CAuSMIC Trial

Final One-Year Results of the CAUSMIC Trial

First United States Randomized Controlled Trial Utilizing 3-Dimensional, Catheter-Based Delivery of Autologous Skeletal Myoblasts for Ischemic Cardiomyopathy

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American Heart Association
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ADVANCED CELL TECHNOLOGY

Mytogen

Presenter Disclosure Information

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Disclosure Information...
The following relationships exist related to this presentation:

Nabil Dib, MD, MSc, FACC *- Shareholder for Mytogen, Inc.; Significant level relationship*

Jonathan Dinsmore *- Employee and Shareholder for Mytogen, Inc.; Significant level relationship*

Ann Campbell *– Consultant for Mytogen, Inc.; Significant level relationship*

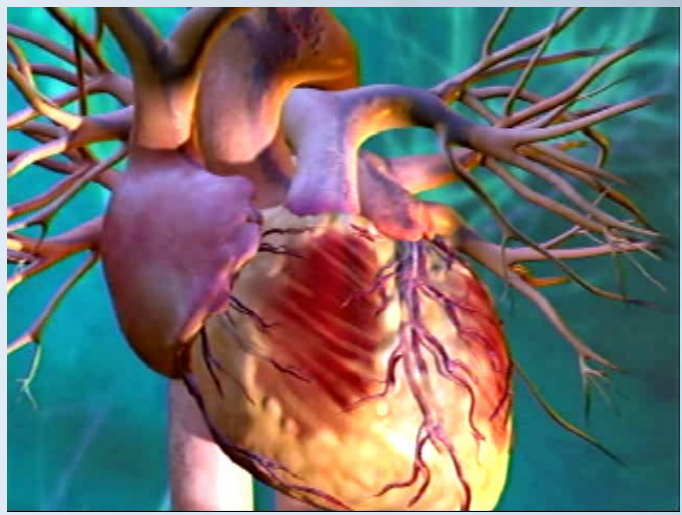
Zaki Lababidi, Bee White, Susan Moravec, Katayoun Seyedmadani, Amy Rosenbaum, Wael A. Jaber, Craig Ridenhour *– No relationship to disclose*

Edward B. Diethrich *– Shareholder for Mytogen Inc.; Significant level relationship*

Myocardial Regeneration
MYOGENESIS

Congestive Heart Failure

Population Group	Prevalence 2002	Incidence (New Cases)	Mortality 2001	Hospital Discharges 2002	Cost 2005
Total Population	4,900,000 (2.3%)	550,000	52,828	970,000	$27.9B



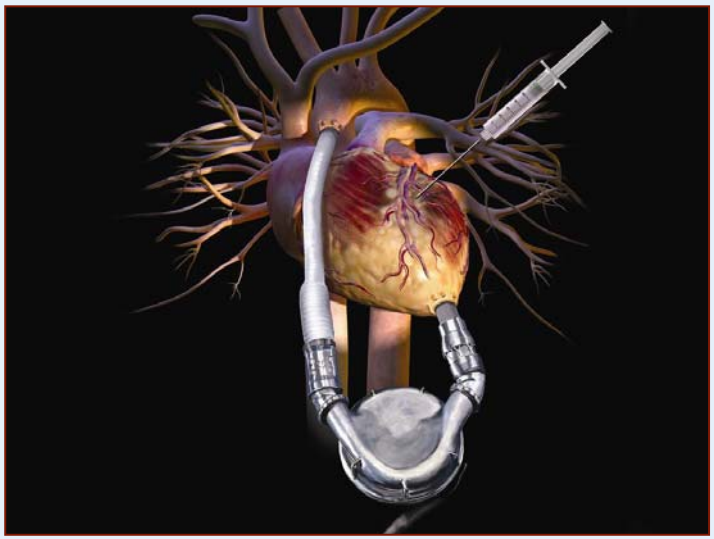
Coronary Heart Disease

Population Group	Prevalence CHD 2002	Prevalence MI 2002	New & Recurrent MI & Fatal CHD	New & Recurrent MI	Mortality CHD 2002	Mortality MI 2002	Hospital Discharges CHD 2005	Cost CHD 2005
Total Population	13,000,000 (6.9%)	7,100,000 (3.5%)	1,200,000	865,000	494,382	179,514	2,125,000	$142.1B

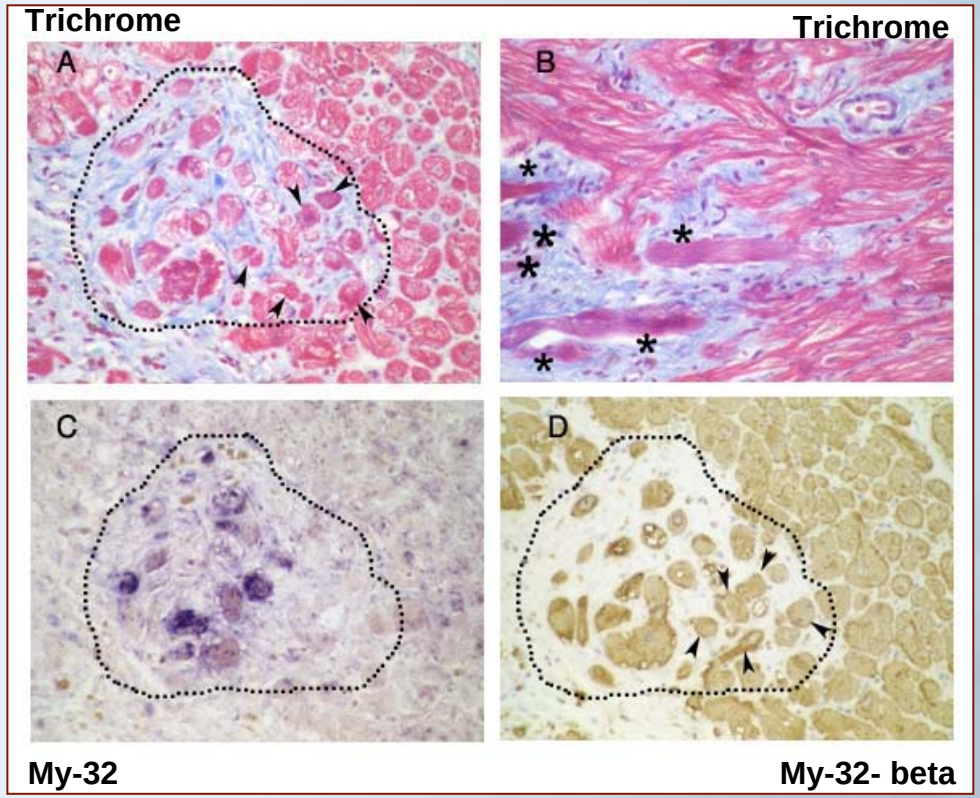
Heart Disease and Stroke Stastics – 2005 Update, AHA

LVAD and Cell Transplantation
Proof of Concept-Engraftment

Pt # 4 (5 months post: 300 X 10^6)



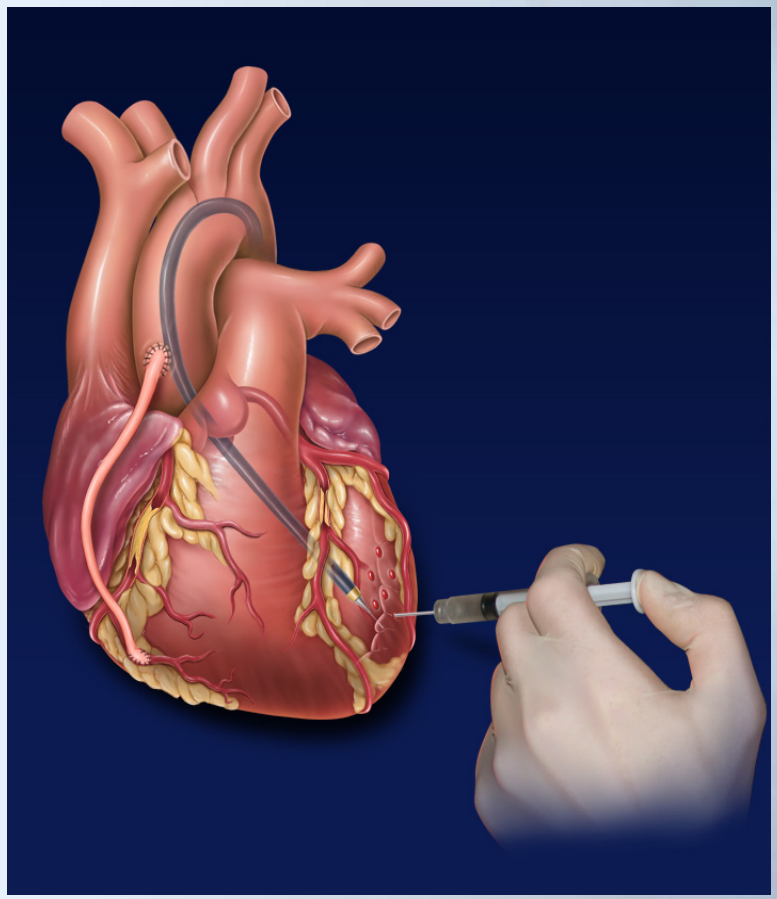
300 million Cells



Pagani et al., J Am Coll Cardiol. 2003: 41:879-88

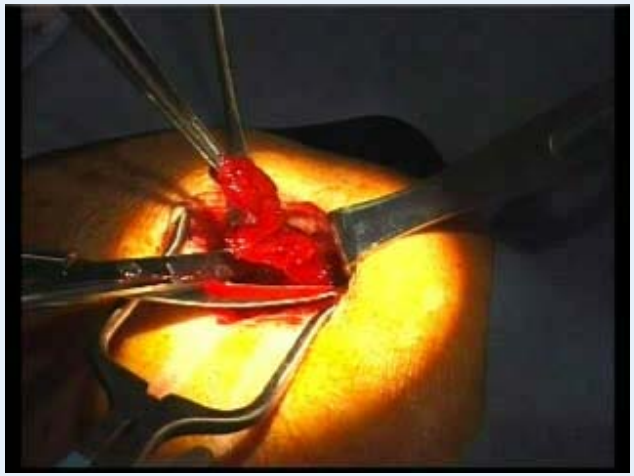
Percutaneous vs. Surgical

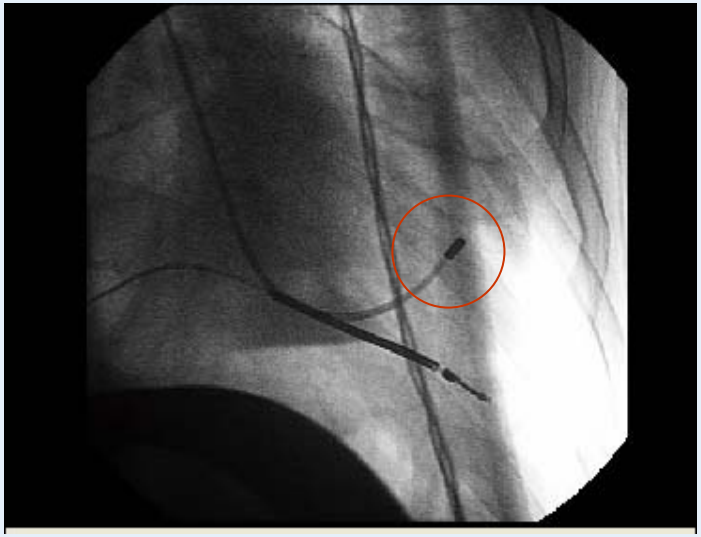
- Less invasive
- High risk patient
- Repetition



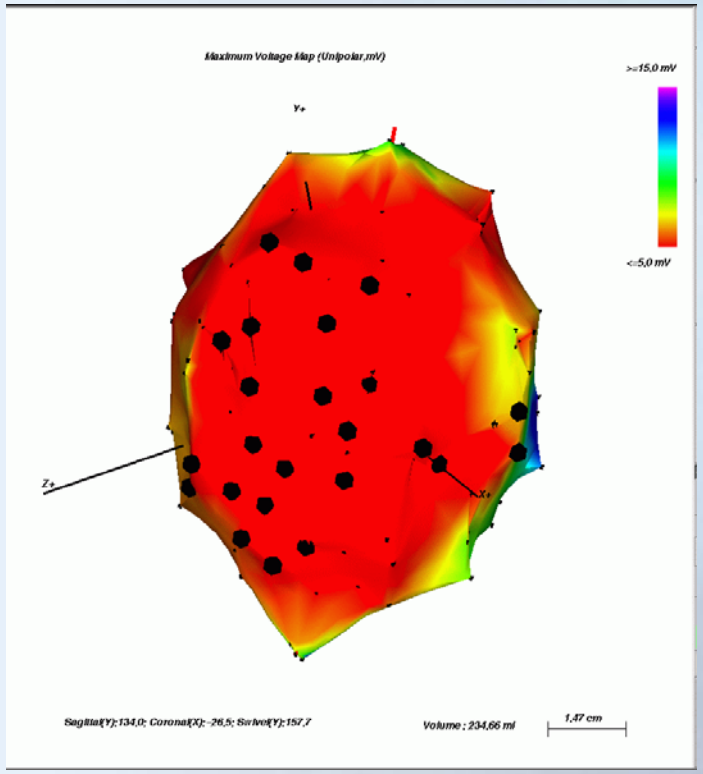
Procedure

Myoblast Procurement, Isolation / Expansion





Electromechanical Mapping Injections with the NOGA® System



24 injections, 600 X 10^6 cells

Study Design

Phase I, single center, prospective randomized 1:1 open label, dose escalating clinical trial

23 subjects with Ischemic Cardiomyopathy EF ≤40%

↓

1:1 Randomization

Control group
Optimal medical therapy (*n*=11)

ASM Transplantation (n=12)
3 subjects per dose group
$30x10^6$, $100x10^6$, $300x10^6$, $600x10^6$
3-24 injections, 0.25 mL over 20 sec.

No FDA requirements for ICD or anti-arrhythmic medication

CAuSMIC

Objective

Primary

To evaluate the safety and feasibility of transplanting ASM into infarcted myocardium using a 3-D guided catheter-based delivery system.

Secondary

To evaluate Efficacy assessed by changes at 3, 6 and 12 m

- ***Quality Of Life:***
  - **NYHA classification**
  - **Minnesota Living With Heart Failure Questionnaire**

- ***Myocardial viability* assessments performed:**
  - **electromechanical mapping (NOGA® system)**

- ***Heart Function:***
  - **echocardiography**

Inclusion / Exclusion Summary

Inclusion

- **Previous MI** documented by gated SPECT imaging demonstrating fixed defect
- **Ejection fraction ≤ 40%** as measured by stress nuclear / viability assessment with gated imaging
- Congestive heart failure (**NYHA Class II - IV**) on optimal medical therapy for a minimum of 2 months and confirmed by an independent medical monitor

Exclusion

- Left ventricular **wall thickness < 5mm**
- Cardiac resynchronization therapy (**CRT) within 6 months**
- Idiopathic cardiomyopathy
- Hospitalization within 4 weeks for ACS, MI, unstable angina or CVA
- Contraindications for left ventricular mapping, i.e. thrombus, severe peripheral arterial disease, uncontrolled atrial and ventricular arrhythmias
- Mechanical valve replacement
- Severe renal insufficiency or liver disease
- Loop Recorder or device interrogation (baseline, 24 hour, week 1, months 1, 3, 6, 12)

Baseline Demographics

	ASM Treated	*Control*	*P*
Number Patients	12	11	NS
Gender (%)			
Male	91	82	NS
Female	9	18	NS
Age (yr)	65.1	62	NS
NYHA	2.8	2.4	NS
MLHFQ Score	47	47	NS
Ejection fraction (echocardiogram) (%)	30	34	NS
Previous MI (%)	100	100	NS
Average MI age (yrs)	13.2	11.3	NS
Diabetes (%)	25	27	NS
Hyperlipidemia (%)	100	90	NS
Previous PCI (%)	75	63	NS
Previous CABG (%)	66	72	NS
Ventricular arrhythmias (%)	67	64	NS
Atrial arrhythmias (%)	42	55	NS
Implantable cardioverter-defibrillator (%)	92	82	NS
Cardiac resynchronization therapy (%)	58	0	0.001

Results: Safety

Independent Data Safety Monitoring

- No deaths, MI, or cerebrovascular events were observed in either group
- One subject in each group was hospitalized for congestive heart failure
- All ASM transplant procedures were performed successfully without injection-related complications
- 2 VT events, requiring cardioversion, occurred during mapping, prior to performing the ASM injections
- One patient in the ASM group was found to have colon adenocarcinoma with metastasis at 11 month follow-up

Ventricular Arrhythmias

Sustained Events					
Treated			**Control**		
Subject	**Baseline**	**6 Months Follow-Up**	**Subject**	**Baseline**	**6 Months Follow-Up**
1	0	0	3	0	0
4	0	0	5	0	0
6	0	0	8	0	0
16	0	0	12	0	0
17	0	0	25	0	0
18	0	0	28	0	0
20	0	0	30	0	0
21	2	0	31	0	0
22	0	**4(3 shocks, 1 ATP[a])**	**32**	0	**2 ATP**
24	2	0	33	0	0
26	0	**4(2 shocks, 2 ATP[b])**	34	0	0
37	0	0			
n=12	**4**	**8**	**n=11**	**0**	**2**

Recorded by 48 hour Holter monitor or implanted device interrogation

[a] event at 8 months

[b] event at 9 days

ATP=antitachycardia pacing

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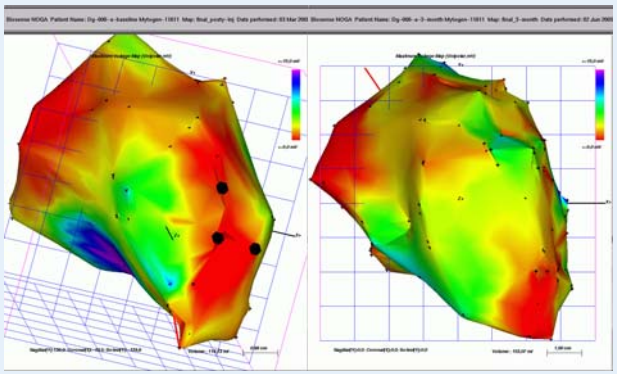
NOGA® Mapping

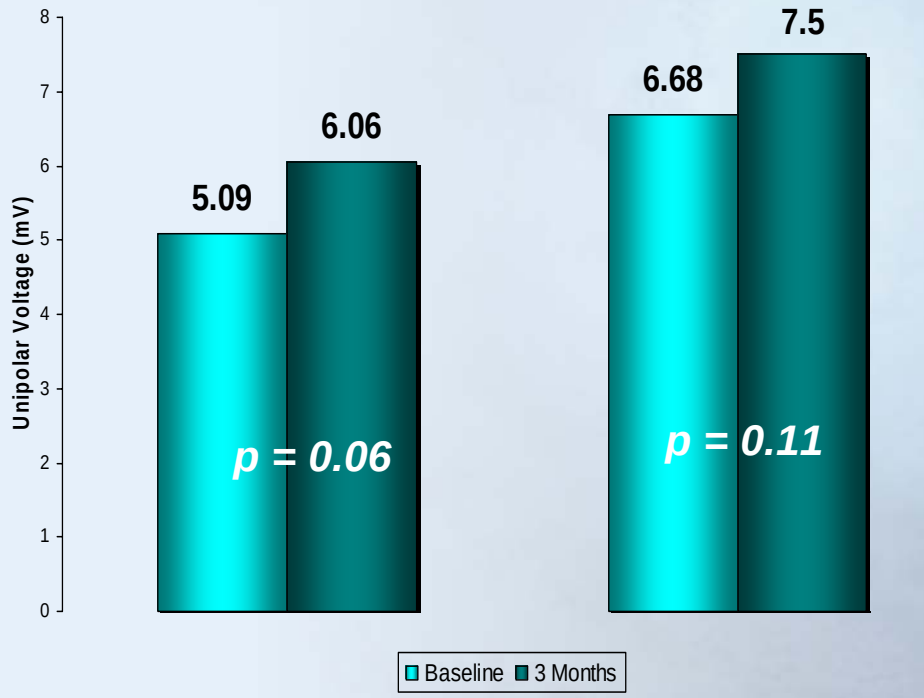
Unipolar Voltage Measurements within Infarct Region vs All Mapped Regions

Baseline **3 months**



30 million cells

n=12



Injected Regions **All Mapped Regions**

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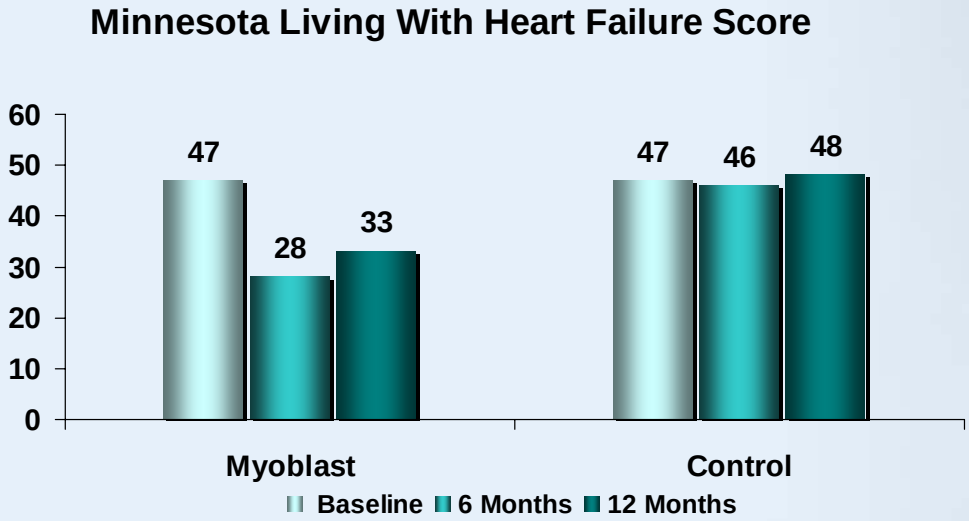
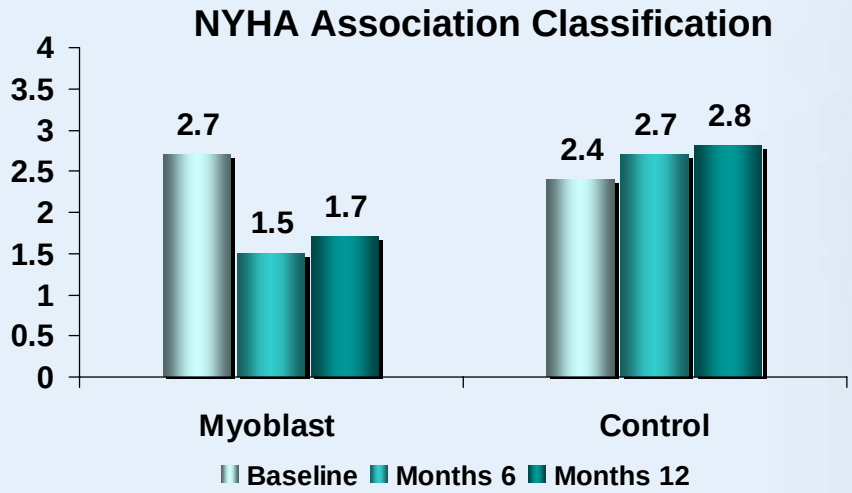
Quality of Life & Functional Capacity



6mos: p = 0.02, t-test, n = 23
12mos: p = 0.002, t-test, n = 23



6 mos: p < 0.0001, t-test, n = 23
12 mos: p < 0.0001, t-test, n = 23

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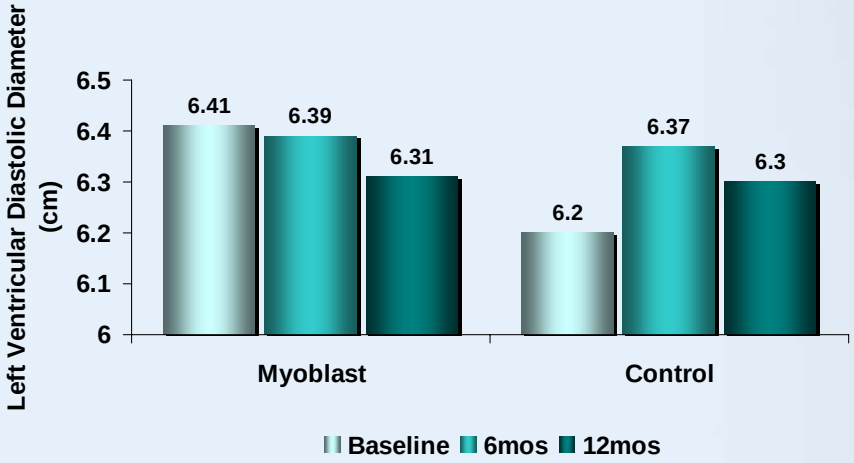
Echo Core lab
Left Ventricular Dimensions



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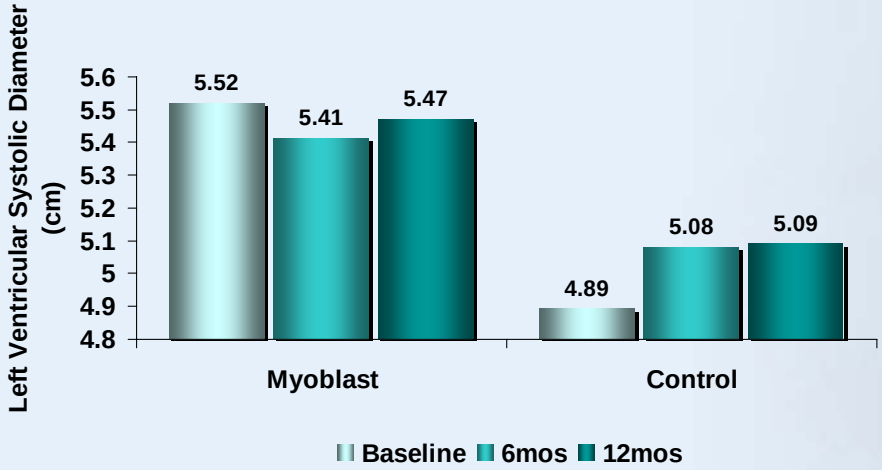
12mos: p = 0.07, t-test, n = 23



6mos: p = 0.07, t-test, n = 23
12mos: p = 0.13, t-test, n = 23

CAuSMIC

Conclusion

3-Dimensional Guided, Catheter-Based Delivery of Autologous Skeletal Myoblasts for Ischemic Cardiomyopathy has shown:

- feasibility and safety
- improvement in viability (unipolar voltage) assessed by 3-D NOGA® mapping
- improvement in quality of life assessed by NYHA Classification and Minnesota Living with Heart Failure Questionnaire
- Strong trend toward improvement in heart function and potentially reversing remodeling as assessed by echocardiography
- A larger 165 patient, phase II, randomized, double- blind, placebo-controlled multicenter clinical trial has been cleared by the FDA