



CTSN Satellite Site Guidelines

Overview:

The primary goal of the Cardiothoracic Surgical Trials Network (CTSN) is to design, conduct, and analyze multiple, collaborative, proof-of-concept, clinical protocols to evaluate surgical and minimally invasive strategies to improve the treatment of cardiovascular disease in adult populations. The CTSN will develop and conduct a number of proof-of-principal clinical studies as an important step in developing a culture of systematic scientific clinical evaluation within the field of cardiac surgery that will inform the use of new interventions in surgical practice and improve the scientific basis of care in cardiovascular disease.

The purpose of this document is to describe the roles, responsibilities, and benefits of being a satellite site in the CTSN. The satellite sites will participate in the CTSN trial ***SURGICAL ABLATION VERSUS NO SURGICAL ABLATION FOR PATIENTS WITH PERSISTENT OR LONGSTANDING PERSISTENT ATRIAL FIBRILLATION UNDERGOING MITRAL VALVE SURGERY (AFIB trial)*** to enhance recruitment, provide additional clinical expertise, and participate in the intellectual output of the CTSN.

Purpose of the Study: The primary aim of this proof-of-concept trial is to determine if surgical ablation for persistent or longstanding persistent AF is more effective than MVS alone in reducing occurrence of post-MVS AF at 6 months and 1 year. Inclusion of 2 different lesion sets in the ablation group (pulmonary vein isolation only [PVI] and a biatrial Maze lesion set) will provide preliminary data to guide development of a follow-up study comparing effectiveness of these 2 lesion sets. In addition to 72-hour continuous rhythm assessment at 6 months and 1 year (Holter), we will employ weekly transtelephonic monitoring to inform follow-up strategies for future trials of rhythm control in AF.

STUDY DESIGN: This is a prospective, multi-center, randomized, controlled clinical trial. The trial will be conducted in up to 23 clinical sites. Two hundred and sixty (260) patients will be randomized. Accrual is expected to take 21 months, and all patients will be followed for 12 months post randomization.

Application and Approval Process:

In order to be considered for participation in this CTSN trial, each satellite site will complete a detailed protocol specific application document. This application requires the satellite site to document:

- Site's clinical trials experience and infrastructure,
- Site's track record in recruiting patients for clinical trials and
- Site's enrollment capabilities for the current CTSN trial (AFIB)

The Satellite Site will submit their application to the CTSN Data Coordinating Center (DCC), International Center for Health Outcomes and Innovation Research (InCHOIR), Mount Sinai School of Medicine, NY, NY. The application will then be reviewed by the CTSN Satellite Site Sub-Committee and when deemed complete, forwarded to the CTSN Steering Committee for a decision. Key review considerations are the satellite site investigator's qualifications and ability to recruit the patients of interest, as well as the availability of adequate resources and appropriate lines of communication with the DCC. The Steering Committee will discuss and make a final decision by majority vote.

Satellite Site Selection Criteria

The CTSN Operations Committee will be responsible for initial review of satellite site applications. Applications will be reviewed for responsiveness to the requirements specified and ability to perform all study duties within the budget approved by NHLBI.

All sites, regardless of previously expressed interest must apply and undergo review. Additional information may be required from potential satellite sites prior to making a final decision on site selection. Final selection of satellite sites will be made by the Steering Committee by majority vote.

Sub-Contract Information

Satellite sites are not primary awardees of the CTSN. Satellite sites will function as a subcontract to the DCC at the Mount Sinai School of Medicine, NY, NY.

Financial Information:

Satellite sites will receive an infrastructure budget and reimbursement for successful patient enrollment.

Infrastructure Payment

Each selected site will receive fixed funding of up to \$5,000 total costs (including indirect costs), to be paid out after enrollment of the second, fourth, sixth, eighth and tenth patients (see below). This funding will support infrastructure costs, training of study personnel and travel to Steering Committee meetings. Steering Committee meetings occur three times annually in Bethesda, MD. The principal investigator (PI) and one coordinator are expected attendees. These payments will be administered by the DCC. Invoices are generated by the DCC based on data completion in the electronic data capture system.

Payment for Patient Enrollment

During enrollment, sites will be paid \$2714 (including indirect costs) on a per capita basis for each patient successfully enrolled in the AFIB trial. Reimbursement for patient enrollment includes protocol-related costs that are not considered standard of care and for data collection efforts. The payment schedule is as follows: 50% upon enrollment, 30% at year 1 and 20% at year 2. Payment intervals will be quarterly based on patient data entered into the electronic data capture system (EDC). Failure to complete protocol specified data collection may result in a reduced payment.

Payment Schedule

Payments are made quarterly. All patients randomized within a quarter will be paid in the following quarter. Supplemental payments will be made as outlined above. After the first 10 patients randomized, subsequent payments will be for the per capita patient fee only.

Role of the DCC (InCHOIR):

Satellite sites require the same administrative and regulatory oversight as the core, affiliate and ancillary sites. The satellite site must agree that the DCC will serve in the central oversight role.

Once approved by the Steering Committee, the Satellite Site must undergo a study initiation visit/teleconference by the DCC prior to trial enrollment during which time the satellite PI, co-investigator (co-I), collaborating investigators, and clinical research staff will be trained. In addition to reviewing the relevant protocols and CTSN Operations Manuals, the initiation conference will include evaluation and confirmation that:

There is a collaborative relationship between the cardiothoracic surgery investigator and cardiology investigators (Interventional Cardiology, Heart Failure and Echocardiography);

A procedure is in place for ensuring that information in source documents is accurately captured on the case report forms (CRFs) and reported to the DCC in accordance with the CTSN Manual of Operations;

A procedure is in place for handling data queries and discrepancies identified by the study monitor;

Compliance with the CTSN requirements in order to ensure that all required regulatory documents (e.g., IRB approvals, financial disclosures, signed and dated curricula vitae (CVs), copies of medical/nursing licenses, documented trainings, etc.) are in place at each satellite site and that these documents (or copies of these documents, as appropriate) are sent to the DCC for their files before enrollment can begin at a satellite;

A procedure is in place for ensuring that the consent process is being conducted in accordance with the protocol, Good Clinical Practice (GCP) and any applicable Federal, State, and Local regulations, such that study subjects understand the nature of their participation, risks associated with participation, etc.;

A procedure is in place for satellite site staff to comply with the protocol, adverse event assessment and reporting, and other medical issues that arise during the course of the study;

A procedure is in place for correcting problems identified by study personnel, outside monitors or auditors, or other parties involved in the conduct of the study;

Documentation has been provided to the DCC regarding the necessary certification for investigators and coordinators;

Conflict of interest (COI) forms have been submitted and either no COI exists or it has been mitigated and/or managed.

Once the approved satellite site is certified by the DCC as having completed the above process, and a sub-contract has been executed, patient enrollment can start. The DCC will monitor regulatory compliance, including quality control review of regulatory documents and data submissions, site monitoring, fielding site's questions, document control, and training and certification oversight as outlined in each protocol.

Role and Responsibilities of Satellite Sites:

For participation in the AFIB trial, all satellite sites must meet the following requirements:

Willing and able to follow the RANDOMIZATION schema: Patients will be randomized to one of two treatment groups:

Group 1: mitral valve surgery with ligation/excision of left atrial appendage PLUS surgical ablation

Group 2: mitral valve surgery with ligation/excision of left atrial appendage (control group)

Patients will be randomized in a 1:1 fashion. By this arrangement, 50% of the patients will undergo ablation lesions (Group 1) and 50% will not (Group 2).

All patients will undergo ligation or excision of LAA.

Patients randomized to the ablation (Group 1) will be further randomized (1:1) to one of two lesion sets:

Group 1a: *pulmonary vein isolation*

Group 1b: *biatrial lesions*

Note: Randomization will be performed intra-operatively following anesthesia and TEE.

Principal Investigator and Co-investigator: Principal investigators will be cardiothoracic surgeons with expertise in mitral valve surgery and surgical ablation and Co-Investigators will be cardiologists with experience in caring for patients with mitral valve disease and arrhythmias.

PI must have performed at least 10 surgical AF ablations and 10 mitral valve procedures over a 2 year period. Surgical qualifications for all participating surgical investigators will be collected on the Surgical Certification Form and faxed to the DCC prior to accreditation. The site's PI will be responsible for overseeing the ongoing performance of the other participating surgical investigators at that site over the course of the study. In addition, each surgical investigator will participate in at least one of the bi-annual meetings of the Clinical Management Committee. Each Satellite site PI's and co-I's responsibility will also include the following:

Establish working relationships between Cardiothoracic Surgery and Cardiology, including general cardiology, echocardiography, and interventional cardiology in order to facilitate patient identification and enrollment;

Obtain IRB approval for the CTSN protocols and informed consent (and their revisions) in a timely manner;

Recruit patients, collect data and enter it accurately in the EDC;

Faithfully follow the protocols and adhere to the standards of GCP;

Provide the DCC with the information necessary for interim, annual, and final reports;

Provide source documents, data and regulatory documents for study monitors to review;

Provide prompt responses to DCC inquiries;

Participate in Investigator Committee and subcommittee meetings and conference calls as a non-voting member;

Participate in analyses and reporting study results, including potential participation on manuscript development subcommittees;

Submit COI forms to DCC on annual basis.

Previous Experience: Satellite sites must demonstrate prior and ongoing experience with patient-oriented research, preferably in surgically treated patients, including prospective studies requiring patient recruitment into clinical trials. Satellite sites must also have dedicated clinical coordinators (e.g., research nurses) to assist with screening and enrolling patients and act as liaison between surgeons and cardiologists, including the echocardiography and catheterization laboratory personnel.

Volume of Recrutable Patients: Sites must demonstrate a large patient population eligible to participate. Sites must be able to demonstrate through prospective screening log that they have a patient volume sufficient to recruit at least 3-5 patients per month.

Ability to Recruit Patients from Cardiothoracic Surgical services: Participating sites must have concurrence from Cardiothoracic Surgical leadership that equipoise exists and patients will be enrolled and randomized. If equipoise does not exist on the part of specific surgeons, then measures will be taken to allow those patients to be enrolled by surgeons collaborating on these trials.

Ability to Recruit Patients from Cardiology services: Participating sites must have access to echocardiography and catheterization laboratory facilities and the ability to recruit patients within those facilities.

All satellite sites must adhere to the following timelines in conducting the clinical trial:

Commitment of dedicated personnel for at minimum 36 months, especially since the majority of personnel effort will be required during the 1st month of patient screening and randomization;

Completion of patient follow-up (up to 12 months). Completion of data collection and closing out queries as per DCC standard operating procedures.

Attachments: Protocol Synopsis (V4.2)

AFIB Data Collection Schedule of Events

Satellite Site Application

Satellite Site Screening Log