

# Autologous Cell Therapy May Curb Pathological Ventricular Remodeling in Chronic Ischemic HFrEF Patients Selected for Favorable Cell Characteristics

*On behalf of the CardiAMP HF Trial Investigators*

Amish Raval, MD

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# Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

## Nature of Financial Relationship

Grant/Research Support

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## Ineligible Company

BioCardia Inc.

Shockwave Medical

# Motivation

- Bone marrow mononuclear cells (MNCs) show beneficial effects in ischemic HFrEF models ( $\uparrow$  vessel density,  $\downarrow$  fibrosis) <sup>1,2</sup>
- Intramyocardial delivery of unfractionated MNC was safe and associated with positive efficacy in the prior CardiAMP Phase 1 & 2 trials <sup>3,5</sup>
- Clinical responders were identified, particularly for patients receiving higher doses of certain enriched cell populations, such as CD34+ <sup>3,4</sup>
- MNCs may be beneficial for microvascular dysfunction
  - immunosuppression not required
  - low potential for arrhythmias
  - all therapeutic options remain available to patients

# Patient Centered Point of Care Approach

## Objective:

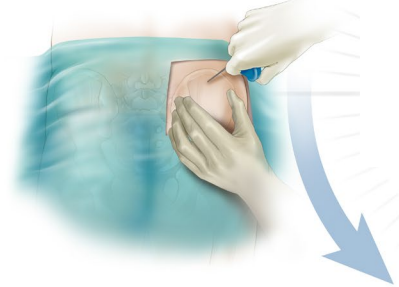
Determine safety and efficacy of high dose auto-MNC treatment in patients with ischemic HFrEF whose cells met prespecified cell population analysis.

### 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



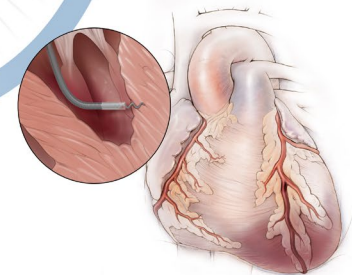
### 2 Cell Processing

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



### 3 Cell Delivery

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

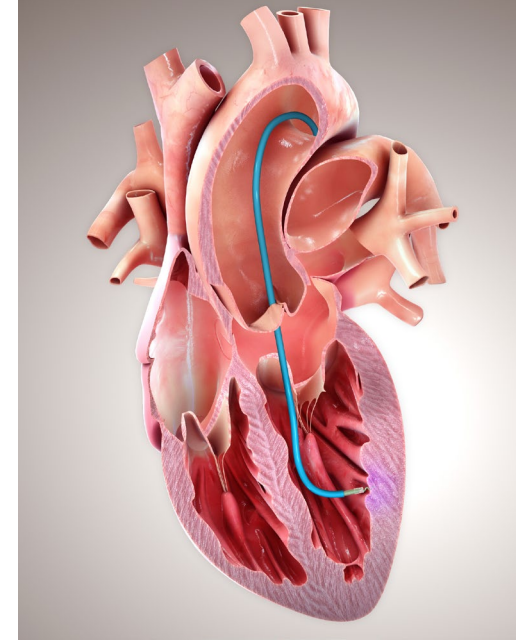
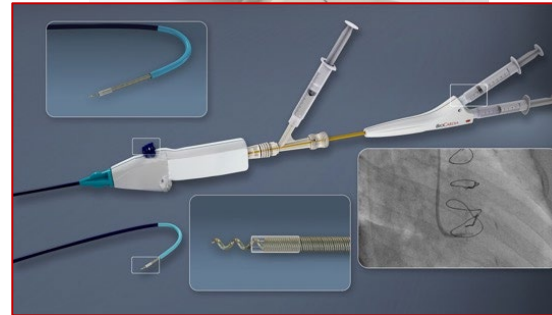


Post-procedure, patient discharged after overnight stay.

## Key Eligibility Criteria

- Chronic ischemic HFrEF with LVEF 20-40%
- NYHA II/III on max tolerated GDMT/device therapy
- Baseline 6MWD 100 - 450 meters
- Flow cytometry-based cell population analysis by core lab

## Investigational Devices



***FDA Breakthrough Device Designation***

**Trial Design:** Double-blind RCT 3:2 active: procedure-placebo control  
33 activated sites (U.S.A and Canada)

**Primary Outcome:** Hierarchical composite ranking using Finkelstein Schoenfeld:

**Tier 1. All cause death, cardiac transplant, LVAD**

**Tier 2. Non-fatal MACE (HF hospitalizations, MI, stroke)**

**Tier 3. Change in 6MWD from baseline to last follow-up**

**Pre-specified Secondary Outcome:**

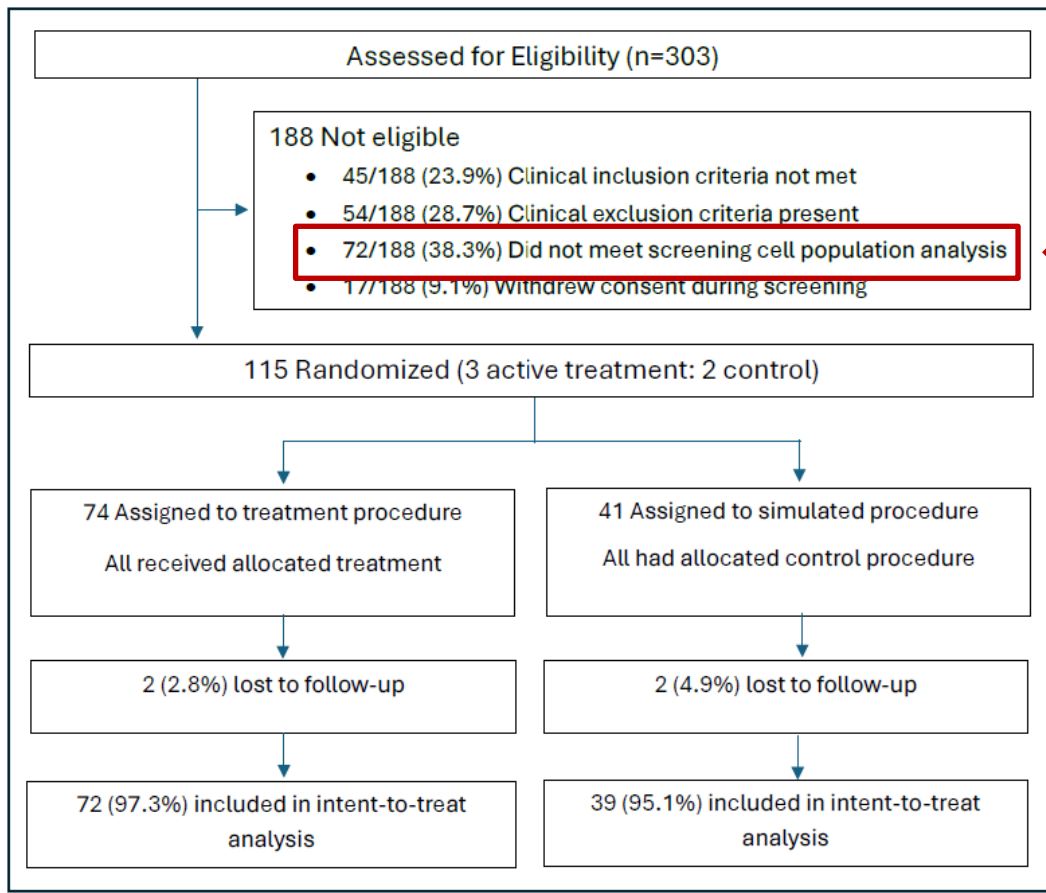
**Tier 3. Change in Quality of Life (MLHFQ)**

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Planned interim analysis July 2023:

- Although safety/futility thresholds were not crossed, the DSMB recommended *pausing* the trial early as the primary outcome using 6MWD in 3<sup>rd</sup> Tier was unlikely to be met.
- Sponsor *stopped* the trial after enrolling 115 of the planned 250 patients.
- Phase II trial predicted 80 pts needed (90% power) for the 3-tier primary.

# CONSORT Diagram



38% did not meet CPA criteria

| Baseline                     | Treatment (n=74) | Control (n=41) |
|------------------------------|------------------|----------------|
| <b>Demographics / Med Hx</b> |                  |                |
| Age*                         | 65.6±10.2        | 66.3±8.1       |
| Male (%)                     | 89.2             | 92.7           |
| White (%)                    | 90.5             | 92.7           |
| BMI, kg/m*                   | 30.5±4.4         | 30.3±5.9       |
| NYHA Class II/III (%)        | 73 / 27          | 78 / 22        |
| <b>Medical History</b>       |                  |                |
| Diabetes mellitus (%)        | 40.5             | 51.2           |
| Hypertension (%)             | 83.7             | 85.4           |
| Hyperlipidemia (%)           | 75.7             | 82.9           |
| Smoking hx (%)               | 69.9             | 62.5           |
| Afib / Flutter (%)           | 23.0             | 36.6           |
| Prior stroke/TIA (%)         | 17.5             | 12.2           |
| Prior CABG (%)               | 40.5             | 46.3           |
| ICD (%)                      | 60.8             | 53.7           |
| CRT-D (%)                    | 18.9             | 24.4           |

| Baseline  | Treatment (n=74) | Control (n=41) |
|---|------------------|----------------|
| <b>Medical Therapy &gt;3M before enrollment</b> |                  |                |
| ACEi, ARB, ARNI (%)                             | 74.3             | 76.5           |
| Beta-blocker (%)                                | 86.5             | 80.4           |
| MRA (%)   | 79.7             | 72.6           |
| SGLT2i (%)                                      | 41.9             | 37.3           |
| GLP-1 Agonists (%)                              | 5.4              | 7.3            |
| <b>Outcome Measures</b>                         |                  |                |
| 6MWD, meters*                                   | 344±80           | 355±66         |
| MLHFQ, points*                                  | 40±25            | 40±24          |
| % LVEF*   | 32±6             | 32±6           |
| LVEDVi*   | 99.7±30.1        | 99.4±28.7      |
| LVESVi*   | 68.5±24.7        | 68.4±23.1      |
| *mean±SD  |                  |                |

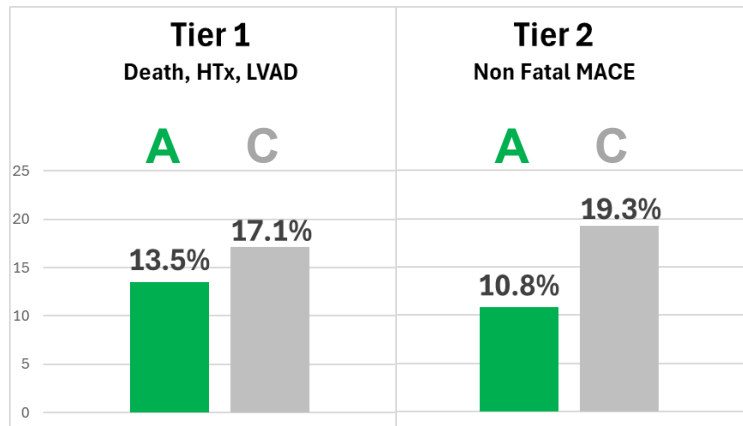
**Periprocedural Safety**

- 3 pericardial effusions
- No sustained arrhythmias



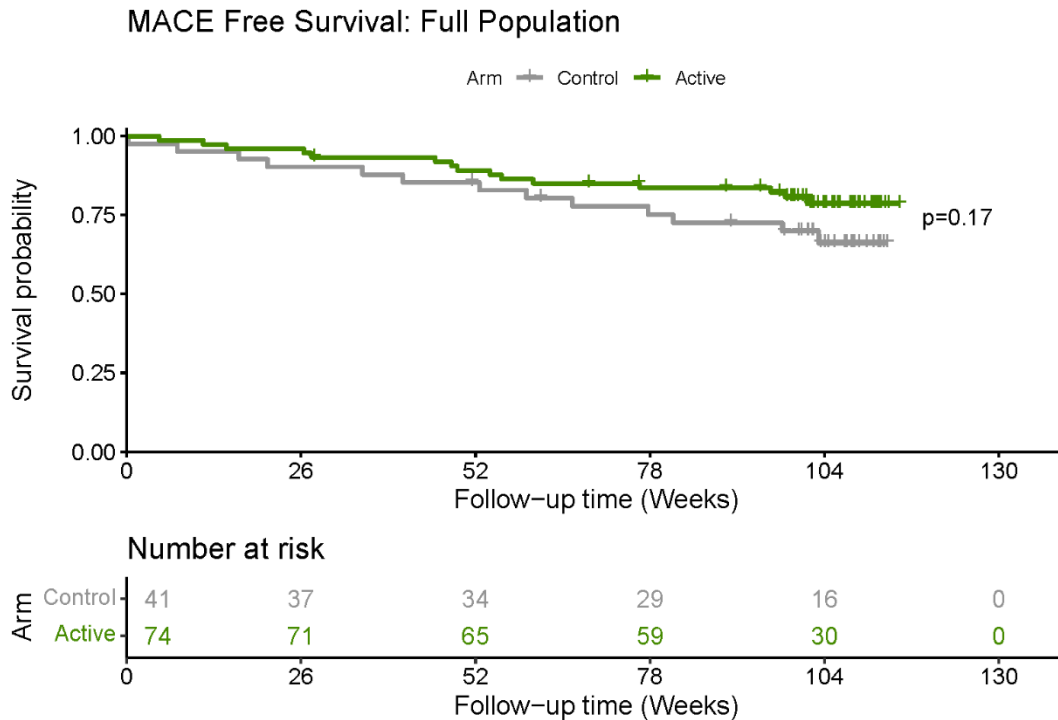
*Independent, Blinded Core Lab - Yale*

# Primary and Key Secondary Outcomes



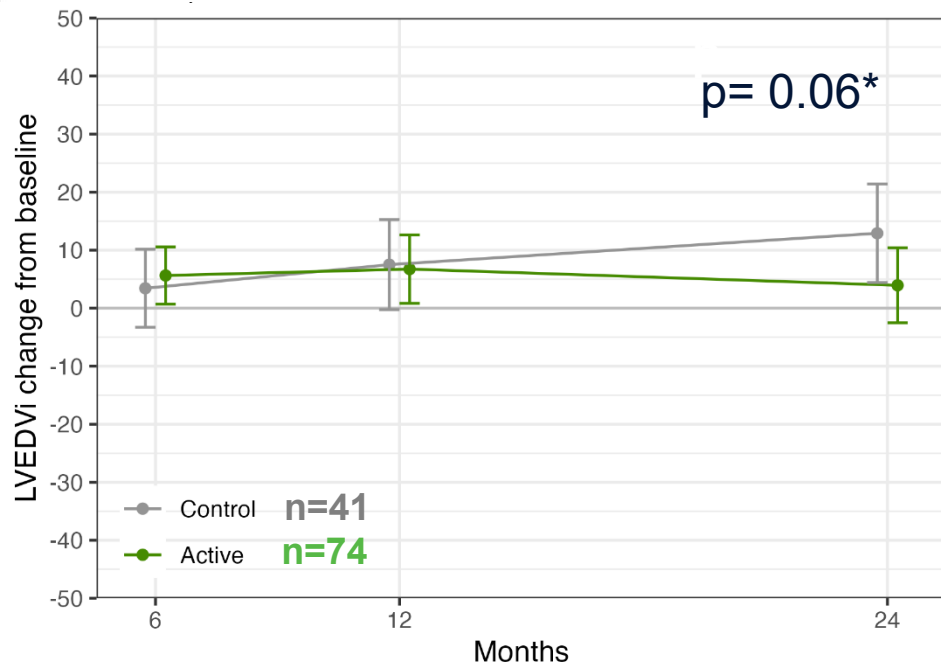
**6MWD** **Tier 3** **MLHFQ**  
**+5.7m** **+27.1m** **5.5 pts**  
**improvement**

**WR = 0.99** **WR = 1.42**  
 (CI: 0.63-1.56) (CI: 0.91-2.22)  
 p = 0.96 p = 0.14

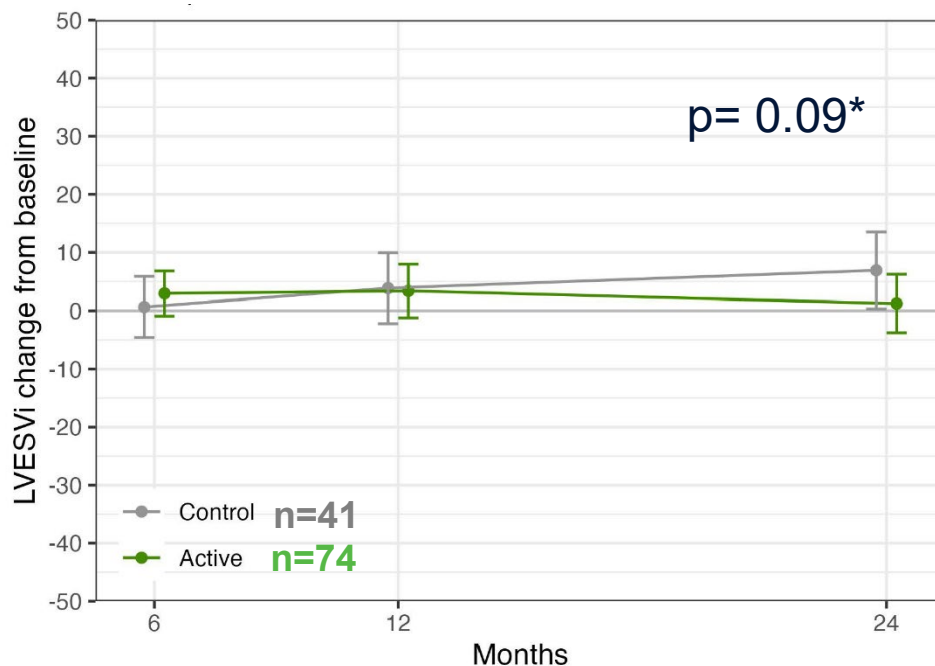


# LV Volume Indices-Full population

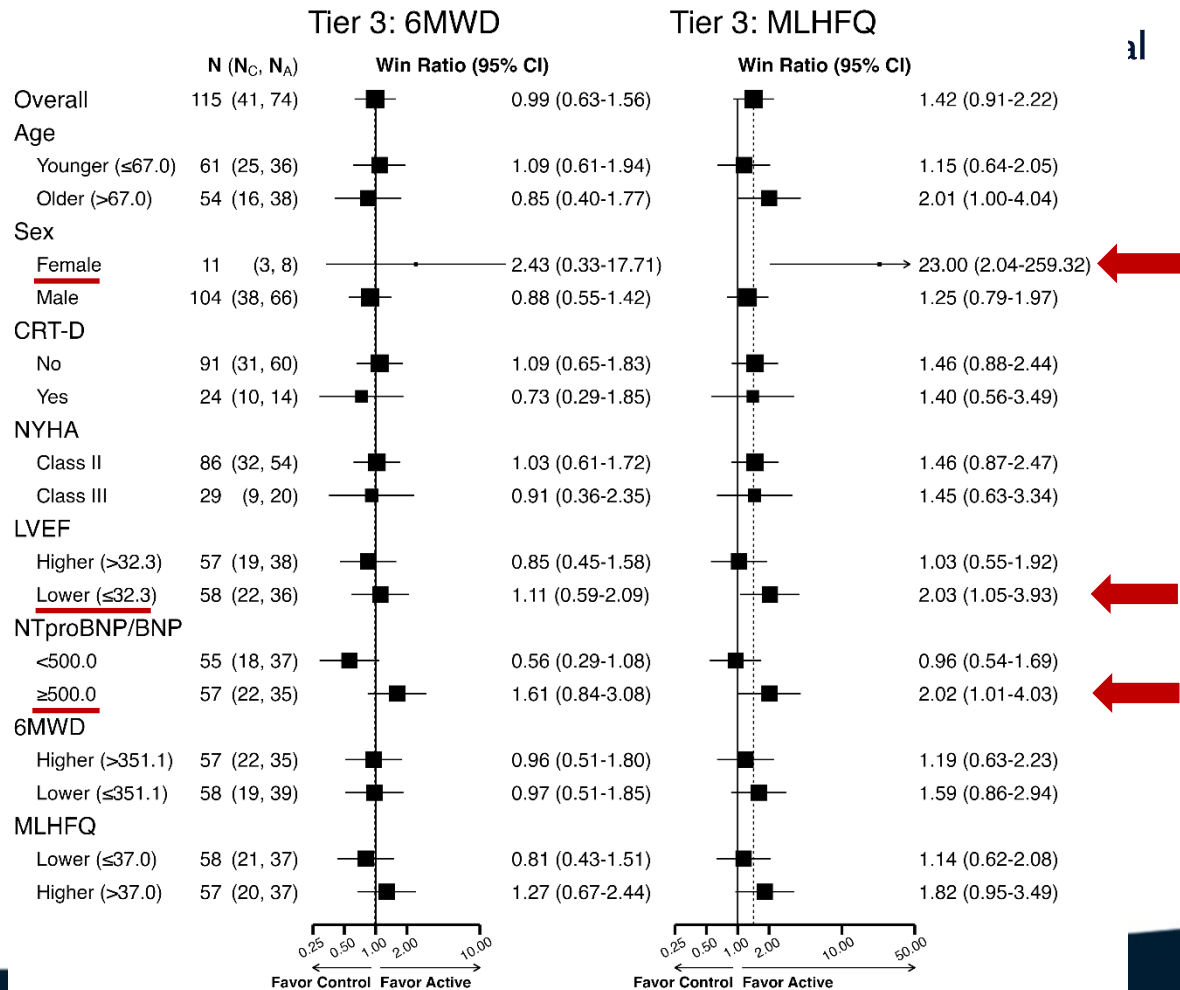
## LVEDVi



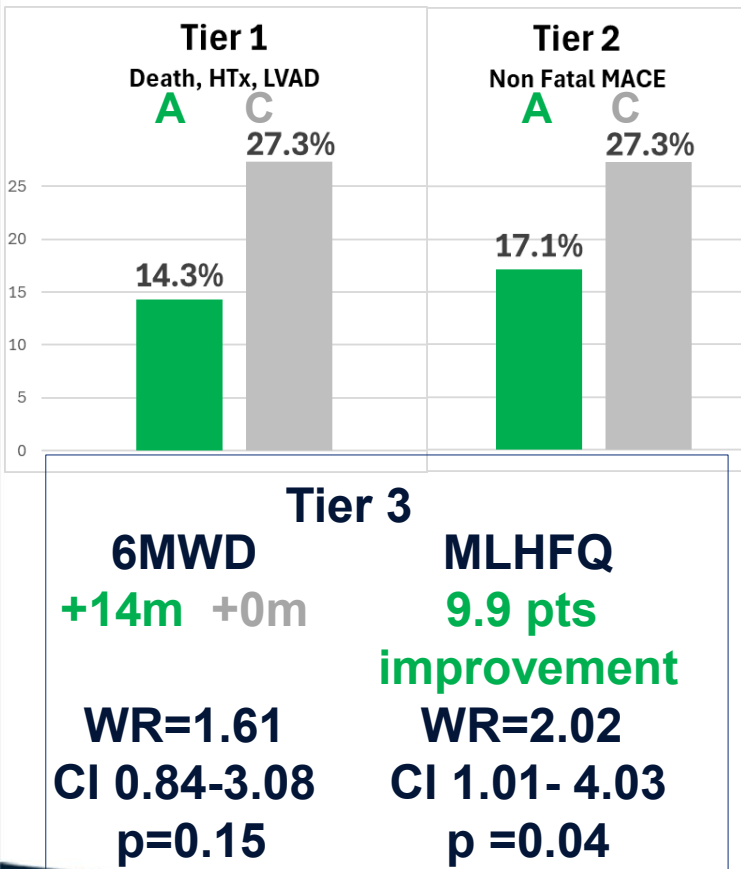
## LVESVi



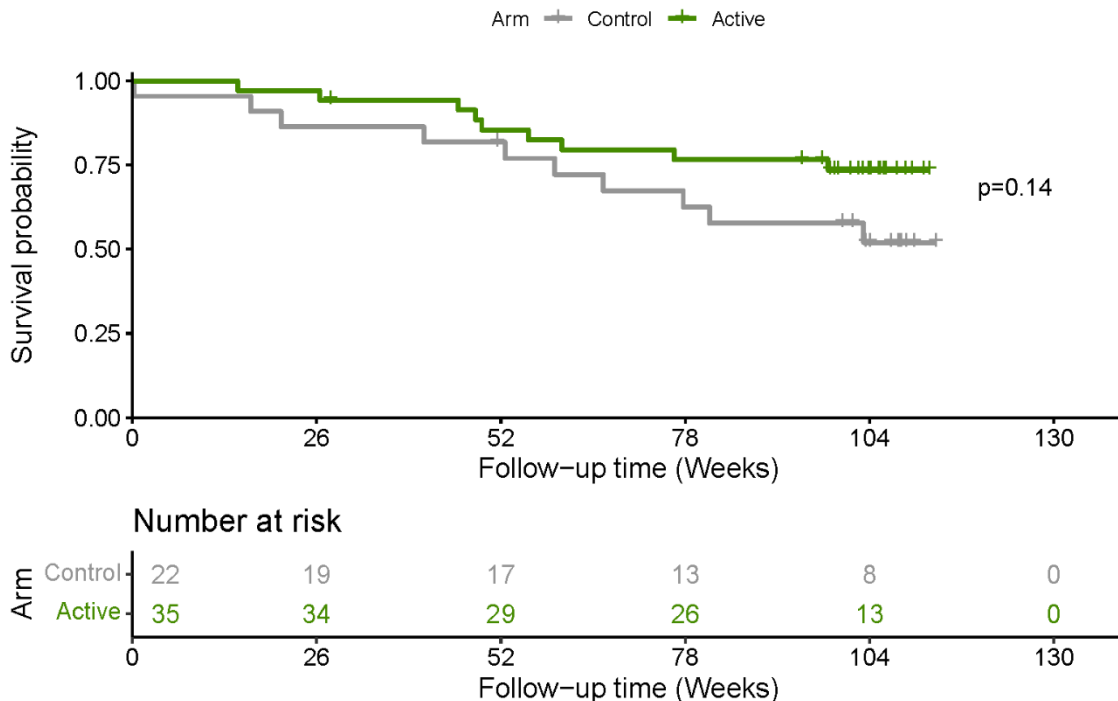
# Prespecified Subgroup Analysis



# Subgroup with NTproBNP/BNP >500 pg/ml

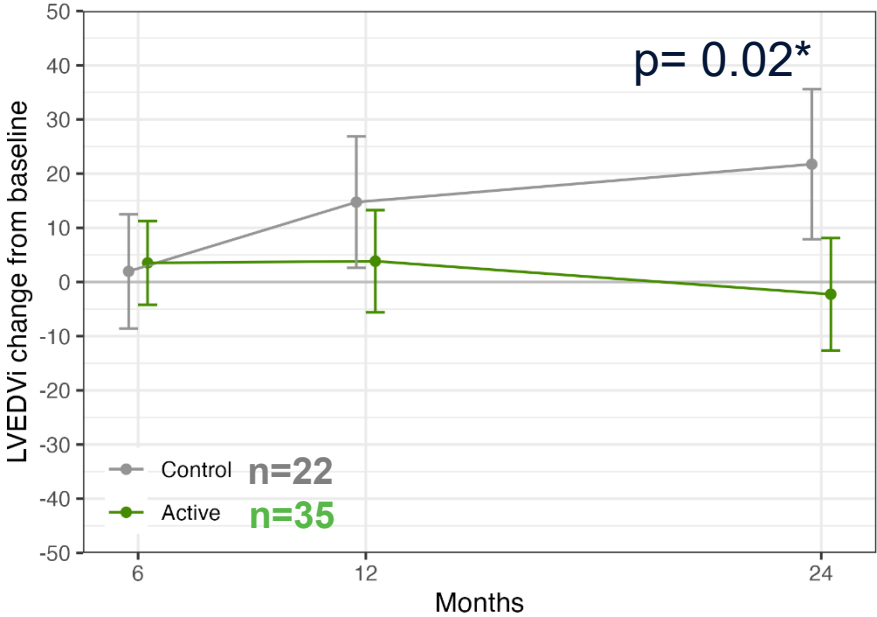


MACE Free Survival: NTproBNP/BNP >500 pg/ml Subgroup

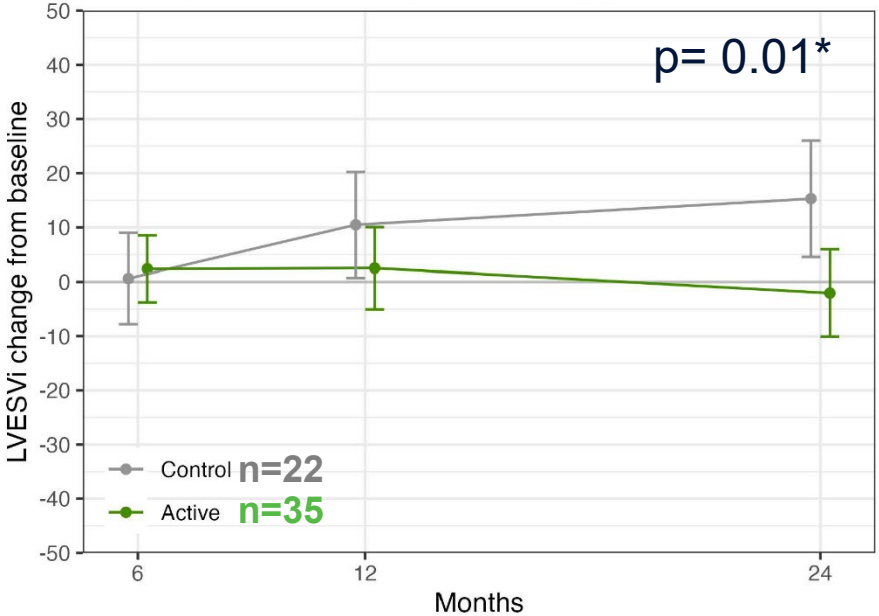


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## LVEDVi



## LVESVi



# Conclusions

- Autologous MNC (CardiAMP) therapy for chronic ischemic HFrEF was safe, had nominally less fatal & non-fatal MACE but the primary 3-tier composite outcome was neutral.
- Subgroup with baseline elevated NTproBNP/BNP had an improved 3-tier composite outcome with MLHFQ (Tier 3), and less LV dilatation ( $p < 0.05$ ).
- Additional LV/RV strain analysis, LV volume-pressure correlations, and mitral/tricuspid valve assessment are under review

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CardiAMP HF Trial

|   |  |  |
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|                              |   |
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| Data Safety Monitoring Board | George W. Vetrovec (Chair), Ori Ben-Yehuda,<br>Joseph M. Massaro, Rickey E. Carter                  |
| Data Reporting & Biostats    | Thomas D. Cook,<br>Statistical Data Analysis Center, Univ of WI-Madison                             |
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