COAPT Trial: Overview

Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation

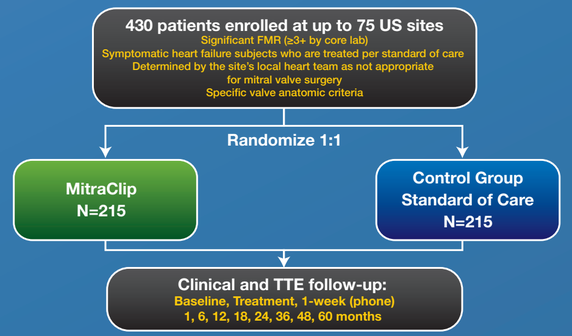
Purpose

- COAPT is a landmark trial to further study the MitraClip device in symptomatic FMR patients with heart failure
- The study will generate important clinical and economic data to support reimbursement and evidence to support the development of treatment guidelines
- COAPT is the first randomized controlled clinical trial to compare non-surgical (medical) standard of care treatment to a percutaneous intervention to reduce MR

Objective

- To evaluate the safety and effectiveness of the MitraClip System for treatment of functional mitral regurgitation (FMR ≥3+) in symptomatic heart failure subjects who are treated per standard of care and who have been determined by the site's local heart team as not appropriate for mitral valve surgery

Trial Design



Clinical Investigational Plan 11-512: Version 5.1, November 11, 2013.
COAPT protocol approved by FDA July 27, 2012.

Key Inclusion Criteria

- Functional MR ≥3+ due to cardiomyopathy of either ischemic or non-ischemic etiology
  - Qualifying TTE must be obtained after subject has been stabilized on optimal therapy
- Symptomatic (NYHA class II, III or ambulatory IV)
- Local Site Heart Team (CT surgeon and HF specialist investigators) and the Central Eligibility Committee concur that surgery will not be offered as a treatment option and that medical therapy is the intended therapy for the subject, even if the subject is randomized to the Control group.
- The subject has had at least 1 HF hospitalization in the 12 months prior to enrollment and/or a corrected BNP ≥300 pg/ml or nT-proBNP ≥1500 pg/ml measured within 90 days prior to registration.
- Subject has been adequately treated per applicable standards for CAD, LV dysfunction, MR or HF (CRT, revascularization, and/or OMT).
- The primary regurgitant jet is non-commissural. If secondary MR jets exist, they must be considered clinically insignificant.
- CK-MB obtained within prior 14 days less than local laboratory upper limit of normal (ULN)

Key Exclusion Criteria

- Leaflet anatomy which may preclude MitraClip implantation, proper MitraClip positioning on the leaflets, or sufficient MR reduction by the MitraClip.
- MV orifice area <4 cm^2, confirmed by the Site 90 days prior to registration
- CABG or PCI in prior 30 days
- CVA within 30 days prior to subject registration
- Carotid surgery within 30 days prior to subject registration
- Severe symptomatic carotid stenosis (>70% by ultrasound)
- Physical evidence of right-sided congestive heart failure with echocardiographic evidence of moderate or severe right ventricular dysfunction
- Tricuspid valve disease or aortic valve disease requiring surgery
- ACC/AHA Stage D heart failure

Primary Endpoints

Primary Effectiveness (minimum 1-year follow-up on all patients)
- Recurrent heart failure hospitalizations

Primary Safety (1 year)
- Composite of Single Leaflet Device Attachment (SLDA), device embolizations, endocarditis requiring surgery, Echocardiography Core Laboratory confirmed mitral stenosis requiring surgery, and any device related complications requiring non-elective cardiovascular surgery at 12 months

Secondary Endpoints

Secondary Effectiveness
- MR severity at 12 months
- Change in 6MWD at 12 months
- Change in Quality of Life score (KCCQ) at 12 months
- Change in LVEDV at 12 months
- Reduction to NYHA Functional Class I/II at 12 months
- Hierarchical composite of death and recurrent HF hospitalization (analyzed when the last subject completes 12 months of follow-up)
- Recurrent hospitalizations – all-cause (analyzed when the last subject completes 12 months of follow-up)

Secondary Safety
- Composite of death (all-cause), stroke, MI, non-elective CV surgery for device related complications in Device group at 30 days

Status

Enrollment as of August 18, 2014:

Screened	477
Randomized	113
Roll-ins	37

Data on file at Abbott Vascular

For more information, please contact:
info@COAPTtrial.com
http://www.COAPTtrial.com

Study Organization

National PIs
Michael Mack, M.D.
Gregg W. Stone, M.D.

Heart Failure Co-PIs
William Abraham, M.D.
JoAnn Lindenfeld, M.D.

Sponsor
Evalve, Inc., a subsidiary of Abbott Vascular Inc.

Multidisciplinary Steering Committee

Interventional Cardiologists
Gregg W. Stone, M.D. (Co-Chair)
Ted Feldman, M.D.
Samir Kapadia, M.D.

Cardiothoracic Surgeons
Michael Mack, M.D. (Co-Chair)
Steve Bolling, M.D.
Patrick McCarthy, M.D.

Heart Failure Specialists
William Abraham, M.D.
JoAnn Lindenfeld, M.D.

Echocardiographer
Paul Grayburn, M.D.

Sponsor Representative
Gary Thompsom

Advisory Committees

Heart Failure
William Abraham, M.D
Joann Lindenfeld, M.D.
Michael Zile, M.D.

Interventional Cardiology
Gregg W. Stone, M.D.
Ted Feldman, M.D.
Saibal Kar, M.D.
Brian Whisenant, M.D.
Samir Kapadia, M.D.
William Gray, M.D.
James Hermiller, M.D.
Howard Hermann, M.D.

Surgery
Michael Mack, M.D.
Patrick McCarthy, M.D.
Steven Bolling, M.D.
Craig Miller, M.D
Marc Gillinov, M.D.

Echocardiography
Paul Grayburn, M.D.
Maurice Sarano, M.D.
Neil Weissman, M.D.
Elyse Foster, M.D.
Robert Siegel, M.D.
Rebecca Hahn, M.D.

Central Eligibility Committee

Role:
- Responsible for approving that the subject has been optimally treated prior to being considered for the trial and that the patient is not appropriate for mitral valve surgery, even if randomized to the Control group

Composition:
- Physician moderator
- Cardiothoracic Surgeon with experience in mitral valve surgery
- Heart Failure Specialist

Format:
- Weekly meetings: Site PI and site mitral valve surgeon present to the committee
- Patients will be approved, denied or deferred

Heart Failure Specialists
Michael Zile, M.D.
James Udelson, M.D.
William Abraham, M.D.
JoAnn Lindenfeld, M.D.

Physician Moderators
Gregg W. Stone, M.D.
Paul Grayburn, M.D.
Scott Lim, M.D.

Cardiothoracic Surgeons
Rakesh Suri, M.D.
James Gammie, M.D.
Marc Gillinov, M.D.
Steve Bolling, M.D.
Patrick McCarthy, M.D.
Donald Glower, M.D.
David Heimansohn, M.D.

Echocardiographic Core Laboratory (ECL)
Neil Weissman, MD, Director
MedStar Health Research Institute
(Hyattsville, MD)

Clinical Events Committee (CEC)
Alejandra Guerichoff, Ph.D
Cardiovascular Research Foundation
(New York, NY)

Data Monitoring Committee
Alejandra Guerichoff, Ph.D
Cardiovascular Research Foundation (New York, NY)