cell Delivery

Bone marrow cells injected into damaged heart tissue through a catheter-based procedure
~30 to 45 minutes

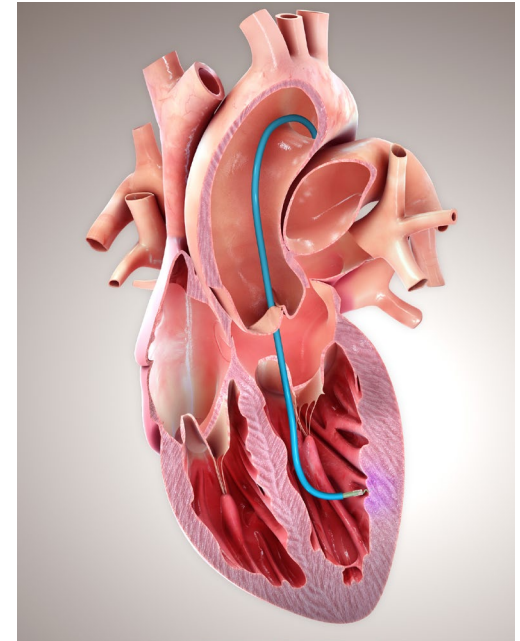
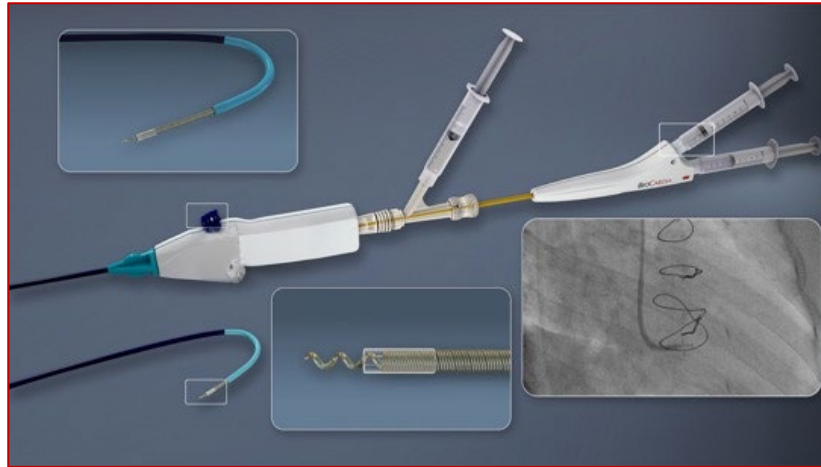
200 M cell
0.5 mL/injection
10 Injections

Target: Ischemic but not infarcted regions



CardiAMP CMI

FDA Breakthrough Device Designation



CardiAMP CMI

Key Eligibility Criteria

- Chronic stable angina due to obstructive CAD (CCS III-IV)
- On stable maximally tolerated anti-anginal treatment
- No revascularization options
- LVEF \geq 40%*
- Baseline ETT: 3 - 10 minutes
- Flow cytometry-based cell population analysis by core lab**

Central Screening Eligibility Committee

- Symptom classification
- Medication optimization
- Coronary angiography
- Myocardial Perfusion imaging
- Echocardiography
- Injection site strategy

* *Yale Echo Core Lab*

** *Baylor CPA analysis lab*

Outcome Measures

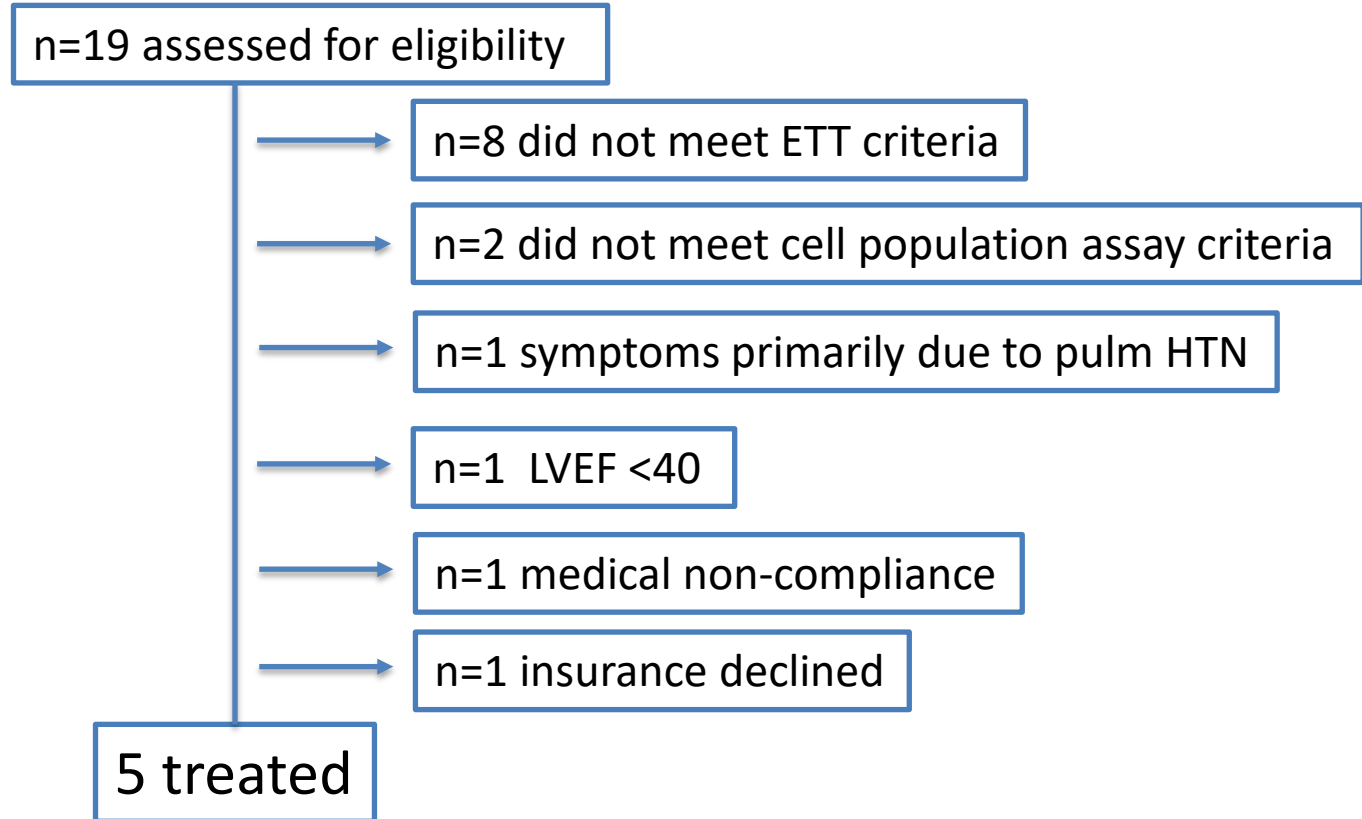
Primary Efficacy:

- Change from baseline in total exercise time on Exercise Tolerance Test (ETT) using modified Bruce protocol

Key Secondary:

- Change in from baseline for angina frequency (episodes per week)

Screening



Baseline Demographics

Age (mean)	75.4 (66-82)
Male Sex	5/5
Diabetes	2/5
HTN	5/5
HLD	4/5
Smoking Hx (never)	3/5
Prior CABG	5/5
Prior PCI	5/5

B-blocker	5/5
CCB	3/5
Long-Acting Nitrate	3/5
Ranolazine	3/5
LVEF (mean)	51% (40-60%)
CCS class III/IV	5/5
Baseline TET (sec)	402 (267-572)

Roll-in Cohort Feasibility and Safety

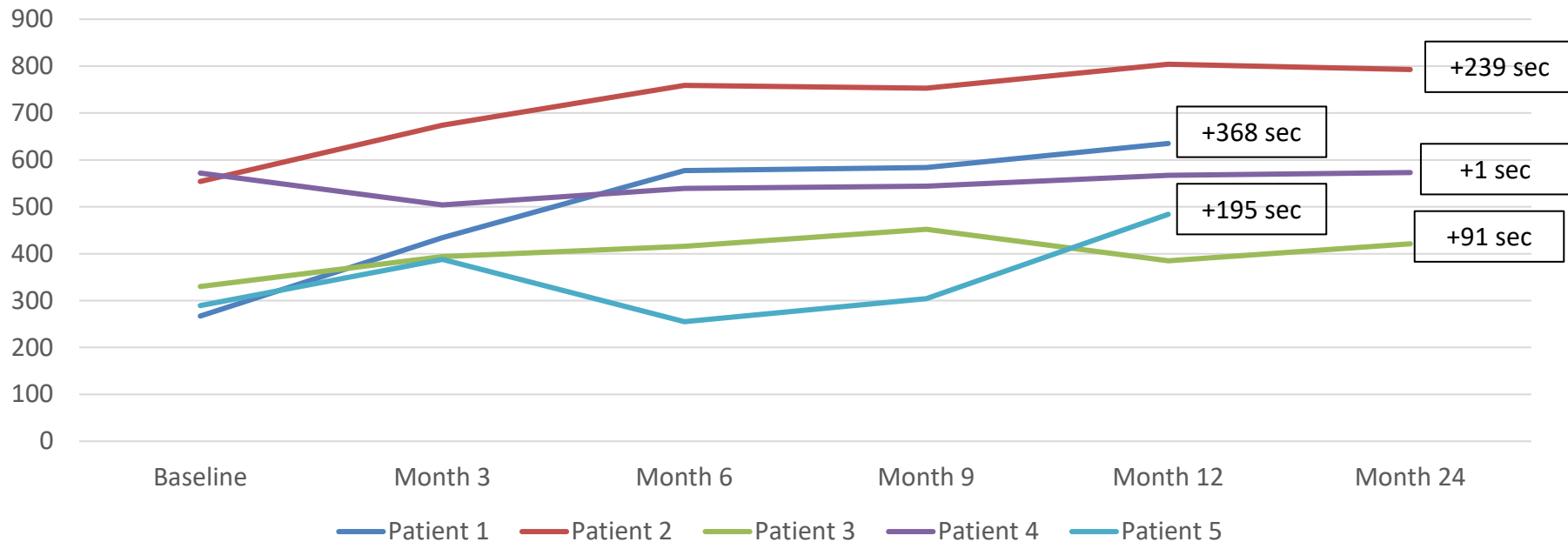
Successful treatment injections in all 5 patients

Treatment emergent adverse events:

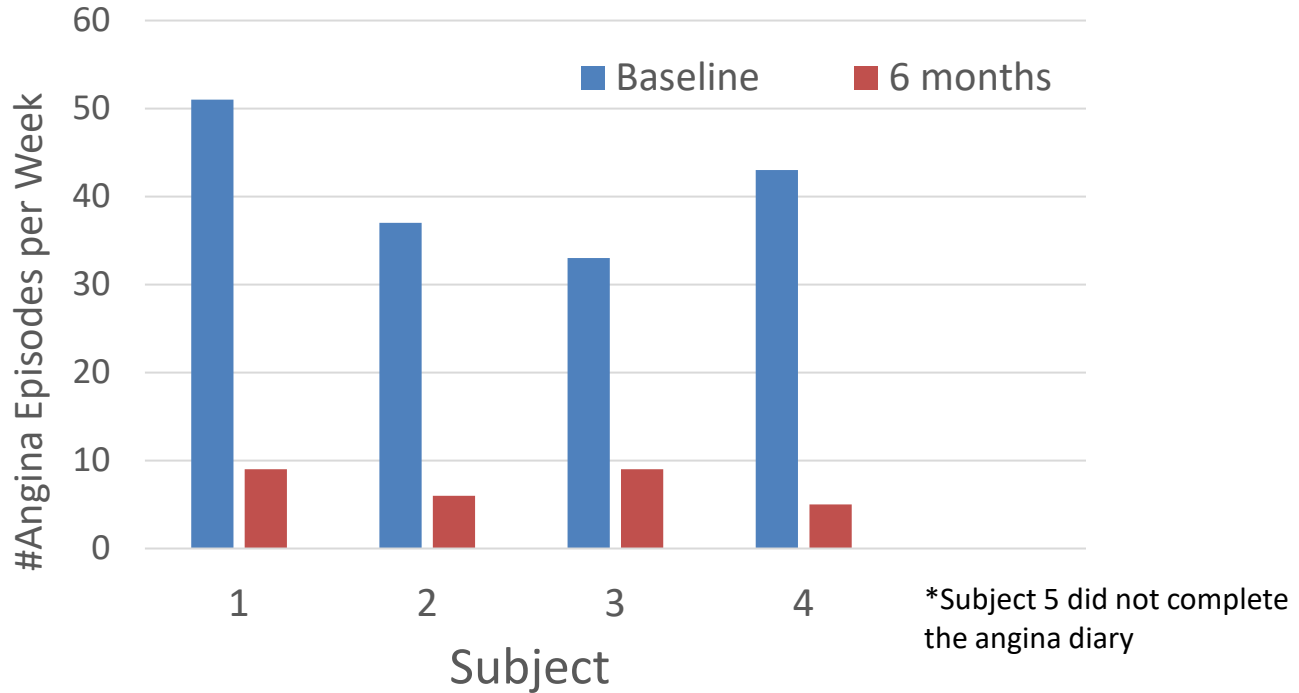
- n=1 asymptomatic, small, non-circumferential pericardial effusion
 - no hemodynamic changes,*
 - complete resolution on echo by day 11*
- No ventricular arrhythmias
- No major bleeding complications

Total Exercise Tolerance Time

Total Exercise Tolerance Time Through Month 24



Angina Frequency



Conclusion

- Transendocardial injection of autologous mononuclear cell therapy for “no option” chronic refractory angina patients was feasible, safe and initial benefits were observed in this roll-in cohort
- Randomized, double blind, sham-controlled trial data is required to confirm these preliminary findings



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