MITRACLIP™ DATA FACT SHEET

WHAT IS MITRACLIP?

Abbott's MitraClip™ is the world's first transcatheter mitral valve repair (TMVr) therapy that provides select people living with primary and secondary mitral regurgitation (MR) with a minimally invasive treatment option. The MitraClip system is the first-of-its-kind and only transcatheter mitral valve therapy with more than 16 years of clinical experience and proven safety, survival, and durable clinical outcomes focused on addressing the critical unmet needs of people who are not candidates for open-heart surgery.

The device is a small metal clip covered with a polyester fabric that is implanted in the mitral valve to repair primary and secondary MR. The nonsurgical, minimally invasive device repairs leaky mitral valves and is delivered to the heart through a small incision in the leg. The therapy works by grasping together portions of the leaflets, or flaps, of the mitral valve to reduce MR, which allows the heart to pump blood more efficiently, thereby relieving symptoms and improving patient quality of life. Backed by years of positive long-term outcomes, and built on the foundation of findings from the EVEREST, REALISM and COAPT studies, the device is proven to achieve the highest MR reduction[1] and is now in its fourth-generation of innovation. MitraClip G4 provides more treatment options by offering a tailored repair and predictable procedure experience for physicians.[1,2]

MITRACLIP IS APPROVED IN MORE THAN 75 COUNTRIES WORLDWIDE, SPANNING REGIONS IN ASIA, AFRICA, EUROPE, THE AMERICAS, AND AUSTRALIA.

MITRACLIP CLINICAL DATA

COAPT TRIAL

The landmark **C**ardiovascular **O**utcomes **A**ssessment of the MitraClip **P**ercutaneous **T**herapy for Heart Failure Patients with Functional Mitral Regurgitation (COAPT™) trial investigated MitraClip for the treatment of secondary MR due to left ventricular dysfunction. The study unequivocally showed that patients who received the MitraClip device not only lived longer but were hospitalized less frequently for heart failure and had a better quality of life compared to patients who received only medical therapy.[3]

Three-year data from the COAPT trial using MitraClip in patients with heart failure and severe MR found that transcatheter mitral leaflet approximation with MitraClip was safe, reduced hospitalization rates and improved survival and quality of life, compared to medical therapy alone. The findings demonstrated that MitraClip is the first therapy shown to improve prognosis by reducing secondary MR.[4]

Results published in *Circulation* (2019), also showed that transcatheter mitral valve repair using the MitraClip device in heart failure patients with secondary MR was cost-effective and projected to increase life-expectancy and quality of life improvements at an incremental cost, compared to guideline-directed medical therapy (GDMT) alone.[5] These results may further help inform a coverage review being conducted by the Centers for Medicare & Medicaid Services' (CMS) for an expanded National Coverage Determination (NCD) designation for MitraClip,[6] with the proposed decision memo expected in 2020.

THERE ARE TWO TYPES OF MR:

Primary (degenerative) and secondary (functional) MR. **Primary MR** is usually due to an abnormality of the mitral valve, which can be related to age, a birth defect, or underlying heart disease, while **secondary MR** occurs in patients with coronary disease or heart failure.

See Important Safety Information referenced within.

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EXPAND STUDY

The multi-center, global EXPAND study was initiated to evaluate real-world clinical outcomes associated with the third-generation MitraClip NTR/XTR Clip Delivery Systems, which has expanded the treatment of MR to a broader range of anatomies in an all-comer population. Data from this study continues to support the safety and efficacy of the MitraClip device. The EXPAND study enrolled a total of 1,041 patients at 57 sites in the United States, Europe, and the Middle East and represents the largest real-world Echo-Core Lab dataset reported to date.[1]

The EXPAND study late-breaking data presented at the 2020 virtual PCR e-Course demonstrated that primary and secondary MR patients treated with MitraClip NTR/XTR System experienced significantly greater MR reduction (compared to older generation systems), low mortality rates as well as improvements in quality of life and functional capacity. These results confirmed the safety and efficacy of the MitraClip NTR/XTR system at reducing MR in a real-world setting.[1] Additional analyses and longer-term follow-up is currently underway for patients enrolled in the EXPAND study.

POST-APPROVAL STUDY 1 MITRACLIP REGISTRY

The Society of Thoracic Surgeons (STS)/ACC Transcatheter Valve Therapy (TVT) Registry™ is a benchmarking tool developed to track patient safety and real-world outcomes related to transcatheter valve replacement and repair procedures and emerging treatments for valve disease patients.

The real-world Post-Approval Study 1 MitraClip Registry is based on data extracted from the first 2,000 MitraClip patients consecutively entered into the TVT Registry. According to 30-day and one-year data from the first and largest study of site-reported echocardiographic and clinical (functional and quality of life) outcomes for the MitraClip System provided meaningful symptom improvement and quality of life in primary MR.[7]

RESEARCH UNDERWAY

REPAIR MR TRIAL

The first-of-its-kind prospective, randomized, controlled trial, REPAIR MR is evaluating the impact of MitraClip therapy on long-term clinical outcomes in moderate surgical risk patients with severe primary MR who are often limited to open-heart surgery, which is the current standard of care. The trial's design addresses the issue that, despite symptoms or other co-morbidities, elderly patients suffering from primary MR are often undertreated by open-heart mitral valve surgery. The trial is intended to show whether, in such patients, MitraClip offers an alternative treatment option, compared to open-heart surgery.

The primary endpoint was determined after careful review of the risks and benefits associated with the device and surgery, and is a composite of mortality, stroke, acute kidney injury or cardiac hospitalizations (excluding hospitalizations within 30-days) at two years, with follow-up continuing to 10 years. Abbott announced FDA approval for the trial in January 2020 and seeks to enroll 500 patients at 60 sites in the United States, Canada, and Europe to evaluate MitraClip's effectiveness in this patient population. This trial is another example of Abbott's commitment to providing solutions that offer improved benefit-to-risk, compared to the existing standard of care.

EXPAND G4

The EXPAND G4 prospective, multi-center, single arm, observational study of the fourth-generation MitraClip is an international post-market evaluation of the device being used for the treatment of MR in a contemporary real world setting.

ABBOTT'S COMMITMENT

Abbott creates life-changing technologies to help people with serious heart abnormalities, such as damaged heart valves or other heart defects. As a global healthcare leader that helps people live more fully at all stages of life, we have the most comprehensive structural heart portfolio in the industry. Through its cardiac devices and research, Abbott is addressing the critical unmet needs of people by providing life-saving therapies and offering patients a renewed chance at life.

References

1. Rottbauer W. D. Contemporary Clinical Outcomes with MitraClip™ (NTR/XTR) System: Core-lab Echo Results from +1000 Patient the Global EXPAND Study. Data presented at PCR 2020.
2. Tests performed by and data on file at Abbott.
3. Nishimura RA. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2017;136(9):1-123. DOI: 10.1161/CIR.0000000000000503.
4. Mack, M., Abraham, W. T., Lindenfeld, J. A., & Stone, G. W. (n.d.). A Randomized Trial of Transcatheter Mitral Valve Leaflet Approximation in Patients with Heart Failure and Secondary Mitral Regurgitation. Data presented at Transcatheter Cardiovascular Therapeutics (TCT) 2019.
5. Baron, S. J., Wang, K., Arnold, S. V., Magnuson, E. A., Whisenant, B., Brieke, A., Cohen, D. J. (2019). Cost-Effectiveness of Transcatheter Mitral Valve Repair Versus Medical Therapy in Patients With Heart Failure and Secondary Mitral Regurgitation. Circulation, 140(23), 1881–1891. doi: 10.1161/circulationaha.119.043275
6. Medicare Coverage Database. National Coverage Analysis (NCA) Tracking Sheet for Transcatheter Mitral Valve Repair (TMVR) (CAG-00438R). August 2019.
7. Hermiller J. The Abbott Post-Approval Study 1 MitraClip Registry: 1-Year Results of the First 2,000 Patients in the STS/ACC TVT Registry. Data presented at SCAI 2018.

See Important Safety Information referenced within.

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IMPORTANT SAFETY INFORMATION

MITRACLIP CLIP DELIVERY SYSTEMS

Rx ONLY

INDICATION FOR USE

- The MitraClip™ G4 System is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR ≥ 3+) due to primary abnormality of the mitral apparatus [degenerative MR] in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation.

- The MitraClipTM G4 System, when used with maximally tolerated guideline-directed medical therapy (GDMT), is indicated for the treatment of symptomatic, moderate-to-severe or severe secondary (or functional) mitral regurgitation (MR; MR ≥ Grade III per American Society of Echocardiography criteria) in patients with a left ventricular ejection fraction (LVEF) ≥ 20% and ≤ 50%, and a left ventricular end systolic dimension (LVESD) ≤ 70 mm whose symptoms and MR severity persist despite maximally tolerated GDMT as determined by a multidisciplinary heart team experienced in the evaluation and treatment of heart failure and mitral valve disease.

CONTRAINDICATIONS

The MitraClipTM G4 System is contraindicated in patients with the following conditions:

- Patients who cannot tolerate, including allergy or hypersensitivity to, procedural anticoagulation or post procedural anti-platelet regimen
- Patients with known hypersensitivity to clip components (nickel / titanium, cobalt, chromium, polyester), or with contrast sensitivity
- Active endocarditis of the mitral valve
- Rheumatic mitral valve disease
- Evidence of intracardiac, inferior vena cava (IVC) or femoral venous thrombus

WARNINGS

- **DO NOT use MitraClip™ outside of the labeled indication.**
- The MitraClip™ G4 Implant should be implanted with sterile techniques using fluoroscopy and echocardiography (e.g., transesophageal [TEE] and transthoracic [TTE]) in a facility with on-site cardiac surgery and immediate access to a cardiac operating room.
- Read all instructions carefully. Use universal precautions for biohazards and sharps while handling the MitraClip™ G4 System to avoid user injury. Failure to follow these instructions, warnings and precautions may lead to device damage, user injury or patient injury, including:
  - MitraClip™ G4 Implant erosion, migration or malposition
  - Failure to deliver MitraClip™ G4 Implant to the intended site
  - Difficulty or failure to retrieve MitraClip™ G4 system components
- Use caution when treating patients with hemodynamic instability requiring inotropic support or mechanical heart assistance due to the increased risk of mortality in this patient population. The safety and effectiveness of MitraClip™ in these patients has not been evaluated.
- For the Steerable Guide Catheter and Delivery Catheter only:
  - The Guide Catheter: the distal 65 cm of the Steerable Guide Catheter with the exception of the distal soft tip, is coated with a hydrophilic coating.
  - The Delivery Catheter: coated with a hydrophilic coating for a length of approximately 131 cm.
  - Failure to prepare the device as stated in these instructions and failure to handle the device with care could lead to additional intervention or serious adverse event.
- The Clip Delivery System is provided sterile and designed for single use only. Cleaning, re-sterilization and / or re-use may result in infections, malfunction of the device and other serious injury or death.
- Note the product "Use by" date specified on the package.
- Inspect all product prior to use. Do not use if the package is open or damaged, or if product is damaged.

PRECAUTIONS

- Prohibitive Risk Primary (or degenerative) Mitral Regurgitation
  - Prohibitive risk is determined by the clinical judgment of a heart team, including a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, due to the presence of one or more of the following documented surgical risk factors:
    - 30-day STS predicted operative mortality risk score of
      - ≥8% for patients deemed likely to undergo mitral valve replacement or
      - ≥6% for patients deemed likely to undergo mitral valve repair
  - Porcelain aorta or extensively calcified ascending aorta.
  - Frailty (assessed by in-person cardiac surgeon consultation)
  - Hostile chest
  - Severe liver disease / cirrhosis (MELD Score > 12)
  - Severe pulmonary hypertension (systolic pulmonary artery pressure > 2/3 systemic pressure)
  - Unusual extenuating circumstance, such as right ventricular dysfunction with severe tricuspid regurgitation, chemotherapy for malignancy, major bleeding diathesis, immobility, AIDS, severe dementia, high risk of aspiration, internal mammary artery (IMA) at high risk of injury, etc.
  - Evaluable data regarding safety or effectiveness is not available for prohibitive risk primary patients with an LVEF < 20% or an LVESD > 60 mm. MitraClip™ should be used only when criteria for clip suitability for primary have been met.
  - The heart team should include a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease and may also include appropriate physicians to assess the adequacy of heart failure treatment and valvular anatomy.
- Secondary Mitral Regurgitation
  - Evaluable data regarding safety or effectiveness is not available for secondary MR patients with an LVEF < 20% or an LVESD > 70 mm.
  - The multidisciplinary heart team should be experienced in the evaluation and treatment of heart failure and mitral valve disease and determine that symptoms and MR severity persist despite maximally tolerated GDMT. rohibitive Risk Primary (or degenerative) Mitral Regurgitation

POTENTIAL COMPLICATIONS AND ADVERSE EVENTS

The following ANTICIPATED EVENTS have been identified as possible complications of the MitraClip™ G4 procedure.
Death; Allergic reactions or hypersensitivity to latex, contrast agent, anaesthesia, device materials (nickel / titanium, cobalt, chromium, polyester), and drug reactions to anticoagulation, or antiplatelet drugs; Vascular access complications which may require transfusion or vessel repair including: wound dehiscence, catheter site reactions, Bleeding (including ecchymosis, oozing, hematoma, hemorrhage, retroperitoneal hemorrhage), Arteriovenous fistula, pseudoaneurysm, aneurysm, dissection, perforation / rupture, vascular occlusion, Emboli (air thrombotic material, implant, device component), Peripheral Nerve Injury; Lymphatic complications; Pericardial complications which may require additional intervention, including: Pericardial effusion, Cardiac tamponade, Pericarditis; Cardiac complications which may require additional interventions or emergency cardiac surgery, including: Cardiac perforation, Atrial septal defect; Mitral valve complications, which may complicate or prevent later surgical repair, including: Chordal entanglement / rupture, Single Leaflet Device Attachment (SLDA), Thrombosis, Dislodgement of previously implanted devices, Tissue damage, Mitral valve stenosis, Persistent or residual mitral regurgitation, Endocarditis; Cardiac arrhythmias (including conduction disorders, atrial arrhythmias, ventricular arrhythmias); Cardiac ischemic conditions (including myocardial infarction, myocardial ischemia, and unstable / stable angina); Venous thromboembolism (including deep vein thrombosis, pulmonary embolism, post procedure pulmonary embolism); Stroke / Cerebrovascular accident (CVA) and Transient Ischemic Attack (TIA); System organ failure: Cardio-respiratory arrest, Worsening heart failure, Pulmonary congestion, Respiratory dysfunction / failure / atelectasis, Renal insufficiency or failure, Shock (including cardiogenic and anaphylactic); Blood cell disorders (including coagulopathy, hemolysis, and Heparin Induced Thrombocytopenia (HIT)); Hypotension / hypertension; Infection including:, Urinary Tract Infection (UTI), Pneumonia, Septicemia
Nausea / vomiting; Chest pain; Dyspnea; Edema; Fever or hyperthermia; Pain; Fluoroscopy, Transesophageal echocardiogram (TEE) and Transthoracic echocardiogram (TTE) –related complications: Skin injury or tissue changes due to exposure to ionizing radiation, Esophageal irritation, Esophageal perforation, Gastrointestinal bleeding.

See Important Safety Information referenced within.

CAUTION: This product is intended for use by or under the direction of a physician. Prior to use, reference the Instructions for Use, inside the product carton (when available) or at eifu.abbottvascular.com or at medical.abbott/manuals for more detailed information on Indications, Contraindications, Warnings, Precautions and Adverse Events.

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