Cardiovascular Cell Therapy Research Network

Echo Core Lab Application- 2014

Network: We are a network of physicians, scientists, and support staff dedicated to studying stem cell therapy for treating heart disease. The goals of the Network are to complete research studies that will potentially lead to more effective treatments for patients with cardiovascular disease, and to share knowledge quickly with the healthcare community.

Purpose: The mission of the CCTRN is to achieve public health advances for the treatment of cardiovascular disease, through the conduct and dissemination of collaborative research leading to evidence-based treatment options and improved outcome for patients with heart disease.

Expectations for Core Labs: It is expected that Network core labs will:

1. Work closely with the Steering Committee to determine the analysis needs of proposed protocols, provide a corresponding scope of work and budget to address those needs, and provide procedures for the proper collection, shipment, analysis, and storage of study data.
2. Employ sufficient personnel to ensure the primary analysis (at least one individual and a back-up), timely data entry/data transmission, and timely invoicing.
3. Regularly review, update, and re-issue SOPs to clinical centers at established intervals and as warranted by changes to the protocol.
4. Provision of and inventory monitoring of supplies needed to provide data from the sites to the core (e.g., Fed Ex account, shipping boxes, package labels, checklists of materials to be included)
5. Submit appropriate applications and annual reports to their institutional review board for approval to conduct analysis on de-identified data.
6. Submit periodic progress reports to the Data Coordinating Center (DCC) and to attend and participate in regularly scheduled Steering Committee meetings.
7. Adhere to the NHLBI and CCTRN policies on 1) presentations/publications, 2) intellectual property rights, and 3) access to and sharing data.
8. Provide timely provision of data deliverables to the DCC.
9. Provide monthly invoicing to the DCC to receive payment which includes detail support (patient identification numbers, visit type, etc.).

Application and Review Process:

Applications (no more than 6 pages in length) will be reviewed by the CCTRN Executive Committee and an NHLBI-appointed review group. Selected core labs will be notified via email from the DCC within 60 days of the close of the application period.

Applications must include 1) a copy of the lab director's current CV and 2) an application addressing the core lab elements listed beginning on page 4. In support of the application, a listing of relevant publications of previous or ongoing work may also be provided. The application must include the following elements:

Section I. Laboratory Description

A. Name and address of Core Lab
B. List of key lab personnel (including the Director), their credentials, and experience in cellular therapy field
C. Brief description of the lab; including any off site facilities or personnel utilized (can include years of operation, previous projects or programs on which the lab has functioned as a core, accreditations, special awards, acknowledgments, etc.). Please specify clinical trial experience.
D. Indicate any accreditation that the lab has and provide current documentation (i.e. certificates).
E. Provide descriptions of the types of analysis provided by the lab with respect to the type and nature of Network protocols.
F. Please provide background on the lab's experience in collection and interpretation of echoes in LVAD patients?

Section II. Training and Management Plan for Sample Collection and Shipment

A. Describe training to be conducted by your laboratory with the clinical center personnel prior to data collection (e.g., site training visits, development of SOPs, teleconferences, distribution of materials, qualification information)
B. Describe the qualification process that your lab conducts-(e.g., site equipment validation, number of qualification runs needed to meet assurance, etc)
C. List any ongoing education sessions available to clinical centers by your lab (e.g. refresher training on coordinator calls, emails to technicians at clinical centers, etc)
D. Describe management processes for maintaining inventory/shipment of collection supplies to centers.

Section III. Communication Strategies with Centers and Sponsor

A. Describe circumstances, frequency and method of communication with clinical centers
B. Describe circumstances, frequency and method of communication with Sponsor (DCC)
C. Describe how your lab resolves/reports communication failures with clinical center personnel

Section IV. Laboratory Quality Control Processes

A. Describe your process for receipt and tracking of data received from clinical centers (e.g. logging system including date of receipt, date of analysis, condition of the data, etc.)
B. Describe process for addressing data issues: missing labels, media, or paperwork from clinical centers

C. List equipment and/or software used by your lab for analysis of data in the CCTRN trials
D. Provide additional info on software validation (standard used, frequency of calibration, etc.)
E. Describe your system for managing blinded quality control review

Section V. Sample Storage and Data Submission

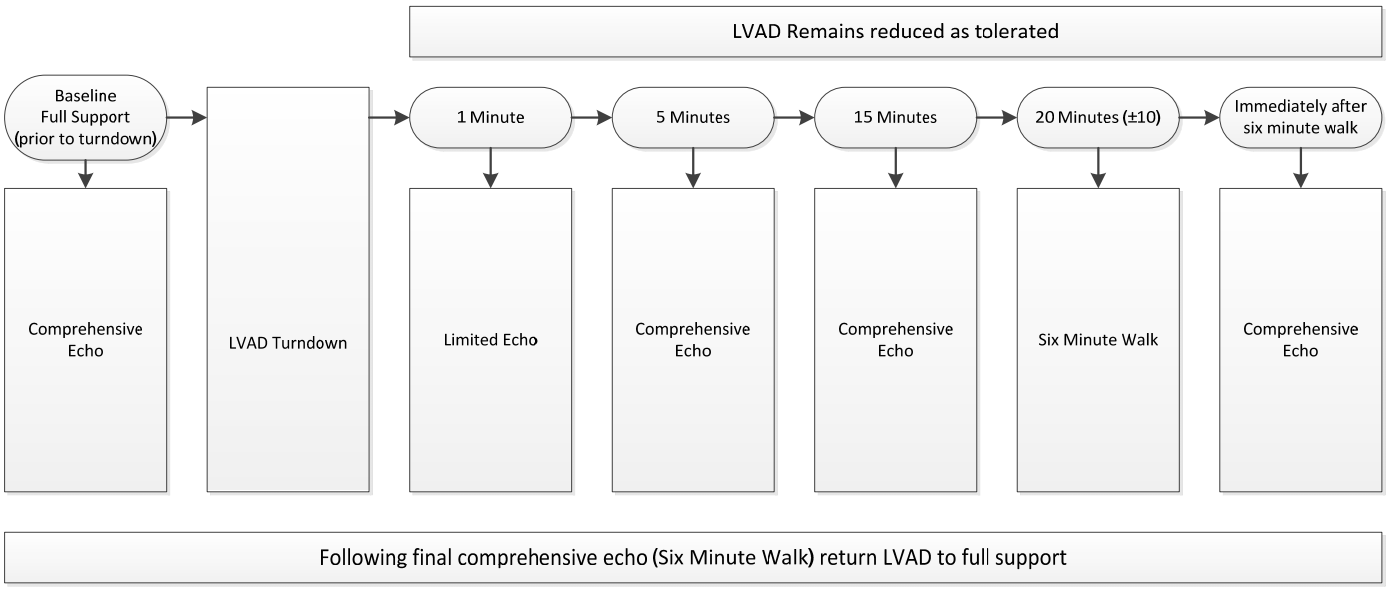
A. Provide information on data storage (under what conditions are the data kept, how long are they kept, destruction methods, any security measures that are in place)
B. Describe your data backup process for data processed by your lab; including any off-site data storage
C. Provide information on your data transmission capabilities (secure upload, database entry, submission of spreadsheets, etc.)

Section VI. Budget

The budget should include cost for carrying out the analysis procedures, any necessary (non-electronic) shipping of image data, and storage (if appropriate) of study data. Cost should be reported on a "cost per patient" basis.

As part of the CELLVAD protocols echoes will be collected in patients with left ventricular assist devices (LVAD). Echoes will be collected both while the pump is running at full speed, as well as when the pump speed is reduced. Both limited and complete echoes will be collected as part of this turn down protocol (see figure).

Figure: TIMELINE OF FUNCTIONAL ASSESSMENTS PERFORMED DURING TURNDOWN PROCEDURE



Para-sternal long axis, short axis and axial 4 chamber views should be obtained at each time point and the following measurements taken:

- LV Dimensions and posterior wall thickness in systole and diastole and aortic valve opening time from the parasternal long axis view and all measured on the M-mode
- Simpsons method performed on the apical four chamber view to measure EF
- MR grade, any aortic regurgitation, and whether the aortic valve is opening or not

Echo Elements

PARASTERNAL WINDOW

Long Axis View

1. 2D Parasternal Long
2. M mode of LV with measurement of LV dimensions
3. M-mode Aortic Valve (Several tracings preferable for total of 10 heartbeats)
4. Color Doppler Mitral Valve
5. Color Doppler Aortic Valve

Short Axis View

6. 2D Papillary muscle level
7. 2D Aortic valve level

APICAL WINDOW

8. Color Doppler imaging of the LVAD inflow cannula
   [*This should be acquired in the apical window which best demonstrates the cannula.*]
9. CW Doppler of the LVAD inflow cannula
   [*This image should be optimized to show both the peak inflow and any retrograde flow through the cannula*.]

4-Chamber View

10. 2D 4-Chamber
11. Color Doppler Mitral Valve
12. CW Doppler Mitral Valve (MR velocity and mitral gradient if stenosis/prosthesis)
13. Color Doppler Tricuspid Valve
14. CW Doppler Tricuspid Valve (TR velocity)
15. PW Doppler Mitral inflow with sample volume at the MV leaflet tips
16. Tissue Doppler (lateral mitral annulus)
17. M-mode of the lateral tricuspid valve annulus (TAPSE)
18. Several beats to be recorded to view the LV function and EF assessed by Simpson's rule

5-Chamber View

19. 2D 5-Chamber
20. Color Doppler Aortic Valve
21. PW Doppler Left Ventricular Outflow Tract
    [*This image needs to be optimized to measure the flow (if any) ejected via the LV outflow tract into the aorta*.]
22. CW Doppler Aortic Valve

CHAMBER SIZES:

1. LA diameter
2. LV end diastolic diameter (from the M mode performed in the parasternal long axis view)
3. LV end systolic diameter
4. LV end diastolic volume (Biplane Simpson's method)
5. LV end systolic volume (Biplane Simpson's method)
6. RV diastolic area (4-chamber view)
7. RV systolic area (4-chamber view)
8. Aortic diameter (annulus, root, sino-tubular junction and ascending aorta)
9. Ratio of LVEDD to pre-implant LVEDD

LV FUNCTION:

10. LV ejection fraction (Biplane Simpson's method)
11. LV fractional shortening
12. LV ejected stroke volume (VTI x pi x R^2)
13. Simpson's stroke volume (LVEDV – LVESV)
14. Duration of AV opening (LV ejection time)
15. Percentage of heartbeats with AV opening
16. LV dP/dT from CW Doppler of mitral regurgitation

RV FUNCTION:

17. RV fractional area change
18. TAPSE
19. RV ejected stroke volume (VTI x pi x R^2)

LVAD FUNCTION:

20. Peak inflow cannula flow velocity
21. Average inflow cannula flow velocity
22. Aortic pulsatility index (Ratio of peak systolic to diastolic flow velocity in the descending aorta)

VALVE FUNCTION:

Valvular regurgitation will be graded semi-quantitatively using American Society of Echocardiography (ASE) criteria. Grades will be assigned on a 7-point scale (none, minimal, mild, mild-moderate, moderate, moderate to severe and severe). Particular attention to the degree of aortic valve thickening and calcification will also be assessed on the same 7-point scale.