SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Prosthesis, Tricuspid Valve, Percutaneously Delivered
Device Trade Name:	Edwards EVOQUE Tricuspid Valve Replacement System
Device Procode:	NPW
Applicant Name and Address:	Edwards Lifesciences LLC One Edwards Way Irvine, CA 92614
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P230013
Date of FDA Notice of Approval:	February 1, 2024
Breakthrough Device:	Granted breakthrough device status on December 18, 2019, because the device can provide for more effective treatment of an irreversibly 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 Edwards EVOQUE Tricuspid Valve Replacement System (EVOQUE system) is indicated for the improvement of health status in patients with symptomatic severe tricuspid regurgitation (TR) despite optimal medical therapy (OMT), for whom tricuspid valve replacement is deemed appropriate by a heart team.

III. CONTRAINDICATIONS

The EVOQUE system is contraindicated in patients with the following conditions:

- Active bacterial endocarditis or other active infections.
- Untreatable hypersensitivity to nitinol alloys (nickel and titanium).
- Inability to tolerate an anticoagulation/antiplatelet regimen.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the EVOQUE system labeling.

V. DEVICE DESCRIPTION

The EVOQUE system, as shown in Figure 1, is designed to replace the native tricuspid heart valve without open heart surgery and without concomitant removal of the failed native valve. It comprises the EVOQUE Valve, EVOQUE Tricuspid Delivery System, EVOQUE Dilator Kit, EVOQUE Loading System, and various optional accessories.

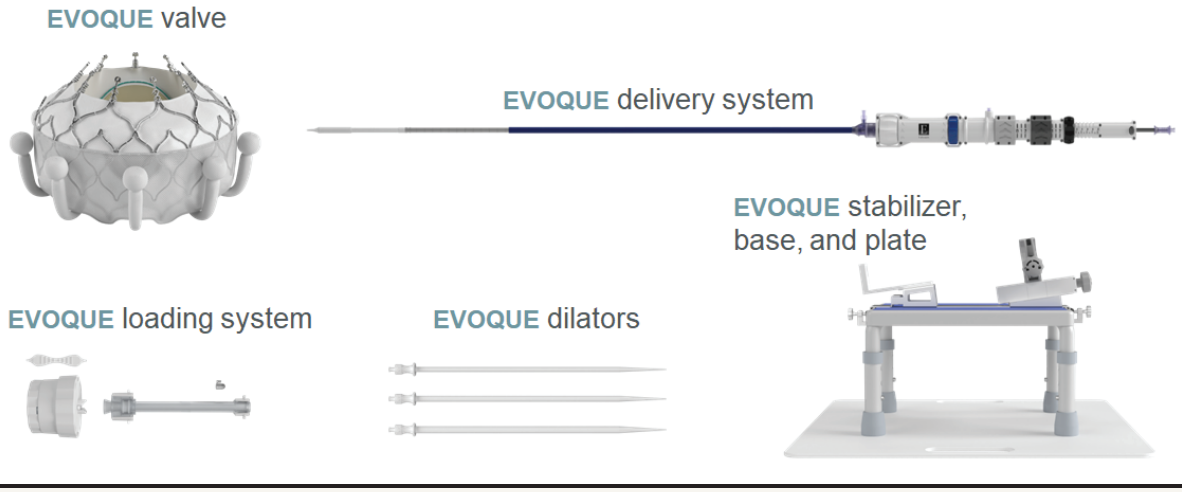


Figure 1. Edwards EVOQUE Transcatheter Tricuspid Valve Replacement System.

Edwards EVOQUE Valve

The EVOQUE valve consists of a 28-mm trileaflet bovine pericardial tissue valve, a self-expanding nitinol frame with anchoring system that can extend between the chordae tendinae of the subvalvular apparatus to engage and capture the free edge of the native tricuspid leaflets (septal, anterior, and posterior), and an intra-annular fabric skirt. The EVOQUE valve is packaged and terminally sterilized in glutaraldehyde using the proprietary Thermafix process. The valve is available in three sizes, with outer frame diameters of 44 mm (9850EV44), 48 mm (9850EV48), and 52 mm (9850EV52). While a 56-mm valve (9850EV56) was introduced into the trial towards the end of the enrollment period, it is not included in the scope for this PMA application.

Edwards EVOQUE Tricuspid Delivery System

The EVOQUE tricuspid delivery system (9850TDS) has an outer diameter of 28 French (Fr) and is designed to deliver the EVOQUE valve via a transfemoral venous approach. The EVOQUE tricuspid delivery system handle contains a primary flex knob, secondary flex knob,

and depth knob to facilitate EVOQUE valve alignment and positioning within the native valve, and a capsule knob and release knob to control the expansion and release of the EVOQUE valve housed in a delivery capsule at the distal end of the delivery system. All three EVOQUE valve sizes (44 mm, 48 mm, and 52 mm) are compatible with the 28 Fr delivery system.

Edwards EVOQUE Dilator Kit

The EVOQUE system is supplied with a hydrophilic-coated EVOQUE dilator kit (9850DK) that includes three dilators of 24 Fr, 28 Fr, and 33 Fr diameter. The dilators are used to dilate the access site, facilitating EVOQUE tricuspid delivery system insertion. All dilators accommodate a 0.035" guidewire and are tapered to minimize access site trauma.

Edwards EVOQUE Loading System

The EVOQUE loading system (9850LS) is intended to facilitate loading and attachment of the EVOQUE valve onto the EVOQUE tricuspid delivery system. It assists in crimping the EVOQUE valve to the appropriate diameter, allowing the capsule to advance over the EVOQUE valve.

Edwards EVOQUE Optional Accessories

The EVOQUE optional accessories include the EVOQUE stabilizer (9850SB), EVOQUE stabilizer base (9850BA), and EVOQUE stabilizer plate (9850PT), which are designed to secure the EVOQUE delivery system at an angle appropriate for the transfemoral venous approach and to enable fine adjustments of the position of the EVOQUE tricuspid delivery system during the implantation procedure.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are other alternatives for the treatment of TR, including medical therapy and surgery. 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 EVOQUE system is commercially available in the European Union, Switzerland, and United Kingdom. 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 EVOQUE system:

- Death
- Abnormal laboratory values
- Allergic reaction to anesthesia, contrast media, anticoagulation medication, or device materials
- Anaphylactic shock
- Anemia or decreased hemoglobin (Hgb), which may require transfusion
- Aneurysm or pseudoaneurysm
- Angina or chest pain
- Arrhythmia – atrial (i.e., atrial fibrillation, supraventricular tachycardia)
- Arrhythmias – ventricular (i.e., ventricular tachycardia, ventricular fibrillation)
- Arterio-venous fistula
- Bleeding
- Cardiac arrest
- Cardiac (heart) failure
- Cardiac injury, including perforation
- Cardiac tamponade / pericardial effusion
- Cardiogenic shock
- Chordal entanglement or rupture that may require intervention
- Coagulopathy, coagulation disorder, bleeding diathesis
- Conduction system injury, which may require implantation of a pacemaker (temporary or permanent)
- Conversion to open heart surgery
- Coronary artery occlusion
- Damage to or interference with function of pacemaker or implantable cardioverter defibrillator (ICD)
- Edema
- Electrolyte imbalance
- Embolization including air, particulate, calcific material, or thrombus
- Inflammation
- Injury to the tricuspid apparatus including chordal damage, rupture, papillary muscle damage
- Local and systemic infection
- Mesenteric ischemia or bowel infarction
- Multi-system organ failure
- Myocardial infarction
- Nausea and/or vomiting
- Nerve injury
- Neurological symptoms, including dyskinesia, without diagnosis of transient ischemic attack (TIA) or stroke
- Non-emergent reoperation
- Pain
- Pannus formation
- Paralysis
- Percutaneous valve intervention
- Peripheral ischemia
- Permanent disability
- Pleural effusion
- Pneumonia
- Pulmonary edema
- Pulmonary embolism
- Reaction to anti-platelet or anticoagulation agents
- Rehospitalization
- Renal failure
- Respiratory failure, atelectasis, which may require prolonged intubation
- Retroperitoneal bleed
- Right ventricular outflow tract (RVOT) obstruction
- Septicemia, sepsis
- Skin burn, injury, or tissue changes due to exposure to ionizing radiation
- Stroke
- Structural deterioration (wear, fracture, calcification, leaflet tear, leaflet thickening, stenosis of implanted device, or new leaflet motion disorder)
- Thromboembolism

- Emergent cardiac surgery
- Endocarditis
- Esophageal irritation
- Esophageal perforation or stricture
- EVOQUE system component(s) embolization
- Failure to retrieve any EVOQUE system components
- Fever
- Gastrointestinal bleeding
- Hematoma
- Hemodynamic compromise
- Hemolysis / hemolytic anemia
- Hemorrhage requiring transfusion/surgery
- Hypertension
- Hypotension
- TIA
- Valve endocarditis
- Valve explant
- Valve leaflet entrapment
- Valve malposition
- Valve migration
- Valve paravalvular leak (PVL)
- Valve regurgitation (new or worsening tricuspid, aortic, mitral, pulmonary)
- Valve thrombosis
- Vascular injury or trauma, including dissection or occlusion
- Vessel spasm
- Wound dehiscence, delayed or incomplete healing

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

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

Nonclinical laboratory studies on the EVOQUE 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 valve substitutes implanted by transcatheter techniques*, along with relevant FDA guidance documents.

1. Biocompatibility

Biocompatibility assessments were completed on the EVOQUE system 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 EVOQUE system valve, delivery system, and dilator kit components are summarized in Table 1, Table 2, and Table 3, respectively.

Table 1. Summary of EVOQUE Valve Biocompatibility Assessments.		
Biological Effect Per ISO 10993-1	**Test Method**	**Results**
Cytotoxicity	Medium eluate method using human fibroblast cells	Non-cytotoxic
Sensitization	Guinea pig maximization test	Non-sensitizing
Irritation/ Intracutaneous Reactivity	Rabbit intracutaneous reactivity test	Non-irritating
Pyrogenicity	Rabbit pyrogen test – materials mediated	Non-pyrogenic
Acute systemic toxicity	Mouse systemic injection test	Not inducing significantly greater biological reactions than the control extracts
Hemocompatibility	*In vitro* hemolysis (indirect contact)	Non-hemolytic
	In vitro hemolysis (direct contact)	Non-hemolytic
	Complement activation test	No risk to activate complement
	In vivo thrombogenicity with domestic sheep	No evidence of thrombosis or hemolysis after implantation for up to 20 weeks
Genotoxicity	Ames assay/bacterial reverse mutation test	Non-mutagenic
	Chromosomal aberration assay	Non-clastogenic
Physicochemical	Chemical characterization of volatile organic compounds, semi-volatile organic compounds, non-volatile organic compounds, elements and toxicological risk assessment	Compounds 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

Table 2. Summary of EVOQUE Tricuspid Delivery System Biocompatibility Assessments.		
Biological Effect Per ISO 10993-1	**Test Method**	**Results**
Cytotoxicity	Medium eluate method using L-929 mouse fibroblast cells	Non-cytotoxic
Sensitization	Guinea pig maximization test	Non-sensitizing
Irritation/ intracutaneous reactivity	Rabbit intracutaneous reactivity test	Non-irritating
Hemocompatibility	*In vitro* hemolysis (indirect contact)	Non-hemolytic
	In vitro hemolysis (direct contact)	Non-hemolytic

	Partial thromboplastin time test	No impact on the Unactivated Partial Thromboplastin Time
	Complement activation test	No risk to activate complement
	Platelet and leukocyte count test	No impact on platelet and leucocyte counts
	In vivo thrombogenicity with domestic pigs	No clinically significant risk of thrombosis or thromboembolism
Pyrogenicity	Rabbit pyrogen test – materials mediated	Non-pyrogenic
Acute systemic toxicity	Mouse systemic injection test	Not inducing a significantly greater biological reaction than the control extracts

Table 3. Summary of EVOQUE Dilator Kit Biocompatibility Assessments.

Biological Effect Per ISO 10993-1	Test Method	Results
Cytotoxicity	Medium eluate method using human fibroblast cells	Non-cytotoxic
Sensitization	Guinea pig maximization test	Non-sensitizing
Irritation/ intracutaneous reactivity	Rabbit intracutaneous reactivity test	Non-irritating
Hemocompatibility	*In vitro* hemolysis (indirect contact)	Non-hemolytic
	In vitro hemolysis (direct contact)	Non-hemolytic
	Partial thromboplastin time test	Minimal impact to Partial Thromboplastin Time
	Complement activation test	No risk to activate complement
	Platelet and leukocyte count test	No impact on platelet and leucocyte counts
	In vivo thrombogenicity with domestic pigs	No clinically significant risk of thrombosis or thromboembolism
Pyrogenicity	Rabbit pyrogen test – materials mediated	Non-pyrogenic
Acute systemic toxicity	Mouse systemic injection test	Not inducing a significantly greater biological reaction than the control extracts

2. **Bench Testing**

A summary of the bench testing results is provided in Table 4.

Table 4. Summary of EVOQUE System Bench Testing.		
Test	**Purpose**	**Results**
EVOQUE Valve		
Frame fatigue testing	To assess the fatigue resistance of the inner and outer EVOQUE valve frames under cyclic loading for up to 600-million cycles.	No fractures observed at minimum 10x magnification following 600 million cycles of fatigue testing.
Migration testing	To assess the resistance of the EVOQUE valve to migration that would compromise hemodynamic performance or result in embolization.	No migration or embolization.
Corrosion resistance	To evaluate the corrosion resistance of the EVOQUE valve frame in accordance with ASTM F2129.	Met prespecified corrosion resistance acceptance criteria.
Magnetic resistance imaging (MRI) compatibility	To evaluate MRI safety and compatibility of the implant and ensure that the implant is not affected by scanning at 1.5 Tesla and 3.0 Tesla field strengths.	Valve can be labeled "MR Conditional."
Hydrodynamic assessment	To determine the hydrodynamic performance of the valve in terms effective orifice area and regurgitation under tricuspid cardiac conditions.	Met prespecified minimum hydrodynamic performances.
Flow visualization	To qualitatively investigate flow characteristics of the valve under tricuspid conditions.	Exhibited similar flow as the reference valve.
Chronic outward force / radial resistive force	To characterize chronic outward force and radial resistive force.	Resisted permanent deformation and generated acceptable radial compressive forces.
Crush resistance	To characterize the crush resistance of the frame from opposing lateral force after reaching final diameter.	Resisted permanent deformation and generated acceptable crush resistance forces.
Accelerated wear testing	To assess valve durability to 200 million cycles.	Met minimum prespecified hydrodynamic performance specifications and no abnormal wear patterns observed.

Valve expansion and foreshortening	To evaluate the relationship of the valve length and diameter during expansion.	Demonstrated to have acceptable expansion dimensions.
Valve recoil	To characterize the final frame dimensions following simulated-use conditioning and crimping.	Met all dimensional requirements.
Dynamic failure mode testing	To characterize potential failure modes affecting the durability of the valve.	Demonstrated a gradual degradation failure mode consistent with the commercial reference valve.
Particle image velocimetry	To assess quantitatively the flow fields and hemolytic potential downstream of the valve.	Exhibited similar flow characteristics to the commercial reference valve.
Bernoulli relationship	To verify whether the Bernoulli relationship applies to clinical pressure drop measurements.	Exhibited similar pressure drop and Bernoulli coefficient values to the commercial reference valve.
Finite element analysis	To determine mechanical strain during valve loading, deployment and cyclic loading. Results used to assess the fatigue life of the device.	No fracture of implant structural components predicted within a minimum of 600 million cycles under clinically representative challenging conditions.
EVOQUE Tricuspid Delivery System and Accessories		
Dimensional inspections	To verify system level dimensions to ensure product meets specifications.	Met design requirements and acceptance criteria.
Depth verification	To verify the maximum ventricular translation distance of the delivery catheter.	Met design requirements and acceptance criteria.
Deployment evaluation	To verify that the force to flex and flex angles of the steerable catheter and valve deployment are within pre-specified limits.	Met design requirements and acceptance criteria.
Tensile verification	To verify that tensile strength of bonds meets pre-defined specifications	Met design requirements and acceptance criteria.
Visual inspection	To verify that the external surface of catheter working length is free from defects.	Met design requirements and acceptance criteria.
Bond/joint verification	To verify that the bonds of the delivery system meet specification based on loading and deployment force	Met design requirements and acceptance criteria.

	characterization or ISO 10555-1.	
Hemostasis	To verify that the delivery system maintains hemostasis with a guidewire.	Met design requirements and acceptance criteria.
Corrosion	To evaluate the corrosion resistance of the delivery system in accordance with ISO 10555-1.	No signs of corrosion observed.
Particulate characterization	To evaluate and characterize the particulate and fiber counts of the delivery system.	Particulate sizes and counts within established limits.
Simulated use	To verify the functionality of the delivery system and accessories under simulated use.	Met design requirements and acceptance criteria.
EVOQUE Dilator Kit		
Dimensional inspections	To verify system level dimension to ensure product meets specifications.	Met design requirements and acceptance criteria.
Visual inspection	To verify that the external surface of the dilators is free from defects.	Met design requirements and acceptance criteria.
Radiopacity	To verify that the working length of the dilator is visible under fluoroscopy.	Visible under fluoroscopy.
Flushing and syringe compatibility	To verify that the inner lumen of the dilator can be flushed with standard syringes.	Met design requirements and acceptance criteria.
Hemostasis	To verify that the dilator kit maintains hemostasis with a guidewire.	Met design requirements and acceptance criteria.
Tensile verification	To verify that the tensile strength of bonds meets pre-defined specifications.	Met design requirements and acceptance criteria.
Particulate characterization	To evaluate and characterize the particulate and fiber counts of the dilator kit.	Particulate sizes and counts within established limits.

B. Animal Studies

The EVOQUE system underwent Good Laboratory Practice-compliant preclinical *in vivo* evaluations in an ovine model (chronic study) and porcine model (acute study), as summarized in Table 5.

Table 5. Summary of EVOQUE System Animal Studies.	
Chronic 90-Day and 20-Week Study	
Sample size / animal model	10 adult sheep (4 at 90 days and 6 at 140 days)
Test articles	10 EVOQUE valves (44 mm), 10 EVOQUE Delivery Systems, and 10 EVOQUE Loading Systems
Technique	The valves were loaded and crimped and then implanted via an on-pump surgical bypass technique. To overcome the annular dilation that might occur due to the frailty of native tricuspid annulus in an ovine, a 'De Vega' suture annuloplasty was performed on the native annulus prior to valve implantation.
Objective	To evaluate the chronic *in vivo* safety of the valve with respect to the following items: – adverse clinical events – device performance – systemic toxicity
Results	For the 90-day cohort, three (3) animals survived to their 90-day endpoint and passed all protocol requirements. One animal was inadvertently euthanized prematurely at day 87. For the 140-day cohort, all six (6) animals survived to their 140-day endpoint and passed the protocol requirements.
Conclusion	All the implants showed appropriate healing, no structural damage or deterioration, or any evidence of device embolization, migration or any other clinically significant device-related events under gross and histopathological assessment.
Acute Study	
Sample size / animal model	2 adult pigs
Test articles	2 EVOQUE valves (44 mm), 2 EVOQUE Delivery Systems, 2 EVOQUE Dilator Kits, and 2 EVOQUE Loading Systems
Technique	The valve was implanted through a transfemoral approach according to the Instructions for Use, utilizing the delivery system.
Objective	To evaluate the acute *in vivo* safety of the EVOQUE system with respect to the following items: – delivery system performance (load, deploy, track, visibility) – valve performance (deployment, visibility, and compatibility) – hemocompatibility
Results	The EVOQUE valve and EVOQUE delivery system were all visible on echocardiogram and fluoroscopy. The positioning of each implant

	was stable and predictable throughout each procedure. Activated clotting time (ACT) levels were maintained at double baseline and below 600 seconds throughout the procedures until the completion of the study and euthanasia. There were no clinically significant signs of thrombus observed on the EVOQUE delivery system.
Conclusion	The valves were successfully loaded, deployed, and met all acceptance criteria. There were no clinically significant signs of thrombus caused by the delivery system or dilator kit.

C. Sterilization

The EVOQUE valve is sterilized via terminal liquid sterilization (TLS) in accordance with ISO 14160:2020, *Sterilization of health care products -- Liquid chemical sterilizing agents for single-use medical devices utilizing animal tissues and their derivatives.* The validated TLS sterilization process demonstrated a minimum Sterility Assurance Level (SAL) of 10^{-6}.

The EVOQUE delivery system, dilator kit, loading system, and stabilizer 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 EVOQUE stabilizer base and EVOQUE stabilizer plate are provided non-sterile.

D. Packaging and Shelf-Life

The EVOQUE valve is stored in a jar filled with a sterile glutaraldehyde solution, which is tightly sealed with an integrated gasket lid to form the primary sterile barrier. The jar is contained within the inner packaging assembly and inserted into a shelf carton to complete the protective packaging system for the EVOQUE valve.

The EVOQUE delivery system, dilator kit, loading system, and stabilizer are secured to a high-density polyethylene (HDPE) card with preformed protective connectors and tunnels. The HDPE card is inserted into a Tyvek/poly pouch, which is sealed and inserted into a shelf carton and then a shipping carton.

The EVOQUE stabilizer base and plate are packaged in stand-alone shipper boxes and distributed separately from the rest of the system.

The packaging validation for the sterile components of the EVOQUE system was conducted per EN ISO 11607-1:2020, *Packaging for terminally sterilized medical devices – Part 1: Requirements for materials, sterile barrier systems and packaging systems*, and EN ISO 11607-2:2020, *Packaging for terminally sterilized medical devices – Part 2:*

Validation requirements for forming, sealing and assembly processes. 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 life for all sterile components of the EVOQUE system (valve, delivery system, dilator kit, loading system, and stabilizer) is 1 year, as demonstrated by packaging integrity and product functional testing on aged samples.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the EVOQUE system for patients with severe symptomatic TR under Investigational Device Exemption (IDE) G190289 (titled the "TRISCEND II trial"). Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The TRISCEND II trial was a prospective, global, multi-center, randomized (2:1), controlled trial, comparing transcatheter tricuspid valve replacement using the EVOQUE device plus OMT (device group) vs. OMT alone (control group) in patients with severe TR. It enrolled a total of 400 patients (denoted as "Full Cohort"), with the primary endpoint being evaluated at 1 year. Given the breakthrough device designation of the device, the unmet clinical need, and anticipated slow enrollment, the trial employed a phased primary analysis plan. The current PMA application included a health status improvement indication supported by the 6-month results of the first 150 patients (denoted as "Breakthrough Pathway Cohort"). In addition, the sponsor provided initial descriptive results of the available data from the Full Cohort, in support of the current PMA application. A second future PMA supplement is planned to request expansion of the indication to include morbidity/mortality improvement based on the final results of the Full Cohort, as illustrated in Figure 2.

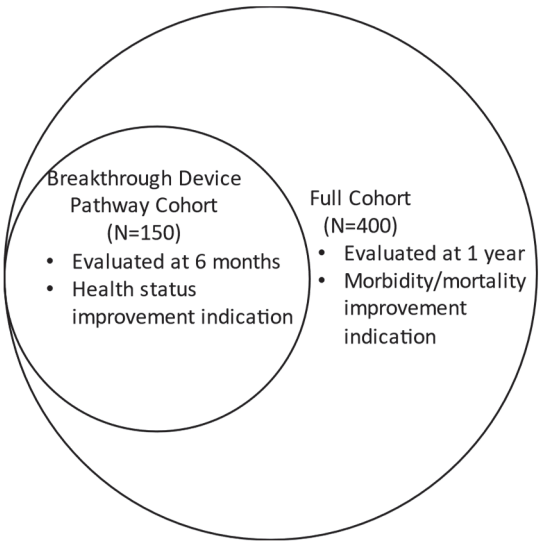


Figure 2. Construct of the TRISCEND II Trial Data Analysis Plan.

In addition to the Randomized Cohort, the trial also included a Single-Arm Cohort for patients deemed ineligible for randomization. This summary focuses on data from the Randomized Cohort.

The TRISCEND II trial utilized a Central Screening Committee (CSC) to ensure patient suitability for enrollment, an independent Data Safety Monitoring Board (DSMB) to oversee safety or compliance, a Clinical Events Committee (CEC) to adjudicate endpoint-related events, and an Echocardiographic Core Laboratory (ECL) to independently analyze all echocardiograms.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the TRISCEND II trial was limited to patients who met the following inclusion criteria:

   - Age ≥18 years old.
   - Despite OMT per the local heart team, patient has signs of TR, symptoms from TR, or prior heart failure (HF) hospitalization from TR. Patient must be on OMT per the local heart team at the time of TR assessment (transthoracic echocardiogram; TTE) for trial eligibility. OMT includes stable oral diuretic medications, unless patient has a documented history of intolerance.
   - Functional and/or degenerative TR graded as at least severe on a TTE (assessed by the ECL using a 5-grade classification proposed by Hahn et al. [2017]).
   - The local heart team determines that the patient is appropriate for transcatheter tricuspid valve replacement.
   - Patient is willing and able to comply with all study evaluations and provides written informed consent.

Patients were not permitted to be enrolled in the TRISCEND II trial if they met any of the following exclusion criteria:

- Anatomy precluding proper device delivery, deployment, and/or function.
- Left ventricular ejection fraction (LVEF) < 25%.
- Evidence of severe right ventricular dysfunction.
- Any of the following pulmonary pressure parameters:
    - Pulmonary arterial systolic pressure (PASP) >60 mmHg by Doppler echocardiogram (unless right heart catheterization [RHC] demonstrates PASP ≤70 mmHg)
    - PASP >70 mmHg by RHC
    - Pulmonary Vascular Resistance (PVR) >5 Wood units by RHC (unless PVR ≤5 Wood units and systolic blood pressure >85 mmHg after vasodilator challenge)
- Previous tricuspid surgery or intervention.
- Presence of trans-tricuspid pacemaker or defibrillator lead with any of the following:
    - Implanted in the right ventricle within the last 90 days
    - Patient is pacemaker dependent on trans-tricuspid lead without alternative pacing option
    - Has delivered appropriate implantable cardioverter defibrillator (ICD) therapy
- Severe aortic, mitral, and/or pulmonic valve stenosis and/or regurgitation.
- Active endocarditis within the last 90 days or infection requiring antibiotic therapy (oral or intravenous) within the last 14 days.
- Hemodynamically significant pericardial effusion.
- Significant intra-cardiac mass, thrombus, or vegetation.
- Clinically significant, untreated coronary artery disease requiring revascularization, evidence of acute coronary syndrome, recent myocardial infarction within the last 30 days.
- Any of the following cardiovascular procedures:
    - Percutaneous coronary, intracardiac or endovascular intervention within the last 30 days
    - Carotid surgery within the last 30 days
    - Direct current cardioversion within the last 30 days
    - Leadless right ventricular pacemaker implant within the last 30 days
    - Cardiac surgery within the last 90 days
- Known history of untreated severe symptomatic carotid stenosis (>50% by ultrasound) or asymptomatic carotid stenosis (>70% by ultrasound).
- Need for emergent or urgent surgery for any reason, any planned cardiac surgery within the next 12 months (365 days), or any planned percutaneous cardiac procedure within the next 90 days.
- Hypotension (systolic pressure <90 mmHg) or requirement for inotropic support or hemodynamic support within the last 30 days.

- Patient with refractory HF that requires or required advanced intervention (i.e., left ventricular assist device or transplantation) (American College of Cardiology/American Heart Association/ European Society of Cardiology/ European Association for Cardio-Thoracic Surgery Stage D HF).
- Deep vein thrombosis or pulmonary embolism in the last 6 months (180 days)
- Stroke within the last 90 days.
- Modified Rankin Scale ≥4 disability.
- Severe renal insufficiency with estimated glomerular filtration rate (eGFR) ≤25 mL/min/1.73m^2, calculated using the Modification of Diet in Renal Disease (MDRD) equation, or requiring chronic renal replacement therapy.
- Patients with hepatic insufficiency, or cirrhosis with Child-Pugh score class C.
- Patient is oxygen-dependent or requires continuous home oxygen.
- Chronic anemia with transfusion dependency or Hgb <9 g/dL not corrected by transfusion.
- Unable to walk at least 100 meters in a 6-minute walk test (6MWT).
- Thrombocytopenia (platelet count <75,000/mm^3) or thrombocytosis (platelet count >750,000/mm^3).
- Known bleeding or clotting disorders or patient refuses blood transfusion.
- Active gastrointestinal bleeding within the last 90 days.
- Pregnant, breastfeeding, or planning pregnancy within the next 12 months (365 days).
- Patients in whom (any of the following):
    - transesophageal echocardiography (TEE) is contraindicated or cannot be completed.
    - tricuspid valve anatomy is not evaluable by TTE or TEE
- In the opinion of the investigator, access to and through the femoral vein/inferior vena cava with a guide sheath and delivery catheter is deemed not feasible (e.g., occluded femoral veins, occluded or thrombosed inferior vena cava filter).
- Untreatable hypersensitivity or contraindication to any of the following: all antiplatelets, all anticoagulants, nitinol alloys (nickel and titanium), bovine tissue, glutaraldehyde, or contrast media.
- Currently participating in another investigational biologic, drug or device study
- Co-morbid condition(s) that, in the opinion of the investigator, limit life expectancy to <12 months (365 days).
- Presence of infiltrative cardiomyopathy or valvulopathy, including carcinoid, amyloidosis, sarcoidosis, hemochromatosis, or significant uncorrected congenital heart disease, including but not limited to hemodynamically significant atrial septal defect, right ventricular dysplasia, and arrhythmogenic right ventricle.
- Any condition, in the opinion of the investigator, making it unlikely the patient will be able to complete all protocol procedures and follow-ups.
- Other medical, social, or psychological conditions that preclude appropriate consent and follow-up, including patients under guardianship.
- Any patient considered to be vulnerable.

2. Follow-up Schedule

The follow-up time points included 30 days, 3 months (select health status questionnaires only), 6 months, and 12 months post-procedure (for device group) or post-randomization (for control group), and will continue annually through 5 years. The device group patients were also assessed intra-procedurally, within 12-24 hours post-procedure (post-procedure/pre-discharge), and at discharge (or 7-days post-index procedure, whichever occurred first).

Baseline and follow-up assessments included physical assessments (e.g., physical examination, 6MWT, volume overload assessments), medical history, laboratory tests, imaging studies, and health status surveys. Adverse events and complications were recorded at all visits.

3. Clinical Endpoints

Primary Safety Endpoint – Breakthrough Pathway Cohort

The primary safety endpoint for the Breakthrough Pathway Cohort was a composite of major adverse events (MAEs) at 30 days consisting of the following components:

- Cardiovascular mortality
- Myocardial infarction
- Stroke
- New need for renal replacement therapy
- Severe bleeding (fatal, life-threatening, extensive, or major bleeding, as defined in the Mitral Valve Academic Research Consortium (MVARC) consensus document)
- Non-elective tricuspid valve re-intervention, percutaneous or surgical
- Major access site and vascular complications
- Major cardiac structural complications due to access-related issues
- Device-related pulmonary embolism
- Arrhythmia and conduction disorder requiring permanent pacing

The hypothesis for the primary safety endpoint was as follows:

H_0: $P(\text{MAE}) \geq 70\%$
H_1: $P(\text{MAE}) < 70\%$

where P(MAE) was the proportion of patients with an MAE at 30 days and 70% was a performance goal derived from reported safety outcomes after isolated tricuspid valve replacement surgery. The null hypothesis would be rejected if the one-sided 97.5% confidence interval was less than 70%.

Primary Effectiveness Endpoint – Breakthrough Pathway Cohort

There were two co-primary effectiveness endpoints for the Breakthrough Pathway Cohort, as listed below:

- Co-primary effectiveness endpoint #1: TR grade reduction to moderate or less at 6 months
- Co-primary effectiveness endpoint #2: A hierarchical composite endpoint at 6 months of the following components:

    - Health status improvement assessed by KCCQ overall summary score (KCCQ score, hereafter) of ≥10 points
    - New York Heart Association (NYHA) functional class improvement of ≥1 class
    - 6-minute walk distance (6MWD) improvement of ≥30 meters

The hypothesis for co-primary effectiveness endpoint #1 was as follows:

$$H_0: P_D(\text{TR}) - P_C(\text{TR}) \leq 0$$
$$H_1: P_D(\text{TR}) - P_C(\text{TR}) > 0$$

where $P_T(TR)$ and $P_C(TR)$ were the proportions of patients with TR grade reduction to moderate or less at 6 months in the device and control groups, respectively. The alternative hypothesis that $P_T(TR)$ was superior to $P_C(TR)$ was tested at a one-sided significance level of 0.025.

The hypothesis for co-primary effectiveness endpoint #2 was as follows:

H_0: None of the components is improved by the device
H_1: At least one component is improved by the device

The alternative hypothesis that the device group was superior to the control group in at least one component of co-primary effectiveness endpoint #2 was tested using the Finkelstein-Schoenfeld method at a one-sided significance level of 0.025. As a supplementary analysis, the unmatched win-ratio approach was also used to evaluate the composite endpoint. In the analysis, each pair of patients from the device group and the control group were compared in the order of the defined hierarchy; and the win ratio was defined as the number of winners divided by the number of losers in the device group.

Primary Safety and Effectiveness Endpoint – Full Cohort

The primary safety and effectiveness endpoint for the Full Cohort was a hierarchical composite at 1 year of the following components:

- All-cause mortality
- Right ventricular assist device (RVAD) implantation or heart transplant
- Tricuspid valve surgical or percutaneous intervention
- Annualized rate of heart failure hospitalizations

- KCCQ score improvement of ≥10 points
- NYHA functional class improvement of ≥1 class
- 6MWD improvement of ≥30 meters

Additional Outcomes – Breakthrough Pathway Cohort

Additional outcomes assessed for the Breakthrough Pathway Cohort included the following:

- Echocardiographic parameters by echocardiogram core laboratory assessment
- Clinical and functional parameters

The Breakthrough Pathway Cohort included a sample size of 150 patients (100 in the device group and 50 in the control group), which provided >80% power to test the hypotheses for the primary safety and effectiveness endpoints. Study success of the Breakthrough Pathway Cohort was defined as meeting the primary safety endpoint and meeting both the co-primary effectiveness endpoints. The statistical analysis plan also prespecified that at the time of the initial PMA application based on the Breakthrough Pathway Cohort data, the primary endpoint for the Full Cohort and its individual components would be examined descriptively for trending based on available data.

B. Accountability of PMA Cohort

The enrollment in the Breakthrough Pathway Cohort of the TRISCEND II trial took place between May 2021 and April 2022. A total of 153 patients were randomized at 30 investigational sites in the U.S. and Germany.

The dispositions of patients in the Breakthrough Pathway Cohort are detailed in Figure 3.

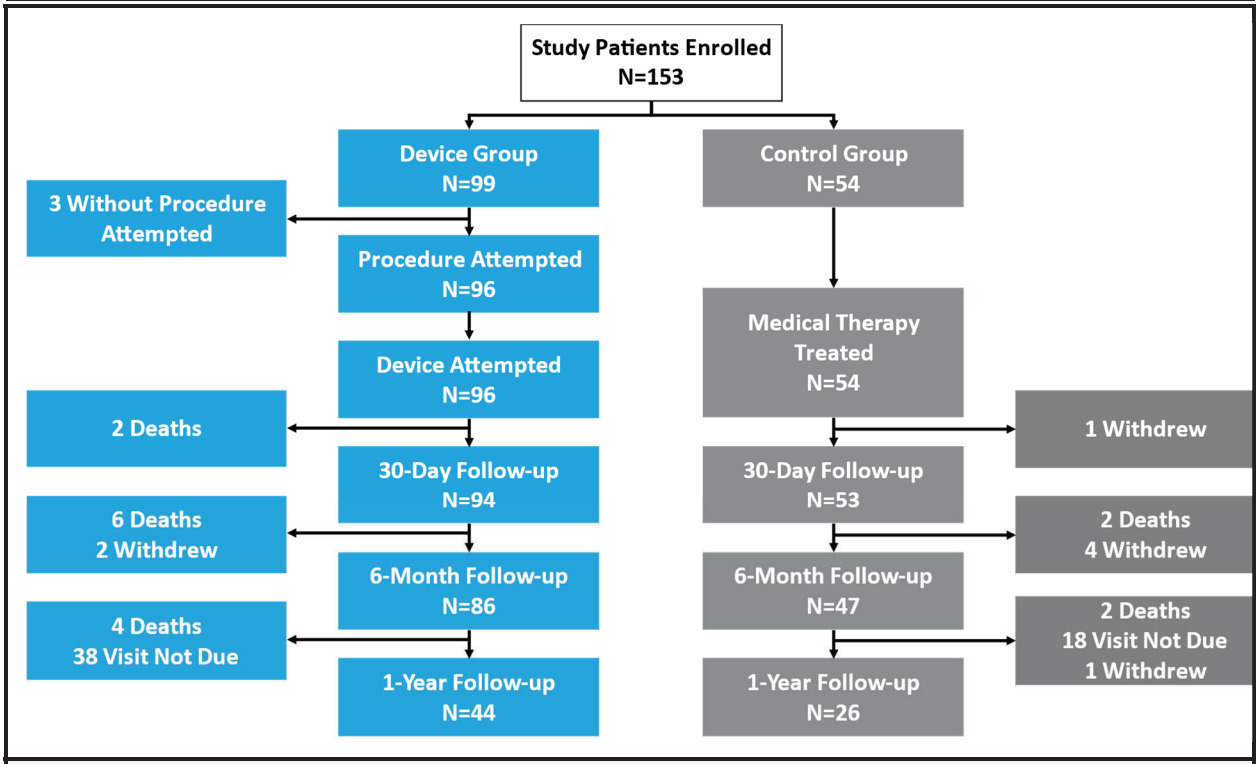


Figure 3. Patient Disposition – Breakthrough Pathway Cohort.

The analysis populations for the Breakthrough Pathway Cohort are defined in Table 6. The primary safety and effectiveness analyses were performed on the mITT Safety and mITT Effectiveness Populations, respectively.

Table 6. Analysis Populations - Breakthrough Pathway Cohort.

Analysis Population	Definition	Number of Patients	
		Device Group	Control Group
Intent-to-Treat (ITT)	All patients randomized to each treatment group.	99	54
Modified ITT (mITT) Safety	All ITT patients who had the study procedure attempted (initiation of skin incision to access the femoral vein) in the device group or who were randomized to the control group.	96	54
mITT Effectiveness	All patients in the mITT Safety Population who had a study device attempted (insertion of guide sheath into femoral vein) in the device group or who were randomized to the control group.	96	54

As-Treated (AT)	All patients in the mITT Effectiveness Population who had a study device implanted at exit from procedure room in the device group or who were randomized to the control group and treated with medical therapy.	92*	54

*Four (4) patients had aborted procedures due to challenging anatomy or imaging.

At the time of database lock, of the randomized patients eligible for the 6-month visit, 96.5% in the device group and 95.7% in the control group completed the visit, as shown in Table 7.

Table 7. Visit Compliance - Breakthrough Pathway Cohort mITT (Safety) Population

Visit Status	30 Days		6 Months	
	Device Group (N=96)	Control Group (N=54)	Device Group (N=96)	Control Group (N=54)
Ineligible for visit	2	1	10	7
Eligible for visit*	94	53	86	47
Follow-up visit completed†	95.7% (90/94)	90.6% (48/53)	96.5% (83/86)	95.7% (45/47)

*Patients were considered eligible if they completed the visit, or their visit windows were open, they were alive, and had not exited the study prior to the window opening.
†Categorical variables: % (no./total no.)

C. Study Population Demographics and Baseline Characteristics

The demographics and baseline characteristics of the study population in the Breakthrough Pathway Cohort are summarized in Table 8, which are typical for a TR study performed in the U.S. A majority of the study patients were female and White. Ethnicity information was not collected in the study. Overall, the two treatment groups were well-balanced except that there were more patients in the device group than in the control group that were in NYHA functional class III/IV (79.2% vs. 70.4%) or had a prior stroke (19.8% vs. 5.6%), and there were fewer patients in the device group than in the control group that had myocardial infarction (5.2% vs. 14.8%) or had ≥1 prior open-heart surgeries (31.2% vs. 42.6%).

Table 8. Patient Demographics and Baseline Characteristics - mITT (Safety) Population

Demographics and Baseline Characteristics	Summary Statistics* (N=150)	
	Device Group (N=96)	Control Group (N=54)
Age (years)	79.4 ± 7.71 (96)	78.2 ± 8.32 (54)
Female	82.3% (79/96)	75.9% (41/54)
Race		

American Indian or Alaskan Native	1.0% (1/96)	0.0% (0/54)
Asian	7.3% (7/96)	9.3% (5/54)
Black or African American	6.3% (6/96)	1.9% (1/54)
White	65.6% (63/96)	68.5% (37/54)
Not available	11.5% (11/96)	11.1% (6/54)
Other	8.3% (8/96)	9.3% (5/54)
Body mass index (BMI, kg/m²)	26.4 ± 5.93 (96)	26.6 ± 5.68 (54)
New York Heart Association (NYHA) functional class		
Class I	1.0% (1/96)	0.0% (0/54)
Class II	19.8% (19/96)	29.6% (16/54)
Class III	75.0% (72/96)	68.5% (37/54)
Class IV	4.2% (4/96)	1.9% (1/54)
Left ventricular ejection fraction (LVEF, %)	55.1 ± 8.60 (96)	52.4 ± 11.57 (54)
Society of Thoracic Surgeons (STS) Mortality Score - mitral valve replacement (%)	10.2 ± 5.66 (96)	9.4 ± 4.49 (54)
STS Mortality Score - mitral valve repair (%)	7.0 ± 4.58 (96)	6.7 ± 4.17 (54)
European System for Cardiac Operative Risk Evaluation (EuroSCORE) II (%)	5.3 ± 3.28 (96)	5.4 ± 3.33 (54)
Katz Activities of Daily Living Score	5.8 ± 0.44 (96)	5.9 ± 0.39 (54)
Canadian Study of Health and Aging (CSHA) Clinical Frailty Score		
Non-frail to mildly frail (1-5)	85.3% (81/95)	90.7% (49/54)
Moderate-to-severely frail (6-9)	14.7% (14/95)	9.3% (5/54)
Cardiomyopathy	13.5% (13/96)	16.7% (9/54)
Dilated	9.4% (9/96)	16.7% (9/54)
Restrictive	1% (1/96)	0% (0/54)
Hypertrophic	2.1% (2/96)	0% (0/54)
Coronary artery disease (≥50% stenosis)	26.0% (25/96)	29.6% (16/54)
Hypertension	91.7% (88/96)	87.0% (47/54)
Pulmonary Hypertension	70.8% (68/96)	74.1% (40/54)
Myocardial infarction	5.2% (5/96)	14.8% (8/54)
Stroke	19.8% (19/96)	5.6% (3/54)
Atrial fibrillation	97.9% (94/96)	96.3% (52/54)
Pacemaker/implantable cardioverter defibrillator	36.5% (35/96)	42.6% (23/54)
Percutaneous coronary intervention (PCI)/stent	12.5% (12/96)	11.1% (6/54)
Total number of prior open-heart surgeries (valve or coronary artery bypass grafting)		

0	65.6% (63/96)	57.4% (31/54)
1	22.9% (22/96)	38.9% (21/54)
≥2	8.3% (8/96)	3.7% (2/54)
Number of hospitalizations for heart failure in the last 12 months prior to consent	1.7 ± 0.96 (30)	1.7 ± 0.92 (17)
Total number of days hospitalized for heart failure in the last 12 months (for those who had heart failure hospitalization)	9.3 ± 7.48 (28)	11.8 ± 9.31 (17)
Diabetes	19.8% (19/96)	27.8% (15/54)
Chronic obstructive pulmonary disease (COPD)	19.8% (19/96)	16.7% (9/54)
Renal insufficiency or failure	48/96 (50.0%)	57.4% (31/54)
Stage I (eGFR ≥90)	0.0% (0/96)	0.0% (0/54)
Stage II (eGFR 60-89)	7.3% (7/96)	5.6% (3/54)
Stage III (eGFR 30-59)	38.5% (37/96)	44.4% (24/54)
Stage IV (eGFR 15-29)	4.2% (4/96)	7.4% (4/54)
Stage V (eGFR <15)	0.0% (0/96)	0.0% (0/54)
History of renal replacement therapy (e.g., dialysis)	0.0% (0/96)	1.9% (1/54)
Baseline KCCQ Overall Score	49.1 ± 21.47 (95)	49.7 ± 22.30 (54)
Baseline 6MWD (meter)	232.2 ± 89.61 (96)	244.0 ± 91.02 (54)
TR severity greater than severe[†]		
Severe	43.8% (42/96)	40.7% (22/54)
Massive	21.9% (21/96)	27.8% (15/54)
Torrential	34.4% (33/96)	31.5% (17/54)
Pulmonary arterial systolic pressure (PASP; mmHg)	37.5 ± 9.57 (93)	38.0 ± 11.53 (54)
TAPSE (mm)	15.9 ± 4.25 (80)	16.0 ± 4.00 (45)

eGFR: estimated glomerular filtration rate; KCCQ: Kansas City Cardiomyopathy Questionnaire; 6MWD: 6-minute walk distance; TR: tricuspid regurgitation; TAPSE: tricuspid annular plane systolic excursion.

[*]Categorical variables: % (no./total no.); continuous variables: mean ± standard deviation (no.)

[†]TR severity was evaluated on the 5-grade scale by Hahn et al. (2017).

D. Safety and Effectiveness Results

This section summarizes the results of the Breakthrough Pathway Cohort, unless otherwise noted.

1. Primary Safety Endpoint

The primary safety endpoint results are presented in Table 9. The proportion of patients with MAEs at 30 days was 27.4% in the device group, with a one-sided 97.5% upper confidence bound of 36.9%, which was less than the pre-specified performance goal of 70%. Thus, the primary safety endpoint was met.

Table 9. MAEs at 30 Days – Breakthrough Pathway Cohort mITT (Safety) Population.

Endpoint	No. Events	Event Rate*	One-sided 97.5% Upper Confidence Bound†	Endpoint Result
Composite MAEs	36	27.4% (26/95)	36.9% < 70%	Endpoint met
Cardiovascular mortality	3	3.2% (3/95)	-	-
Myocardial infarction	1	1.1% (1/95)	-	-
Stroke	0	0.0% (0/95)	-	-
New need for renal replacement therapy	1	1.1% (1/95)	-	-
Severe bleeding‡	10	10.5% (10/95)	-	-
Non-elective tricuspid valve re-intervention, percutaneous or surgical	0	0.0% (0/95)	-	-
Major access site and vascular complications	3	3.2% (3/95)	-	-
Major cardiac structural complications due to access-related issues	2	2.1% (2/95)	-	-
Device-related pulmonary embolism	1	1.1% (1/95)	-	-
Arrhythmia and conduction disorder requiring permanent pacing	14	14.7% (14/95)	-	-

MAEs: major adverse events

*% (no./total no.). Denominator included patients who had been in the trial for ≥30 days or had an MAE prior to 30 days. One patient had an aborted procedure and withdrew from the trial on post operative day (POD) 22 without experiencing an MAE and thus was not included in the denominator.

†Based on the normal approximation method with continuity correction for the proportion of patients with the MAEs and compared to the pre-specified performance goal of 70%.

‡Fatal, life-threatening, extensive, or major bleeding, as defined by Mitral Valve Academic Research Consortium (MVARC; Stone et al. 2015).

There were 3 cardiovascular mortalities at 30 days, all of which were adjudicated by the CEC to be device- and procedure-related. The primary causes of death were biventricular heart failure in 2 patients and right ventricular heart failure in 1 patient.

New-onset arrhythmia and conduction disorder requiring permanent pacing was the most frequent MAE observed at 30 days, which occurred in 22.6% (14/62) of all device patients without pre-existing pacemakers or ICDs. All 14 patients received a permanent pacemaker (vs. ICD), 13 of which had pre-existing cardiac arrhythmias, including atrial fibrillation (n=13), right bundle branch block (RBBB; n=3), and 1st degree atrioventricular block (n=2). One patient had procedure-related complete heart block prior to device implant.

Severe bleeding, defined as fatal, life-threatening, extensive, or major bleeding per Mitral Valve Academic Research Consortium (MVARC) consensus document (Stone et al. 2015), was the second most frequent MAE observed at 30 days, occurring in 10.5% (10/95) of device patients. The details of the severe bleeding events are presented in Table 10.

Table 10. Severe Bleeding within 30 Days of Index Procedure - mITT Safety Population.

Source of Severe Bleeding	Reported Events	Event Counts							
		Total Events	Severity*				Causal Relationship*		
			Fatal	Life-threatening	Extensive	Major	Device	Procedure	AP/AC
Associated with major complication due to access issue	– Cardiac perforation: 2 – Retroperitoneal hematoma: 1 – Shock hemorrhagic: 1 – Vascular access site hematoma: 1	5	0	3	0	2	5	5	0
Other source of bleeding	– Anemia: 1 – Gastrointestinal hemorrhage: 1 – Hemodilution: 1 – Hypovolemic shock: 1 – Mallory-Weiss syndrome: 1	5	0	1	1	3	3	5	1

Total:	-	10	0	4	1	5	8	10	1

AP: antiplatelet; AC: anticoagulation
*Severity and causal relationship adjudicated by CEC. Events adjudicated as possibly, probably, or related (causal relationship) to device, procedure, or adjunctive antiplatelet/anticoagulation medication are considered "related" for this analysis.

2. Primary Effectiveness Endpoints

Co-primary Effectiveness Endpoint #1:

The primary analysis result of co-primary effectiveness endpoint #1 is shown in Table 11. The proportions of patients with TR reduction to moderate or less at 6 months were 98.8% (80/81) in the device group and 21.6% (8/37) in the control group, a difference of 77.1% between the two groups, with one-sided p-value of <0.001, which was less than the pre-specified one-sided significance level of 0.025. Thus, co-primary effectiveness endpoint #1 was met, indicating superiority of the device group to the control group.

Table 11. Co-Primary Effectiveness Endpoint #1 Result - mITT Effectiveness Population.

	Summary Statistics*		**Difference**	**p-Value†**	**Endpoint Result**
	Device Group (N=96)	**Control Group (N=54)**			
TR grade reduction to moderate or less at 6 months	98.8% (80/81)	21.6% (8/37)	77.1%	<0.001	Endpoint met

*% (no./total no.). The total number of patients included patients with available data only. Fifteen (15) device patients did not have a 6-month TR grade available: 3 had aborted procedures; 8 died prior to the visit; and 4 missed the visit or did not have transthoracic cardiogram (TTE) collected. Seventeen (17) control patients did not have a 6-month TR grade available: 2 died; 1 missed the visit; 4 were pending records from outside hospitals; 4 had TTE with unmeasurable TR grade; and 6 withdrew consent prior to the visit.
†Pooled Z-test with continuity correction. Compared with one-sided significance level of 0.025.

Co-primary Endpoint #2:

The primary analysis result of co-primary effectiveness endpoint #2 is shown in Table 12. The Finkelstein-Schoenfeld test statistic result was 5.299 with a one-sided p-value of <0.001, which is less than the pre-specified one-sided significance level of 0.025. Thus, co-primary effectiveness endpoint #2 was met indicating the device group was superior to the control group.

Table 12. Co-Primary Effectiveness Endpoint #2 Result - mITT Effectiveness Population			
Primary Endpoint	**Test Statistic**	**p-Value***	**Result**
Finkelstein-Schoenfeld analysis	5.299	<0.001	Endpoint met

*One-sided p-value calculated using the Finkelstein-Schoenfeld method. Compared with one-sided significance level of 0.025.

The supplementary win ratio analysis of co-primary effectiveness endpoint #2 is shown in Figure 4. The win ratio of the device group vs. the control group was 4.6 (95% confidence interval: [2.6, 8.0]).

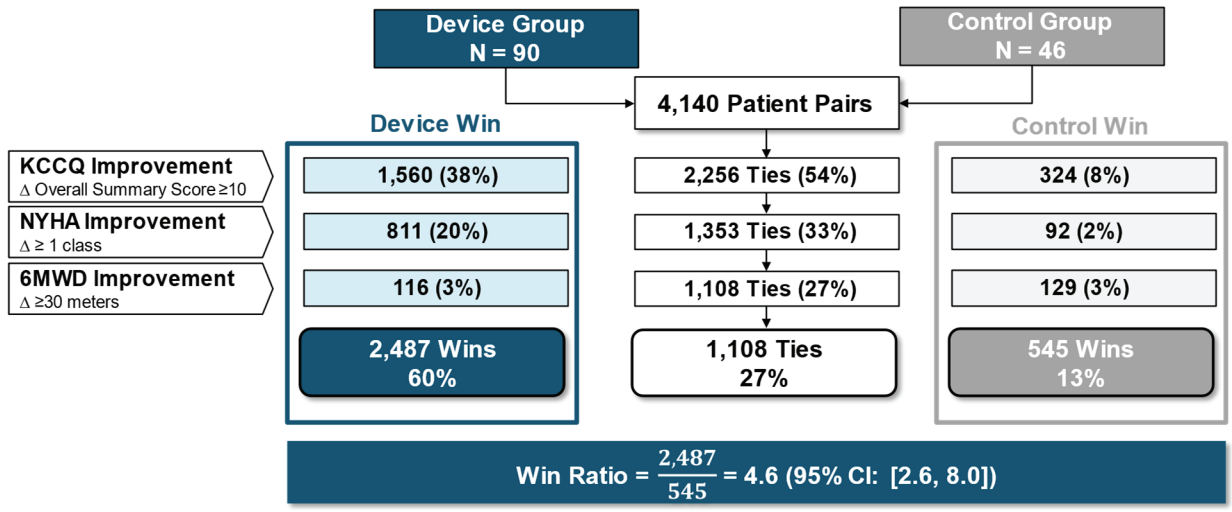


Figure 4. Win Ratio Analysis of Co-Primary Effectiveness Endpoint #2 Result - mITT Effectiveness Population. KCCQ: Kansas City Cardiomyopathy Questionnaire; NYHA: New York Heart Association; 6MWD: 6-minute walk distance; CI: confidence interval.

3. Adverse Events

The site-reported device-or procedure-related serious adverse events that occurred through 6 months in the Breakthrough Pathway Cohort are presented in Table 13.

Table 13. Site-Reported Device- or Procedure-Related Serious Adverse Events - mITT (Safety) Population.

Event	Device Group (N=96)			
	30 Days		6 Months	
	No. Events	Event Rate*	No. Events	Event Rate*
Acute kidney injury	4	4.2% (4/96)	4	4.2% (4/96)
Acute left ventricular failure	0	0.0% (0/96)	1	1.0% (1/96)
Acute respiratory distress syndrome	1	1.0% (1/96)	1	1.0% (1/96)
Acute respiratory failure	1	1.0% (1/96)	1	1.0% (1/96)
Altered mental status	1	1.0% (1/96)	1	1.0% (1/96)
Anemia	2	2.1% (2/96)	2	2.1% (2/96)
Arrhythmia	2	2.1% (2/96)	2	2.1% (2/96)
Arterial repair	1	1.0% (1/96)	1	1.0% (1/96)
Atrial fibrillation	2	2.1% (2/96)	3	3.1% (3/96)
Atrioventricular block complete	11	11.5% (11/96)	11	11.5% (11/96)
Bradycardia	4	4.2% (4/96)	5	5.2% (5/96)
Cardiac arrest	1	1.0% (1/96)	1	1.0% (1/96)
Cardiac failure	7	7.3% (7/96)	9	9.4% (9/96)
Cardiac perforation	2	2.1% (2/96)	2	2.1% (2/96)
Cardiogenic shock	3	3.1% (3/96)	3	3.1% (3/96)
Cellulitis	1	1.0% (1/96)	1	1.0% (1/96)
Chest pain	1	1.0% (1/96)	1	1.0% (1/96)
Decubitus ulcer	1	1.0% (1/96)	1	1.0% (1/96)
Deep vein thrombosis	1	1.0% (1/96)	1	1.0% (1/96)
Fall	1	1.0% (1/96)	1	1.0% (1/96)
Hemorrhagic shock	1	1.0% (1/96)	1	1.0% (1/96)
Heparin-induced thrombocytopenia	1	1.0% (1/96)	1	1.0% (1/96)
Hepatic congestion	1	1.0% (1/96)	1	1.0% (1/96)
Hypotension	2	2.1% (2/96)	2	2.1% (2/96)
Hypovolemic shock	1	1.0% (1/96)	1	1.0% (1/96)
Ileus paralytic	1	1.0% (1/96)	1	1.0% (1/96)
Intracardiac thrombus	1	1.0% (1/96)	2	2.1% (2/96)
Jailed pacing lead	1	1.0% (1/96)	1	1.0% (1/96)
Junctional rhythm	1	1.0% (1/96)	1	1.0% (1/96)

Leukocytosis	2	2.1% (2/96)	2	2.1% (2/96)
Low cardiac output syndrome	1	1.0% (1/96)	1	1.0% (1/96)
Mallory-Weiss tear	1	1.0% (1/96)	1	1.0% (1/96)
Pleural effusion	3	3.1% (3/96)	3	3.1% (3/96)
Prosthetic cardiac valve malfunction	0	0.0% (0/96)	1	1.0% (1/96)
Prosthetic cardiac valve thrombosis	0	0.0% (0/96)	2	2.1% (2/96)
Prosthetic valve endocarditis	0	0.0% (0/96)	1	1.0% (1/96)
Pulmonary edema	5	5.2% (5/96)	5	5.2% (5/96)
Pulmonary embolism	1	1.0% (1/96)	1	1.0% (1/96)
Respiratory failure	1	1.0% (1/96)	1	1.0% (1/96)
Respiratory insufficiency	1	1.0% (1/96)	1	1.0% (1/96)
Retroperitoneal hematoma	1	1.0% (1/96)	1	1.0% (1/96)
Right bundle branch block	1	1.0% (1/96)	1	1.0% (1/96)
Right ventricular dysfunction	4	4.2% (4/96)	4	4.2% (4/96)
Right ventricular failure	2	2.1% (2/96)	2	2.1% (2/96)
Septic shock	1	1.0% (1/96)	1	1.0% (1/96)
Thrombocytopenia	1	1.0% (1/96)	1	1.0% (1/96)
Thrombosis	1	1.0% (1/96)	1	1.0% (1/96)
Uremia	1	1.0% (1/96)	1	1.0% (1/96)
Vascular access site bleeding	2	2.1% (2/96)	2	2.1% (2/96)
Vascular access site hematoma	1	1.0% (1/96)	1	1.0% (1/96)
Vascular access site infection	0	0.0% (0/96)	1	1.0% (1/96)
Ventricular extrasystoles	1	1.0% (1/96)	1	1.0% (1/96)

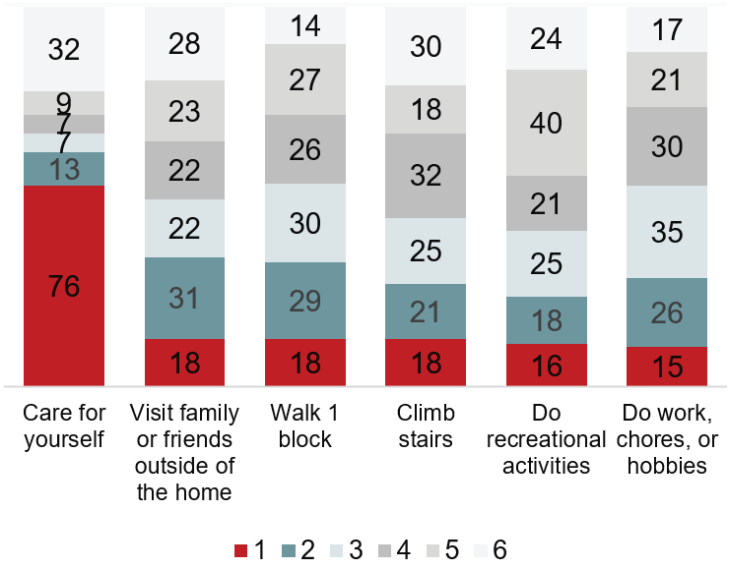
*% (no./total no.)

4. Other Study Observations

Patient Preference Survey Result:

A patient preference survey was administered at baseline to all patients participating in the TRISCEND II pivotal trial to understand the patient priorities for relief from TR symptoms and patient disease burden and experience. The responses to 2 ranking questions on activity and symptom importance are shown in Figure 5, where patients were asked to rank activities or symptoms on a scale of 1 to 6, with 1 being the "most important" and 6 being the "least important" activity or symptom to improve. Fifty-three percent (53%; 76/144) of the patients ranked "caring for yourself"' as the most important activity for improvement, and 41% (59/144) of patients rated "shortness of breath" as the most important symptom to see improvement.

A. Activity Importance



B. Symptom Importance

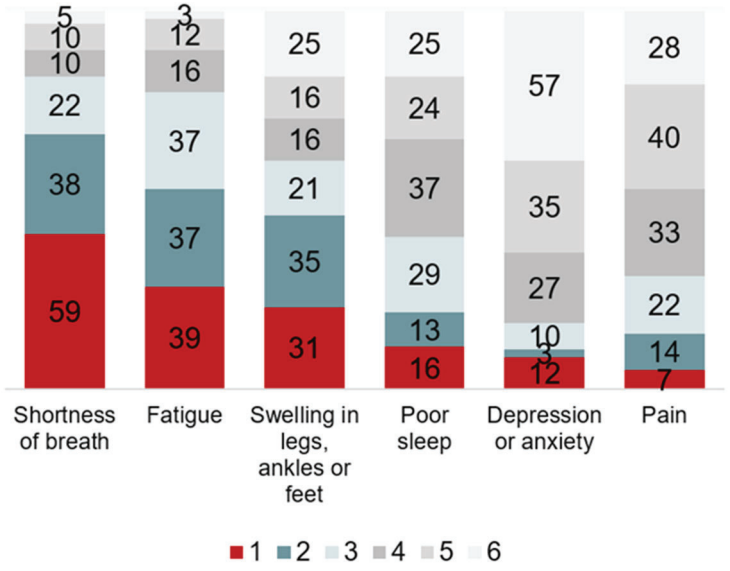


Figure 5. Patient Preference Survey Baseline Data - mITT Safety Population. A total of 144 of the 150 patients were included in the analysis. One (1) patient did not complete the baseline patient preference survey, and 5 patients had incomplete responses.

TR Severity Grade:

The TR severity grades by visit are presented in Figure 6. The proportion of patients with severe or greater TR decreased from 100% at baseline in both groups to 1.2% in the device group compared to 78.4% in the control group at 6 months.

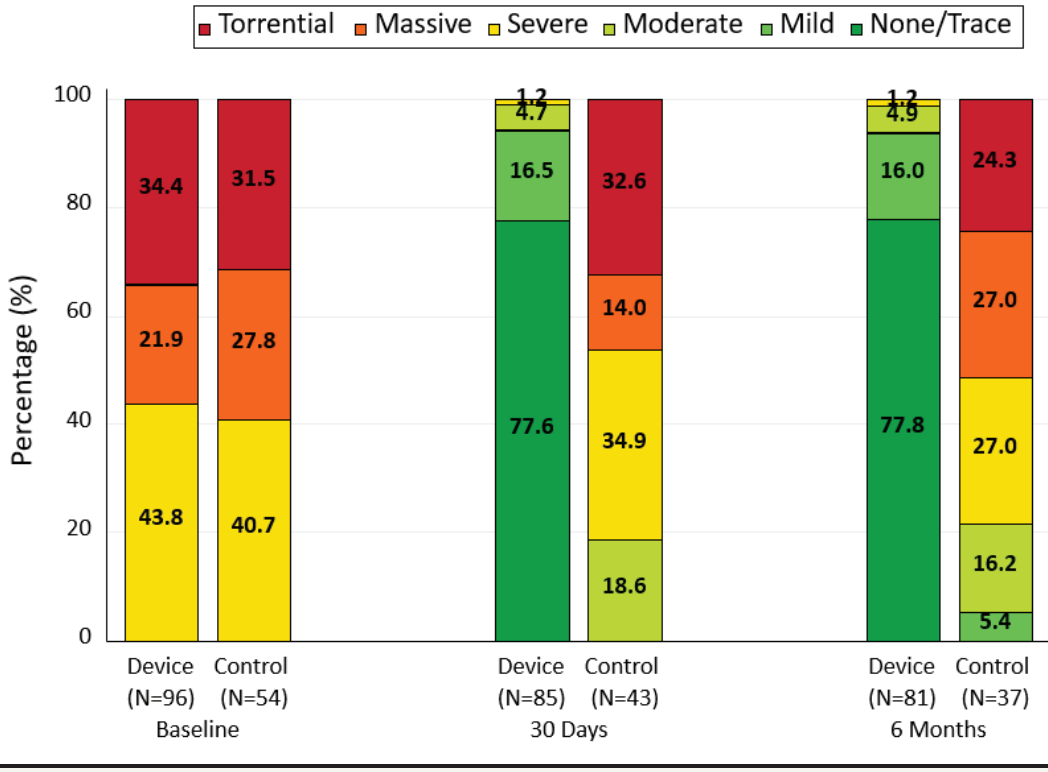


Figure 6. TR Severity Grade by Visit – mITT (Effectiveness) Population.

KCCQ Score:

The results for the KCCQ score are presented in Figure 7. The mean score increased from 49.1 at baseline to 67.4 at 30 days and 72.2 at 6 months in the device group, while it remained mostly unchanged from baseline (49.7) to 30 days (49.2) and increased slightly at 6 months (54.9) in the control group.

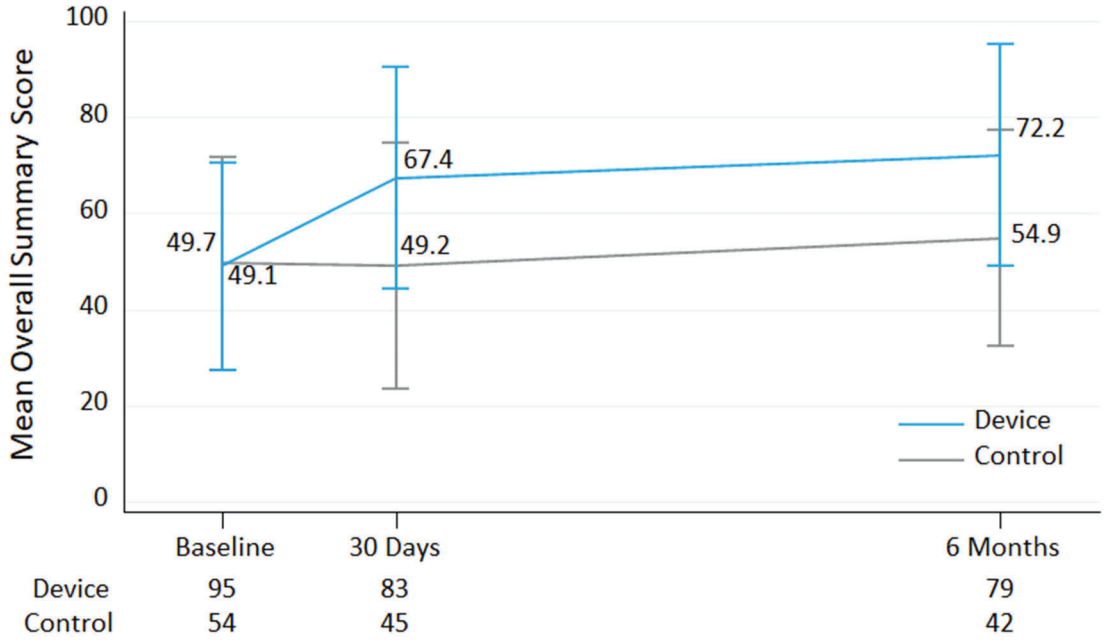


Figure 7. KCCQ Overall Summary Score by Visit – mITT (Effectiveness) Population. The error bars represent standard deviations.

EQ-5D-5L Score:

The results for the EQ-5D-5L visual analog score (VAS) are presented in Figure 8. The mean score in the device group increased from 63.2 at baseline to 73.3 at 30 days and mostly sustained at 6 months (74.7). In contrast, the mean score in the control group remained largely unchanged from baseline (59.8) to 30 days (58.5) and to 6 months (59.1).

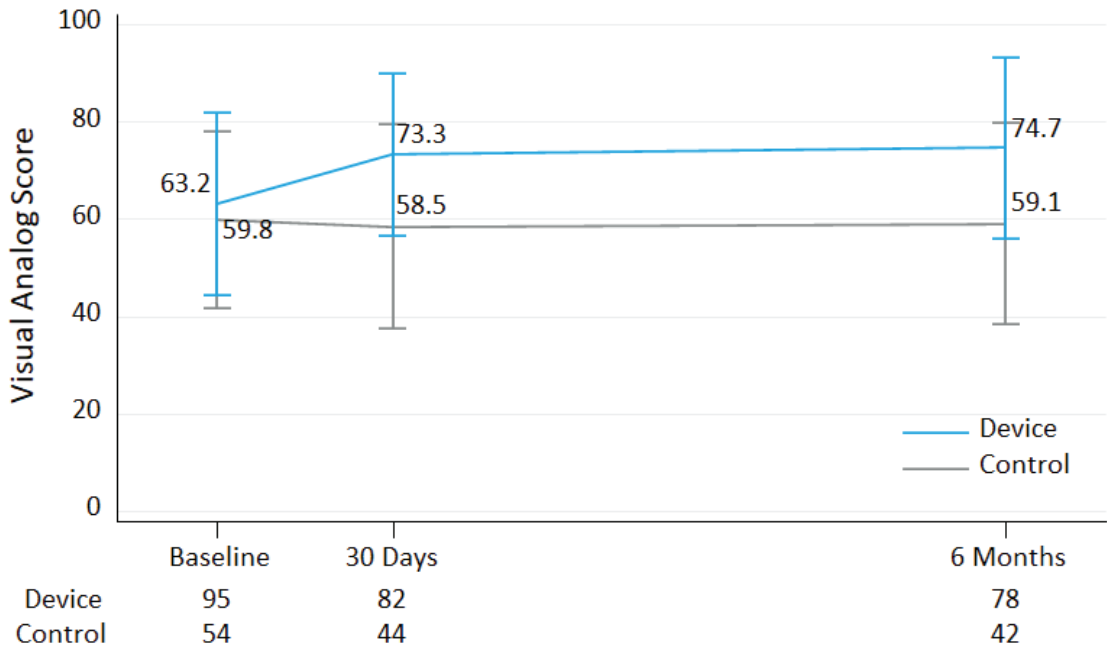
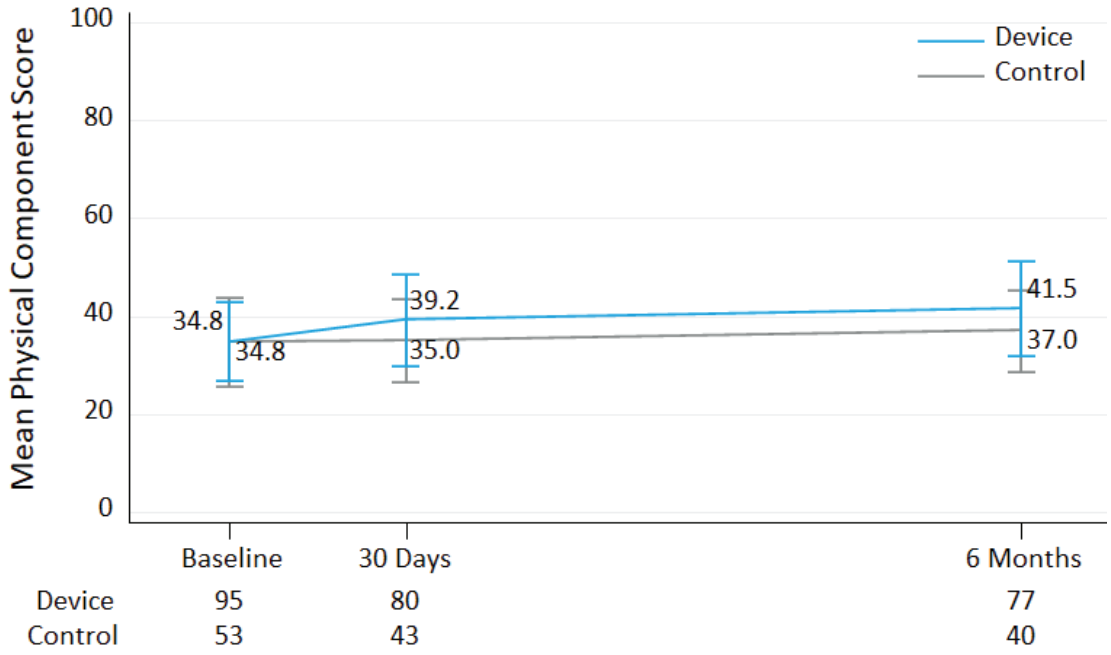


Figure 8. EQ-5D-5L Visual Analog Score by Visit - mITT (Effectiveness) Population. The error bars represent standard deviations.

SF-36 Score:

The results for the SF-36 physical component summary score and mental component summary score are presented in Figure 9. In the device group, the mean SF-36 physical component score increased from baseline by 4.4 points at 30 days and 6.7 points at 6 months, while in the control group, it remained mostly unchanged from baseline to 30 days and increased slightly by 2.2 points from baseline to 6 months. The mean SF-36 mental component score increased from baseline by 2.1 points at 30 days and 4.2 points at 6 months, while it decreased slightly from baseline to 30 days and 6 months in the control group.

A. Physical Component Summary Score



B. Mental Component Summary Score

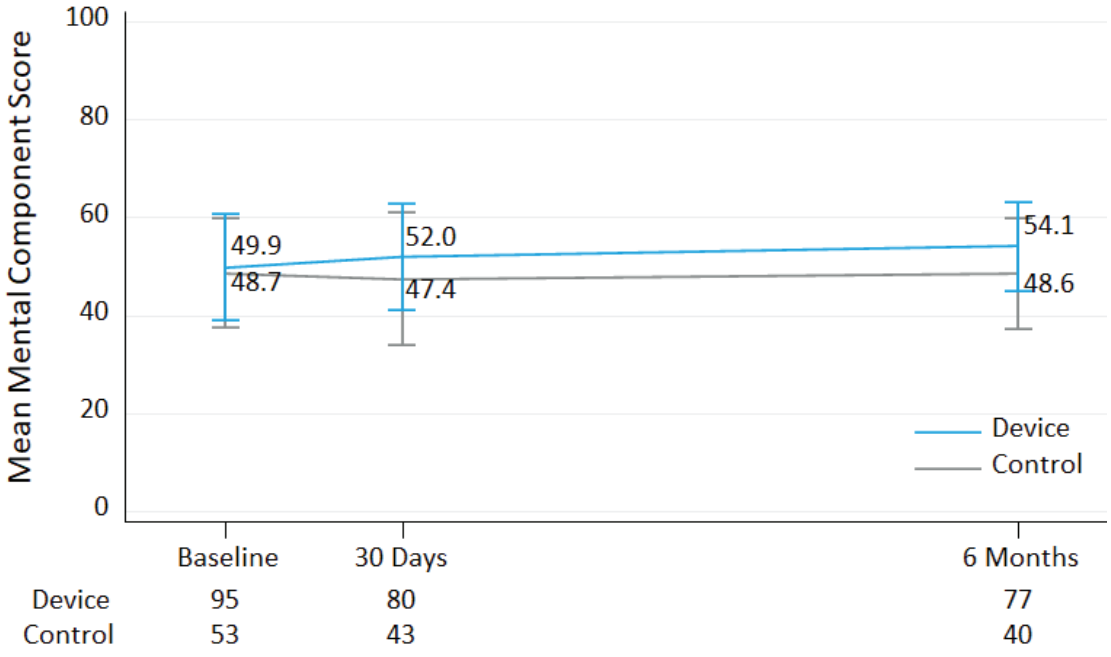


Figure 9. SF-36 Score by Visit – mITT (Effectiveness) Population. The error bars represent standard deviations.

NYHA Functional Class:

The NYHA functional class by visit are presented in Figure 10. At baseline, 79.2% of device patients and 70.4% of control patients were in NYHA class III/IV. The proportion of patients in NYHA class III/IV decreased to 10.1% in the device group compared to 65.9% in the control group at 6 months.

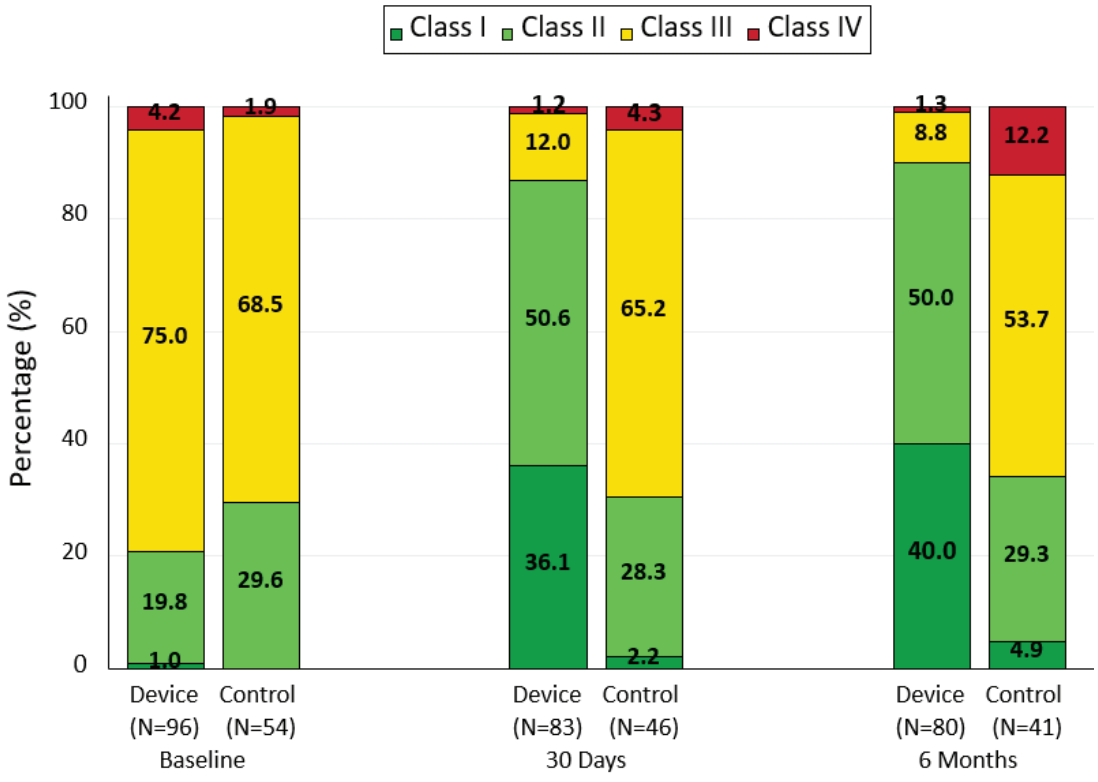


Figure 10. NYHA Functional Class by Visit – mITT (Effectiveness) Population.

6MWD:

The 6MWD results are presented in Figure 11. The mean 6MWD increased by about 25 meters from baseline to 6 months in the device group compared to about 1.1 meters in the control group.

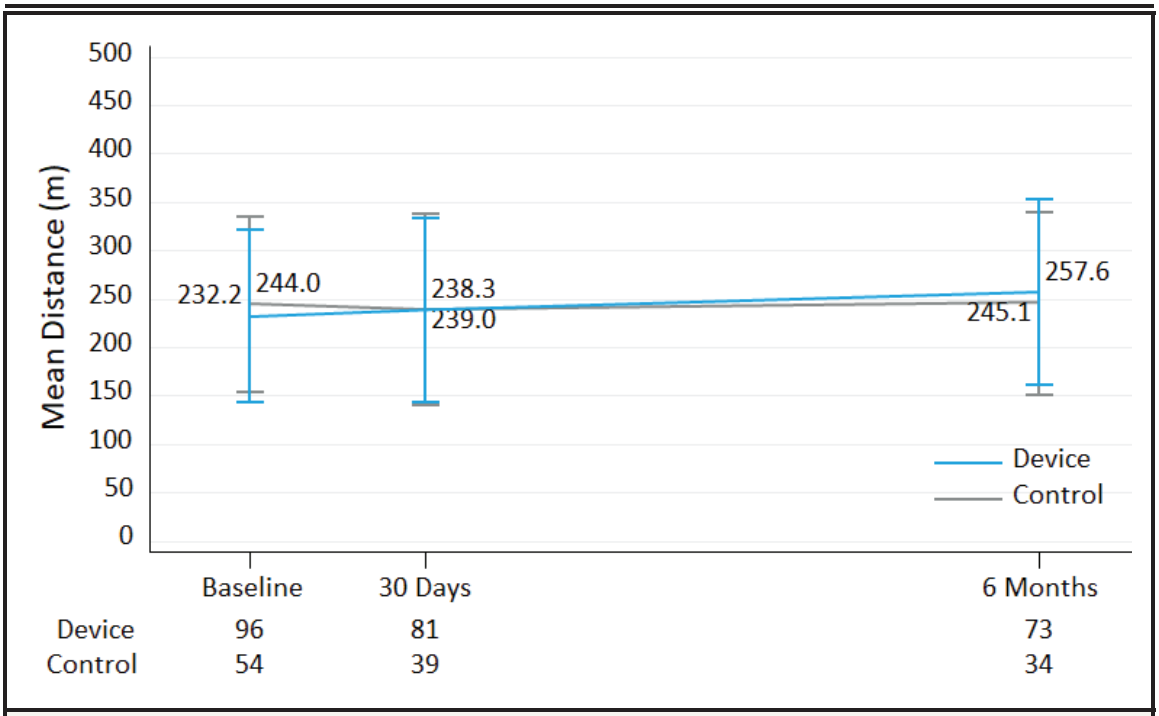


Figure 11. 6MWD by Visit – mITT (Effectiveness) Population. The error bars represent standard deviations.

Echocardiographic Parameters:

Key echocardiographic (TTE) parameters for the mITT Effectiveness population at baseline, 30 days, and 6 months are presented in Table 14.

Table 14. Echocardiographic Parameters – mITT Effectiveness Population (Unpaired)

Variable	Summary Statistics*					
	Baseline		30 Days		6 Months	
	Device Group (N=96)	Control Group (N=54)	Device Group (N=88)	Control Group (N=45)	Device Group (N=81)	Control Group (N=41)
Cardiac output (LVOT; L/min)	3.9 ± 1.97 (92)	3.7 ± 1.64 (54)	4.3 ± 1.34 (80)	4.3 ± 2.38 (44)	4.4 ± 1.58 (73)	4.3 ± 1.95 (40)
CW TV mean gradient (mmHg)	1.8 ± 0.98 (94)	1.7 ± 1.16 (51)	4.3 ± 1.83 (87)	2.0 ± 1.70 (44)	3.3 ± 1.33 (80)	1.5 ± 0.89 (41)
RV fractional area change (%)	40.2 ± 8.36 (85)	39.4 ± 10.00 (50)	25.7 ± 9.90 (68)	36.5 ± 9.63 (36)	27.5 ± 12.54 (67)	36.0 ± 8.46 (39)

RV end diastolic mid diameter (mm)	39.0 ± 8.51 (94)	39.2 ± 6.30 (52)	34.2 ± 7.65 (76)	38.9 ± 7.35 (39)	33.1 ± 7.61 (69)	38.0 ± 7.64 (39)
RVOT VTI (cm)	11.1 ± 3.54 (90)	10.8 ± 4.19 (48)	13.0 ± 4.11 (84)	10.8 ± 3.66 (44)	13.0 ± 4.35 (73)	10.8 ± 3.37 (38)
RVOT stroke volume (mL)	52.0 ± 22.20 (80)	53.2 ± 27.13 (45)	71.5 ± 41.57 (72)	60.7 ± 24.53 (33)	68.6 ± 29.32 (54)	58.3 ± 23.38 (30)
RV free wall longitudinal strain (3D only; %)	-20.7 ± 7.38 (28)	-20.0 ± 8.17 (20)	-13.4 ± 5.23 (29)	-22.0 ± 8.06 (21)	-11.3 ± 4.49 (33)	-21.1 ± 5.95 (23)
IVC diameter (expiration; mm)	25.0 ± 5.78 (94)	24.2 ± 7.10 (54)	22.1 ± 5.33 (82)	23.9 ± 8.14 (39)	20.5 ± 5.18 (79)	23.9 ± 7.91 (39)
Hepatic vein flow						
S-dominant	8.5% (7/82)	11.1% (5/45)	31.6% (18/57)	5.3% (2/38)	25.0% (15/60)	8.8% (3/34)
D-dominant	6.1% (5/82)	15.6% (7/45)	40.4% (23/57)	21.1% (8/38)	56.7% (34/60)	23.5% (8/34)
S-reversal	85.4% (70/82)	73.3% (33/45)	28.1% (16/57)	73.7% (28/38)	18.3% (11/60)	67.6% (23/34)
PASP (mmHg)	37.5 ± 9.57 (93)	38.0 ± 11.53 (54)	35.8 ± 10.45 (31)	36.9 ± 11.74 (38)	34.3 ± 10.25 (33)	37.5 ± 11.37 (38)
TAPSE (mm)	15.9 ± 4.25 (80)	16.0 ± 4.00 (45)	11.8 ± 4.42 (64)	15.6 ± 3.83 (39)	11.3 ± 3.28 (61)	15.4 ± 4.41 (36)

LVOT: left ventricular outflow tract; CW: continuous wave; TV: tricuspid valve; RV: right ventricular; RVOT: right ventricular outflow tract; VTI: velocity time integral; 3D: 3-three dimensional; IVC: inferior vena cava; PASP: pulmonary artery systolic pressure; TAPSE: tricuspid annular plane systolic excursion.
*Continuous variables: mean ± standard deviation (no.); categorical variables: % (no./total no.)

Procedural Data:

The general procedural data for the randomized cohort AT population are summarized in Table 15.

Table 15. General Procedure Data - AT Population.

Variable	Result* (N=92)
General anesthesia	100.0% (92/92)
Implant rate†	100.0% (92/92)

Total procedure time (min)[‡]	115.7 ± 48.93 (92) 101.0 (53.0, 351.0)
Device time (min)[§]	65.7 ± 28.42 (91) 60.0 (31.0, 167.0)
Fluoroscopy duration (min)	30.6 ± 14.03 (92) 27.5 (10.0, 72.0)
Total length of stay in days for the index hospitalization (from procedure date)	5.9 ± 6.09 (92) 4.0 (1.0, 46.0)

[*]Continuous variables: Mean ± standard deviation (n); median (min, max); categorical variables: % (no/total no.).
[†]Implant rate: % of patients who had study device implanted, deployed as intended, and delivery system retrieved successfully.
[‡]Total procedure time: from procedure start time (femoral vein puncture/skin incision) to femoral vein access closure.
[§]Device time: from implant system insertion to removal.

5. 1-Year Outcomes for Available Full Cohort Patients

During FDA's PMA review, a total of 259 patients were randomized to the device group and had an attempted procedure, and 133 patients were randomized to the control group (Full Cohort mITT Safety Population), of which 220 (84.9%) device patients and 98 (73.7%) control patients completed the 1-year visit as of December 15, 2023 (Table 16).

Table 16. Available Full Cohort Patients - mITT Safety Population.

	Device Group	**Control Group**
Total number of patients	259	133
30-day visit complete	245 (94.6%)	124 (93.2%)
6-month visit complete	231 (89.2%)	112 (84.2%)
1-year visit complete	220 (84.9%)	98 (73.7%)
Total withdrawals	10 (3.9%)	18 (13.5%)

Available descriptive 1-year results of the Full Cohort primary endpoint and its components are shown in Figure 12 through Figure 16. There was no RVAD implantation or heart transplantation in either group. The results showed favorable trends in the device group compared to the control group in the win ratio result of the primary endpoint and in the descriptive results of all the primary endpoint components with observed events.

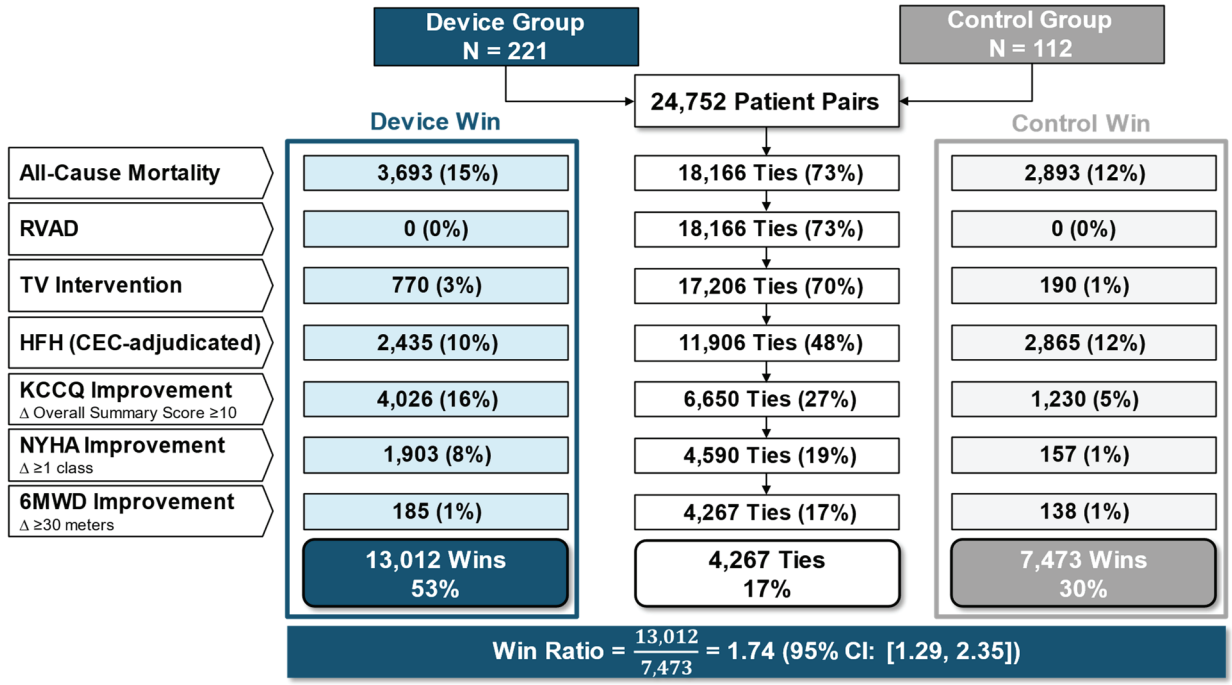


Figure 12. Win Ratio Analysis of Primary Safety and Effectiveness Endpoint - Available Full Cohort mITT Effectiveness Population. RVAD: right ventricular assist device; TV: tricuspid valve; HFH: heart failure hospitalization; CEC: Clinical Events Committee; KCCQ: Kansas City Cardiomyopathy Questionnaire; NYHA: New York Heart Association; 6MWD: 6-minute walk distance; CI: confidence interval.

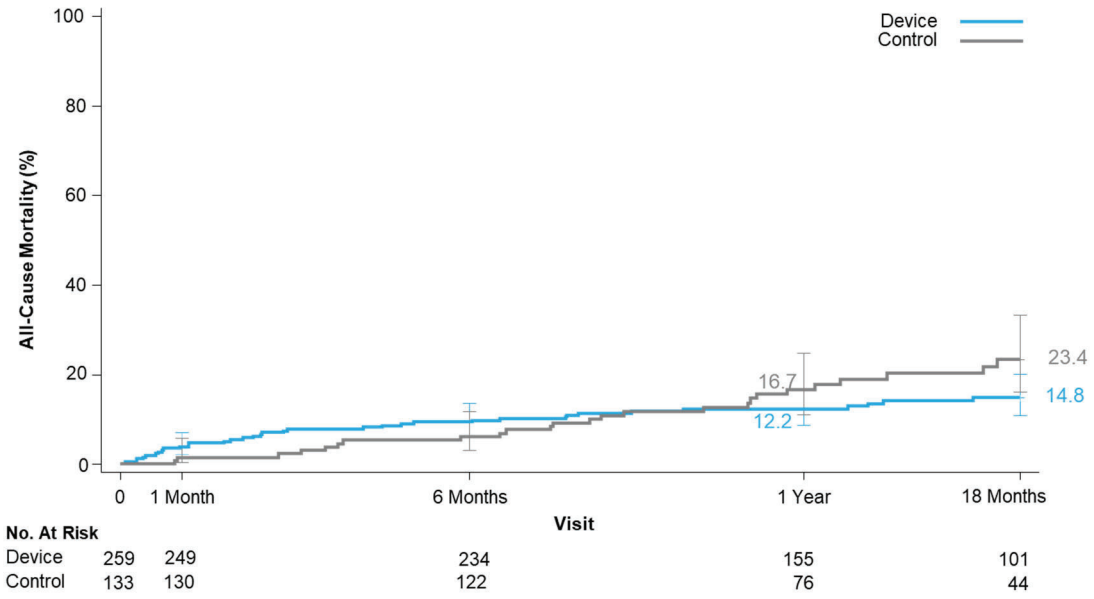


Figure 13. Kaplan-Meier Analysis of Sited-Reported All-Cause Mortality – Available Full Cohort mITT Safety Population.

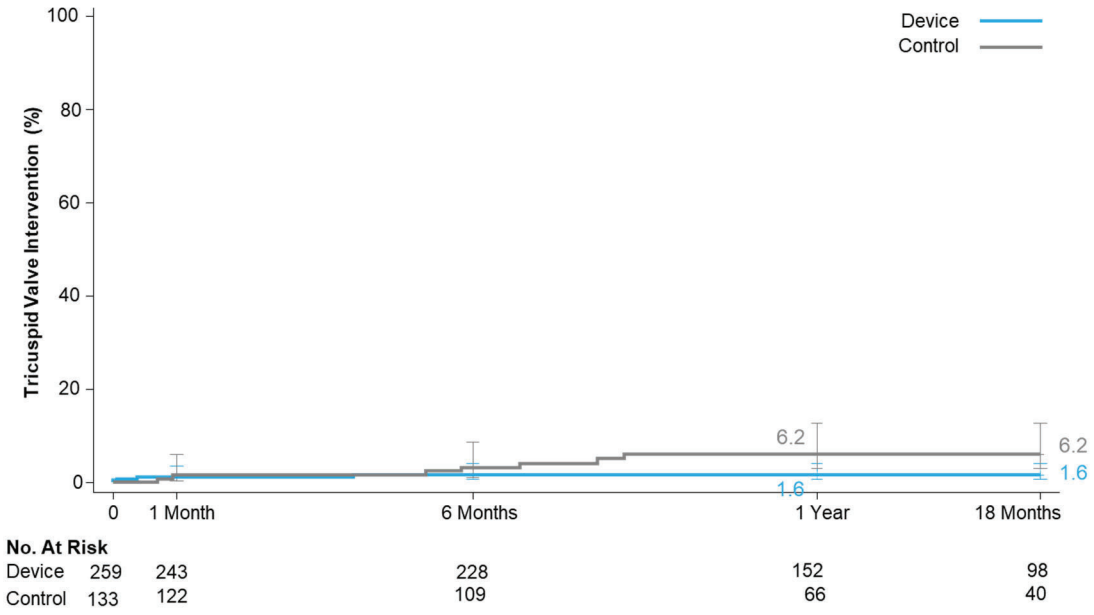


Figure 14. Kaplan-Meier Analysis of Sited Reported Tricuspid Valve Surgical or Percutaneous Intervention – Available Full Cohort mITT Safety Population.

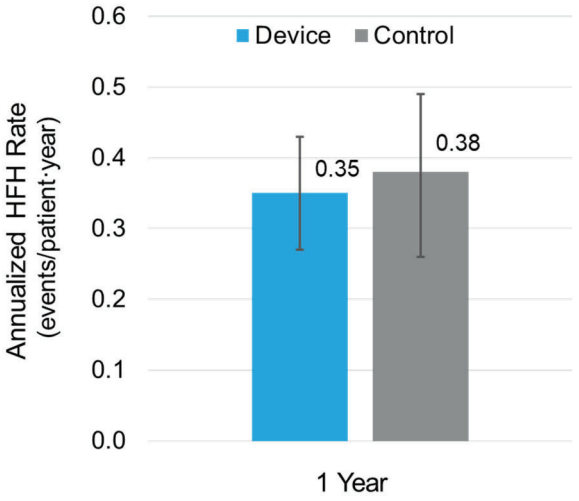


Figure 15. Annualized HF Hospitalization Rate – Available Full Cohort mITT Safety Population. HFH: heart failure hospitalization. The error bars represent the 95% confidence interval (CI). The CIs were calculated without multiplicity adjustment. The adjusted CIs could be wider than presented here.

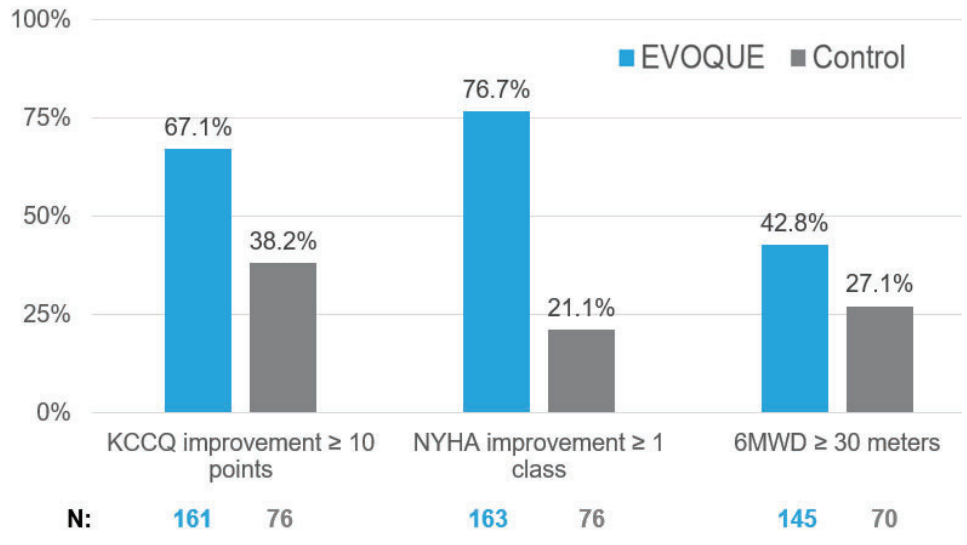


Figure 16. KCCQ, NYHA, and 6MWD Improvements at 1 Year – Available Full Cohort mITT Safety Population. KCCQ: Kansas City Cardiomyopathy Questionnaire; NYHA: New York Heart Association; 6MWD: 6-minute walk distance.

6. Subgroup Results

Prespecified subgroup analyses were performed on the primary safety and effectiveness endpoints of the Breakthrough Pathway Cohort by sex (male vs. female) and age (≤65 years vs. >65 years; ≤80 years vs. >80 years). There were no statistically significant interaction effects between treatment groups and sex or age for the primary safety or effectiveness endpoints.

The primary safety endpoint result, co-primary effectiveness endpoint #1 result, and co-primary effectiveness endpoint #2 components results by race for the Breakthrough Pathway Cohort are shown in Table 17 through Table 19.

Table 17. Primary Safety Endpoint Result by Race - mITT Safety Population.

Race	Composite MAEs at 30 days	
	No. Events	No./Total No. Patients
American Indian or Alaskan Native	0	0/1
Asian	5	4/7
Black or African American	0	0/5
Native Hawaiian or Other Pacific Islander*	0	0/0
White	28	20/63
Not available†	3	2/11
Other‡	0	0/8

MAE: major adverse events.

*No patients in the race category enrolled.

†Europeans regulations did not allow the race information to be collected for patients enrolled in Germany.

‡Other includes racial denominations not covered by broad categories and/or mixed race.

Table 18. Co-Primary Effectiveness Endpoint #1 Result by Race - mITT Safety Population.

Race	TR Grade Reduction to Moderate or Less at 6 Months	
	Device Group	Control Group
American Indian or Alaskan Native	1/1	0/0
Asian	5/5	3/4
Black or African American	4/4	0/1

Native Hawaiian or Other Pacific Islander*	0/0	0/0
White	52/53	4/24
Not available†	11/11	0/4
Other‡	7/7	1/4

TR: tricuspid regurgitation. The numbers shown were no. of patients with events/total no. of patients.

*No patients in the race category enrolled.

†Europeans regulations did not allow the race information to be collected for patients enrolled in Germany.

‡Other includes racial denominations not covered by broad categories and/or mixed race.

Table 19. Co-Primary Effectiveness Endpoint #2 Components Results by Race - mITT Safety Population.

Race	ΔKCCQ ≥10 Points§		ΔNYHA ≥1§		Δ6MWD ≥30 Meters§	
	Device Group	Control Group	Device Group	Control Group	Device Group	Control Group
American Indian or Alaskan Native	1/1	-	1/1	-	0/1	-
Asian	4/5	0/4	5/5	2/4	4/5	1/4
Black or African American	1/5	0/1	3/5	0/1	0/3	0/1
Native Hawaiian or Other Pacific Islander*	0/0	0/0	0/0	0/0	0/0	0/0
White	35/50	9/28	43/51	6/27	21/46	7/22
Not available†	6/11	2/4	7/11	2/4	6/11	1/3
Other‡	5/7	1/5	4/7	1/5	3/7	2/4

KCCQ: Kansas City Cardiomyopathy Questionnaire; NYHA: New York Heart Association; 6MWD: 6-minute walk distance.

*No patients in the race category enrolled.

†Europeans regulations did not allow the race information to be collected for patients enrolled in Germany.

‡Other includes racial denominations not covered by broad categories and/or mixed race.

§The improvements were evaluated at 6 months compared to baseline. The numbers shown were no. of patients with events/total no. of patients.

7. Pediatric Extrapolation

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

E. 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 conducting clinical studies covered by the regulation. The TRISCEND II pivotal clinical trial included 678 investigators. Of these, none were full-time or part-time employees of the sponsor, and 47 investigators had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and 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: 44
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: 4

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.

XI. 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 Systems Devices panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

In the TRISCEND II pivotal trial, the two co-primary effectiveness endpoints of the Breakthrough Pathway Cohort were met. The device group achieved superior TR reduction to the control group. The proportion of patients with moderate or less TR at 6 months (co-primary effectiveness endpoint #1) was 98.8% (80/81) in the device group compared to 21.6% (8/37) in the control group, a difference of 77.1% ($p<0.001$). In addition, the device group was shown to be superior to the control group for the hierarchical composite effectiveness endpoint of KCCQ, NYHA, and 6MWD improvement from baseline to 6 months (co-primary effectiveness endpoint #2), using the Finkelstein-Schoenfeld method ($p<0.001$). The win ratio for co-primary effectiveness endpoint #2 was 4.6, with a lower

bound of the one-sided 97.5% confidence interval of 2.6, in favor of the device group. Furthermore, the available 1-year results of the Full Cohort showed favorable trends in the device group vs. the control group in the primary endpoint components of annualized rate of HF hospitalizations (0.35 vs. 0.38 events/patient-year), KCCQ score improvement ≥10 points (67.1% vs. 38.2%), NYHA functional class improvement ≥1 class (76.7% vs. 21.1%), and 6MWD improvement ≥30 meters (42.8% vs. 27.1%).

B. Safety Conclusions

The risks of the EVOQUE 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 and durability) and animal studies demonstrated that the EVOQUE valve is suitable for long-term implant.

In the Breakthrough Pathway Cohort of the TRISCEND II pivotal trial, the 30-day composite MAEs rate was 27.4%, with a one-sided 97.5% upper confidence bound of 36.9%, which was less than the pre-specified performance goal of 70.0%. Thus, the primary safety endpoint was met. The most frequent MAEs observed were new-onset arrythmia and conduction disorder requiring permanent pacing (22.6%) and severe bleeding (10.5%). In addition, the available 1-year results of the Full Cohort showed favorable trends in the device group vs. the control group in the primary endpoint components of all-cause mortality (12.2% vs. 16.7%; site reported) and tricuspid valve surgical or percutaneous intervention (1.6% vs. 6.2%; site reported).

C. Benefit-Risk Determination

The probable benefits of transcatheter tricuspid valve replacement with the EVOQUE system in patients with severe or greater TR include significant TR reduction and clinically meaningful improvements in health status as measured by KCCQ, NYHA functional class, and 6MWD.

The probable risks of the EVOQUE system include MAEs, such as cardiovascular death, severe bleeding, conduction disturbances requiring a new pacemaker, major access site and vascular complications, major cardiac structural complications due to access-related issues, myocardial infarction, new need for renal replacement therapy, and device-related pulmonary embolism.

Additional factors considered when determining the probable risks and benefits for the EVOQUE system included:

1. Patient Perspectives

   Patient perspectives considered during the review included patient reported outcomes as measured by KCCQ, EQ-5D-5L, and SF-36, as well as the results of the patient preference survey.

In conclusion, given the available information summarized above, the data support that for

patients with at least severe TR, the probable benefits of transcatheter tricuspid valve replacement with the EVOQUE system outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the EVOQUE system for the improvement of health status in patients with symptomatic severe TR who are refractory to OMT.

XIII. CDRH DECISION

CDRH issued an approval order on February 1, 2024. The final clinical conditions of approval cited in the approval order are described below.

The applicant must conduct one post-approval study:

Registry-Based Real-World Use Surveillance: The surveillance will be carried out to assess the real-world performance of the EVOQUE system and the clinical outcomes of the device in patient populations underrepresented in the TRISCEND II pivotal trial. It will involve all consecutive patients treated within the first 2 years following device approval or a total of 5,000 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). Data collection will continue for underrepresented racial and ethnic groups (Black/African American, Asian, American Indian/Alaskan Native, Native Hawaiian/Pacific Islander, and Hispanic or Latino ethnicity) until each group has enrolled a minimum of 100 patients. 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, tricuspid valve reintervention, and hospitalization) 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).

XIV. 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.

XV. REFERENCES

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