Evaluating surgical approaches for cardiac disease

CTSN CARDIOTHORACIC SURGICAL TRIALS network

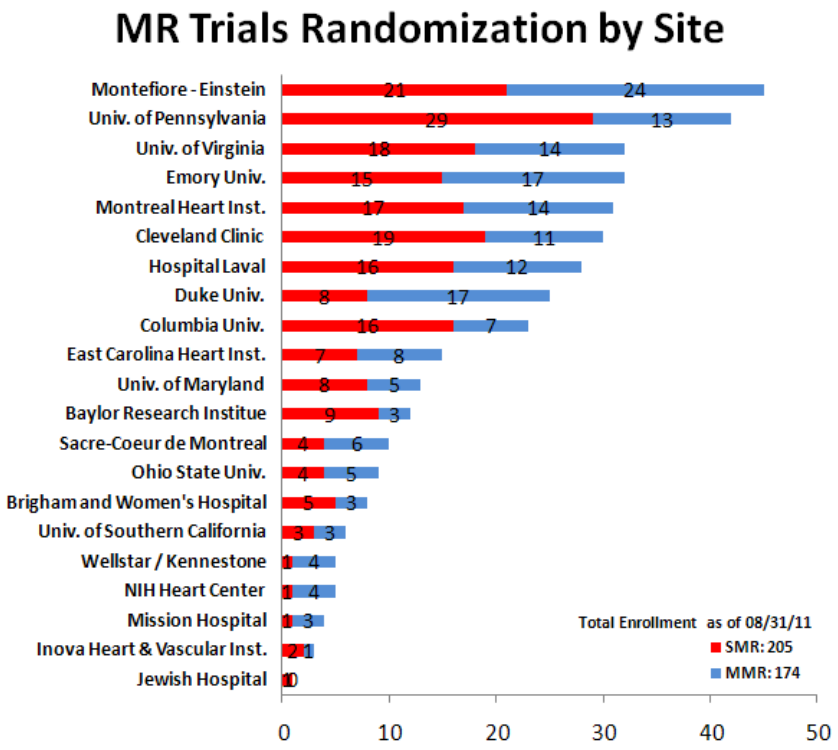
THE NETWORK NEWS

September 2011

Trials Update

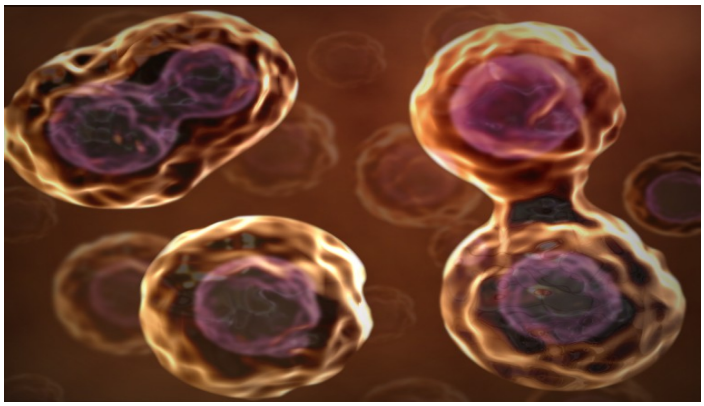
SMR and AF Trials Hit Major Enrollment Milestones

August has been a very successful month for the Network, as the University of Pennsylvania randomized the 200th patient in the severe ischemic mitral regurgitation (SMR) trial. As of 8/31/11, the Network randomized 205 patients in this trial that evaluates the efficacy and safety of mitral valve repair and replacement for severe MR patients. A companion trial, the moderate MR (MMR) trial, evaluates the safety and efficacy of mitral valve repair and CABG vs. CABG alone. The results of these trials will be timely and important as the optimal approach to treatment of patients with ischemic MR remains controversial, leading to significant variations in surgical practice. Investigators expect to complete enrollment in the SMR trial (n=250) in the fall of 2011, and in the MMR trial (n=300) by summer of next year.



In August, we reached another milestone: the University of Virginia randomized the 100th patient in the atrial fibrillation (AF) trial. AF affects an estimated 2.2 million Americans and accounts for over 460,000 hospitalizations annually. AF coexists in 50% of patients undergoing mitral valve surgery; half of those have long-standing AF. The Network designed a comparative effectiveness randomized trial of surgical ablation with left atrial appendage (LAA) closure versus LAA closure alone in patients with (longstanding) persistent AF undergoing MVS. Nested within this trial, is a further randomized comparison of 2 different lesions sets (pulmonary vein isolation only and Maze lesion set). Currently, we randomized 104 patients; the 3 top enrolling sites are the Cleveland Clinic, Montefiore-Einstein and Columbia University. The FDA recently approved expansion from 13 to 23 clinical centers. These new sites are now being launched to enable completion of enrollment in 2012.

FDA Approves LVAD-Cell Therapy Trial



LVAD therapy has disseminated widely and outcomes have improved over time. However, adverse events could be minimized and QoL improved if the duration of support could be limited by inducing myocardial recovery through cell therapy. In collaboration with the Cardiovascular Cell Therapy Research Network, CTSN developed a translational trial that will evaluate the safety, and explore the efficacy, of direct myocardial injection of off-the-shelf mesenchymal precursor cells in LVAD recipients.

The FDA recently approved the protocol, start-up activities are underway and training of site coordinators will begin in mid-fall.

Stem Cell Therapy in Cardiac Transplantation Recipients

The Network's stem cell research portfolio includes a study exploring the safety and feasibility of intra-coronary injections of autologous cardiac stem cells following cardiac transplantation. This trial will provide important exploratory information regarding safety and the ability of stem cells to engraft and differentiate within the scaffold of the transplanted heart. The rationale for this research is to modulate tolerance and reduce the incidence of allograft rejection. A pre-IND meeting to discuss the protocol with the FDA will take place in September.

Ticagrelor Post CABG

In collaboration with the VA Cooperative Clinical Studies Program, the Network is designing a large, simple trial evaluating the effect of adding ticagrelor to aspirin after CABG. The primary efficacy endpoint is MACCE and the primary safety endpoint is severe bleeding. The sample size in this event-driven trial will be close to 5,000 patients, and the trial is designed to detect a 20% reduction in the primary efficacy endpoint.

What's New ?

Upcoming meetings:

October 11—All Canadian Investigator Meeting (Toronto)
October 19—Investigator Meeting (Bethesda, MD)
November Coordinator Meeting TBD

Predictors of Infections Following Cardiac Surgery

Infection Type	# of events	# of patients	% of patients
Pneumonia	125	123	2.4%
C. Difficile Colitis	49	48	0.9%
Bloodstream Infection	41	39	0.8%
Deep Incision Surg site infection (sternum)	27	26	0.5%
Mediastinitis	12	12	0.2%
Deep Incision Surg site infection (groin/leg)	10	10	0.2%
Myocarditis or pericarditis	5	4	0.1%
Device-related percut site infection	4	4	0.1%
Empyema	3	2	0.04%
Endocarditis	3	3	0.04%
LVAD Pocket infection	1	1	0.02%

Hospital-acquired infections represent the major non-cardiac complication after heart surgery, which are associated with substantial morbidity, mortality and prolonged hospitalizations. The Network enrolled nearly 5200 patients in a prospective cohort study to identify modifiable management practices and patient characteristics predictive of post-op infections. *Major infections* occurred in 5% of patients; interestingly, although much of the focus in the surgical literature has been on sternal wound infections and mediastinitis, 75% of major infections in our study are pneumonia, C. Diff. colitis, and bloodstream infections. These results will be presented at upcoming national meetings, and publications are in process.

Core Clinical Centers

Cleveland Clinical Foundation (E. Blackstone, M. Gillinov)
Columbia University Medical Center (M. Argenziano)
Duke University (P. Smith)
East Carolina Heart Institute (B. Ferguson)
Emory University (J. Puskas)
Montefiore Medical Center - Albert Einstein College of Medicine (R. Michler)
Montreal Heart Institute (L. Perrault)
NIH Heart Center at Suburban Hospital (K. Horvath)
University of Pennsylvania (M. Acker)
University of Virginia Health Systems (I. Kron)

Ancillary Clinical Centers

Hôpital du Sacré-Cœur de Montréal (P. Pagé)
Inova Heart & Vascular Institute (A. Speir)
Institut Universitaire de Cardiologie de Québec (Hôpital Laval) (P. Voisine)
Ohio State University Medical Center (S. Sudhakar)
WellStar Health System, Kennestone Hospital (W. Cooper)

Satellite Clinical Centers

Baylor Research Institute (M. Mack)
Baystate Medical Center (J. Rousou)
Brigham and Women's Hospital (F. Chen)
Christiana Care Health System (R. Blackwell)
Lankenau Institute for Medical Research (S. Goldman)
Mission Hospital, Inc. (M.Groh)
Sunnybrook Health Sci.Centre (G. Cohen-Nehemia)
University of Alberta Hospital (J. Mullen)
University of Chicago (V. Jeevanandam)
University of Maryland Medical Center (J. Gammie)
University of Michigan (S. Bolling)
University of North Carolina—Chapel Hill (A. Kiser)
University of Southern California (M. Bowdish)
Washington Univ. School of Medicine (R. Damiano)
Yale University (A. Mangi)

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Find us on the web:
http://www.ctsurgerynet.org
Or contact:

Ellen Moquete, RN, BSN
ellen.moquete@inchoir.org