



Heart & Vascular Center **ADVANCES**

MOMENTUM 3 Results Lead Late Breaking Clinical Trial News at 2016 AHA Scientific Sessions

At the November 2016 American Heart Association (AHA) Scientific Sessions in New Orleans, Mandeep R. Mehra, MD, Executive Director of the Center for Advanced Heart Disease and Medical Director of the Heart & Vascular Center at Brigham and Women's Hospital (BWH), announced groundbreaking results of the first primary endpoint from the MOMENTUM 3 clinical trial. The results were published simultaneously online in the *New England Journal of Medicine* and will appear in a future issue of the publication.

MOMENTUM 3 (*Multi-center Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3*) is the largest and fastest enrolling left ventricular assist device (LVAD) trial to date. Dr. Mehra is the national co-principal investigator and Chair of the Publications Committee of this randomized study evaluating a novel centrifugal flow pump (HeartMate 3™ left ventricular assist system) compared with a commercial axial flow pump (HeartMate II™ left ventricular assist system) in patients with advanced heart failure at 69 experienced centers throughout the United States.

The primary endpoint of this study was a composite of survival at six months, free of disabling stroke or reoperation to replace or remove the device. In this six-month pre-specified Intent to Treat (ITT) analysis, patients were enrolled regardless of whether the pump was intended as bridge to transplantation or destination therapy.

"This study is a practice changer in the ventricular assist device arena and a culmination of what we have learned over more than two decades of research and innovation," said Dr. Mehra. "It represents an incremental benefit for our patients in need of left heart support to relieve their suffering from advanced heart disease."

Pragmatic Design Accelerates Study Timeline

The adaptive and pragmatic style of MOMENTUM 3 has enabled the research team to dramatically reduce the overall trial timeline from the typical seven-to-nine years to two years by applying the therapy to an all-comer patient

continued on page 4

brighamandwomens.org/heart

Contact us:

(617) 732-9894

bwhreferrals@partners.org

Page 2

New Biologic Vessel Studied for Its Promise for Patients with Advanced Peripheral Arterial Disease and End Stage Renal Disease

Page 3

BWH Chief Leads International One Brave Idea Team to Define Early Markers and Causes of Coronary Artery Disease

BWH News



New Biologic Vessel Studied for Its Promise for Patients with Advanced Peripheral Arterial Disease and End Stage Renal Disease

Vascular surgeons at Brigham and Women's Hospital (BWH) are at the forefront of several trials of a novel tissue-engineered vascular conduit that may alleviate challenges seen with synthetic vascular grafts and autologous vessels.

"This is the first truly bioengineered vessel that has reached this stage of clinical development for vascular use," according to Michael Belkin, MD, Chief of the Division of Vascular and Endovascular Surgery at BWH. "We are hopeful that the vessel will demonstrate advantages over the currently available treatment options for patients with PAD and ESRD."

Composed of human collagen and other extracellular matrix proteins, the vessel is built by human cells. Then, it undergoes a multi-step process to clear the cells, cellular debris, and antigenic material that could lead to immune response. A recently completed Phase II study showed no detectable immune response from study subjects.

Earlier studies of the vessel also suggest that the collagen matrix comprising the vessel may be infiltrated and remodeled with host cells following implantation, which potentially could positively affect the vascular access. The vessel has the potential to be stored onsite in a hospital – making it readily available for implementation.

National Early-phase Study in PAD

Dr. Belkin is the Principal Investigator for an NIH-supported national study of the vessel in patients with peripheral arterial disease (*A Phase 2 Study for the Evaluation of Safety and Efficacy of Humacyte's Human Acellular Vessel for Use as a Vascular Prosthesis for Femoro-Popliteal Bypass in Patients with Peripheral Arterial Disease*). BWH is one of four sites in the United States that have been selected to participate in this prospective, open-label single-treatment-arm Phase II study to evaluate the safety and efficacy of the Human Acellular Vessel (HAV) in patients with peripheral arterial disease who are undergoing femoro-popliteal bypass surgery.

One of the primary objectives of the study will be to determine the patency of the HAV at 12 months post-implantation. Secondary objectives include further assessment of safety in terms of patient immune response and determination of the rates of HAV interventions required to keep the HAV patent. *For more information, or to refer a patient for this trial, please contact Michael Belkin, MD, at mbelkin@partners.org.*

International Phase 3 Study in ESRD

BWH Vascular Surgeon C. Keith Ozaki, MD, is the Site Principal Investigator of an international randomized two-arm Phase III study comparing the new vessel with expanded polytetrafluoroethylene (ePTFE) grafts as conduits for hemodialysis in ESRD patients who are not candidates for fistula placement –



Vascular surgeons Michael Belkin, MD, and C. Keith Ozaki, MD, are leading trials of a tissue-engineered vascular conduit.

An Assessment of Humacyte's Human Acellular Vessel in Patients Needing Renal Replacement Therapy: A Comparison With ePTFE Grafts as Conduits for Hemodialysis (HUMANITY). Randomization occurs at the time of surgery and is stratified by upper arm or forearm placement based on the Principal Investigator's clinical determination.

Each subject will be followed by study-specific visits until they complete 24 months of follow-up after implantation, regardless of patency status. After two years, only subjects with a patent conduit will be followed up to five years post-implantation at routine study visits. This study is ongoing and recruiting participants. *For more information, or to refer a patient for this trial, please contact C. Keith Ozaki, MD, at ckozaki@partners.org.*

"If the new vessel proves to be beneficial in patients with ESRD and PAD, it may be able to assist with vascular therapies in other areas as well, including the heart," said Dr. Ozaki.



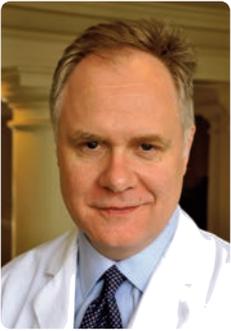
Michael Belkin, MD
Chief, Division of Vascular and Endovascular Surgery



C. Keith Ozaki, MD
Vascular Surgeon, Division of Vascular and Endovascular Surgery

Contact Us – To learn more or to refer a patient, please call our referral coordinators at (617) 732-9894.

BWH NEWS



BWH Chief Leads International One Brave Idea Team to Define Early Markers and Causes of Coronary Artery Disease

Calum MacRae, MD, PhD, Chief of the Division of Cardiovascular Medicine at Brigham and Women's Hospital (BWH), is leading a global team to identify the earliest genetic and molecular signs of coronary heart disease and introduce new preventative and therapeutic strategies. The team was selected among more than 340 applicants to receive the One Brave Idea™ Research Award, a five-year, \$75 million award from the American Heart Association (AHA), Verily Life Sciences (formerly Google Life Sciences), and AstraZeneca. "BWH has been at the forefront of coronary heart disease advances, from aspirin and thrombolytics to stents and statins, for more than 50 years," said Dr. MacRae. "We are now building on our knowledge by bringing

together an unprecedented team of experts to examine and address coronary heart disease from its very beginnings – decades before symptoms appear and adverse events occur."

Key Initiatives

Primary areas of focus for the team will include:

- Use of modern wearable technologies to measure blood vessel reactivity and other physiological changes in families and in large populations in order to better detect the earliest abnormalities related to the risk of coronary artery disease.
- Development of large biological data sets to inform disease research. Validation phases of the study will employ two established study groups – the Framingham Heart Study and the Million Veteran Program (MVP).
- Deep examination of families at high risk for coronary artery disease to determine new biomarkers, new cell biology and behavioral factors that may be prevalent in broader populations.
- Novel strategies to leverage existing and emerging medications in new ways, such as identifying patients who may benefit from therapeutic interventions earlier.
- Researching alternate ways to use time spent with patients in clinic visits by directly engaging patients in data collection.



Gerard M. Doherty, MD, Named Chair of Department of Surgery

Gerard M. Doherty, MD, recently joined Brigham and Women's Hospital as Chair of the Department of Surgery and Surgeon-in-Chief, from Boston Medical Center, where he served as Surgeon-in-Chief. Dr. Doherty has dedicated his career to advancing the care of patients with endocrine tumors and conditions and his research interests include regeneration of parathyroid cells in hypoparathyroid patients. Dr. Doherty is a member of the Complex General Surgical Oncology Board for the American Board of Surgery and is the developer of the AccessSurgery platform for disseminating surgical information including books, images and videos for training. Additionally, he has written more than 250 peer-reviewed articles.

Marc A. Pfeffer, MD, PhD, Earns HFSA Lifetime Achievement Award

Marc A. Pfeffer, MD, PhD, of the Division of Cardiovascular Medicine, recently received a lifetime achievement award for his contributions to the understanding of ventricular remodeling and treatments for heart failure. The award was presented at the Heart Failure Society of America's (HFSA's) annual scientific assembly. Dr. Pfeffer is a highly cited international medical scientist and clinician who has also been awarded the American Heart Association's Herrick Award and Clinical Research Prize, the William Harvey Award of the American Society of Hypertension and the Okamoto Award from the Japanese Circulatory Society.



Peter Libby, MD, Honored with 2016 Ernst Jung Gold Medal for Medicine

Peter Libby, MD, of the Division of Cardiovascular Medicine, received the 2016 Ernst Jung Gold Medal for Medicine, presented by the Ernst Jung Foundation in Hamburg, Germany, which honors exceptional contributions to medical progress and the entire lifetime achievement of a scientist in research and clinical work. Among his many achievements, Dr. Libby served as chief of the Division of Cardiovascular Medicine from 1998 to 2014 and director of Vascular Medicine from 1990 to 1998. His areas of clinical expertise include general and preventive cardiology, with current research focusing on the role of inflammation in vascular diseases, such as atherosclerosis. He is an editor of *Braunwald's Heart Disease*.

MOMENTUM 3 Results Lead Late Breaking Clinical Trial News at 2016 AHA Scientific Sessions...

continued from cover

population with refractory heart failure in need of a circulatory support pump regardless of transplant candidacy. Traditional trials in this arena first undergo safety testing followed by testing younger populations with less co-morbidity who are candidates for a heart transplantation. Typically, the broad population of patients ineligible for transplantation must wait for several years before application of such therapy.

“This is important to our patient population, as one third of patients do not fall neatly into bridge-to-transplant or destination therapy, 28 percent of patients who are initially deemed transplant eligible are still on LVAS support after two years, and over 40 percent of patients are removed from the transplant list over time due to complications or clinical preference,” said Dr. Mehra. “Removing restrictions based on transplant status resulted in a unique study that has been extremely successful in its enrollment and highly expeditious in delivering results.”

Greater Durability Demonstrated

For the pivotal six month analysis, 294 patients were enrolled, with 152 receiving the HeartMate 3 centrifugal flow pump and 142 receiving the Heartmate II axial flow pump between September 2014 and October 2015 at 47 of the 69 sites. The primary outcome of survival with no disabling stroke or reoperation to replace or remove the device was met in 86 percent of patients who received the new centrifugal flow pump and 77 percent of patients who received the axial flow pump. While there was no statistical difference between the devices in terms of deaths or disabling strokes, reoperation for pump malfunction was significantly less with the centrifugal flow pump. No pump thrombosis occurred in the centrifugal flow pump during the six-month study period compared with 18 cases in 14 patients who received the axial flow pump, representing a 45 percent improvement in favor of the centrifugal flow pump.

Two-year Analysis Expected in Late 2018

To date, 1,028 patients total have been enrolled in the full cohort of the MOMENTUM 3 trial. In May 2015, the trial began its expansion phase and completed enrollment by August 2016. The MOMENTUM 3 trial’s analysis at 24 months will provide long-term information about survival, stroke rates, and durability of the new device.



Mandeep R. Mehra, MD
Executive Director, Center for Advanced Heart Disease,
Medical Director, Heart & Vascular Center

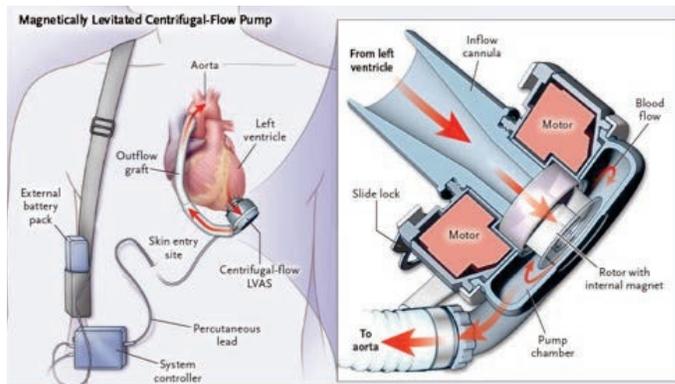
Key Technological Advantages of the Centrifugal Flow Pump

The HeartMate 3 is a revolutionary fully magnetically levitated frictionless pump without mechanical bearings that is designed to reduce shear stress on blood elements and avoid pump thrombosis. Although this pump is smaller in profile than the Heartmate II pump, this pump includes wider blood-flow passages that reduce wear and tear on circulating blood cells. The novel device is also programmable to change the pump seed which allows for an artificial pulse that is asynchronous with the patient’s native heartbeat to reduce stasis within the pump. The pump’s compact size enables it to be placed directly in the chest rather than in the abdominal cavity area.



HeartMate II LVAS

The HeartMate II LVAS is a mechanical bearing axial continuous-flow blood pump which is the only device in the US approved for both Bridge-To-Transplant (BTT) and Destination Therapy (DT) patients.



HeartMate 3 LVAS

The HeartMate 3 LVAS is a centrifugal-flow, fully magnetically levitated blood pump engineered to minimize destruction of red blood cells and thrombosis.



**BRIGHAM AND
WOMEN'S HOSPITAL**

75 Francis Street, Boston, MA 02115
1-800-MD-TO-BWH

A FOUNDING MEMBER OF **PARTNERS**
HEALTHCARE