AWARD NUMBER:	W81XWH-20-1-0272
TITLE:	A Phase 2B Multicenter Study of the Comparative Efficacy and Safety of Transendocardial Injection of MSC in Patients with Nonischemic Dilated Cardiomyopathy
PRINCIPAL INVESTIGATOR:	Dr. Joshua Hare, MD.
CONTRACTING ORGANIZATION:	University of Miami, 1320 S Dixie Hwy., Ste. 650, Coral Gables, FL 33146-2919
REPORT DATE:	MAY 2024
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PREPARED FOR:	U.S. Army Medical Research and Development Command Fort Detrick, Maryland 21702-5012
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MAY 2024	Year 3 Annual Technical Report	1MAY2023 - 30APR2024

4. TITLE AND SUBTITLE

A Phase 2B Multicenter Study of the Comparative Efficacy and Safety of Transendocardial Injection of MSC in Patients with Nonischemic Dilated Cardiomyopathy

5a. CONTRACT NUMBER
W81XWH-20-1-0272

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S) **Dr. Joshua Hare, MD**

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

University of Miami
1320 S Dixie
Hwy., Ste. 650
Coral Gables, FL 33146-2919

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S NUMBER(S) – N/A

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This proposal addresses the FY19 PRMRP Topic Area of Cardiomyopathy. Non-ischemic dilated cardiomyopathy (NIDCM) is one of the more common causes of heart failure in young adults, a leading cause of disability and death, and accounts for approximately 50% of heart transplants performed. As such this disorder is a lead candidate for cell-based therapy. Patients with NIDCM have an enlarged, structurally damaged heart muscle with reduced function. Our group and others have shown that cell-based therapy using mesenchymal stem cells (MSCs) holds great promise as a new approach to produce durable and sustainable improvements in heart function and structure in patients with heart failure due to NIDCM. If these effects can be clinically established and optimized, there is enormous potential for improving clinical outcomes for the many patients suffering from NIDCM. Our group has extensive experience with catheter delivery of bone marrow-derived MSCs in patients with heart failure due to heart attack as well as NIDCM. There is substantial scientific and public interest for cardiac regenerative cell therapy strategies, based on pre-clinical, translational, and early Phase I/II clinical studies. In the POSEIDON-DCM clinical trial, we identified a meaningful increase in cardiac function in a cohort of patients with NIDCM who received MSCs. One-third of the patients transitioned from heart failure with reduced cardiac function to heart failure with recovered function, which is associated with reductions in disease-related symptoms and complications as well as death. Since NIDCM is associated with genetic mutations in a significant proportion of patients, we hypothesized that NIDCM genotype influences patient responsiveness to MSC therapy. Accordingly, we conducted a sub study in the POSEIDON-DCM patients by performing a detailed genotyping using a comprehensive cardiomyopathy gene panel. Our novel preliminary findings show a benefit of MSC therapy, namely improvement in cardiac function, quality of life, major adverse cardiac events, and survival, in patients that lack a known pathogenic mutation, suggesting that patients devoid of pathogenic mutations represent a 'super-responder' group compared to those that have a pathogenic mutation. This Phase IIB clinical trial proposal will test whether MSC therapy is effective in improving cardiac function, as compared to placebo, in patients with NIDCM. Patients will be genotyped and the efficacy of MSC therapy will be compared to placebo in patients that lack a known disease-causing mutation (genotype A), patients with mutations of unknown significance (genotype B), and in those that have a known disease-causing mutation in NIDCM associated genes (genotype C). We expect that patients without a disease-causing mutation will respond better to MSC therapy than those with known mutations or mutations of unknown significance. The primary outcome will be assessed using cardiac magnetic resonance imaging to measure cardiac function at 12 months. This study is clinically important because it will help physicians determine which patients are more likely to respond to specific therapies and will help us develop more individualized therapies for patients with heart failure due to NIDCM. The proposed trial is currently approved by the FDA under IND BB-14419.

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
					USAMRMC
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER *(include area code)*
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TABLE OF CONTENTS

1. INTRODUCTION: *Narrative that briefly (one paragraph) describes the subject, purpose, and scope of the research.*

Non-ischemic dilated cardiomyopathy (NIDCM) represents a significant public health challenge as a prevalent cause of heart failure among young adults, significantly contributing to disability, mortality, and the need for heart transplants. In this context, our research aims to evaluate the efficacy of mesenchymal stem cells (MSCs) therapy, a promising cell-based treatment that has demonstrated potential in improving heart function and structure in previous clinical settings, including our POSEIDON-DCM trial. This trial notably indicated that patients, particularly those without pathogenic genetic mutations, showed improved cardiac function and quality of life after receiving MSC therapy. The current Phase IIB clinical trial seeks to extend these findings by systematically assessing the impact of genetic background on the efficacy of MSC therapy in NIDCM patients. We will compare therapeutic outcomes across three patient groups categorized by genotype: those without known disease-causing mutations, those with mutations of unknown significance, and those with confirmed pathogenic mutations. By correlating genetic profiles with treatment response, this study aims to tailor and enhance therapeutic strategies, contributing to the personalized treatment of heart failure. This approach not only promises to refine clinical outcomes but also aligns with the growing demand for individualized medicine in cardiac care.

2. KEYWORDS: *Provide a brief list of keywords (limit to 20 words).*

Mesenchymal Stem Cell
Heart Failure
Non-ischemic dilated cardiomyopathy (NIDCM)
Genotype
Transendocardial injection
Cellular Therapy
Cardiovascular Disease
Current Good Manufacturing Practices
Allogeneic

3. ACCOMPLISHMENTS: *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.*

- **What were the major goals of the project?**
  - *List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project identify these dates and show actual completion dates or the percentage of completion.*

Accomplished

Tasks	Timeline (Months)				
Major Task1 Subtask 1: Regulatory Documents		% of Completion	Initiated/ Work in Progress	Completed	Note
Finalize consent form & human subjects' protocol	1-3	100%		✓	Submitted to single IRB (BRANY IRB) and Masterfile approval received on 4/27/20.
Site submission to sIRB for initial approval	1-6	100%		✓	Final site approval on 10/26/2020
Submit Initial Protocol to HRPO and ongoing review	3-6 Initial Ongoing	100%		✓	Initial approval was obtained on 4/7/2021. Ongoing: 6/24/2022; 6/9/2023.
Completion of initial regulatory approvals and	3-6 Initial Ongoing	100%		✓	DSMB membership has been secured. Charter document has been finalized. Meeting frequency is semi-annual.

Tasks	Timeline (Months)				
ongoing (FDA/DSMB)					Meetings this reporting period; 06/17/21, Ongoing: 12/16/21, 12/15/2022, 06/23/2022, 06/15/2023 and12/7/2023.
Development and approval of CRFs	1-6	100%		✓	full set of CRFs has been developed and DCC programming has completed the electronic data capture system
Finalize MOP and eCRF users guide	1-12	100%		✓	MOP is completed and materials are posted in secured section of trial website. eCRF users guide of electronic database capture system is also complete and available on website.
Submit amendments, adverse events and protocol deviations as needed	As Needed			✓	Amendments to the protocol were approved by BRANY IRB on 5/13/2021, 1/3/2022, 10/7/2022 and 11/30/2023 . AEs and deviations will be reported as needed. Corresponding documentation is forwarded to HRPO for their records.
Continuing review (CR) submission by Sites to sIRB	Annually			✓	CRs are occurring at regular intervals. All sites are up to date with submissions and approvals
Milestone Achieved: Local IRB approval at all sites	3	**100%**		✓	Final site approval on 10/26/2020
Milestone Achieved: HRPO approval for all protocols	3-6	**100%**		✓	Approval on 4/7/2021
Major Task 1 Subtask 2: Site Management		% of Completion	Initiated/ Work in Progress	Completed	Note
Contract with identified sites and core labs	1-6	100%		✓	All contracts are finalized.
Comprehensive lab plan/product SOP development	1-6	100%		✓	All lab SOPs and manual are completed. Final training for sites is complete.
Finalize data & safety monitoring and data management plan	1-6	100%		✓	DSMB charter is finalized. Medical Monitoring Plan is finalized.
Finalize organization/communication and site performance plans	1-6	100%		✓	Site recruitment plans received and reviewed 01/25/2021 (updated 2/11/2022, 5/8/2023 and 02/05/2024). Study team meetings held 2x per month. Research Coordinator meetings held monthly.
Finalize clinical trial management plan	1-6	100%		✓	• Manual of Operations (complete) • Clinical Research Monitoring Plan (complete) • Medical Monitoring Plan (complete) • Data and Safety Monitoring Plan. (complete) • Stat Analysis Plan (complete)
Finalize data completeness & quality monitoring plan	1-6	100%		✓	Clinical Research Monitoring Plan is finalized. Monthly email alerts to sites for incomplete missing data.

Tasks	Timeline (Months)				
Deploy secure website for sharing study materials	1-6	100%		✓	Web site is deployed. Training materials are posted.
Complete and deploy EDC-system set-up	6-12	100%		✓	Test and production databases complete. EDC training completed for coordinators and cell processors. Training webinar posted for refresher along with EDC user's guide.
Implement site training plan (including MRI, FMD, Cell processing)	1-6	100%		✓	Training is complete. SOPs, worksheets, and videos posted to the website.
Activate initial site(s) (at least 2 sites out of 4)	1-12	100%		✓	All sites Activated: University of Miami – 05/07/2021 Stanford University – 05/19/2021 Texas Heart Institute – 07/21/2021 University of Louisville –09/10/2021
Design information to ClinicalTrials.gov	6-7	100%		✓	NCT04476901 Registry updated every 6mos or as needed (e.g. protocol amendments, contact changes)
Major Task 2 Subtask 1: Participant Recruitment –		% of Completion	Initiated/ Work in Progress	Completed	Note
Coordinate with Sites for flow chart for all study steps, web data collection and database requirements	4-8	100%		✓	Coordinator training was completed 11/18/2020 with training sessions completed for MOP, safety/event reporting, and electronic database. Frequently asked questions mechanism deployed on website. Monthly coordinator meetings initiated.
Deploy randomization system	6-12	100%		✓	System complete.
Deploy specimen tracking system	6-12	100%		✓	System complete.
Finalize assessment measurements	1-3	100%		✓	All clinical assessments (including core lab evaluations) finalized
Milestone Achieved: Study begins	6-12	**100%**		✓	University of Miami – 05/07/2021 Stanford University – 05/19/2021 Texas Heart Institute – 07/21/2021 University of Louisville –09/10/2021
Major Task 2 Subtask 2: Genetic Screening and Randomization –		% of Completion	Initiated/ Work in Progress	Completed	Note
Genetic Screen	3-30	100%		✓	Testing and reporting processes established, webinar on collection held 1/26/2021. Sample collection kits provided to sites. Genotype classification SOP established. Testing has begun.
Randomization	3-30	100%		✓	EDC access for entry of genetic info complete. Randomization scheme incorporates genotype. Will be deployed once enrollment starts
Milestone Achieved: Ongoing	3-30	**23%**	✓		Randomization has initiated (49 of 136 randomized)

Tasks	Timeline (Months)				
randomization during enrollment					
Major Task 3 Subtask 1: Allogeneic MSC manufacture		% of Completion	Initiated/ Work in Progress	Completed	Note
Donor recruitment	3-12	100%	✓		The allogeneic MSCs were obtained from 5 different donors.
Cell manufacture and quality assessment	3-12	80.5%		✓	A total of 87 product units have been produced; 53 units have been utilized, issued to other sites, or otherwise allocated. Another 34 are available in stock.
Product shipment	6-12	49%	✓		27 units have been shipped to other sites. 26 units have been used at University of Miami Total 53 units
Milestone achieved: Reach production requirement for the entire trial	3-12	80.5%	✓		A total of 87 product units have been produced. A total of 88 units plus 20 extras are needed to complete the trial (total 108 units).
Major Task 3 Subtask 2: Therapy Implementation		% of Completion	Initiated/ Work in Progress	Completed	Note
Follow-up visit and assessment at 1 week and at months 1, 3, 6, and 12	3-42	18.4%	✓		Twenty-five of the projected 136 participants have completed all follow-ups.
Milestone Achieved: Perform blinded therapy and follow-up visits	12-48	36% Randomized 34.5% Received Blinded Therapy. 18.38% Completed Follow-up. 0.74% Expired. 3.67 % Withdrawn. 14.7 % in follow-up	✓		Projected participants = 136 Randomized participants = 49 Received blinded therapy = 47 Completed follow ups = 25 Expired = 1 Withdrew = 5 Currently in follow-up = 20
Major Task 3 Subtask 3: Evaluation		% of Completion	Initiated/ Work in Progress	Completed	Note
Assessment of site protocol performance	Ongoing		✓		Ongoing progress monitoring toward meeting recruitment goals.

- **What was accomplished under these goals?**

  For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Major Activities	Specific Objectives	Significant Results or Key Outcomes
Core Lab quality control monitoring	Refinement of procedures; Staff proficiency; Certification of any newly added technicians; Quality control review	Data transmission progressing: Quality Control (QC) feedback provided by Core Labs, ensuring ongoing

		improvement and adherence to standards.
Cell Lab quality control monitoring	Refinement of procedures; Staff proficiency; Certification of any newly added technicians; Quality control review	Shipments and QC activities progressing smoothly, indicating efficient operations and maintenance of quality standards.
Completion of cell manufacture and quality assessment	Manufacture cells for full trial	Manufacturing progressing with only a few units remaining; demonstrates effective production and quality control.
Enrollment	Bi-weekly discussion of screening/enrollment activity; Monthly discussion of enrollment targets and eligibility criteria.	Enrollment advancing with timely submissions of data and images; Genetic screening results returned within 1-3 weeks; Adverse event reporting ongoing, ensuring participant safety and compliance.
Ongoing monitoring of recruitment	Refinement of recruitment action plans; Initiation of a variety of recruitment efforts; Bi-weekly investigator meetings; Monthly coordinator meetings	Regular communication among investigators and teams; Open exchange between sites and project management; Initiation of new recruitment methods to bolster trial numbers, enhancing trial execution and participant diversity.
Ongoing monitoring of data completeness/quality	Continuance of secured remote upload system for clinical research monitoring; Generation of monthly email alerts related to missing/incomplete data; Semi-annual schedule of core lab data upload system with quality control review; Generation of cumulative site monitoring reports to IND Sponsor	Database submissions current; Data quality monitoring up to date; Core lab transmissions and monitoring reports are current, ensuring data integrity and prompt addressing of any issues.
Ongoing evaluation of adverse events	Continuance of secured remote upload system for redacted medical record review of adverse events; Ongoing medical monitoring and MedDRA coding of events; Semi-annual review by Data Safety Monitoring Board (DSMB); Development of reports for regulatory oversight groups	A comprehensive, data driven program that provides ongoing capture and analyses of safety data and issues timely notifications, event specific reports, and scheduled cumulative trial reports of safety issues

- **What opportunities for training and professional development has the project provided?**
    - *If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."*
    - *Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.*

Nothing to Report

- **How were the results disseminated to communities of interest?**
    - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
    - *Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.*

Nothing to Report

- **What do you plan to do during the next reporting period to accomplish the goals?**
    - *If this is the final report, state "Nothing to Report."*
    - *Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives*

Tasks
Following tasks will be done during next reporting period. 1. **Update** www.clinicaltrials.gov**:** The clinical trial registry will be updated to reflect any changes made to the trial protocol or alterations in contact personnel. 2. **Maintain regular meeting schedule with DSMB (Data Safety Monitoring Board):** Semi-annual meetings will be held in June and December with the DSMB to review safety data and discuss any concerns related to trial progress or participant safety. 3. **Maintain regular bi-weekly meeting schedule with site Investigators:** Every two weeks, meetings will be conducted with the site investigators to discuss trial progress, address any issues, and ensure that all sites are aligned with the trial's standards and objectives. This routine helps maintain consistency and promptly address challenges. 4. **Maintain regular monthly meeting schedule with site coordinators:** Monthly meetings will be held with site coordinators to oversee the operational aspects of the trial at each site, including patient management, data collection, and adherence to protocol. 5. **Continue with therapy implementation and follow-up per enrollment schedule:** The administration of the therapy and subsequent follow-ups will continue according to the predefined enrollment schedule. This involves monitoring the treatment's effectiveness and participant adherence to the treatment regimen. 6. **Continue to track site recruitment per recruitment action plans and troubleshoot as needed:**

Ongoing tracking of participant recruitment will be conducted in line with the recruitment action plans for each site. Issues in recruitment rates or processes will be identified and addressed through strategic troubleshooting and adjustments to the recruitment strategies.

7. **Review protocol compliance to inform necessary protocol amendments:**
   Regular reviews of protocol compliance will be conducted to determine if the protocol is being followed correctly or if amendments are needed to enhance clarity, improve participant safety, or address operational challenges.
8. **Assess, track, and report any incoming adverse events per protocol:**
   A continuous assessment and tracking system will be in place to log any adverse events reported during the trial. These events will be analyzed and reported in accordance with the trial's protocol to ensure that any potential risks are managed promptly and effectively.

4. IMPACT: *Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

- **What was the impact on the development of the principal discipline(s) of the project?**
  - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
  - *Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).*

Nothing to Report

- **What was the impact on other disciplines?**
  - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
  - *Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.*

Nothing to Report

- **What was the impact on technology transfer?**
  - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
  - *Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:*
    - *transfer of results to entities in government or industry;*
    - *instances where the research has led to the initiation of a start-up company; or*
    - *adoption of new practices.*

Nothing to Report

- **What was the impact on society beyond science and technology?**
  - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
  - *Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:*
    - *improving public knowledge, attitudes, skills, and abilities;*

- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report

5. **CHANGES/PROBLEMS:** *The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

- **Changes in approach and reasons for change**
  - *Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.*

Nothing to Report

- **Actual or anticipated problems or delays and actions or plans to resolve them**
  - *Describe problems or delays encountered during the reporting period and actions or plans to resolve them.*

Barriers to recruitment have included the following:

- Unlike patients who have had a heart attack, patients with DCM have often not had an impactful life-threatening cardiac event; they "feel well" and so do not identify with the serious, progressive nature of their disease.
- The wider use of the medication, Entresto and SGLT2 inhibitors has impacted participation.
- Decline in interest to participating in research (mistrust in research); no return of calls by prospective participants.
- Increasing numbers of participants who are traveling to participating center and requiring financial travel assistance.

Actions being taken:

- Investigators are making presentations in their local hospitals/communities about the trial (e.g. grand rounds; lunch and learn sessions, emails to cardiologists for referrals)
- Site representation at local DCM patient support group meetings to provide information about the trial.
- Working with the centers on a case-by-case basis to approve and reimburse travel expenses for interested participants.
- One clinic has conducted an in-service session to educate device clinics and staff about the trial in order to expand outreach to potential participants.
- One center is participating in the DIVERSE Network/TOTAL Project. This is an AHA funded project which leverages digital methods including culturally tailored internet and social media ads to increase minority enrollment.
- Continuously visiting transplant centers to inform attending physicians about the study and engage them in the referral process.

- **Changes that had a significant impact on expenditures**
  - *Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.*

Nothing to Report

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

- *Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.*

- **Significant changes in use or care of human subjects**

Nothing to Report

- **Significant changes in use or care of vertebrate animals.**

Nothing to Report

- **Significant changes in use of biohazards and/or select agents**

Nothing to Report

6. PRODUCTS: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

Nothing to Report

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to Report

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Public facing website is available (www.dcmii.org). Electronic data capture system is available via secured access from public facing website. Training modules from core lab training sessions are posted to secured website for new personnel/refresher training. Clinicaltrials.gov registry is available (NCT04476901). Public facing website for www.DCMFoundation.org has a small blurb regarding the trial.

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

  Nothing to Report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

  Nothing to Report

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

  - *data or databases;*

    The Data Coordinating Center (DCC) has developed and maintains a comprehensive, feature-rich framework of web-based applications that support data capture, data transfer and harmonization, randomization, specimen management, and reporting services for the DCMII trial. Adverse event reporting and MedDRA classification are supported as well. Clinical sites enter electronic case report forms data through a web interface provided by the secured electronic data capture (EDC) portal, where data checks are performed to validate all data before committing it to the EDC system. The DCC system also provides services for transferring core laboratory and specimen data from a variety of sources, and can accept files in a variety of standard formats; this data can then be merged with existing clinical data.

  - *biospecimen collections; Nothing to Report*
  - *audio or video products; Nothing to Report*
  - *software; Nothing to Report*
  - *models; Nothing to Report*
  - *educational aids or curricula; Nothing to Report*
  - *instruments or equipment; Flow Mediated Dilation (FMD) Testing System – System has been used to measure FMD of patients enrolled in the trial prior to treatment and then at 3, 6, and 12 months post-treatment time points.*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models); Nothing to Report*
  - *clinical interventions; Nothing to Report*
  - *new business creation; and Nothing to Report*
  - *other. Nothing to Report*

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

- **What individuals have worked on the**.
    - *Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."*

***Example**:*

Name:	*Mary Smith*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award).*

Institution	Name	Project Role	Proposed Effort	Actual Effort	Person Mths Worked	Contribution to Project
University of Miami	Joshua Hare	Principal Investigator (Contact)	10%	10%	1.20	**Attending bi-monthly meetings (2x per month), protocol development, compliance review, report development and review**
University of Miami	Dushyantha Jayaweera	Principal Investigator	3%	3%	0.36	Attending bi-monthly meetings (2x per month), protocol development, compliance review
University of Miami	Aisha Khan	Principal Investigator	10%	9.3%	1.12	Attending bi-monthly meetings (2x per month), protocol development, compliance review, report development and review, establishing contracts with collaborators, cell manufacturing, training sites
University of Miami	Raul Mitrani	Co-Investigator	10%	10%	1.20	Attending bi-monthly meetings (2x per month), protocol development, compliance review
University of Miami	Robert Myerburg	Co-Investigator	5%	5%	0.60	Attending bi-monthly meetings (2x per month), protocol development, compliance review
University of Miami	Chris Schettino	Co-Investigator	1.5%	1.5%	0.18	Attending bi-weekly meetings (2x per week), protocol development, MRI reading and analysis
University of Miami	Yoel Siegel	Co-Investigator	0.00%	1.50%	0.05	Attending bi-weekly meetings (2x per week), protocol development, MRI reading and analysis
University of Miami	Antonio Izquierdo	Administrator	5%	5%	0.60	Attending bi-monthly meetings (2x per month), providing budgetary and resource guidance, compliance review
University of Miami	Yee-Shuan Lee	Assist. Scientist	10%	10%	1.20	Attending bi-monthly meetings (2x per month), protocol development, compliance review, cell manufacturing,

Institution	Name	Project Role	Proposed Effort	Actual Effort	Person Mths Worked	Contribution to Project
						testing, release, shipping IP, documentation
University of Miami	Ketty Bacallao	Assist. Scientist	10%	10%	1.20	Attending bi-monthly meetings (2x per month), protocol development, compliance review, cell manufacturing, testing, release, shipping IP, documentation
University of Miami	Bangon Longsomboon	Manager, Quality Assurance	10%	10%	1.20	Attending bi-monthly meetings (2x per month), protocol development, compliance review, cell manufacturing, testing, release, shipping IP, documentation
University of Miami	Lina Caceres	Manager, Quality Assurance	10%	10%	1.20	Attending bi-monthly meetings (2x per month), protocol development, compliance review, review monitoring reports, attend monthly CRCs meetings, monitor recruitment
University of Miami	Russell Saltzman	Regulatory Analyst	10%	10%	1.20	Attending bi-monthly meetings (2x per month), protocol development, compliance review
University of Miami	Varaporn Suwunrut	Sr. Clinical Trial Program Coordinator	10%	10%	1.20	Attending bi-monthly meetings (2x per month), protocol development, compliance review, invoicing, progress reports, annual reports, budget implementation
University of Miami	Jehan Corpuz	Senior Project Coordinator	10%	10%	1.20	Overseeing bi-monthly meetings (2x per month), QA training of site on IP handling and documentation and administrative organization of the project.
University of Miami (Vascular Core)	Barry Hurwitz	Core Leader	5%	5%	0.60	Leader of the Vascular Core who developed and supervised the construction of the equipment to perform the vascular endothelial brachial artery reactive hyperemia test across each of the 4 study sites. Protocol development and supervises collection of core measures. Performs final pass quantitation of vascular measures. Attends bi-monthly meetings. Participates in the interpretation of findings, preparation of scientific manuscripts.
University of Miami (Vascular Core)	Alex Gonzalez	Research Associate	5%	5%	0.60	Staff training and ultrasound vascular assessment certification at each test site. Continued technical support for troubleshooting hardware and software issues. Data transfer from each site to secure servers.
University of Miami (Vascular Core)	Meela Parker	Ultrasound Technician	5%	5%	0.60	Continued training and support of ultrasound imaging protocol. Preliminary QA review of acquired image data, with site feedback. Performs first and second pass quantitation of the vascular measures
University of Texas Health	Barry Davis	Principal Investigator (RETIRED)	0%	0%	0.00	None
University of Texas Health	Dejian Lai	Principal Investigator (Prev. Co-I)	15%	15%	0.45	Statistical analysis plan development, protocol amendment review, Investigator meeting attendance

Institution	Name	Project Role	Proposed Effort	Actual Effort	Person Mths Worked	Contribution to Project
University of Texas Health	Ruosha Li	Co-Investigator	5%	5%	0.15	Statistical analysis plan development, protocol amendment review, Investigator meeting attendance
University of Texas Health	Lara Simpson	Safety Officer	40%	40%	1.20	Clinical endpoint adjudication definitions, protocol amendment review, testing of EDC system for event reporting/adjudication, Investigator meeting attendance, review of adverse events
University of Texas Health	Judy Bettencourt	Clinical Trials Project Manager (RETIRED)	30.00%	0%	0.00	None
University of Texas Health	Shelly Sayre	Clinical Trials Project Manager (RETIRED)	65.00%	0%	0.00	None
University of Texas Health	Sibi Mathew	Clinical Research Monitor	50%	50%	1.50	Recruitment action plan development, template recruitment plans, EDC testing, and meeting attendance, and generation of Investigator meeting minutes, remote monitoring review of source documents
University of Texas Health	Gina DeWildt	Programmer Analysis	50%	25%	0.75	Continued programming of EDC, payment invoicing report development; FAQ system; DSMB draft tables/reports
University of Texas Health	Avichal Aggarwal	Medical Monitor (MD)	5%	5%	0.15	Review of adverse event reports for distribution to regulatory oversight groups, clinical endpoint adjudication
University of Texas Health	Kiran Mansoor	Clinical Trials Project Manager	30%	30%	0.90	Hired in Nov 2023 as Shelly and Judy retired as of Dec 2023. Updates to public facing website, Investigator meeting attendance, testing of the EDC system; EDC user account management; programming requests, IRB ongoing correspondence (continuing reviews), clinicaltrials.gov registry maintenance, biweekly Investigator meeting organization, EDC testing, posting of materials from trainings to website, finalization of trial documents
University of Texas Health	Mahrukh Jamil	Assistant Clinical Trials Project Manager	18%	18%	0.54	Hired March 2024. Investigator meeting attendance, testing of the EDC system; EDC user account management; programming requests, IRB ongoing correspondence (continuing reviews), clinicaltrials.gov registry maintenance, biweekly Investigator meeting organization, posting of materials from trainings to website.
Johns Hopkins	Joao Lima	Principal Investigator	8.33%	10.00%	0.30	provide scientific input in MR image data acquisition, develop the MRI protocol; participate in monthly investigator calls
Johns Hopkins	Bharath Ambale-Venkatesh	Co-Investigator	10.00%	9.00%	0.27	review MRI protocol, eligibility criteria, oversee quality control, assist in regulatory activities
Johns Hopkins	Chikara Noda	Post Doctoral Fellow	30.00%	25.00%	0.75	conduct quality control review of all MRI images received and provide extensive feedback reports to sites; participate in data reporting template to the coordinating center
Johns Hopkins	Ela Chamera	Technician	35.00%	25.00%	0.75	assist in quality control review; assist in data reporting template to the

Institution	Name	Project Role	Proposed Effort	Actual Effort	Person Mths Worked	Contribution to Project
						Coordinating Center; read all incoming MRI images for analysis and interpretation
Johns Hopkins	Jason Ortman	Technician	5.00%	5.00%	0.15	oversee image transfer, receipt, storage, and archive of images from sites; maintain access to portal; troubleshoot image transfer issues
Johns Hopkins	Vinithra Varadarajan	Post Doctoral Fellow	0.00%	0.00%	0.00	develop data dictionary, conduct export of raw data, complete data cleaning and validation, upload data results to the Coordinating Center
Johns Hopkins	Ashkan Abdollahi	Post Doctoral Fellow	0.00%	10.00%	0.30	develop data dictionary, conduct export of raw data, complete data cleaning and validation, upload data results to the Coordinating Center
Johns Hopkins	Bruna Scarpa	Post Doctoral Fellow	0.00%	50.00%	1.50	reviews incoming MRI images for clinical findings, overreads technician reads, prepares dataset of results
Univ. of Louisville	Roberto Bolli	Principal Investigator	10.00%	10.0%	0.30	Attending bi-weekly meetings (2x per week), compliance and patient record reviews
Univ. of Louisville	Heidi Wilson	Clinical Research Coordinator	20.00%	27.7%	0.83	Continued patient recruitment and prescreening, writing orders for the upcoming injections and visits, maintaining source documents for the study, coordinating study procedures with different departments for the required procedures
Stanford University	Phillip Yang	Principal Investigator	8.33%	8.33%	0.25	Overseeing weekly site meetings, administering the project (IRB, protocol, and budget), recruiting pts (liaison and PR w/ HF, Interventional, Gen Cards and Imaging attendings) and advice and guidance for study eligibility diagnostic tests (MRI, and SPI). Completed Protocol and safety training.
Stanford University	Kendall Harrington	Clinical Research Coordinator	35.00%	32.00%	0.96	Preparation for weekly meetings, organization of the administrative efforts (BRANY IRB continuing review, Informed Consent amendments, DOA log and budget preparation), screening medical records for recruitment prep and communication with self-referred patients, coordination of setup and completion of site CPL, FMD Core lab trainings. Completion of CRC Protocol, Safety, 6MWT trainings and EDC certification.
Texas Heart	Emerson Perin	Principal Investigator	10.00%	2%	0.06	Attendance of DCM II virtual meetings, Completion of all required regulatory documents for start-up and trainings, institutional operational management with James and team
Texas Heart	James Chen	Clinical Research Coordinator	35.00%	5%	0.15	Attendance of DCM II virtual meetings, Regulatory work (i.e.: IRB submission, site start-up requirements by U of Miami), institutional operational management (i.e.: coordinator huddles, meetings/discussions with local hospital departments)

Institution	Name	Project Role	Proposed Effort	Actual Effort	Person Mths Worked	Contribution to Project
Texas Heart	Nichole Piece	Clinical Research Coordinator	0.00%	5%	0.15	Institutional operational management (i.e.: coordinator huddles, meetings/discussions with local hospital departments), patient recruitment, coordination of trial activities, patient safety
Texas Heart	Kimberly Walker	Clinical Research Coordinator	0.00%	0%	0.00	Institutional operational management (i.e.: coordinator huddles, meetings/discussions with local hospital departments), patient recruitment, coordination of trial activities, patient safety

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**
    - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
    - *If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.*

    Nothing to Report

- **What other organizations were involved as partners?**
    - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
    - *Describe partner organizations - academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) - that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.*
      Provide the following information for each partnership:
        - **Organization Name:**

Site 1: **University of Miami, Miller School of Medicine**
Clinical Coordinating Center

Interdisciplinary Stem Cell Institute
Biomedical Research Building
1501 NW 10th Avenue, Room 903
Miami, Florida 33136

PIs: Joshua Hare, MD; Aisha Khan, MSc, MBA.
Project Manager: Lina Caceres, MHS

Site 2: **University of Louisville Research Foundation, Inc.**

Department of Medicine,
Institute of Molecular Cardiology
300 E. Market Street, Suite 300
Louisville, KY 40202

PI: Roberto Bolli, MD
Coordinator: Heidi Wilson

Site 3: **Texas Heart Institute**

6770 Bertner Avenue, Houston TX 77225

Site 4: **Stanford University School of Medicine Research Management Group**
3172 Porter Drive, Palo Alto, CA 94304-1212

PI: Emerson Perin, MD/PhD
Coordinator: Huang (James) Chen, RN, BSN

University of Texas, School of Public Health

1200 Pressler St. W-916, Houston, TX 77030

PI: Dejian Lai, PhD, Co-I: Lara Simpson, PhD, Ruosha Li, PhD
Project Manager: Kiran Mansoor, MBBS; Mahrukh Jamil, MS.

PI: Phillip C. Yang, MD
Coordinator: Fouzia Khan, MBBS

Johns Hopkins University, MRI Core Center

600 N. Wolfe Street, Blalock 524, Baltimore, MD 21287

PI: Joan Lima, MD
Co-I: Bharath Ambale -Venkatesh

- **Location of Organization:** *(if foreign location list country)*
- **Partner's contribution to the projec**t *(identify one or more)*
  - **Financial support;**
  - **In-kind support** *(e.g., partner makes software, computers, equipment, etc., available to project staff)*;
  - **Facilities** *(e.g., project staff use the partner's facilities for project activities)*;
  - **Collaboration** *(e.g., partner's staff work with project staff on the project)*;
  - **Personnel exchanges** *(e.g., project staff and/or partner's staff use each other's facilities, work at each other's site)*; and
  - **Other.**

8. SPECIAL REPORTING REQUIREMENTS –

- **COLLABORATIVE AWARDS:** *N/A*
- **QUAD CHARTS:** *N/A*

9. APPENDICES: ***N/A***