The Circulatory

Volume 1, Issue 1, December 2013

Welcome!

Welcome to the inaugural issue of *The Circulatory*. We are launching this monthly e-newsletter as part of our new design of the coordinator conference calls. This e-newsletter will provide you with the information covered on the monthly CTSN Coordinators Informational Conference Call, as well as additional information pertinent to trial coordinators. The informational calls will alternate with topic-driven conference calls to discuss trial start up activities, share best practices and concerns, promote mentorship between coordinators, and facilitate working groups. As always, we encourage you to contact the DCC for questions or concerns.

Happy Reading,
The DCC

SMR Trial Update

The follow-up phase of the SMR trial will be complete in early 2014. The DCC is aiming to complete adjudication of all SMR adverse events by late spring 2014 in preparation for trial close out, final analyses and publications. Source documentation requests have been sent to coordinators; a timely response is greatly appreciated.

Mark Your Calendar

The next CTSN Coordinator Call is scheduled for

Tuesday, December 17th

3pm ET

MMR Trial Update

The Month 12 primary endpoint collection for the MMR trial will be completed in May 2014. Kathy McDonald will continue to send email reminders to coordinators 30 days prior to Month 12 study visit window opening in 30 days. Please reply to Kathy's email with the scheduled date of the study visit.

In preparation for the analyses, presentations and publications of the primary endpoint, the EAC meetings in January and April 2014 will adjudicate all MMR AEs that occurred in the first 12 months of follow up. All sites have received source documentation requests for MMR AEs. If you received a request for source documentation, please provide source as soon as possible or let us know of encountered barriers to obtaining source.

CTSN @ AHA

The SMR, LVAD Cell Therapy and Infection trials were recently presented at the American Heart Association Conference in Dallas, TX.

Coordinators' efforts in recruitment, retention and data completion contributed greatly to these presentations.

Thank you for all your hard work and dedication to these trials!

MR Trials: NYHA Guidance

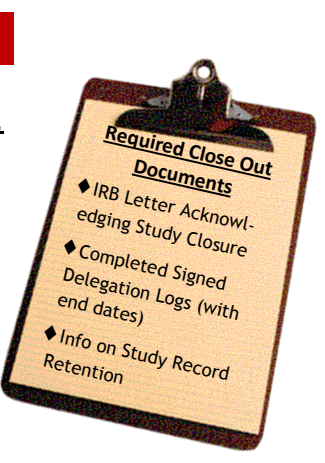
For both SMR and MMR patients whose NYHA assessment was conducted at a different institution, please document the date of the NYHA assessment in the EDC to reflect the date of the physical exam from which the NYHA was evaluated. The note to file will document the date the NYHA was assessed using the source documentation. If new medication or physical exam information is made available through NYHA source, please update the EDC.

AF Trial Update

2014 is an exciting year for the AF Trial with the month 6 and month 12 primary endpoint collection being completed. The last enrolled patient in the trial is expected to complete the month 6 primary endpoint assessment by mid-March and the month 12 primary endpoint assessment by early September. Medicomp has extended the lead time for reaching out to patients to maximize schedule opportunities. Please continue to confirm the Holter start date when conducting the telephone follow-up at month 6 and month 12 and provide Wayne Bowen with any changes to the patient's contact information.

Close Out of the LVAD Cell Therapy Trial

Preparations to close out the LVAD Cell Therapy Trial are underway. In order for a site to close out, **all outstanding regulatory requests, including protocol deviation forms, must be completed**. The DCC will inform sites of outstanding regulatory documentation, and once completed, the DCC will schedule a call with each site's trial PI and coordinators.



Preparing for Close Out

Below is a list of documents that will be required to close LVAD study. More information on study close processes out will be issued on the call with DCC and site PI and coordinator.

- IRB Letter Acknowledging Study Closure
- Completed Signed Delegation Logs (with end dates)
- Information on Study Record Retention

New Trials

There are several exciting new trials in development. The first two trials anticipated to initiate in early 2014 are the Post-Op AF study and LVAD Cell Therapy Stage 2. To inform site selection for all new trials, the DCC will circulate a site assessment form to be completed online through REDCap evaluating a site's ability to conduct individual trials. Additional information on site assessments will be sent in the near future.

LVAD Cell Therapy II Trial

LVAD Cell Therapy II Trial Projected Timeline

November 2013 →	• Non-LVAD Stage 1 sites applications due
December 2013 →	• LVAD Stage 1 sites applications due • PDC Meetings
January 2014 →	• Site Selection • Protocol to DSMB
February 2014 →	• Protocol to FDA • Regulatory package to sites

Planning for the second stage of LVAD Cell Therapy Trial is in full swing. The Protocol Development Committee, composed of principal investigators and coordinators, convened for a conference call on Tuesday, November 26th and are scheduled to meet again on December 10th. The PDC discussed changes to the protocol such as decreased weaning frequency, a sample size of 60-90 patients, and comparing a 150 million MPC does to a control group and possibly adding in the future a third dose as an amendment to the protocol. Also of note, the study product will now be stored in vials and a 1cc gauge needle will be utilized.

From an IND perspective, changes to the protocol will be submitted to the FDA as an amendment; from a regulatory perspective, however, a new application will be submitted for stage 2 of the LVAD trial and new contracts will be issued.

The DCC released a brief survey to sites that did not participate in stage 1. Stage 1 sites were recently contacted and asked to confirming their interest to participate in Stage 2. Interested Stage 1 sites must submit a completed survey by December 17th. For additional information, please contact Janine Lynch at janine.lynch@mountsinai.org.

Post-Op AF Study

Another study in the pipeline is a post-operative atrial fibrillation (AF) study evaluating rate versus rhythm control in patients with no history of afib undergoing CABG, primary valve surgery or combination therapy (CABG + valve). In the spirit of innovation, the DCC is considering the use of technologies such as cell phone applications to monitor patients' heart rhythm. This form of data collection may lessen the study's burden on the patients.

The development of Post-Op AF protocol is making great progress. The DCC will recruit a group of coordinators to review the data collection tables, and the coordinators will be able to review the protocol before it is submitted to the NHLBI's protocol review committee during the first week of January 2014. The protocol will be then submitted to the DSMB during the third week of January. If the protocol is approved, sites may receive a regulatory package by early February.

Post-Op AF Study Projected Timeline

Jan. Week 1	Protocol to NHLBI PRC
Jan. Week 3	Protocol to DSMB
Feb. Week 1	Regulatory package to sites

Call for Sites

In the near future all core and potential consortium CTSN sites will receive a survey requesting information on post-surgery monitoring practices (e.g. duration of telemetry), anticoagulation strategies for patients experiencing atrial fibrillation, and a discharge protocol for patients with AF. Sites interested in participating in the post-op AF study are encouraged to submit a survey.

Neuroprotection

Neuroprotection in the setting of aortic valve replacement surgery is a top priority for the Network, and there are two neuroprotection studies in development.

One area of focus involves the use of an embolic protection device, either from Cardiogard or Edwards. Cardiogard is an Israeli company whose device is a cannula that collects solids and gasses. Edwards is a U.S. company whose device is similar to a net and catches solid materials. Next steps include a discussion with the FDA regarding the regulatory requirements for using one of these devices in a Network trial.

A second research area of focus will involve a study evaluating a HIF compound and the ability to tolerate ischemia. In response to FDA guidance, Glaxo Smith Kline recently contracted a lab to conduct animal testing of the HIF compound before the compound is used in a human trial. Start up of this trial projected to be 9-12 months away.

Stay tuned for more information on upcoming trails!