SUMMARY MINUTES
Observational Study Monitoring Board (OSMB)
Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS) N01 HV58198
Conference call
November 13, 2015
10:00 AM-11:00AM

I. PARTICIPANTS:
OSMB Members Present: Leslee Shaw, PhD (Chair) and Pierre Voisine, MD

OSMB Members Absent: James Anderson, MD, PhD; Dean Follmann, PhD; Robert Levine, MD

Study Investigators: James Young, MD (Study Chair) and Elizabeth Blume, MD

Data Coordinating Center (DCC) Staff: Craig Collum, MPH; Susan Meyers, BBA, QMIS; Mary Lynne Clark; Kathryn Hollifield, BSN, RN; Ryan Canter, MSPH

NHLBI Staff: Catherine Burke, MA (Executive Secretary); Marissa Miller, DVM, MPH (Project Officer); Tim Baldwin, PhD (Deputy Project Officer); Neal Jeffries, PhD; Wendy Taddei-Peters, PhD

II. INTRODUCTION:
This was a regularly scheduled call of the INTERMACS OSMB to review both the study progress and an amendment to the protocol (Protocol Version 5.0). Comprehensive written reports and materials were provided to the OSMB members in advance of the call. Minutes from the November 7, 2014 OSMB meeting were not approved at this time because we did not have a quorum of OSMB members present. The participating OSMB members had no changes to the minutes. The Chair agreed that the Project Officer Update, the DCC Report, and the Protocol Amendment should be presented to the participating members. The absentee members will be asked to provide their reviews of the documents and votes (where applicable) via email. No new conflicts were reported by the OSMB members.

III. PROJECT OFFICER UPDATE –
The NHLBI Project Officer provided an update to the OSMB members regarding changes affecting the INTERMACS enterprise. In August 2015, the FDA notified the NHLBI that they were withdrawing the site medical device reporting exemption granted in 2007. INTERMACS was required to immediately cease providing initial medical device reports (MDRs) to the FDA and device manufacturers on behalf of the hospitals. The DCC immediately complied with this directive, which required informal notification to manufacturers and hospitals, as well as amending the protocol. The protocol amendment will be discussed in detail shortly. The FDA sent out official notification to all sites concerning this change in October 2015.
In May 2015, the NHLBI and FDA in collaboration with INTERMACS held a workshop to: 1) review the available data from INTERMACS and other clinical studies on instances of pump thrombosis in currently marketed VADs; 2) discuss device-associated risks and how best to mitigate them in clinical practice and research settings; 3) identify research needs and trial opportunities; and 4) provide guidance on the conduct of interventional trials in advanced heart failure patients receiving VADs. Attendees included the INTERMACS Executive Committee, members of the scientific community, as well as representatives from the FDA, CMS, and NHLBI. The workshop succeeded in meeting its goals. Moreover, manuscripts utilizing analyses from Workshop presentations have been accepted for publication by the *Journal of Heart and Lung Transplantation (JHLT)*, which the DCC will discuss.

The INTERMACS enterprise continues to look for ways of ensuring sustainability, leadership has been in discussions with the American College of Cardiology, the Society for Thoracic Surgery and the International Society for Heart and Lung Transplantation. From the NHLBI perspective, the enterprise is strong and able to realign itself in a way that provides long term relevance for INTERMACS. The DCC has been able to streamline operations to increase efficiency and decrease costs.

**IV. OPEN SESSION: OVERALL PROGRESS REVIEW:**

Members of the DCC presented study progress focusing on the period from September 1, 2014 to September 30, 2015.

**A. Response to Previous Recommendations:**

- The Board previously noted that continued oversight by the DAAP will be important and that the DCC should consider expanding. The DCC changed the process for reviewing requests for data to make the process more efficient. They have expanded the committee and review proposals as they come in rather than wait until a certain time.
- The Board recommended that the DCC explore the use of the R13 mechanism to support the annual meeting. The DCC noted that they are in the process of preparing an application to be submitted by the December 12, 2015 deadline to help support the 10th annual meeting in March 2016.
- The Board recommended that the DCC look into AHRQ or PCORI for additional funding, which they are doing.

**B. Scientific Achievements of INTERMACS**

- Two manuscripts describing follow-up analyses on pump thrombosis in the Heartmate II device utilizing the same INTERMACS datasets (University of Alabama at Birmingham and The Cleveland Clinic) and a third manuscript (NHLBI and INTERMACS Study Chair), which further explored the same INTERMACS datasets to give perspective to the two described analyses will be published in the next two months. The Chair asked for copies of these articles when they are available.
- Over the last 13 months, six additional manuscripts utilizing INTERMACS data were published.
• Nineteen abstracts were presented at the 2015 International Society of Heart and Lung Transplantation (ISHLT) Scientific Sessions and published in JHLT. The DCC performed the analyses for 15 of the 19 abstracts.

C. Study Progress Update

• Information Security:
  o A Business Continuity Plan (BCP) is near completion and will guide INTERMACS during any natural and manmade disasters that could impact the ability to operate.
  o NIH Privacy Awareness training for all Data and Clinical Coordinating Center staff was completed in 2015.
  o Two factor authentication is required for all users of the web based data entry system.

• Web Based Data Entry System
  o Sites are now authorized to download their own data directly from the web based data entry system
  o Later this month, sites will also be able to generate lists of their own data with additional capabilities being added in 2016.

• New Site Enrollment
  o Over the last year, 14 new centers enrolled in the registry – 3 pediatric and 11 adult only centers.
  o A total of 38 training sessions were held during the last year, of which eight were for pediatric sites. All 14 new sites have received training.

D. Data Quality

• Specific mechanisms to assure data quality have been implemented such as:
  o Remote audits prior to an on-site audit have increased efficiency and effectiveness.
  o 537 out of 613 requests for programming modifications have been responded to and closed over the past 13 months.
  o Implementation of Protocol 5.0 will increase the ability to reconcile industry and INTERMACS implant counts due to the requirement of redacted hospital implant logs.
  o The single reporter exemption was withdrawn by the FDA in August 2015. The DCC ceased reporting MDRs immediately upon notification, removed all MDR-related information from the website, provided updated site contact information to the FDA to allow them to provide official letters to INTERMACS-participating sites, informally informed industry partners and all sites, and provided FDA contact information and a link to the FDA’s MDR website on the INTERMACS website.

• Audits
  During the contract period all centers will undergo at least one routine on-site audit, and 18 centers had full on-site audits performed during this reporting period. Thirty-six additional centers received remote audits as part of the data
quality monitoring (note: any center with less than a 90% compliance rate receives a remote audit).
- All sites receive a specific quarterly Clinical Summaries report. The hospitals are asked to review the report and correct any inconsistencies. Nurse monitors use this report for conducting both remote and on-site audits.
- Regulatory document audits are also conducted. Any lapse in providing required regulatory documents causes the hospital/site to be inactivated.

E. **Protocol 5.0**
- The following updates and modifications to the Protocol and Manual of Operations and Procedures (MOP) were noted:
  - Broadening the international participation to go beyond Canada
  - All language regarding medical device reporting has been removed
  - Broadening the registry to collect data on “legally utilized” devices (i.e., legally marketed and regulated investigational mechanical circulatory support devices, MCSDs)
  - Educational information was moved to the MOP
  - Clearly stating that adverse events are not adjudicated and that patient information sheets are provided as a courtesy and are not a requirement of INTERMACS
  - For the purposes of transparency and completeness, stating the policy for dataset distribution and analyses within and outside the INTERMACS enterprise

- As soon as the protocol amendment is approved by the OSMB and the UAB IRB, it will be forwarded to the sites, who in turn will forward to their IRBs. In general, the local IRB review process takes approximately 60 days to complete.
- Verbal approval was given by the two Board members present on the call. The remaining members will be asked to review and approve the protocol amendment via email.

F. **Financial Update**
- Hospital fees of $10,000 annually for adult and adult/pediatric centers are still in place.
- In July 2015, pediatric center fees of $5,000 annually began
- In January 2016, per device fee will increase to $200 for industry partners.

G. **Reports**
- The following reports are provided to Federal partners, industry partners, and member hospitals in INTERMACS:
  - Quarterly quality assurance report to hospitals
  - Quarterly Statistical Reports to INTERMACS Federal partners
  - Device-specific reports to manufacturers

H. **Additional Activities**
• The DCC reported on the following activities
  o Weekly Executive Committee Conference Calls with NHLBI, the Study Chair, Principal and Co-investigators, and DCC staff.
  o Steering Committee Meetings quarterly or as needed
  o Data Access, Analysis, and Publications Committee (DAAP) met 3 times via conference call to review proposals during this reporting period.
  o Business Advisory Committee now meets annually and last met on July 23, 2015.
  o Pedimacs Committee meets regularly and held an in-person investigator’s meeting on November 8, 2015 in Orlando. The goal of the meeting was to engage the investigators in Pedimacs and encourage the solicitation of new centers.
  o Medimacs Committee meets quarterly via conference call to review patient enrollment numbers and discuss any issues. NHLBI noted that the Registry Evaluation of Vital Information for VADs in Ambulatory Life (REVIVAL), which started in July 2015, complements Medimacs as it included Medamacs leadership, involves more in-depth data collection of the advanced heart failure population, and allows patients in Medimacs who have been followed for at least 1 year and continue to be medically managed to then enter REVIVAL, with all of the data eventually going into Medamacs.
  o Hospital Standards Committee meets quarterly or as needed. As of September 30, 2015, 98% of the sites have a greater than 90% compliance rate.
  o Quality of Life Committee met three times during this reporting period.

I. Annual Meeting
• The Ninth Annual Meeting held in May 2015 in Baltimore, MD was the largest to date with 188 attendees.
• The Tenth Annual Meeting will be held in March 2016 in Atlanta, GA.

J. Collaborations
• The following collaborations were noted:
  o Heartware Propensity Analysis – an evaluation of the comparability of the HeartWare patients and the HeartMate II patients.
  o HeartWare PAS-001 Retrospective mRS Data Collection
  o With Kathleen Grady, PhD: SUSTAIN-IT (Sustaining Quality of Life of the Aged: Heart Transplant or Mechanical Support?) – a study designed to compare health-related quality of life outcomes in older (60-80 years of age) advanced heart failure patients who undergo heart transplantation or MCSD implantation and their caregivers.
  o Organ Procurement and Transplantation Network (OPTN) – combining two datasets to allow for the most complete assessment of outcomes.

IV. Closed Session:
The Board elected not to hold a closed session as there was no need for it.
V. General Recommendations and Comments:
The Board made the following comments and recommendations:

- The Board commented on the outstanding expertise found at the DCC and noted the quality of research that has been done.
- The Board has preliminarily given verbal approval and support for the continuation of the registry.
- Approval of the protocol amendment was deferred until absentee OSMB members have an opportunity to review Version 5.0. Their review and approval will occur via email.
- As of November 24, 2015, two additional Board members approved the protocol amendment via email, which constitutes a quorum of members.

VI. NEXT MEETING:
The next planned review will be scheduled to convene in approximately 12 months with the specific date to be determined.

Respectfully submitted,

Catherine Burke, MA
INTERMACS OSMB Executive Secretary

Leslee Shaw, PhD
INTERMACS OSMB Chair

___ APPROVAL        _____ DISAPPROVAL

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Director, NHLBI                      Date