Effect of Transendocardial Delivery of Autologous Bone Marrow Mononuclear Cells on Functional Capacity, Left Ventricular Function, and Perfusion in Chronic Ischemic Heart Failure: The FOCUS-CCTRN Trial

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Organizational Structure: NHLBI Cardiovascular Cell Therapy Research Network (CCTRN)

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Chair: R. Simari

Steering Committee

Data Coordinating Center
UTSPH
L. Moyé

Cell processing QC Lab

Biorepository, cMRI, Echo, MVO₂, SPECT Core Labs

Texas Heart Institute
J. Willerson

University of Florida*
C. Pepine

Cleveland Clinic
S. Ellis

Minneapolis Heart Institute
T. Henry

Vanderbilt University*
D. Zhao

*Skills Development Core
Cell Therapy in Ischemic Heart Failure

Cell Types

**Autologous Cells**
- Bone marrow mononuclear cells (ABMMNCs)
- Selected bone marrow cells ALDH\(^{br}\) cells

- No immunological Issues
- Variable cell quality and function due to host factors such as age and comorbidities
- Relatively mixed cell population

**Allogeneic Cells**
- Mesenchymal stem cells (MSCs)
- Mesenchymal precursor cells (MPCs)

- Possible immunological Reaction
- Uniform cell quality and function (single/ limited numbers of healthy donors)
- Relatively pure cell population
Double blinded, randomized, multicenter trial
Transendocardial delivery of a dose of 100 million Autologous Bone Marrow Mononuclear Cells
Patients with chronic ischemic heart disease and LV dysfunction with heart failure and/or angina
Uniform local cell processing: Sepax
Centralized Biorepository
CCTRN Biorepository

When a patient enters a clinical study:

- Blood drawn for PC and cytokine measurements
- Shipments Date Entered into Web Interface
- Web Interface Sends an e-mail to Coordinator and Technician to expect shipped samples
- Arrival Logged in Web Interface
- Samples are Prepared
- FACS
- Stem cells
- Cytokines
- Inflammation
- Effect
- Functional Measurements
- Real time status and tracking
- Report generation
- Blinded data analysis
- Easy data sharing
- Regulatory compliance
- Reduced work load

"Biorepository"
Center for Cardiovascular Repair
University of MN/Univ FL
Confidential and Privileged
Inclusion Criteria

- Patients > 18 y old with significant coronary artery disease.
- LVEF ≤ 45% (by echocardiogram) and limiting angina (class II-IV) and/or heart failure (NYHA class II-III).
- Patients should be on maximal medical therapy.
- Presence of reversibility by SPECT (adenosine stress) and/or viability as identified by NOGA.
- Coronary artery disease not well suited to any other revascularization procedure (percutaneous or surgical) in the target region of the left ventricle.
- Hemodynamic stability as defined by systolic BP ≥80mmHg without IV pressors or support devices.
- Women of childbearing age must be willing to use 2 forms of birth control for the duration of the study.
- A signed consent form approved by the Institutional Review Board.
Exclusion Criteria (1)

1. Atrial fibrillation, atrial flutter, and/or significant uncontrolled arrhythmias.
2. ICD shock within 30 days of baseline screening.
3. Unstable Angina.
4. High-risk ACS or a myocardial infarction in the month before evaluation.
5. LV thrombus, as documented by echocardiography or LV angiography.
6. Vascular anatomy that precludes cardiac catheterization.
7. Severe valvular disease or mechanical aortic valve that would preclude safe entry of the catheter into the left ventricle.
8. Platelet count <100K/mm³.
9. WBC <2K/mm³.
10. Revascularization within 30 days of study enrollment.
11. TIA or stroke within 60 days of study enrollment.
12. Bleeding diathesis defined as an INR ≥2.0 in the absence of warfarin therapy.
Exclusion Criteria (2)

13. History of non-basal cell carcinoma malignancy in the last 5 years.
14. Infectious-disease test result positive for HIV, hepatitis B, or hepatitis C.
15. Any previous transplant requiring immunosuppressive medication.
16. LV wall thickness of < 8 mm (by echocardiogram) at the target site for cell injection.
17. Inability to walk on a treadmill, except for class IV angina patients who will be evaluated separately.
18. Enrollment in an investigational device or drug study within the previous 30 days.
19. Hepatic dysfunction as defined by AST and ALT levels.
20. Chronic renal insufficiency.
21. Pregnancy as determined by a positive pregnancy test at baseline.
22. Any other contraindication to enrollment or follow-up.
Study Endpoints
6 Months

Primary Endpoints
• Change in maximum oxygen consumption (MVO2)
• Change in LVESV as assessed by echocardiography
• Change in ischemic (reversible) defect size as assessed by SPECT

Secondary Endpoints
• Wall motion by echocardiography
• Change in LVEDV as assessed by echocardiography
• Change in total and fixed defect size as assessed by SPECT
• Change in functional class (NYHA, CCS) and serum BNP levels

Exploratory Analyses
• LVEF by echocardiography
• Phenotypic and bone marrow function analyses with relevant endpoints
• Relationship of Age and relevant endpoints
FOCUS CCTRN Study Flow

Informed Consent → Meets Inclusion/Exclusion Criteria → Baseline Echo MVO₂ SPECT → 2:1 Randomization

2 BMC:1 Cell-Free

Baseline Echo MVO₂ SPECT

BMCs (n=61)

Cell Free Placebo (n=31)

BM Aspiration/Cell Processing*

Coronary angiography, LV Mapping and Transendocardial Injections

Screening period w/in 60 days (N=92)

6 Month Echo MVO₂ SPECT

Yearly Safety Follow-up up to 4 Years

*CP-Quality Control - Biorepository - Cell Function Core
Cell Processing

- Sepax System
  - Automated processing
  - Includes cell washing
  - Closed system
  - Sterile disposable set
  - Local processing

- BMC Ficoll
  - BM Sepax
  - Ficoll
  - Manual

- Processing
  - Includes cell washing
  - Closed system
  - Sterile disposable set
  - Local processing
Targeting of Stem Cell Injections

Anatomical (angiogram)

Perfusion (SPECT)

Viability/hibernation (EMM)
Transendocardial Injections

- Total of 15 injections
- Volume of 0.2 cc
- Targeted to ischemic myocardium
- Injection Criteria:
  - Unipolar voltage $\geq 6.9$mV
  - Loop Stability $\leq 4$
  - PVC upon needle insertion
Results: Patient Flow

Assessed for Eligibility  
N=273

Randomized  
N=92

Excluded after eligibility assessment (N=181)  
Did not meet eligibility criteria (N=116)  
- No reversible ischemia (n=116)  
- Other cardiac conditions (n=32)  
- EF>45% (n=29)  
- Refused to participate (N=27)  
- Other reasons (N=38)

Assigned to active intervention (N=61)  

Received active intervention (N=57)  

- Did not receive active intervention (N=4)  
  Reasons: Revascularizable lesion at intervention (n=3), Dissection (n=1)

  Included in active group analysis:  
  - MVO$_2$ (N=52)  
  - SPECT (N=50)  
  - Echo (N=54)

Assigned to placebo intervention (N=31)  

Received placebo intervention (N=29)  

- Did not receive placebo intervention (N=2)  
  Reasons: Revascularizable lesion at intervention (n=2)

  Included in placebo group analysis:  
  - MVO$_2$ (N=27)  
  - SPECT (N=26)  
  - Echo (N=28)
### Baseline Characteristics

**Patient Characteristics:**

<table>
<thead>
<tr>
<th></th>
<th>BMC N=61</th>
<th>Placebo N=31</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean (SD)</td>
<td>63.95(10.90)</td>
<td>62.32(8.25)</td>
<td>0.47</td>
</tr>
<tr>
<td>Female</td>
<td>8(13.11)</td>
<td>2(6.45)</td>
<td>0.49</td>
</tr>
<tr>
<td>White</td>
<td>58(95.08)</td>
<td>30(96.77)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3(4.92)</td>
<td>1(3.23)</td>
<td>1.00</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>30.10(6.14)</td>
<td>31.80(6.60)</td>
<td>0.23</td>
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</table>

**NYHA Classification:**

<table>
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<th>Placebo</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Class I</td>
<td>6(9.84)</td>
<td>2(6.45)</td>
<td></td>
</tr>
<tr>
<td>Class II</td>
<td>32(52.46)</td>
<td>14(45.16)</td>
<td></td>
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<tr>
<td>Class III</td>
<td>23(37.70)</td>
<td>15(48.39)</td>
<td>0.59</td>
</tr>
<tr>
<td>Class IV</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
<td></td>
</tr>
</tbody>
</table>

**CCS Classification: (BMC=54, Placebo=25)**

<table>
<thead>
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<th></th>
<th>BMC</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>13(24.07)</td>
<td>10(40.00)</td>
<td></td>
</tr>
<tr>
<td>Class II</td>
<td>24(44.44)</td>
<td>10(40.00)</td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>16(29.63)</td>
<td>5(20.00)</td>
<td></td>
</tr>
<tr>
<td>Class IV</td>
<td>1(1.85)</td>
<td>0(0.00)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

**BP in mmHg, mean (SD):**

<table>
<thead>
<tr>
<th></th>
<th>BMC</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>120.59(19.69)</td>
<td>122.13(15.78)</td>
<td>0.71</td>
</tr>
<tr>
<td>Diastolic</td>
<td>70.95(11.18)</td>
<td>74.77(10.35)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

**Qualifying LVEF (echo), mean (SD) (BMC=60)**

<table>
<thead>
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<th>BMC</th>
<th>Placebo</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>32.43(9.23)</td>
<td>30.19(7.76)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

**Aspiration to Injection Time (hours), mean (SD) (BMC=58, Placebo=29)**

<table>
<thead>
<tr>
<th></th>
<th>BMC</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8.95(1.18)</td>
<td>8.56(2.22)</td>
<td>0.28</td>
</tr>
</tbody>
</table>
## Baseline Characteristics

<table>
<thead>
<tr>
<th>N (%) unless otherwise specified</th>
<th>BMC N=61</th>
<th>Placebo N=31</th>
<th>P-value</th>
</tr>
</thead>
</table>

### Medical History:

- **Diabetes**:
  - BMC: 21 (34.43%)
  - Placebo: 16 (51.61%)
  - P-value: 0.12
- **Hypertension**: 49 (80.33%) vs. 24 (77.42%), P-value: 0.79
- **History of MI (BMC=57)**: 53 (92.98%) vs. 29 (93.55%), P-value: 1.00
- **Prior Revascularization**: 51 (83.61%) vs. 26 (83.87%), P-value: 1.00
- **Prior CABG**: 47 (77.05%) vs. 25 (80.65%), P-value: 0.79

### Number CABG Operations:
- 1: 33 (70.21%) vs. 21 (84.00%), P-value: 0.39
- 2: 13 (27.66%) vs. 4 (16.00)
- 3: 1 (2.13%) vs. 0 (0.00)

### Medications at Time of Randomization:

- **ACEi/ARB**: 37 (60.66%) vs. 22 (70.97%), P-value: 0.37
- **Diuretics**: 41 (67.21%) vs. 23 (74.19%), P-value: 0.63
- **Statins**: 44 (72.13%) vs. 21 (67.74%), P-value: 0.81
- **Ranolazine**: 21 (34.43%) vs. 3 (9.68%), P-value: 0.01

### Laboratory Evaluations:

- **GFR in ml/min/1.73m^2, median (range) (BMC=58, Placebo=29)**: 71.2 (29.6-155.4) vs. 70.1 (30.5-107.3), P-value: 0.96
- **BNP in pg/ml, median (range) (BMC=46, Placebo=23)**: 132.0 (16.0-545.0) vs. 105.0 (26.0-140.0), P-value: 0.68
- **ProBNP in pg/ml, median (range) (BMC=15, Placebo=8)**: 833.0 (50.0-9793.0) vs. 828.0 (103.0-5778.0), P-value: 0.95
# Cell Characteristics and Function

<table>
<thead>
<tr>
<th>N (%), unless otherwise specified</th>
<th>BMC N=61</th>
<th>Placebo N=31</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Nucleated Cells/Product (x10^6), mean (SD)</td>
<td>99.03(5.58)</td>
<td>100.03(0.18)</td>
<td>0.322</td>
</tr>
<tr>
<td>%Viability/product by Trypan blue exclusion, mean (SD)</td>
<td>98.56(1.11)</td>
<td>98.70(0.89)</td>
<td>0.523</td>
</tr>
<tr>
<td>%CD34 cells/product, mean (SD)* (BMC=57, Placebo=30)</td>
<td>2.71(1.19)</td>
<td>2.60(0.93)</td>
<td>0.673</td>
</tr>
<tr>
<td>%CD133 cells/product, mean (SD)* (BMC=57, Placebo=30)</td>
<td>1.21(0.62)</td>
<td>1.14(0.48)</td>
<td>0.588</td>
</tr>
<tr>
<td>Colony Forming Units-Hill/product, mean (SD)* (BMC=55, Placebo=30)</td>
<td>109.41(206.29)</td>
<td>151.33(244.20)</td>
<td>0.404</td>
</tr>
<tr>
<td>Endothelial Colony Forming Cells/product, mean (SD)* (BMC=49, Placebo=28)</td>
<td>131.84(164.62)</td>
<td>156.44(240.12)</td>
<td>0.596</td>
</tr>
</tbody>
</table>

* Four patients either declined participation or had insufficient product for the Biorepository.
Therapy Effect on change in NYHA Class over time

NYHA in Control Group

NYHA in Treated Group

Baseline

6 months

Baseline

6 months
Therapy Effect on change in CCS Class over time

CCS in Control Group

CCS in Treated Group

Baseline
6 months

Baseline
6 months
Primary Endpoint: LVESV

No difference in the change in indexed LVESV by Echo between BMC and Placebo groups from baseline to 6 months.
Primary Endpoint: MVO$_2$

No difference in the change in MVO$_2$ between BMC and Placebo groups from baseline to 6 months.
Primary Endpoint: Reversible Defect

No difference in the change in reversible defect by SPECT between BMC and Placebo groups from baseline to 6 months.
## Clinical Outcomes within 6-month Endpoint Window

<table>
<thead>
<tr>
<th>Event</th>
<th>BMC (n=61)</th>
<th>Placebo (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>New MI</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Rehospitalization for PCI</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rehospitalization for ACS</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Rehospitalization for CHF</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>New AICD implantation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Heart Transplant</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>LVAD</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total Outcomes</strong></td>
<td><strong>7</strong></td>
<td><strong>7</strong></td>
</tr>
<tr>
<td><strong>Patients</strong></td>
<td><strong>4 (7%)</strong></td>
<td><strong>4 (13%)</strong></td>
</tr>
<tr>
<td><strong>Crude Incidence Rate</strong></td>
<td><strong>0.066</strong></td>
<td><strong>0.129</strong></td>
</tr>
</tbody>
</table>
Exploratory Analysis: LVEF

Significant difference in the change in LVEF between BMC and Placebo groups from baseline to 6 months (1.4 vs -1.3, p=0.030)
Only 2 patients had CFU in the “normal” range.
Focus HF

Bone Marrow Sample Analysis

**Age and CFU**

- **P = .04**

**Age and MVO₂**

- **p = 0.038**

*Am Heart J 2011;161:1078-1087*
Pre-Specified Analysis

Relationship of Age with Endpoints

Age (median 62y)

- Age < 62
- Age ≥ 62

Primary and Exploratory Endpoints

- LVESV
- MVO$_2$
- SPECT
- LVEF
## Delta LVEF and Age

### LVEF- Treatment: Age < 62

<table>
<thead>
<tr>
<th></th>
<th>BMC</th>
<th>Mean</th>
<th>SD</th>
<th>Placebo</th>
<th>Mean</th>
<th>SD</th>
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</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td>N 27</td>
<td>35.1</td>
<td>9.0</td>
<td>N 15</td>
<td>32.0</td>
<td>8.0</td>
</tr>
<tr>
<td><strong>Followup</strong></td>
<td>N 27</td>
<td>38.2</td>
<td>11.8</td>
<td>N 15</td>
<td>30.4</td>
<td>7.8</td>
</tr>
<tr>
<td><strong>Change</strong></td>
<td>N 27</td>
<td>3.1</td>
<td>5.2</td>
<td>N 15</td>
<td>-1.6</td>
<td>6.6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Change</th>
<th>Test</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.7</td>
<td>2.55</td>
<td>0.015 0.97 8.37</td>
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</table>

### LVEF- Treatment: Age ≥ 62

<table>
<thead>
<tr>
<th></th>
<th>BMC</th>
<th>Mean</th>
<th>SD</th>
<th>Placebo</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td>N 27</td>
<td>34.2</td>
<td>8.8</td>
<td>N 13</td>
<td>32.5</td>
<td>9.6</td>
</tr>
<tr>
<td><strong>Followup</strong></td>
<td>N 27</td>
<td>33.9</td>
<td>8.9</td>
<td>N 13</td>
<td>31.6</td>
<td>10.5</td>
</tr>
<tr>
<td><strong>Change</strong></td>
<td>N 27</td>
<td>-0.3</td>
<td>4.7</td>
<td>N 13</td>
<td>-0.9</td>
<td>3.0</td>
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</table>

<table>
<thead>
<tr>
<th>Change</th>
<th>Test</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6</td>
<td>0.43</td>
<td>0.668 -2.28 3.52</td>
</tr>
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</table>
Cell Function Heterogeneity

Age and Comorbidities

Low ECFC capacity

High ECFC capacity
Pre-Specified Bone Marrow Analysis

Relationship with Endpoints

Preliminary Bone Marrow Functional and Phenotypic Analyses

- CD 34+
- CD 133+
- CFU Hill
- ECFC

Primary and Exploratory Endpoints

- LVESV
- MVO₂
- SPECT
- LVEF
Correlation between $\Delta$LVEF and $\%$CD34

Unadjusted

Adjusted for Age and Therapy

$R^2 = 8\%$
$P = 0.012$

$R^2 = 16\%$
$P = 0.043$
Pre-Specified Bone Marrow Analysis

Relationship with Endpoints

Preliminary Bone Marrow Functional and Phenotypic Analyses

- CD 34+
- CD 133+
- CFU Hill
- ECFC

Primary and Exploratory Endpoints

- LVESV
- MVO₂
- SPECT
- LVEF
Correlation between $\Delta$LVEF and $\%$CD133

Unadjusted

Adjusted for Age and Therapy

$R^2 = 8\%$
$P = 0.010$

$R^2 = 16\%$
$P = 0.041$
Pre-Specified Bone Marrow Analysis

Relationship with Endpoints

Preliminary Bone Marrow Functional and Phenotypic Analyses

- CD 34+
- CD 133+
- CFU Hill
- ECFC

Primary and Exploratory Endpoints

- LVESV
- MVO$_2$
- SPECT
- LVEF
Pre-Specified Bone Marrow Analysis

*Relationship with Endpoints*

Preliminary Bone Marrow Functional and Phenotypic Analyses

- CD 34+
- CD 133+
- CFU Hill
- ECFC

Primary and Exploratory Endpoints

- LVESV
- MVO₂
- SPECT
- LVEF
Exploratory Endpoint Analysis
ECFCs > 80 (median)

<table>
<thead>
<tr>
<th></th>
<th>BMC</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean</td>
<td>SD</td>
<td>N</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Baseline</td>
<td>20</td>
<td>14.6</td>
<td>3.3</td>
<td>11</td>
<td>15.2</td>
<td>3.1</td>
</tr>
<tr>
<td>Followup</td>
<td>20</td>
<td>15.3</td>
<td>4.8</td>
<td>11</td>
<td>13.4</td>
<td>3.7</td>
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<tr>
<td>Change</td>
<td>20</td>
<td>0.7</td>
<td>2.9</td>
<td>11</td>
<td>-1.8</td>
<td>3.4</td>
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</table>

<table>
<thead>
<tr>
<th>Change</th>
<th>SD</th>
<th>Test Statistic</th>
<th>95% Confidence Interval</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>P-value</td>
</tr>
<tr>
<td>2.5</td>
<td>3.1</td>
<td>2.18</td>
<td>0.037</td>
</tr>
</tbody>
</table>
Conclusions

• In patients with chronic ischemic heart disease and LV dysfunction with heart failure and/or angina there were no significant differences in a priori selected primary endpoints of LVESV, Reversibility by SPECT and MVO$_2$ between subjects treated with 100 million autologous bone marrow mononuclear cells and placebo at 6 month follow-up.

• In this phase II study, exploratory analyses revealed that LVEF improved in the BMC group compared with the placebo group.

• LVEF improvement was significant in patients younger than the median study population age and correlated with the percentage of CD34$^+$ and CD133$^+$ cells in BM samples.
Conclusions cont’d

- A pre-specified analysis of cell function (ECFC) showed significant improvement in MVO2 in those study patients with higher than median ECFC values.

- Evaluating inherent variability in the cell product may provide mechanistic insights and help select patients that are likely to benefit from autologous cell therapy.

- Additional analyses of cell function will be forthcoming from the CCTRN biorepository and should help guide the design of future clinical trials in patients with ischemic heart disease and LV dysfunction.
Acknowledgements

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Effect of Transendocardial Delivery of Autologous Bone Marrow Mononuclear Cells on Functional Capacity, Left Ventricular Function, and Perfusion in Chronic Heart Failure
The FOCUS-CCTRN Trial

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Contact Previous studies using autologous bone marrow mononuclear cells (BMCs) in patients with ischemic cardiomyopathy have demonstrated safety and suggested efficacy. Objective To determine if administration of BMCs through transendocardial injections improves myocardial perfusion, reduces left ventricular end-systolic volume (LVESV), or enhances maximal oxygen consumption in patients with coronary artery disease or LV dyssynchrony, and limiting heart failure or angina. Design, Setting, and Patients A phase 2 randomized double-blind, placebo-controlled trial of symptomatic patients (New York Heart Association classification II-III or Canadian Cardiovascular Society classification II-IV) with a left ventricular ejection fraction of 45% or less, a perfusion defect by single photon emission tomography (SPECT), and coronary artery disease not amenable to revascularization who were receiving maximal medical therapy at 5 National Heart, Lung, and Blood Institute-sponsored Cardiac Cell Therapy Research Network (CCTRN) sites between September 29, 2009, and April 18, 2011. Intervention Bone marrow aspiration (isolation of BMCs using a standardized automated system performed locally) and transendocardial injection of 100 million BMCs or placebo (ratio of 2 for BMC group to 1 for placebo group).

Main Outcome Measures Co-primary end points assessed at 6 months: changes in LVESV assessed by echocardiography, maximal oxygen consumption, and reversibility on SPECT. Phenotypic and functional analyses of the cell product were performed by the CCTRN core repository core laboratory.

Results Of 153 patients who provided consent, a total of 92 (82 men; average age: 63 years) were randomized (n = 61 in BMC group and n = 31 in placebo group). Changes in LVESV (−0.9 mL/meter² [95% CI, −1.2 to 0.1]; P = .095), maximal oxygen consumption (1.09 mL/kg/min [95% CI, 0.73 to 1.46]; P = .35), and reversible defect (1.29% [95% CI, 0.10 to 1.13]; P = .034) were statistically significant. There were no differences found in any of the secondary outcomes, including percent myocardial defect, total defect size, fixed defect size, regional wall motion, and reversibility on SPECT.

Conclusion Among patients with chronic ischemic heart failure, transendocardial injection of autologous BMCs compared with placebo did not improve LVESV, maximal oxygen consumption, or reversibility on SPECT.

Trial Registration clinicaltrials.gov Identifier: NCT00844055

CELL THERAPY HAS EMERGED AS an innovative approach for treating patients with advanced ischemic heart disease, including those with refractory angina and heart failure. Early clinical studies have been performed primarily using autologous stem/progenitor cells. In patients with ischemic heart disease,