SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Prosthesis, mitral valve, percutaneously delivered
Device Trade Name:	Tendyne Transcatheter Mitral Valve System
Device Procode:	NPU
Applicant Name and Address:	Abbott Medical 177 County Road B East St. Paul, MN 55117
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P240042
Date of FDA Notice of Approval:	May 23, 2025
Breakthrough Device:	Granted breakthrough device designation on May 28, 2021, because the device can provide for more effective treatment of an irreversible debilitating disease; as well as represents a breakthrough technology, offers significant advantages over existing approved or cleared alternatives, and is in the best interest of patients.

II. INDICATIONS FOR USE

The Tendyne Transcatheter Mitral Valve System (Tendyne System) is indicated for the treatment of symptomatic severe mitral valve dysfunction (moderate-to-severe or severe mitral regurgitation [MR], severe mitral stenosis [MS], or moderate MR with moderate or greater MS) associated with severe mitral annular calcification (MAC) in patients who are deemed unsuitable for mitral valve surgery or transcatheter edge-to-edge repair by a multidisciplinary heart team.

III. CONTRAINDICATIONS

The Tendyne System is contraindicated in patients with:

- anticoagulation/antiplatelet intolerance;
- sepsis or active endocarditis;
- evidence of left ventricular or left atrial thrombus at risk of embolization;
- a thin or fragile apex rendering the subject unsuitable for a transapical procedure; or

- untreatable hypersensitivity to nickel or titanium.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Tendyne System labeling.

V. DEVICE DESCRIPTION

The Tendyne System is designed to replace the native mitral heart valve without open heart surgery and without concomitant removal of the failed native valve. It is composed of the following components: Tendyne Mitral Valve, Tendyne Apical Pad, Tendyne Loading System, Tendyne Delivery System, Tendyne Pad Positioning System, Tendyne Retrieval System, Tendyne Stand, Tendyne Stand Components, and Tendyne Weight, as shown in Figure 1.

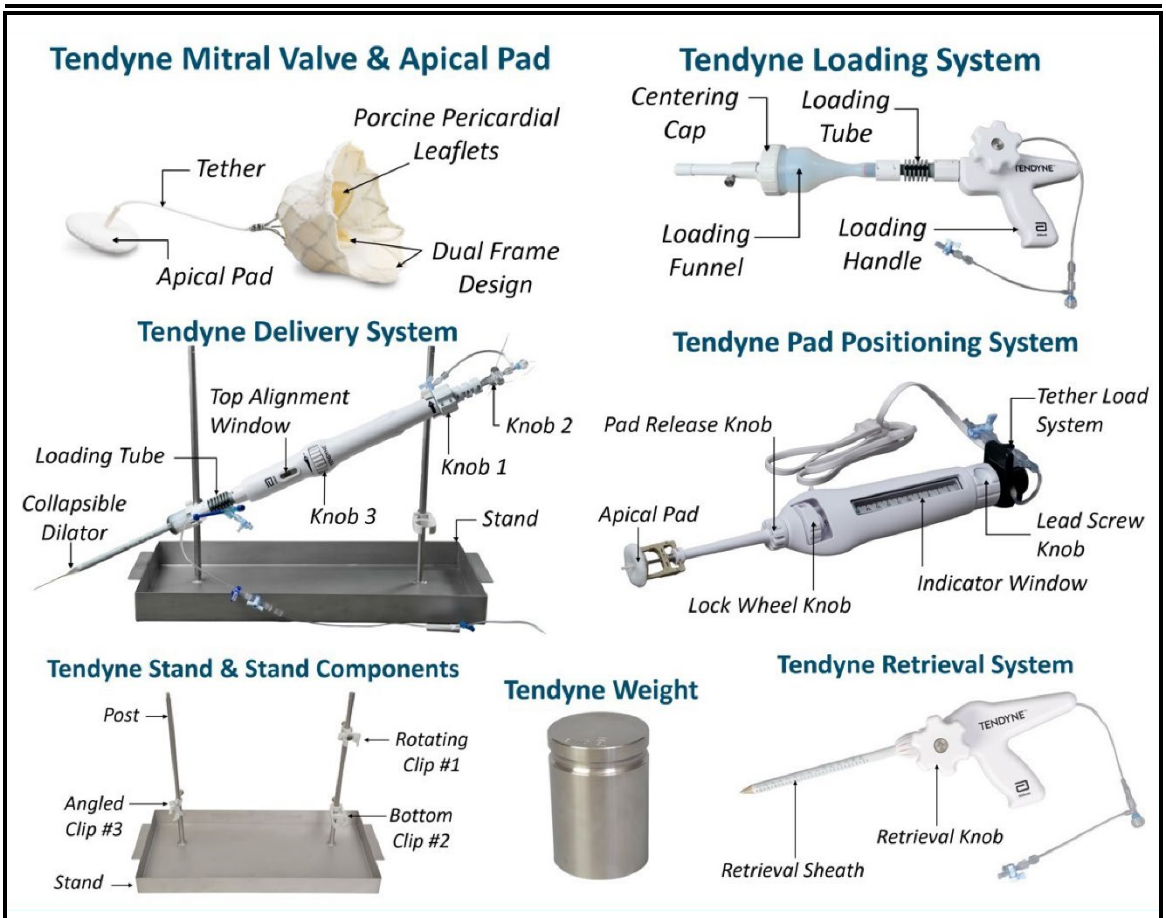


Figure 1. Tendyne Transcatheter Mitral Valve System.

- Tendyne Mitral Valve

The Tendyne Mitral Valve consists of porcine pericardium tissue leaflets, a Nitinol inner

frame, a Nitinol outer frame, and a braided ultra-high molecular weight polyethylene (UHMWPE) tether and is intended for transapical implantation within the native mitral valve annulus. It is anchored to the left apex with the tether and an epicardial hemostatic pad. The valve is fully repositionable and retrievable intraoperatively, until the point in the procedure when the tether is cut. It is available in a Standard Profile (SP) or a Low Profile (LP). The LP valve is designed to accommodate patients with smaller cardiac dimensions.

- Tendyne Apical Pad

  The Tendyne Apical Pad is intended to help maintain tension on the valve tether until tissue ingrowth occurs. It is comprised of a base with polyester fabric and poly tetrafluoro ethylene felt layering.

- Tendyne Loading System

  The Tendyne Loading System is used to properly collapse the valve into the loading tube assembly prior to attachment of the loading tube to the Tendyne Delivery System.

- Tendyne Delivery System

  The Tendyne Delivery System is used to deliver the Tendyne Mitral Valve into the patient anatomy and consists of an introducer needle, delivery handle, collapsible dilator, and delivery sheath.

- Tendyne Pad Positioning System

  The Tendyne Pad Positioning System is designed to adjust the tension on the valve tether and to place and secure the apical pad. It comprises a positioning handle assembly and tether load system assembly.

- Tendyne Retrieval System

  The Tendyne Retrieval System is used intraoperatively to retrieve and remove the Tendyne Mitral Valve if needed. Retrieval allows for use of an alternative valve size if the initial size selected was found to be suboptimal.

- Tendyne Stand

  The reusable Tendyne Stand with the stand components is used to hold the Tendyne Loading, Delivery, and Retrieval Systems during device preparation.

- Tendyne Stand Components

  The single-use Tendyne Stand Components are used in conjunction with the Tendyne Stand to assist in the preparation of the valve and instruments.

- Tendyne Weight

  The reusable Tendyne Weight is used with the Tendyne Pad Positioning System to verify accurate tether tension readings from the Tendyne Tether Loading System.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Patients with severe mitral valve dysfunction due to severe MAC currently lack effective treatment options. Medical therapy does not address the underlying disease condition and offers limited benefit in symptom management. Surgical intervention is often not offered to patients due to the associated technical challenges and procedural risks. Transcatheter edge-to-edge repair is not generally feasible, as the calcification typically encroaches into the valve orifice, reducing the available area of blood flow, which is not well-tolerated by patients. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Tendyne System is marketed in the European Union, Israel, and Saudi Arabia. It has not been withdrawn from marketing for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device:

- Death
- Adverse foreign body response
- Adverse reaction to anesthesia
- Allergic reaction
- Anemia
- Annular dissection
- Aortic insufficiency
- Atrial or ventricular injury
- Atrial Septal Defect (resulting from transeptal mitral valvuloplasty, if performed)
- Bioprosthetic valve dysfunction
- Bleeding complications
- Blood loss which may require transfusion
- Cardiac arrest
- Cardiac perforation
- Esophageal irritation, stricture, or perforation
- Fever
- Foreign body response
- Heart Failure, new or worsening
- Hematoma
- Hemolysis
- Hypotension
- Infection/sepsis
- Leaflet, chordal, papillary or ventricular rupture (resulting from mitral valvuloplasty, if performed)
- Liver failure
- Mitral valve injury
- Mitral valve prolapse/stenosis
- Myocardial infarction
- Obstruction

- Conduction defect, with or without need for pacemaker
- Cardiac arrhythmia, atrial or ventricular
- Damage to cardiac tissue and/or structures
- Decreased LV function and/or cardiac output
- Device embolism
- Device erosion, migration or malposition
- Device thrombosis
- Embolism (air, blood clot, calcium, tissue, etc.)
- Endocarditis
- Pain
- Pleural effusion
- Pulmonary embolism
- Pulmonary hypertension
- Paravalvular leak (PVL)
- Pericardial effusion/tamponade
- Renal insufficiency or failure
- Respiratory difficulty, insufficiency or failure
- Stroke or transient ischemic attack
- Tear or damage to device
- Vascular and access-related complications
- Worsening of MR

For the specific adverse events that occurred in the clinical study, please see Section X.

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

Nonclinical laboratory studies on the Tendyne System were performed in accordance with, but not limited to, ISO 5840-1:2021 *Cardiovascular implants - Cardiac valve prostheses Part 1*: *General Requirements*, and ISO 5840-3:2021 *Cardiovascular implants - Cardiac valve prostheses Part 3*: *Heart valves substitutes implanted by transcatheter techniques*, along with relevant FDA guidance documents.

1. Biocompatibility

Biocompatibility of the Tendyne System was assessed in accordance with ISO 10993-1 *Biological Evaluation of Medical Devices - Part 1: Evaluation and testing within a risk management process*, and the FDA Guidance for Industry and Food and Drug Administration Staff, *Use of International Standard ISO 10993-1, Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process.* The required testing for each component was determined based on the nature and duration of body contact per ISO 10993-1. The test articles consisted of patient-contacting device components after exposure to all manufacturing processes, including sterilization. The biocompatibility test results for the Tendyne Mitral Valve and Apical Pad, Tendyne Delivery System and Loading System, Tendyne Pad Positioning System, and Tendyne Retrieval System are summarized in Table 1.

Table 1. Summary of Tendyne System Biological Safety Evaluation.		
Biological Effect per ISO 10993-1	**Test Method**	**Results**
Tendyne Mitral Valve and Apical Pad		
Cytotoxicity	MEM Elution Assay	Non-cytotoxic
Sensitization	Guinea Pig Maximization	Non-sensitizing
Irritation	Intracutaneous Reactivity	Non-irritating
Systemic toxicity	Material Mediated Pyrogen	Minimal or no reaction when compared with the control article
	Acute Systemic Toxicity	No biologically significant signs of systemic toxicity
Implant toxicity	Implant Toxicity – 4 Weeks	Non-irritant and no patterns of systemic toxicity
	Implant Toxicity – 13 Weeks	Non-irritant and no patterns of systemic toxicity
Hemocompatibility	Hemolysis – Direct Contact and Extract	Non-hemolytic
	Complement Activation Assay – SC5b-9	Equivalent to comparison article
	Partial Thromboplastin Time	Clotting time greater than or not statistically significantly lower than that of the comparison device
	Platelet & Leukocyte	Mean percentage value of the platelet cell counts within 80-100% of the negative control
Genotoxicity	Ames – Bacterial Reverse Mutation	No biologically significant increases in reversion rates
	In vitro Mouse Lymphoma	Non-genotoxic, non-clastogenic
Physicochemical	Chemical characterization of volatile organic compounds, semi-volatile organic compounds, non-volatile organic compounds, and elements and toxicological risk assessment	Compounds and elements detected and identified in extracts of the test articles were present at levels that would not be expected to pose any significant risk of adverse systemic toxicological effects
Tendyne Delivery System and Loading System		
Cytotoxicity	MEM Elution Assay	Non-cytotoxic

Biological Effect per ISO 10993-1	Test Method	Results
Sensitization	Guinea Pig Maximization	Non-sensitizing
Irritation	Intracutaneous Reactivity	Non-irritating
Systemic toxicity	Material Mediated Pyrogen	Minimal or no reaction when compared with the control article
	Acute Systemic Toxicity	No biologically significant signs of systemic toxicity
Hemocompatibility	Hemolysis – Direct Contact and Extract	Non-hemolytic
	Complement Activation Assay – SC5b-9	Equivalent to comparison and/or reference material
	In vivo Thrombogenicity	Clinically acceptable response
Tendyne Pad Positioning System		
Cytotoxicity	MEM Elution Assay	Non-cytotoxic
Sensitization	Guinea Pig Maximization	Non-sensitizing
Irritation	Intracutaneous Reactivity	Non-irritating
Systemic toxicity	Material Mediated Pyrogen	Minimal or no reaction when compared with the control article
	Acute Systemic Toxicity	No biologically significant signs of systemic toxicity
Tendyne Retrieval System		
Cytotoxicity	MEM Elution Assay	Non-cytotoxic
Sensitization	Guinea Pig Maximization	Non-sensitizing
Irritation	Intracutaneous Reactivity	Non-irritating
Systemic toxicity	Material Mediated Pyrogen	Minimal or no reaction when compared with the control article
	Acute Systemic Toxicity	No biologically significant signs of systemic
Hemocompatibility	Hemolysis – Direct Contact and Extract	Non-hemolytic
	Complement Activation Assay – SC5b-9	Equivalent to comparison and/or reference material
	In vivo Thrombogenicity	Clinically acceptable response

2. Bench Testing

A summary of the bench testing results is provided in Table 2.

Table 2. Summary of Tendyne System Bench Testing.

Test	Purpose	Results
Tendyne Mitral Valve		
Frame and tether fatigue testing	To assess the fatigue resistance of the Tendyne valve frame and Tether connection to the Tendyne valve frame under cyclic loading for up to 600-million cycles.	No fractures observed at minimum 8x magnification following test completion
Migration testing	To assess the resistance of the Tendyne Valve to migration that would compromise hemodynamic performance or result in embolization	No migration or embolization
Corrosion	To evaluate the corrosion resistance of the Tendyne Valve frame per ASTM F2129.	Prespecified acceptance criterion met
Hydrodynamic assessment	To determine the valve hydrodynamic performances (i.e., effective orifice area and regurgitation)	Minimum hydrodynamic performances met
Flow visualization	To qualitatively investigate flow characteristics of the valve	No areas of stagnation or turbulence observed
Accelerated wear testing	To assess valve durability to 200-million cycles	Minimum hydrodynamic performances met and no abnormal wear patterns observed
Particle image velocimetry	To assess qualitatively and quantitatively the thrombogenic and hemolytic potential of the valve	Exhibited similar flow characteristics to a commercial reference valve
Magnetic resonance imaging (MRI)	To evaluate MRI safety and compatibility of the implant (including the Apical Pad)	Confirmed the implant can be labeled “MR Conditional” under 1.5- and 3.0-Tesla field strengths
Finite element analysis	To evaluate the long-term fatigue performance of the valve frame under clinically representative challenging physiological loading conditions	No fracture of implant structural components predicted
Tendyne Apical Pad		
Functional	To verify that the Apical Pad meets applicable design requirements	Passed

Test	Purpose	Results
Corrosion	To evaluate the corrosion resistance of the Apical Pad metallic components per ASTM F2129	Prespecified acceptance criterion met
Tendyne Loading System		
Functional	To verify that the Loading System meets applicable design requirements	Passed
Loading Tube tensile strength	To verify that the Loading Tube meets the tensile strength design requirements	Passed
Corrosion	To verify that the metallic, fluid-contacting components of the Loading System are corrosion resistant	Passed
Luer testing	To verify that the applicable luer fittings of the Loading System meets design requirements	Passed
Tendyne Delivery System		
Functional	To verify that the Delivery System, Collapsible Dilator, and Introducer Needle meet applicable design requirements	Passed
Sheath tensile and compression strength	To verify that the Delivery Sheath meets the tensile and compression strength design requirements	Passed
Radiopacity	To verify that the Delivery Sheath meets the applicable requirements associated with radiopacity	Passed
Tether retention	To verify that the tether retention force feature of the Delivery System meets the design requirements	Passed
Corrosion	To verify that the metallic, fluid-contacting components of the Delivery System are corrosion resistant	Passed
Luer testing	To verify that the applicable luer fittings of the Delivery System meets design requirements	Passed
Tendyne Pad Positioning System		
Functional	To verify that the Pad Positioning System meets the design requirements and user needs.	Passed
Corrosion	To verify that the metallic, fluid-contacting components of the Pad	Passed

Test	Purpose	Results
	Positioning System are corrosion resistant	
Tendyne Retrieval System		
Functional	To verify that the Retrieval System meets the design requirements and user needs	Passed
Corrosion	To verify that the metallic, fluid-contacting components of the Retrieval System are corrosion resistant	Passed
Luer testing	To verify that the applicable luer fittings of the Retrieval System meets design requirements	Passed
Tendyne Stand and Weight		
Functional and performance	To verify that the Stand and Weight meet design requirements	Passed
Reprocessing	To validate the reprocessing steps, including cleaning and sterilization	Confirmed both components can be cleaned and sterilized per the Instructions for Use

3. Sterilization

The Tendyne Mitral Valve is sterilized by terminal liquid sterilization (TLS) using 0.65% glutaraldehyde. The Tendyne Apical Pad, Tendyne Loading System, Tendyne Delivery System, Tendyne Pad Positioning System, Tendyne Retrieval System, and single-use Tendyne Stand Components are sterilized via ethylene oxide (EtO) in accordance with EN ISO 11135-1:2014+A1:2018 *Sterilization of health care products – Ethylene oxide – Requirements for development, validation and routine control of a sterilization process for medical devices*. The validated EtO sterilization process demonstrated a minimum Sterility Assurance Level (SAL) of 10^{-6}.

The reusable Tendyne Stand and Tendyne Weight are provided non-sterile and must be cleaned and sterilized prior to each use.

4. Packaging and Shelf Life

The Tendyne Mitral Valve is stored in a jar filled with a sterile glutaraldehyde solution, tightly sealed with a lid to form the primary sterile barrier. The jar is contained within a shelf carton and shipping box to complete the protective packaging system for the valve.

The Tendyne Apical Pad is individually packaged in a vented jar with a lid. The jar is placed in two Tyvek pouches, with the outer pouch forming the primary sterile barrier, and packaged in a shelf carton.

The Tendyne Loading System, Delivery System, Pad Positioning System, Retrieval System, and Stand Components are single-use devices individually placed in an inner tray molded to conform to the specific contents of the tray, with a retainer placed the top. The inner tray and retainer are placed in an outer tray sealed with a Tyvek lid. The sealed tray is placed in a shelf carton.

The non-sterile Tendyne Stand and Weight are packaged in separate corrugated shelf cartons.

The packaging validation for the sterile components of the Tendyne System was conducted per ISO 11607-1:2020 *Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for materials, sterile barrier systems and packaging systems.* The packaging validation demonstrated that the packaging system was able to maintain a sterile barrier after exposure to temperature, distribution conditioning, and aging.

The shelf lives of the sterile Tendyne System components are as follows: Tendyne Mitral Valve, 21 months; Tendyne Apical Pad, 24 months; Tendyne Delivery System, Pad Positioning System, Retrieval System, and Loading System, 12 months; and Tendyne Stand Components, 16 months.

B. Animal Studies

The Tendyne System underwent Good Laboratory Practice-compliant preclinical *in vivo* evaluations in a porcine model, as summarized in Table 3.

Table 3. Summary of Tendyne System Animal Studies.

Chronic Studies	
Animal model	Porcine
Sample size	14 at 140 ± 7 days
Test articles	Tendyne Mitral Valves: 8 SP and 6 LP (modified to fit porcine anatomy)
Technique	Access to the apex of the heart was created via a sternotomy with a purse string closure on the apex. Intra-operative echocardiography was used to guide delivery of the compressed valve mounted on the delivery tool over a guidewire, through the apex of the heart and to the mitral annulus. The test valve was deployed at the native mitral valve annulus. The test article was held in place by a tether that was secured with an apical pad at the apex.
Objective	To evaluate the following: • Valve delivery and deployment • Physical examination • Neurological observation • Hematology • Valve hemodynamic function • Structural integrity of the valve

	• Healing response of the valve
Results	Echocardiographic and fluoroscopic imaging demonstrated clinically acceptable mitral regurgitation. Cardiac output and mitral mean gradients were maintained throughout the studies. There were no safety concerns with the implant and no changes in clinical pathology that were persistent or suggestive of health abnormalities. There were no deaths directly ascribable to the test valve.
Conclusion	These studies demonstrate that the Tendyne Mitral Valve can be properly delivered to the mitral annulus and that the valve and apical pad can remain anchored to the apex with no device embolization.
Acute Studies	
Animal model	Porcine
Sample size	7
Test articles	9 Tendyne Mitral Valves and Tendyne Delivery Systems; 6 Tendyne Retrieval Systems
Technique	Placement and retrieval of the Tendyne Valves via sternotomy with fluoroscopic and echocardiography guidance. An assessment of the gross pathology of the heart and downstream organs was conducted. As part of a sub-study, users answered a series of questions using a Likert scale.
Objective	To conduct design validation testing in an acute *in vivo* environment to ensure the Tendyne Delivery and Retrieval Systems conform to defined user requirements including successful deployment and retrieval of the Tendyne valve.
Results	The Tendyne Mitral Valve Delivery, Pad Positioning, and Retrieval Systems met the acceptance criteria for use by trained independent physicians. The physician users positively assessed performance and handling of the device and no safety concerns were raised in the subsequent pathological assessment.
Conclusion	These studies demonstrate that the Tendyne Systems meet all tested user and performance requirements when used by trained physicians.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the Tendyne System in patients with symptomatic severe mitral valve dysfunction associated with severe MAC under IDE G140240 (entitled the "SUMMIT" trial). The SUMMIT trial included three cohorts, namely, Randomized cohort (Tendyne vs. MitraClip), Non-repairable cohort (non-surgical and non-repairable patients), and Severe MAC cohort. Data from the Severe MAC cohort were the basis for the PMA approval decision. A summary of the Severe MAC cohort clinical study is presented below.

A. Study Design

The SUMMIT trial Severe MAC cohort was a prospective, single-arm study. Patients were enrolled between October 2019 and March 2023. The database for this PMA application reflected data collected through May 20, 2024, and included 103 patients. There were 37 investigational sites in the US and Canada.

The SUMMIT trial utilized: a Subject Eligibility Committee (SEC), which confirmed study subject eligibility and the subject's intended treatment cohort; an Echocardiography Core Laboratory (ECL), which reviewed echocardiography images acquired at baseline and follow-up visits; a Computed Tomography (CT) Core Laboratory, which characterized the morphology, lateral-medial symmetry, and overall distribution shape of MAC; an independent Data Safety Monitoring Board (DSMB), which was instructed to notify the applicant of any safety or compliance issues; and a Clinical Events Committee (CEC), which was responsible for adjudicating endpoint-related events reported during the study.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the SUMMIT trial Severe MAC cohort was limited to patients who met the following inclusion criteria:

   - Symptomatic mitral valve disease associated with MR ≥Grade III (per American Society of Echocardiography criteria), or severe mitral stenosis, or both moderate MR and moderate MS as assessed by the ECL. (Note: MR and MS severity must be determined by assessment of a qualifying transesophageal echocardiogram [TEE] or transthoracic echocardiogram [TTE] obtained within 120 days prior to subject consent.)
   - New York Heart Association (NYHA) Functional Class ≥II (if Class IV, patient must be ambulatory).
   - The site heart team determines that the subject has been adequately treated per applicable standards for coronary artery disease (e.g., revascularization), left ventricular dysfunction (e.g., cardiac resynchronization therapy [CRT]) and heart failure (e.g., guideline-directed medical therapy). The SEC must concur that the subject has been adequately treated.
   - The site heart team deems the degree of MAC renders the subject unsuitable for mitral valve surgery.
   - Age 18 years or older at time of consent.
   - Subject has been informed of the nature of the study and agrees to its provisions, including complying with study required testing, medications, and follow-up visits, and has provided written informed consent.

   Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

   - Mitral valvular vegetation or mass.
   - Left ventricle or left atrium thrombus.
   - Chest condition that prevents transapical access.

- Left ventricular ejection fraction (LVEF) <25%, as assessed by the site based on a TTE obtained within 120 days prior to subject consent and confirmed by the ECL.
- Left ventricular end diastolic diameter (LVEDD) >7.0 cm, as assessed by the site based on a TTE obtained within 120 days prior to subject consent and confirmed by the ECL.
- Prior surgical or interventional treatment of mitral valve involving implantation of prosthetic material (e.g., valve repair or replacement, or MitraClip).
- Mitral pathoanatomy and left ventricular outflow tract (LVOT) anatomy deemed not suitable for Tendyne transcatheter mitral valve implantation.
- Aortic valve disease requiring surgery or transcatheter intervention.
- Tricuspid valve disease requiring surgery or transcatheter intervention.
- Severe tricuspid regurgitation or severe right ventricular dysfunction.
- Any surgical or interventional procedure within the period of 60 days prior to subject registration or planned procedure 60 days following subject registration.
- Implant or revision of CRT device within 90 days prior to intended subject registration.
- Myocardial Infarction (MI) within 30 days prior to intended subject registration.
- Symptomatic, unresolved multi-vessel or unprotected left main coronary artery disease (e.g., active ischemia) requiring stenting or coronary artery bypass grafting (CABG).
- Cerebrovascular accident (CVA) within 6 months prior to intended subject registration.
- Unresolved severe symptomatic carotid stenosis (>70% by ultrasound).
- Cardiogenic shock or hemodynamic instability requiring inotropes or mechanical support devices at the time of planned implant procedure.
- Hypertrophic or restrictive cardiomyopathy, or constrictive pericarditis.
- Any of the following: leukopenia, acute anemia, thrombocytopenia, history of bleeding diathesis, or coagulopathy if cannot be adequately treated.
- History of endocarditis within 6 months of planned implant procedure.
- Active systemic infection requiring antibiotic therapy.
- Known hypersensitivity or contraindication to procedural or post-procedural medications (e.g., contrast solution, anti-coagulation and antiplatelet therapy) that cannot be adequately managed medically.
- Subjects in whom TEE is contraindicated or high risk.
- Known hypersensitivity to nickel or titanium.
- Subject is undergoing hemodialysis due to chronic renal failure.
- Subject has pulmonary arterial hypertension (fixed pulmonary artery systolic [PAS] pressure >70 mmHg). (Note: If PAS pressure >70 mmHg, site must provide documentation that PAS pressure is not fixed in order to be eligible.)
- Subject has chronic obstructive pulmonary disease (COPD) requiring continuous home oxygen therapy or chronic outpatient oral steroid use.
- Subjects with non-cardiac comorbidities that are likely to result in a life expectancy of <12 months.
- Modified Rankin Scale ≥4 disability.
- Status 1 heart transplant or prior orthotopic heart transplantation.
- Pregnant, lactating, or planning pregnancy during the clinical investigation follow-up period. (Note: Female subjects of childbearing age should be instructed to use safe contraception [e.g. intrauterine devices, hormonal contraceptives: contraceptive pills,

implants, transdermal patches hormonal vaginal devices, injections with prolonged release.)
- Currently participating in an investigational drug or another device trial that has not reached its primary endpoint. (Note: Trials requiring extended follow-up for products that were investigational, but have since become commercially available, are not considered investigational trials.)
- Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results.

2. Follow-up Schedule

Follow-up time points included 1 month, 3 months (phone contact), 6 months, and annually through 5 years. Baseline and follow-up assessments included physical assessments, medical history, laboratory tests, imaging studies, and health status surveys. Adverse events and complications were recorded at all visits.

3. Clinical Endpoints

Primary Endpoint

The primary endpoint was freedom from all-cause mortality and heart failure hospitalization (HFH) at 12 months post index procedure.

The null (H_0) and alternative (H_1) hypotheses for the primary endpoint were as follows:

$$H_0: \pi_D \leq 43\%$$
$$H_1: \pi_D > 43\%$$

where π_D was the true event rate and 43% was a performance goal. Kaplan-Meier analysis was used to compute the rate; the standard error and confidence limits were computed using Greenwood's method. A sample size of 103 patients was estimated to provide 90% power to reject the null hypothesis at a one-sided significance level of 2.5%.

Secondary Endpoints

Six (6) secondary endpoints were assessed hierarchically after the primary endpoint was met, as listed in Table 4.

Table 4. Ordered List of Secondary Endpoints for Hierarchical Testing.

Order	Secondary Endpoint	Null and Alternative Hypotheses	Significance Level*
1	Freedom from MR >mild (1+) at 30 days post procedure	H_0: $P_{MR\leq 1+} \leq 75\%$ H_1: $P_{MR\leq 1+} > 75\%$	2.5%
2	Change in KCCQ overall summary score at 12 months over baseline	H_0: $D_{12M} \leq 0$ H_1: $D_{12M} > 0$	2.5%
3	Proportion of NYHA functional class I or II at 12 months compared to baseline	H_0: $P_{12M,\ NYHA\ I/II} \leq P_{B,\ NYHA\ I/II}$ H_1: $P_{12M,\ NYHA\ I/II} > P_{B,\ NYHA\ I/II}$	2.5%
4	Change in 6MWT distance at 12 months over baseline	H_0: $D_{12M} \leq 0$ H_1: $D_{12M} > 0$	2.5%
5	Change in KCCQ overall summary score at 6 months over baseline	H_0: $D_{6M} \leq 0$ H_1: $D_{6M} > 0$	2.5%
6	Change in 6MWT distance at 6 months over baseline	H_0: $D_{6M} \leq 0$ H_1: $D_{6M} > 0$	2.5%

MR: mitral regurgitation; KCCQ: Kansas City Cardiomyopathy Questionnaire; NYHA: New York Heart Association; 6MWT: 6-minute walk test; H_0: null hypothesis; H_1: alternative hypothesis

*One-sided significance level

Descriptive Endpoints

The key descriptive endpoints included the following:

- Freedom from all-cause mortality
- Freedom from HFH
- Freedom from stroke
- Freedom from mitral valve reintervention or reoperation
- KCCQ score
- EQ-5D-5L visual analog score
- Short Form (SF)-12 physical and mental components scores
- NYHA functional class
- 6MWT distance
- MR severity

B. Accountability of the PMA Cohort

At the time of database extract, a total of 103 patients had an attempted procedure, which constituted the primary analysis population. Patient accountability through 12 months is summarized in Figure 2.

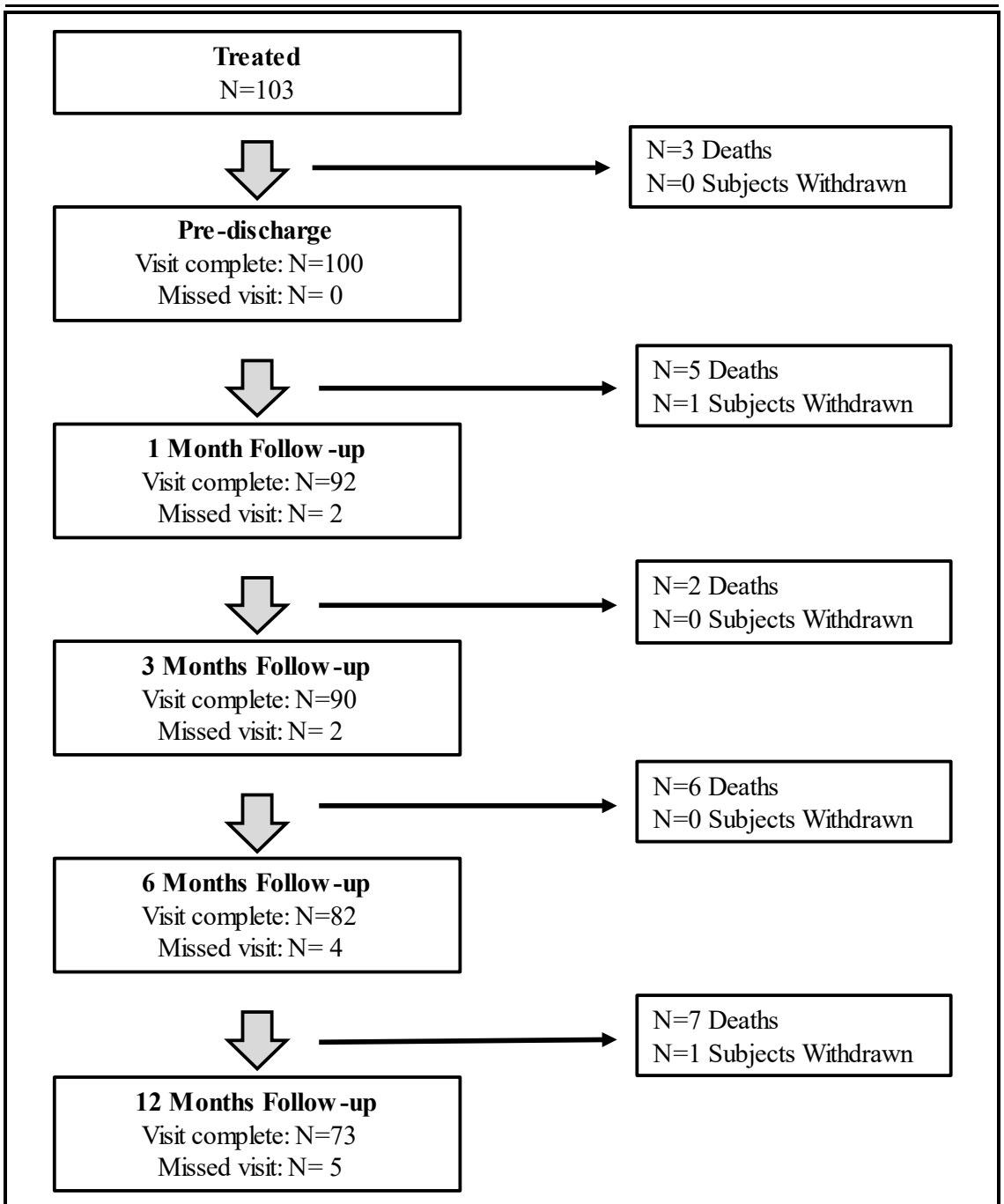


Figure 2. Patient Accountability Through 12 Months.

C. Study Population Demographics and Baseline Characteristics

The demographics and baseline characteristics of the study population are typical for a transcatheter mitral valve replacement device study performed in the U.S. in patients with severe MAC, as summarized in Table 5.

Table 5. Demographics and Baseline Characteristics.

Demographics and Baseline Characteristics	Summary Statistic* (N=103)
Demographics	
Age (year)	78.0 ± 6.5 (103)
Age ≥80 years	48.5% (50/103)
Sex	
Male	44.7% (46/103)
Female	55.3% (57/103)
Race†	
White	98.1% (101/103)
Black or African American	1.9% (2/103)
Native Hawaiian or Other Pacific Islander	0.0% (0/103)
Asian	0.0% (0/103)
American Indian or Alaskan Native	0.0% (0/103)
Other	0.0% (0/103)
Declined or unknown	0.0% (0/103)
Ethnicity	
Hispanic or Latino	1.9% (2/103)
Not Hispanic or Latino	96.1% (99/103)
Declined or unknown	1.9% (2/103)
Medical history and comorbidities	
Diabetes	52.4% (54/103)
Renal insufficiency (GFR <60 mL/min/1.73m^2)	55.3% (57/103)
Lung disease/COPD	28.2% (29/103)
Current or prior smoker	54.4% (56/103)
Liver disease	2.9% (3/103)
Malignant cancer	1.9% (2/103)
Peripheral artery disease	9.7% (10/103)
Carotid stenosis	20.4% (21/103)
Thoracic aortic disease	3.9% (4/103)
Pulmonary arterial hypertension	60.2% (62/103)
Prior stroke	11.7% (12/103)
Prior transient ischemic attack	13.6% (14/103)

Demographics and Baseline Characteristics	Summary Statistic* (N=103)
Hypertension	89.3% (92/103)
Dyslipidemia	77.0% (77/100)
Coronary artery disease	62.1% (64/103)
Prior myocardial infarction	15.5% (16/103)
Infectious endocarditis	1.0% (1/103)
Hospitalization history	
Hospitalization for heart failure in the prior 12 months	29.1% (30/103)
Hospitalization for mitral valve insufficiency in the prior 12 months	15.5% (16/103)
Heart valve disease and conduction abnormalities	
Valvular heart disease other than mitral	94.2% (97/103)
Aortic	52.4% (54/103)
Tricuspid	85.4% (88/103)
Cardiac arrhythmia or conduction abnormalities	78.6% (81/103)
Atrial fibrillation, chronic	32.0% (33/103)
Atrial fibrillation, paroxysmal	26.2% (27/103)
Cardiovascular intervention or device implantation	
Cardiac and vascular interventions	74.8% (77/103)
Aortic valve replacement	51.5% (53/103)
Cardiac rhythm and heart failure devices implanted	
PPM, ICD, CRT-P, or CRT-D	28.2% (29/103)
Risk assessment	
Essential Frailty Toolset score	
0	14.6% (15/103)
1	31.1% (32/103)
2	36.9% (38/103)
3	13.6% (14/103)
4	3.9% (4/103)
5	0.0% (0/103)
STS score - mitral valve replacement (%)	7.13 ± 3.89 (103)
Echocardiography measurements	
MR grade	
None or Trivial	0.0% (0/101)

Demographics and Baseline Characteristics	Summary Statistic* (N=103)
1+	3.0% (3/101)
2+	9.9% (10/101)
3+	37.6% (38/101)
4+	49.5% (50/101)
MR etiology	
Primary or mixed MR	93.2% (96/103)
Secondary MR	6.8% (7/103)
Functional assessment or health status measure	
NYHA functional class	
Class I	0.0% (0/103)
Class II	26.2% (27/103)
Class III	72.8% (75/103)
Class IV	1.0% (1/103)
KCCQ overall summary score	49.2 ± 23.1 (103)
6-minute walk test (meter)	204.14 ± 111.03 (100)

GFR: glomerular filtration rate; COPD: chronic obstructive pulmonary disease; PPM: permanent pacemaker; ICD: implantable cardioverter defibrillator; CRT-P: cardiac resynchronization therapy with a pacemaker; CRT-D: cardiac resynchronization therapy with a defibrillator; STS: Society of Thoracic Surgeons; MR: mitral regurgitation; NYHA: New York Heart Association; KCCQ: Kansas City Cardiomyopathy Questionnaire.
*Continuous measures – mean ± SD (total no.); Categorical measures – % (no./total no.).
†Patients of mixed race are counted in all applicable categories.

The CT Core Laboratory conducted MAC-specific evaluations to characterize the MAC morphology at each of the six mitral segments (A1, A2 and A3 for the anterior annulus, and P1, P2, and P3 for the posterior annulus), the lateral-medial symmetry, and the overall shape of the MAC distribution. The characterization data were used by the SEC to determine patient eligibility, ensuring that only patients with severe MAC were enrolled in the study. The MAC characterization results for the Severe MAC cohort are summarized in Table 6.

Table 6. MAC Characterization by Computed Tomography Core Laboratory.

MAC Characterization	Summary Statistic* (N=103)
MAC morphology†	
P1	
None	13.6% (14/103)
Homogenous	70.9% (73/103)
Spur	9.7% (10/103)
Gutter	5.8% (6/103)
P2	
None	2.9% (3/103)
Homogenous	72.8% (75/103)
Spur	11.7% (12/103)
Gutter	12.6% (13/103)
P3	
None	9.7% (10/103)
Homogenous	73.8% (76/103)
Spur	9.7% (10/103)
Gutter	6.8% (7/103)
A1	
None	43.7% (45/103)
Homogenous	20.4% (21/103)
Spur	35.9% (37/103)
Gutter	0.0% (0/103)
A2	
None	71.8% (74/103)
Homogenous	5.8% (6/103)
Spur	22.3% (23/103)
Gutter	0.0% (0/103)
A3	
None	50.5% (52/103)
Homogenous	12.6% (13/103)
Spur	36.9% (38/103)
Gutter	0.0% (0/103)
MAC distribution	
Circumferential	3.9% (4/103)
C-shape	51.5% (53/103)
J-shape	20.4% (21/103)

MAC Characterization	Summary Statistic* (N=103)
Other	24.3% (25/103)
MAC symmetry	
Symmetric	37.9% (39/103)
Asymmetric	62.1% (64/103)

*Categorical measures – % (no./total no.).
†Homogenous: MAC that did not deviate from the smooth, natural curvature of the mitral annulus was considered; spur: protrusions; gutter: indentations.

D. Safety and Effectiveness Results

1. Primary Endpoint

The primary endpoint results are presented in Table 7 and Figure 3. The rate of freedom from all-cause mortality and HFH at 12 months was 60.4%, with a 97.5% lower confidence bound of 50.2%, which is greater than the performance goal of 43.0% (p=0.0002). Therefore, the primary endpoint was met.

Table 7. Primary Endpoint Analysis.

	Kaplan-Meier Estimate (SE*)	97.5% LCB*	Performance Goal	P-value*
Freedom from all-cause mortality and HFH†	60.4% (4.9%)	50.2%	43.0%	0.0002

HFH: heart failure hospitalization; SE: standard error; LCB: lower confidence bound.
*Assumes asymptotic normal distribution for Kaplan-Meier estimate together with Greenwood's method for estimated variance.
†Two patients who experienced death or hospitalization related to COVID-19 as adjudicated by the CEC had their follow-up information after the COVID-19 related hospitalization excluded.

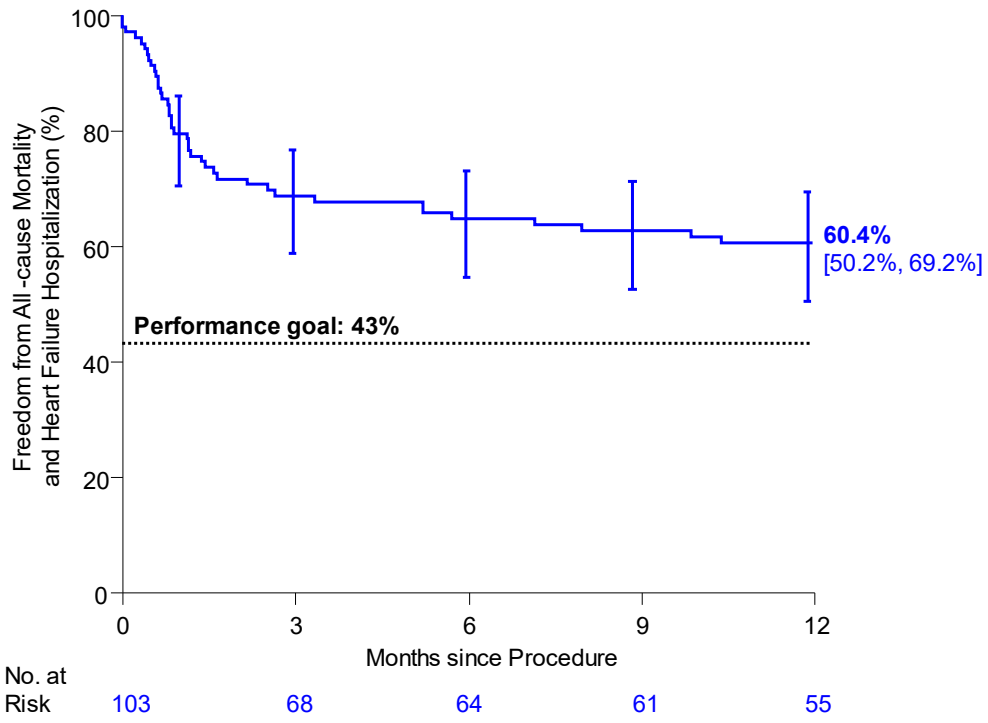


Figure 3. Kaplan-Meier Curve of Freedom from All-Cause Mortality and Heart Failure Hospitalization Through 12 Months. Any patients experiencing a CEC-adjudicated COVID-19-related hospitalization or death had any and all follow-up clinical data censored beginning with the event. Confidence intervals are provided for information purpose only without multiplicity adjustment.

2. Secondary Endpoints

Since the primary endpoint was met, prespecified hypothesis testing was carried out on 6 secondary endpoints sequentially, as summarized in Table 8. The secondary endpoints of freedom from MR >mild (1+) at 30 days post procedure, change in KCCQ overall summary score at 12 months over baseline, proportion of NYHA functional class I or II at 12 months compared to baseline were met. However, there was no significant difference in the change in 6MWT distance at 12 months over baseline. Thus, hypothesis testing was not performed for the remaining endpoints on the hierarchical list.

Table 8. Summary of Hierarchical Testing of Secondary Endpoints.

No.	Endpoint	Summary Statistics*			P-value	Test Result
		Baseline	Follow-Up Visit	Change from Baseline		
1	Freedom from MR >mild (1+) at 30 days post procedure¶	-	100.0% (98/98)	-	<0.0001†	Endpoint met
2	Change in KCCQ overall summary score at 12 months over baseline (paired)**	51.2 ± 23.8 (74)	69.9 ± 23.2 (74)	18.7 ± 24.4 (74)	<0.0001‡	Endpoint met
3	Proportion of NYHA functional class I or II at 12 months compared to baseline**	30.6% (22/72)	87.5% (63/72)	56.9%§	<0.0001‖	Endpoint met
4	Change in 6MWT distance at 12 months over baseline (meter; paired)**,††	218.1 ± 112.2 (65)	238.7 ± 109.0 (65)	20.6 ± 89.3 (65)	0.0338‡	Endpoint not met
5	Change in KCCQ overall summary score at 6 months over baseline (paired)**	49.1 ± 23.9 (79)	67.8 ± 24.9 (79)	18.6 ± 27.1 (79)	-	Not tested
6	Change in 6MWT distance at 6 months over baseline (meter; paired)**,††	216.1 ± 111.9 (71)	213.9 ± 115.4 (71)	-2.3 ± 88.6 (71)	-	Not tested

MR: mitral regurgitation; KCCQ: Kansas City Cardiomyopathy Questionnaire; NYHA: New York Heart Association; 6MWT: 6-minute walk test.

*Continuous measures – mean ± SD (total no.); Categorical measures – % (no./total no.).

†P-value calculated using Exact Binomial test, against a performance goal of 75% at a one-sided significance level of 2.5%.

‡P-value calculated using paired t-test at a one-sided significance level of 2.5%.

§Proportion defined as the proportion of patients who improved from NYHA Class III/IV at baseline to I/II at the 12-month visit, minus the proportion of patients who worsened from NYHA Class I/II at baseline to III/IV at the 12-month visit.

‖P-value calculated using McNemar's test at a one-sided significance level of 2.5%.

¶Missing 30-day MR measurement was imputed from the nearest post-procedure MR measurement obtained from the core laboratory, within 365 days of the scheduled 30-day follow-up visit, if applicable.

**Missing 12-month KCCQ score, 6MWT distance, and NYHA class was imputed from the nearest post 12-month value, within 365 days of the scheduled 12-month visit, if applicable.

††For patients whose 6MWT was not performed due to heart failure, the total distance walked was set to zero.

3. Descriptive Endpoints

Freedom from all-cause mortality

The Kaplan-Meier curve for freedom from all-cause mortality is shown in Figure 4. Seventy-nine percent (79%) of the patients were estimated to be alive at 12 months post-procedure.

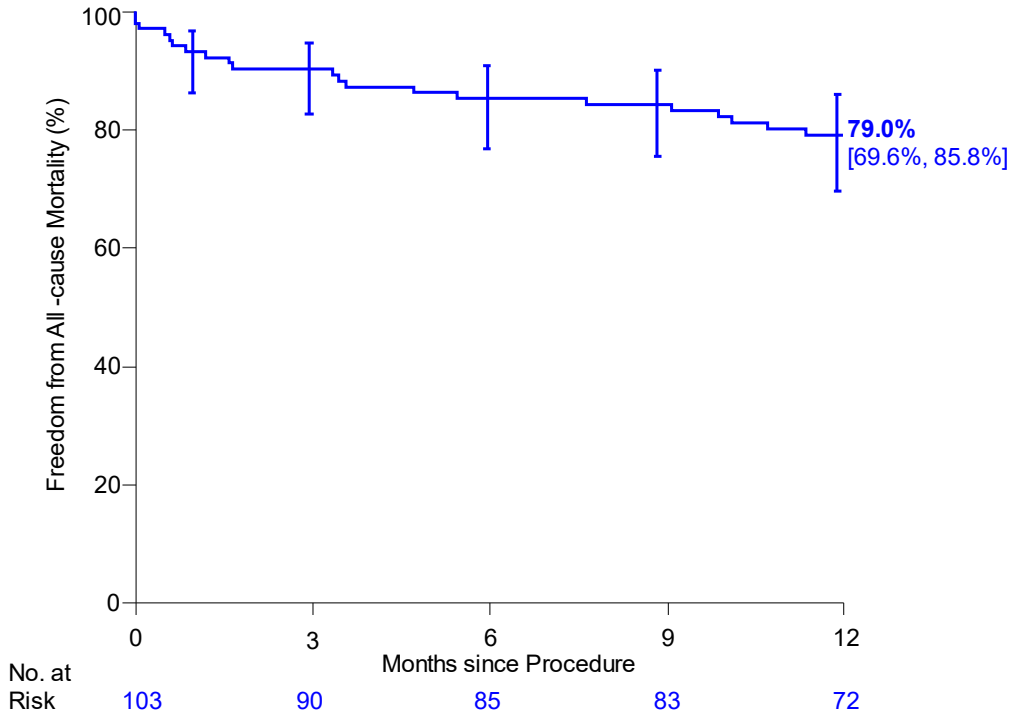


Figure 4. Kaplan-Meier Curve of Freedom from All-Cause Mortality Through 12 Months. Any patients experiencing a CEC-adjudicated COVID-19-related hospitalization or death had any and all follow-up clinical data censored beginning with the event. Confidence intervals are provided for information purpose only without multiplicity adjustment.

Freedom From HFH

The Kaplan-Meier curve for freedom from HFH is shown in Figure 5. An estimated 69.9% of the patients did not experience any HFH at 12 months post-procedure.

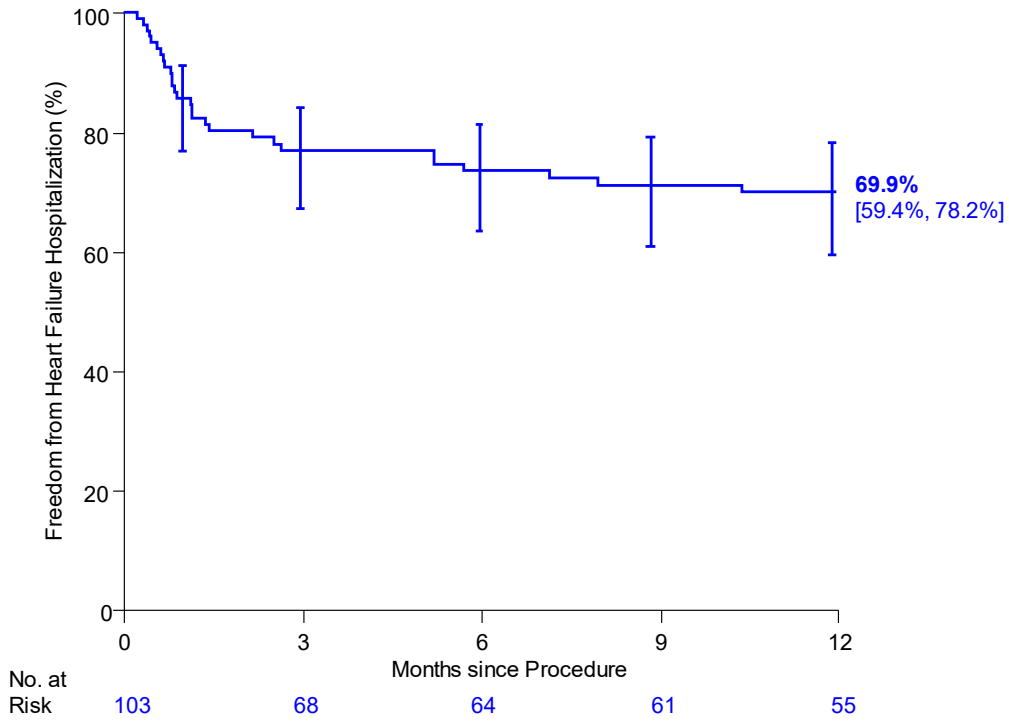


Figure 5. Kaplan-Meier Curve of Freedom from Heart Failure Hospitalization Through 12 Months. Any patients experiencing a CEC-adjudicated COVID-19-related hospitalization or death had any and all follow-up clinical data censored beginning with the event. Confidence intervals are provided for information purpose only without multiplicity adjustment.

Stroke

The Kaplan-Meier curve for freedom from stroke is shown in Figure 6. An estimated 95.9% of the patients were stroke free at 12 months post-procedure.

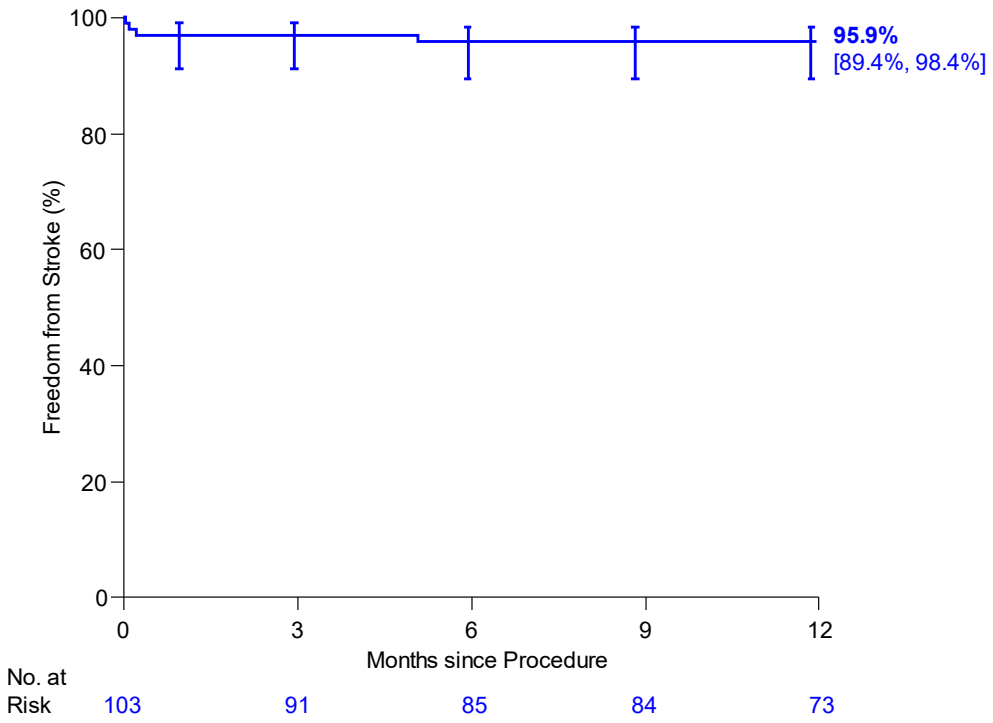


Figure 6. Kaplan-Meier Curve of Freedom from Stroke Through 12 Months. Confidence intervals are provided for information purpose only without multiplicity adjustment.

Freedom from mitral valve reintervention or reoperation

The Kaplan-Meier curve for freedom from mitral valve reintervention or reoperation is shown in Figure 7. An estimated 94.6% of the patients were free from mitral valve reintervention or reoperation at 12 months post-procedure.

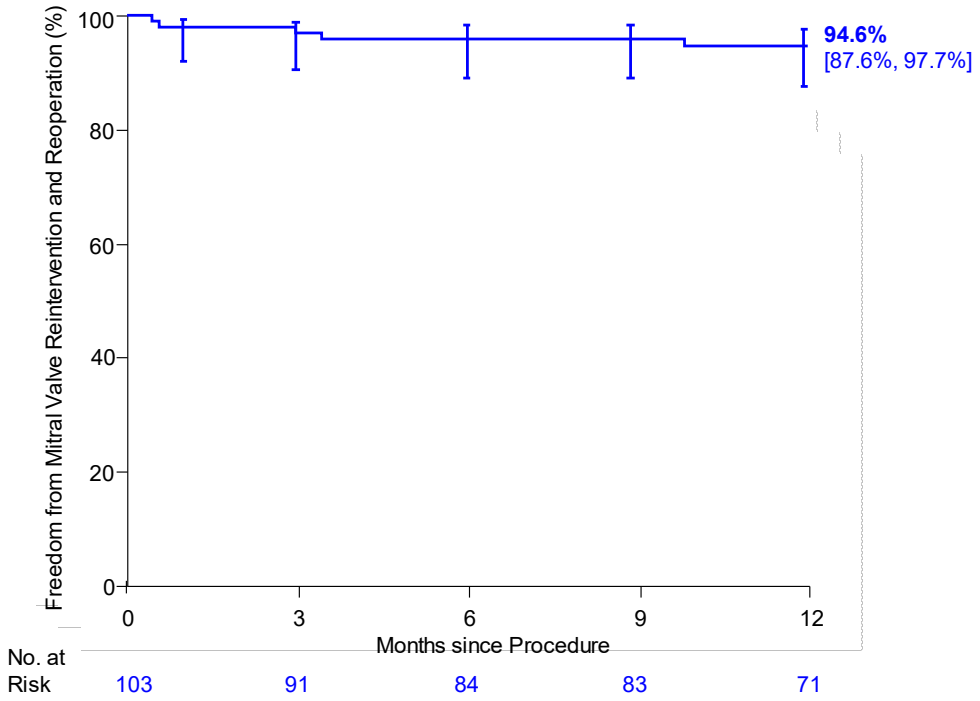


Figure 7. Freedom From Mitral Valve Reintervention or Reoperation Through 12 Months. Confidence intervals are provided for information purpose only without multiplicity adjustment.

KCCQ

The results for the KCCQ overall summary score are shown in Figure 8 (all available data). The mean score increased from 49.2 at baseline to 69.8 at 12 months post-procedure.

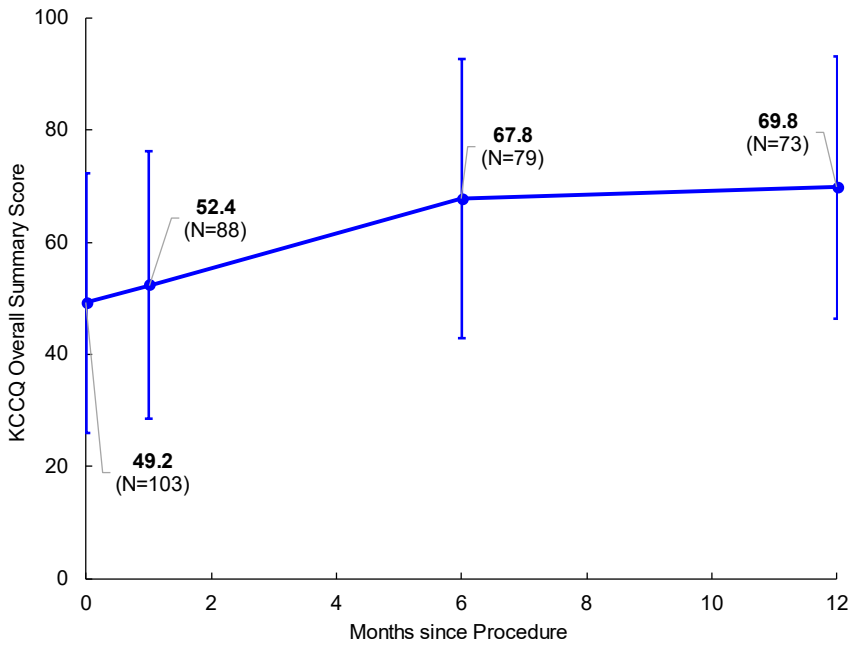


Figure 8. KCCQ Overall Summary Score by Visit (All Available Data). The error bars represent standard deviations.

EQ-5D-5L

The results for the EQ-5D-5L visual analog score (VAS) are presented in Figure 9 (all available data). The mean score was 61.1 at baseline and 72.9 at 12 months post-procedure.

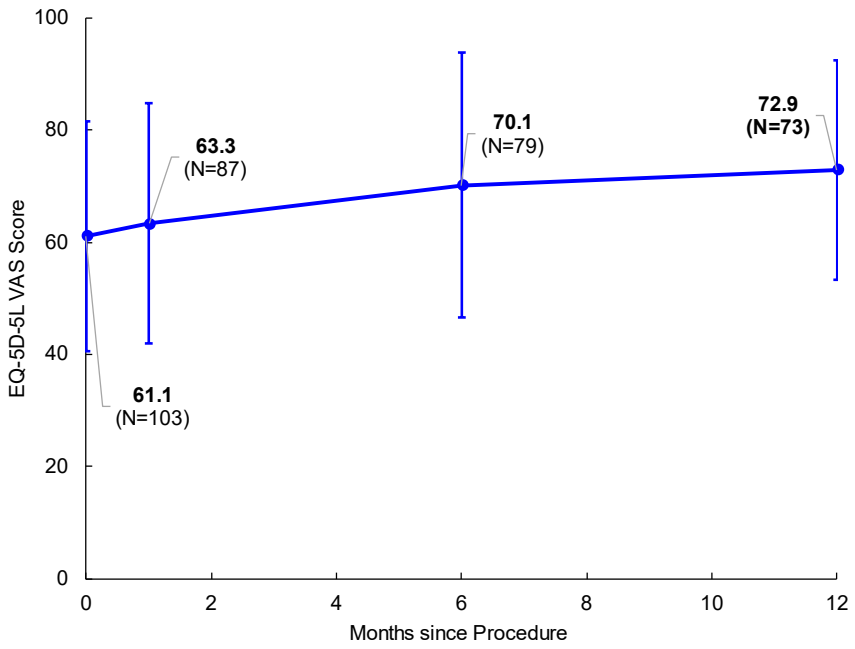
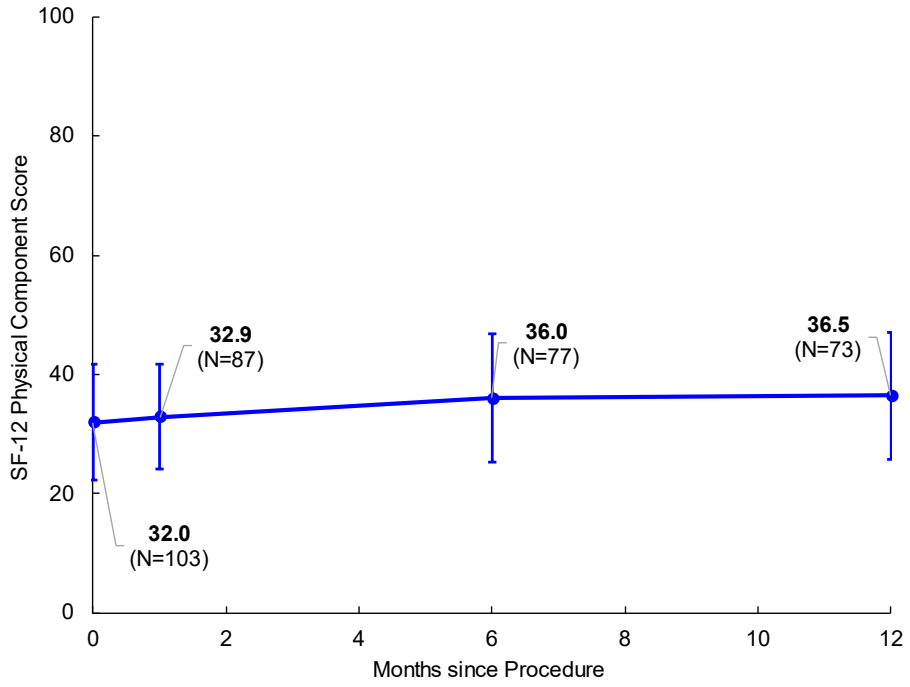


Figure 9. EQ-5D-5L Visual Analog Score by Visit (All Available Data). The error bars represent standard deviations.

SF-12

The results for the SF-12 physical component summary score and mental component summary score are presented in Figure 10 (all available data). The physical component summary score and mental component summary score were 32.0 and 48.3 at baseline and 36.5 and 52.1 at 12 months post-procedure, respectively.

A. Physical Component



B. Mental Component

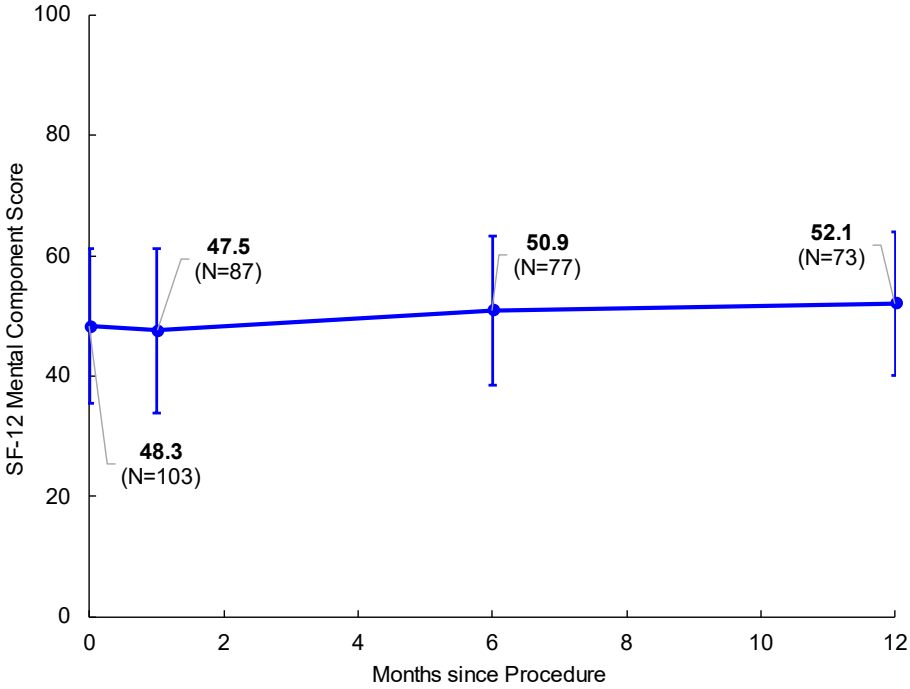


Figure 10. SF-12 Summary Score by Visit (All Available Data). The error bars represent standard deviations.

NYHA functional class

The NYHA functional classes by visit are presented in Figure 11. The proportion of patients in NYHA class I/II increased from 26% at baseline to 87% at 12 months post-procedure.

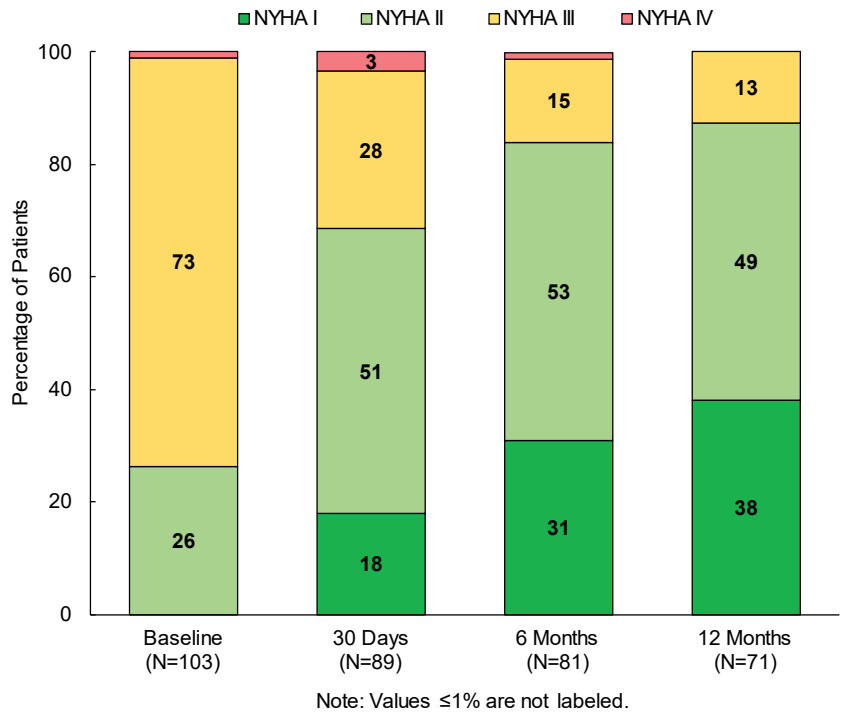


Figure 11. NYHA Functional Class by Visit.

6MWT distance

The results for the 6MWT distance are presented in Figure 12 (all available data). The mean walk distance increased from 204.1 meters at baseline to 239.8 meters.

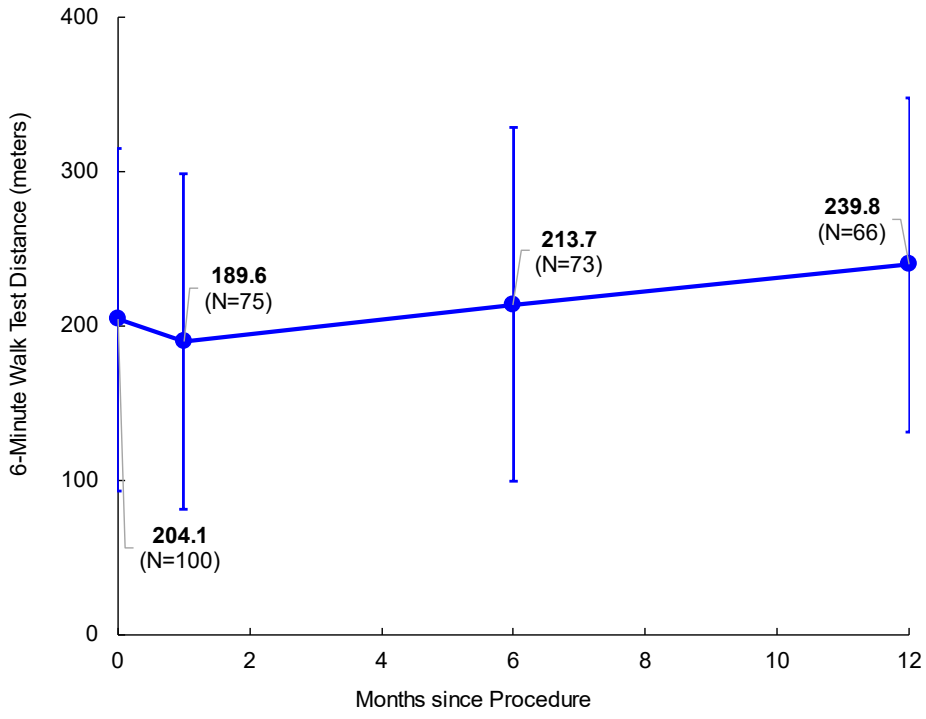


Figure 12. 6MWT Distance by Visit (All Available Data). The error bars represent standard deviations.

MR severity

MR severity by visit is shown in Figure 13. Ninety-one percent (91%) of patients had none/trivial MR at 12 months compared to no patients at baseline.

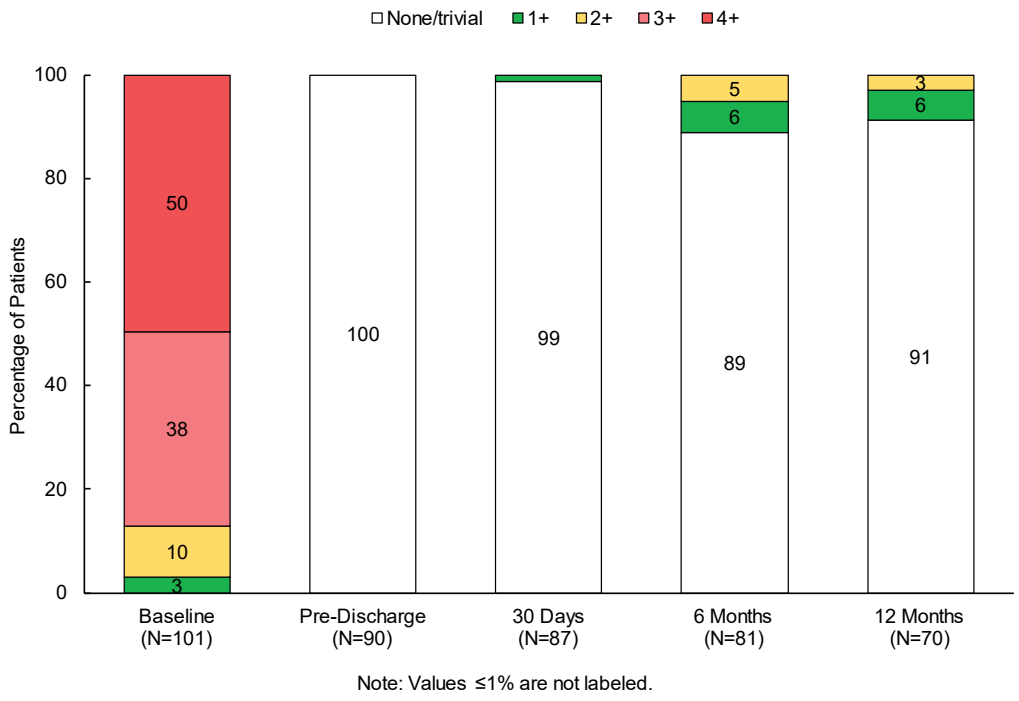


Figure 13. Mitral Regurgitation by Visit.

PVL

PVL grading by visit is shown in Figure 14. At 12 months post-procedure, there were no patients with ≥3+ PVL and 90% of patients had none or trace PVL.

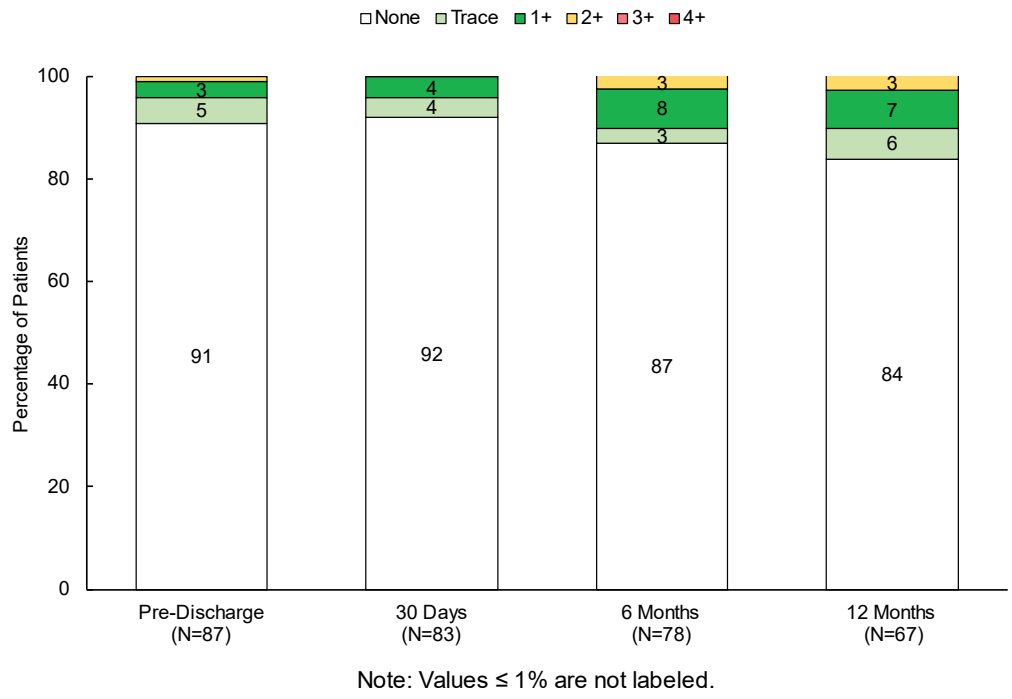


Figure 14. Paravalvular Leak Grading by Visit.

Mitral valve gradient and area

Mitral valve gradient and area by visit are shown in Figure 15 and Figure 16, respectively. The results reflected overall well-functioning mitral valve prostheses without stenosis through 12 months post-procedure.

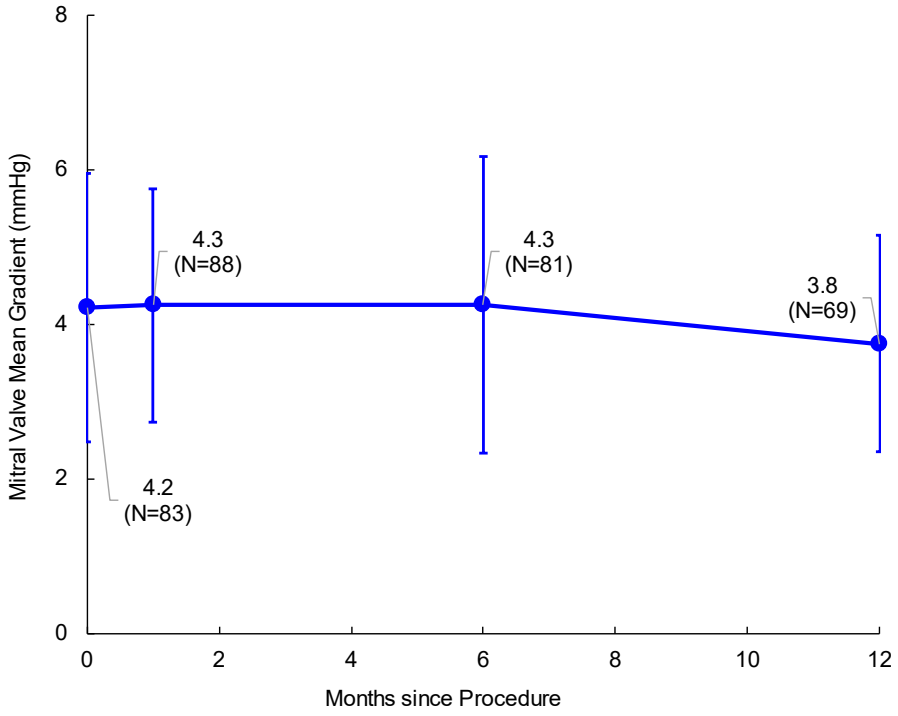


Figure 15. Mitral Valve Gradient by Visit. The error bars represent standard deviations.

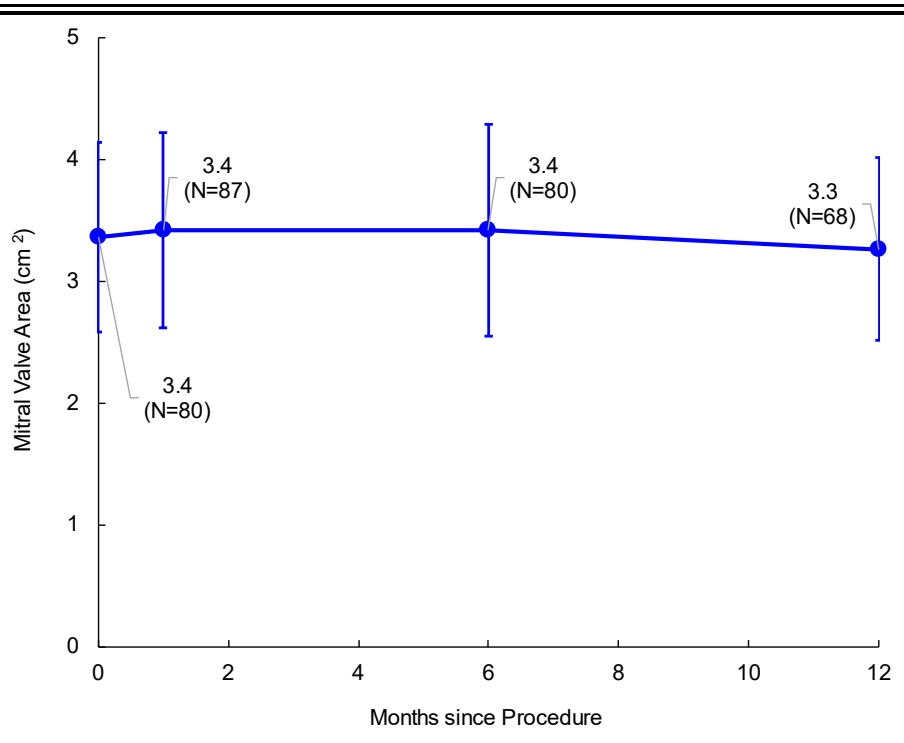


Figure 16. Mitral Valve Area by Visit. The error bars represent standard deviations.

4. Adverse Events

CEC-adjudicated serious adverse events that occurred within the first 30 days and between 31 and 365 days post-procedure are summarized in Table 9.

Table 9. CEC-Adjudicated Serious Adverse Events Within 365 Days Post-Procedure.

Event	Summary Statistics*							
	0 - 30 Days (N=103)				31 - 365 Days (N=95)			
	No. of Events	No. of Patients†	Device Related	Procedure Related	No. of Events	No. of Patients†	Device Related	Procedure Related
Death	7	7 (6.8%)	1	6	16	16 (16.8%)	1	3
HFH	14	14 (13.6%)	0	12	36	23 (24.2%)	2	0
Myocardial infarction	1	1 (1.0%)	0	1	0	0 (0.0%)	0	0
Bleeding	30	28 (27.2%)	2	27	21	16 (16.8%)	1	3
Fatal	3	3 (2.9%)	1	3	1	1 (1.1%)	0	0
Life threatening	7	7 (6.8%)	0	6	2	2 (2.1%)	1	1
Extensive	6	6 (5.8%)	0	6	3	3 (3.2%)	0	0
Major	6	6 (5.8%)	1	5	4	4 (4.2%)	0	1
Minor	8	8 (7.8%)	0	7	11	10 (10.5%)	0	1
Atrial fibrillation	28	27 (26.2%)	1	28	12	10 (10.5%)	0	2
New	14	14 (13.6%)	1	14	1	1 (1.1%)	0	1
Worsening	14	13 (12.6%)	0	14	11	9 (9.5%)	0	1
New PPM/ICD	5	5 (4.9%)	0	5	3	3 (3.2%)	0	0
Acute kidney injury	12	12 (11.7%)	2	12	0	0 (0.0%)	0	0
Device thrombosis	0	0 (0.0%)	0	0	3	3 (3.2%)	3	0
Major	0	0 (0.0%)	0	0	2	2 (2.1%)	2	0
Minor	0	0 (0.0%)	0	0	1	1 (1.1%)	1	0
Stroke or TIA	4	3 (2.9%)	1	4	1	1 (1.1%)	0	0
Disabling stroke	2	2 (1.9%)	1	2	1	1 (1.1%)	0	0
Non-disabling stroke	1	1 (1.0%)	0	1	0	0 (0.0%)	0	0
Undetermined	1	1 (1.0%)	0	1	0	0 (0.0%)	0	0
TIA	0	0 (0.0%)	0	0	0	0 (0.0%)	0	0
Endocarditis	0	0 (0.0%)	0	0	4	4 (4.2%)	3	0

Event	Summary Statistics*							
	0 - 30 Days (N=103)				31 - 365 Days (N=95)			
	No. of Events	No. of Patients†	Device Related	Procedure Related	No. of Events	No. of Patients†	Device Related	Procedure Related
Structural valve dysfunction	0	0 (0.0%)	0	0	0	0 (0.0%)	0	0
Emergency surgery or intervention during index procedure	6	5 (4.9%)	3	6	0	0 (0.0%)	0	0
Mitral valve reintervention	2	2 (1.9%)	2	2	3	3 (3.2%)	3	2

HFH: heart failure hospitalization; PPM: permanent pacemaker; ICD: implantable cardioverter defibrillator; TIA: transient ischemic attack.
*Patients who had at least one day of follow-up available during each period are included in the analysis.
†Number of events (percent of patients experienced at least one event during each period).

5. Subgroup Analysis

The primary endpoint result by race is shown in Table 10.

Table 10. Primary Endpoint Result by Race.

Race	Freedom From All-Cause Mortality and Heart Failure Hospitalization* (N=103)
White or Caucasian	62/101
Black or African American	1/2
Native Hawaiian or Other Pacific Islander	0/0
Asian	0/0
American Indian or Alaskan Native	0/0
Other	0/0
Declined or unknown	0/0

*no. of patients with events/total no. patients in the subgroup.

6. Procedural Information

The procedural data are summarized in Table 11. Successful valve implant was achieved in all attempted patients.

Table 11. Procedure Data.

Procedural Characteristic	Summary Statistics* (N=103)
Total procedure time (min)†	120.9 ± 37.7 (102)
Device time (min)‡	45.6 ± 19.8 (99)
Total fluoroscopy time (min)	18.5 ± 12.3 (99)
Successful valve implant rate	100.0% (103/103)
First valve implanted	99.0% (102/103)
First valve implanted, retrieved, second valve implanted	1.0% (1/103)
Valve type implanted	
SP	18.4% (19/103)
LP	81.6% (84/103)

*Continuous measures – mean ± SD (total no.); categorical measures – % (no./total no.).
†The time elapsed from the start time of anesthesia to time of skin closure.
‡The time elapsed from the start of the apex penetration to the time the tether tensioning ends.

7. Pediatric Extrapolation

In this premarket application, existing clinical data were not leveraged to support approval of a pediatric patient population.

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conduction clinical studies covered by the regulation. The SUMMIT Severe MAC cohort study involved 288 investigators, of which none were full-time or part-time employees of the sponsor and 40 investigators had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f), as described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: None
- Significant payment of other sorts: 40
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: None

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the Act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM THE PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

In the clinical study, the Kaplan-Meier estimate rate of the primary endpoint of freedom from all-cause mortality and HFH at 12 months was 60.4%, with a 97.5% lower confidence bound of 50.2%, which met the prespecified performance goal of 43.0% (p=0.0002). MR was successfully reduced to none/trivial in 100% of patients at discharge and in 91% of patients at 12 months post-procedure. Clinically significant benefits in functional and health status were seen in patients, as evidenced by more patients in NYHA class I/II (87.5% vs. 30.6%) and an almost 19-point average increase in KCCQ overall summary score at 12 months compared to baseline (paired analysis). In addition, the 6MWT distance increased by about 20 meters on average from baseline to 12 months (paired analysis).

B. Safety Conclusions

The risks of the Tendyne System are based on nonclinical laboratory and animal studies as well as data collected in a clinical study conducted to support PMA approval as described above. The results from the nonclinical laboratory (e.g., biocompatibility, hydrodynamic performance, durability, and structural integrity) and animal studies demonstrated that this device is suitable for long-term implant.

Despite the high degree of technical challenge that severe MAC poses for implanting a prosthetic valve, successful valve implant was achieved in all attempted patients. CEC-adjudicated severe adverse events at 30 days included death (6.8%), HFH (13.6%), mitral valve reintervention (1.9%), stroke (2.9%), fatal bleeding (2.9%), life threatening bleeding (6.8%), acute kidney injury (11.7%), new onset atrial fibrillation (13.6%), and worsening atrial fibrillation (12.6%).

C. Benefit-Risk Determination

The probable benefits of transcatheter mitral valve replacement with the Tendyne System in patients with symptomatic severe mitral valve dysfunction associated with severe MAC

include reduction in MR and clinically meaningful improvements in health and functional statuses as measured by KCCQ and NYHA functional class, respectively.

The probable risks of the Tendyne System include device- and/or procedure-related severe adverse events, such as death, HFH, mitral valve reintervention, stroke, bleeding, acute kidney injury, and new onset or worsening atrial fibrillation.

1. Patient Perspectives

   Patient perspectives considered during the review included patient reported outcomes as measured by KCCQ, EQ-5D-5L, and SF-12.

In conclusion, given the available information above, the data support that for patients with symptomatic severe mitral valve dysfunction due to severe MAC, the probable benefits of transcatheter mitral valve replacement with the Tendyne System outweigh the probable risks.

D. Overall Conclusions

The data in this application support a reasonable assurance of safety and effectiveness of the Tendyne System in patients with symptomatic severe mitral valve dysfunction associated with severe MAC who are deemed unsuitable for mitral valve surgery or transcatheter edge-to-edge repair by a multidisciplinary heart team.

XIV. CDRH DECISION

CDRH issued an approval order on May 23, 2025. The final conditions of approval cited in the approval order are described below.

The applicant must conduct two post-approval studies:

1. **Continued Follow-up of SUMMIT MAC Premarket Cohort**: The study will consist of all living patients who were enrolled under the IDE, including those enrolled in the continued access protocol (CAP) investigation. The objective of this study is to characterize the clinical outcomes annually through 5 years post-procedure. The safety and effectiveness endpoints include all-cause mortality, all stroke, cardiovascular hospitalization, number of days alive and out of hospital, annualized rate of HFH, mitral valve reintervention or reoperation, 6MWT distance, KCCQ score, EQ-5D-5L score, SF-12 score, NYHA functional class, and echocardiographic endpoints.

2. **Registry-Based Real-World Use Surveillance**: The surveillance will be carried out to assess the real-world performance of the Tendyne System. It will involve all consecutive patients with severe MAC treated within the first 2 years following device approval or a total of 200 consecutively treated patients, whichever is greater, who are entered into the Society of Thoracic Surgeons (STS)/American College of Cardiology (ACC) Transcatheter Valve Therapy (TVT) Registry (enrollment period). All patients will be followed through 5 years post-procedure (follow-up duration). The clinical data through

one (1) year will be collected through the TVT Registry. The follow-up data (including all-cause mortality, stroke, mitral valve reintervention, and heart failure hospitalizations) from year 2 through year 5 post-procedure will be obtained through linking the TVT Registry data with the Centers for Medicare and Medicaid Services (CMS) claims database.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See final approved labeling (Instructions for Use).

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the final labeling (Instructions for Use).

Post-approval Requirements and Restrictions: See Approval Order.