Edwards

Edwards EVOQUE Tricuspid Valve Replacement System

Instructions for Use

Rx only

Caution: Implantation of the transcatheter tricuspid valve should only be performed by physicians who have received training for the Edwards EVOQUE tricuspid valve replacement system.

- Do not attempt to use the Edwards EVOQUE valve (herein referred to as the EVOQUE valve), delivery system, or associated accessories before completely reading and understanding the information contained in this booklet.
- Failure to follow these instructions, warnings, and precautions may lead to device damage or patient injury. Use of the EVOQUE system should be restricted to those physicians trained to perform invasive endovascular procedures and to those physicians trained in the proper use of the system.
- Consult with authorized Edwards personnel for appropriate selection of EVOQUE valve size.
- The EVOQUE valve, delivery system, dilator kit, loading system, and stabilizer are supplied STERILE. The single-use accessories (base and plate) and reusable accessories (rail, platform, and plate) are supplied NON-STERILE.
- For the Edwards reusable platform and plate, refer to the reprocessing instructions in the Edwards Reusable Accessories IFU for wipe down steps. For the Edwards reusable rail assembly, refer to the reprocessing instructions in the Edwards Reusable Rail Set IFU. All other devices are supplied for single-use only. After use, dispose in accordance with hospital administrative and/or government policy.

1.0 Introduction

The Edwards EVOQUE tricuspid valve replacement system (herein referred to as the EVOQUE system) is designed to replace the native tricuspid valve in patients with tricuspid valve regurgitation without the need for conventional open-heart surgery. The EVOQUE system consists of four (4) elements which are used with either of the two (2) accessories sets, as outlined below:

<table>
<tr><th>Product Name</th><th>44 mm</th><th>48 mm</th><th>52 mm</th><th>56 mm</th></tr>
<tr><td>Edwards EVOQUE Valve (EVOQUE Valve)</td><td>9850EV44</td><td>9850EV48</td><td>9850EV52</td><td>9850EV56</td></tr>
<tr><td rowspan="2">Edwards EVOQUE Loading System</td><td colspan="3">9850LS</td><td>-</td></tr>
<tr><td colspan="4">9850LSA</td></tr>
<tr><td>Edwards EVOQUE Loading System and Trimmer</td><td colspan="4">9850LSB</td></tr>
<tr><td>Edwards EVOQUE Tricuspid Delivery System</td><td colspan="4">9850TDS</td></tr>
<tr><td>Edwards EVOQUE Dilator Kit</td><td colspan="4">9850DK</td></tr>
</table>

<table>
<tr><th colspan="2">Accessories Set 1</th></tr>
<tr><th>Product Name</th><th>Model Number</th></tr>
<tr><td>Edwards EVOQUE Stabilizer</td><td>9850SB</td></tr>
<tr><td>Edwards EVOQUE Stabilizer Base</td><td>9850BA</td></tr>
<tr><td>Edwards EVOQUE Stabilizer Plate</td><td>9850PT</td></tr>
</table>

Accessories Set 2	
Product Name	**Model Number**
Edwards EVOQUE Stabilizer	9850SZ
Edwards Reusable Rail	10500RL
Edwards Reusable Platform	10000UP
Edwards Reusable Plate	10000PT

Note: The EVOQUE system is designed for use with either Accessories set 1 or Accessories set 2. Accessories set 1 is considered an optional and single-use set for use with the EVOQUE system. Components from set 1 and set 2 are not interchangeable.

Note: The devices that comprise the EVOQUE system are intended to be used together and are not intended to be used as standalone devices. The information in this IFU is applicable to all the EVOQUE system devices.

2.0 Device Description

- **Edwards EVOQUE Valve (Figure 1)**

The EVOQUE valve consists of a trileaflet bovine pericardial tissue valve, nitinol frame, and fabric skirt, and is packaged and terminally sterilized in glutaraldehyde.

Valve size recommendations are based on native valve annulus size, as measured by computed tomography (CT). Patient anatomical factors and imaging modalities should be considered during valve size selection.

Device Diameter (Recommended Valve Size)	Systole		Diastole	
	Recommended Treatable Perimeter - Derived Diameter Range (mm)	Maximum Treatable Annulus Length (mm)	Recommended Treatable Perimeter - Derived Diameter Range (mm)	Maximum Treatable Annulus Length (mm)
44	36.5 - 43	45.5	39.6 - 45.5	50
48	40 - 47	49.5	43.2 - 49.5	54
52	45 - 51	53.5	46.8 - 53.5	58
56	48 - 55	57.5	50.4 - 57.5	62

- **Edwards EVOQUE Tricuspid Delivery System (Figure 2, Figure 3, and Figure 4)**

The delivery system has an outer diameter of 28 F and is intended to deliver the EVOQUE valve in the crimped position via the transfemoral venous approach. The delivery system handle contains a primary flex knob, secondary flex knob, and depth knob to facilitate EVOQUE valve alignment and positioning in the native valve, and a capsule knob and release knob to control the expansion and release of the EVOQUE valve.

- **Edwards EVOQUE Dilator Kit (Figure 5)**

The 24 F, 28 F, and 33 F diameter hydrophilic-coated dilators are intended to dilate the access site, facilitating delivery system insertion. All dilators accommodate a 0.035 inch (0.89 mm) guidewire and are tapered to minimize access site trauma.

- **Edwards EVOQUE Loading System (Figure 6) / Loading System and Trimmer (Figure 7)**

The loading system, which consists of multiple components, is intended to facilitate loading and attachment of the EVOQUE valve onto the delivery system. The loading system assists in crimping the EVOQUE valve to the appropriate diameter, which allows the outer capsule to advance over the EVOQUE valve.

- **Edwards EVOQUE System Accessories Set 1: Stabilizer (Model 9850SB), Base, and Plate (Figure 8)**

The single-use stabilizer with single-use base and plate are intended to secure the delivery system at an angle appropriate for the transfemoral venous approach and to enable fine adjustments of the position of the delivery system during the implantation procedure. The base is height-adjustable to accommodate patient lower extremities and is intended to provide a stable base for the stabilizer. The plate is intended to provide a stable, flat surface for the base on the operating table.

- **Edwards EVOQUE System Accessories Set 2: Stabilizer (Model 9850SZ) and Reusable Rail, Platform, and Plate (Figure 9)**

The reusable accessories compatible with the EVOQUE system include the reusable rail, platform, and plate. The reusable rail is a stable, sterilizable rail that provides a surface to secure compatible stabilizer to the reusable platform. The reusable platform allows for positioning and stabilization of Edwards transcatheter replacement delivery systems through adjustable leg height and a stable platform. The reusable plate is placed below the reusable platform, providing a flat and stable surface during use. The single-use stabilizer is intended to aid with positioning and stabilization of the EVOQUE system during implantation procedures. For the Accessories set utilizing reusable accessories (Figure 9), refer to the Edwards Reusable

Accessories IFU for set up of the platform and plate. If reusable rail is non-sterile or if unpackaging for the first time, refer to the Edwards Reusable Rail Assembly IFU.

3.0 Facilities and Training Requirement

Facilities that intend to perform an implantation procedure utilizing the EVOQUE system must have access to cine fluoroscopy and transesophageal echocardiography (TEE) throughout the procedure. In addition, the implanting physicians must have prompt access to facilities with the necessary equipment, instruments, supplies, and personnel to perform emergency tricuspid valve surgery, if required.

A comprehensive training program is provided by Edwards Lifesciences and must be completed by the implanting physicians before use of the EVOQUE system. The implanting physicians should have advanced technical knowledge and experience in related catheter-based procedures.

4.0 Indications for Use

4.1 Intended Use

The EVOQUE tricuspid valve replacement system is indicated for the improvement of health status in patients with symptomatic severe tricuspid regurgitation despite being treated optimally with medical therapy for whom tricuspid valve replacement is deemed appropriate by a Heart Team.

5.0 Contraindications

The EVOQUE valve is contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen, who have active bacterial endocarditis or other active infections, or who have untreatable hypersensitivity to nitinol alloys (nickel and titanium).

6.0 Warnings

- The EVOQUE valve, delivery system, loading system, dilator kit, and stabilizer are designed, intended, and distributed for STERILE single-use only. The EVOQUE stabilizer base and EVOQUE stabilizer plate are provided nonsterile for single-use only. Do not resterilize or reuse any of the single-use devices. There are no data to support the sterility, nonpyrogenicity, or functionality of the single-use devices after reprocessing.
- Ensure proper sterile techniques are utilized during the preparation, transfer, and use of the devices.
- Do not use the valve if the tamper evident seal is broken, the storage solution does not completely cover the valve, the temperature indicator has been activated, the valve is damaged, or the expiration date has elapsed. The EVOQUE valve must remain hydrated at all times. The valve cannot be exposed to solutions, antibiotics, or chemicals other than its shipping storage solution and sterile physiologic saline solution. This will help prevent leaflet damage that may impact valve functionality. Keep the EVOQUE valve hydrated with normal saline until ready for implantation.
- Ensure the correct valve size is selected. Implantation of the improper size (i.e., undersizing or oversizing) may lead to paravalvular leak (PVL), migration, embolization, and/or annular damage.
- Patients with previously implanted devices (e.g., inferior vena cava (IVC) filter) should be carefully assessed prior to insertion of the delivery system to avoid potential damage to vasculature or a previously implanted device.
- Patients with pre-existing cardiac leads should be carefully assessed prior to implantation to avoid potential adverse interaction between devices.
- Care should be taken when implanting cardiac leads after EVOQUE valve implantation to avoid potential adverse interaction between the devices.
- Patients implanted with the EVOQUE valve should be maintained on anticoagulant/antiplatelet therapy as determined by their physicians in accordance with current guidelines, to minimize the risk of valve thrombosis or thromboembolic events.
- There are no data to support device safety or effectiveness if the patient has:
  - Echocardiographic evidence of severe right ventricular dysfunction;
  - Pulmonary arterial systolic pressure (PASP) > 70 mmHg by echo Doppler;
  - A trans-tricuspid pacemaker or defibrillator lead that has been implanted in the RV within the last 3 months;
  - Dependency on a trans-tricuspid pacemaker without alternative pacing options.

7.0 Precautions

7.1 Precautions Prior to Use

- The patient's eligibility depends on the anatomic conditions based on CT scan.
- It is advised that a multi-disciplinary heart team be of the opinion that EVOQUE valve implantation is preferable to alternative percutaneous device solutions, including minimally-invasive open heart surgery.
- It is advised that a multi-disciplinary heart team takes into consideration the severity of disease and the chances of reversibility of right heart failure based on a complete hemodynamic assessment.

7.2 Precautions

- The EVOQUE valve is to be used only with the EVOQUE delivery system and EVOQUE loading system.
- The procedure should be conducted under appropriate imaging modalities, such as transesophageal echocardiography (TEE), fluoroscopy, and/or intracardiac echocardiography (ICE).
- Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to, or breathing of, the solution. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water; in the event of contact with eyes, seek immediate medical attention. For more information about glutaraldehyde exposure, refer to the Safety Data Sheet available from Edwards Lifesciences.
- Conduction disturbances may occur before, during, or following implantation of the EVOQUE valve, which may require continuous ECG monitoring before hospital discharge. If a patient has confirmed or suspected conduction disturbances, consider patient monitoring and/or electrophysiology evaluation. The risk of conduction disturbances may increase with the 56 mm valve size.
- Appropriate antibiotic prophylaxis is recommended post-procedure in patients at risk for prosthetic valve infection and endocarditis.
- Long-term durability has not been established for the EVOQUE valve. Regular medical follow-up is advised to evaluate EVOQUE valve performance.
- Implantation of the EVOQUE valve should be postponed in patients with (1) a history of myocardial infarction within one month (30 days) of planned intervention, (2) pulmonary emboli within 3 months (90 days) of planned intervention, (3) cerebrovascular accident (stroke or TIA) within 3 months (90 days) of planned intervention, (4) active upper GI bleeding within 3 months (90 days) prior to procedure requiring transfusion.

8.0 Potential Adverse Events

Potential adverse events related to standard cardiac catheterization, use of anesthesia, the EVOQUE valve, and the implantation procedure include:

- Abnormal lab values
- Allergic reaction to anesthesia, contrast media, anti-coagulation medication, or device materials
- Anaphylactic shock
- Anemia or decreased hemoglobin (Hgb), 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)
- Death
- Edema
- Electrolyte imbalance
- Embolization including air, particulate, calcific material, or thrombus
- 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
- 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 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 – 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
- Transient ischemic attack (TIA)
- Valve dislodgement/embolization
- 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

9.0 Additional Equipment

The implantation procedure requires additional equipment that is not supplied with the EVOQUE system. The additional equipment is provided below.

9.1 Equipment for EVOQUE Valve Loading

Note: Volumes reflect adequate amount for preparing 1 implant.

- 3500 ml (minimum) sterile physiological saline solution at ambient temperature (~ 23 °C)
- 500 ml (minimum) heparinized saline solution (2 units/ml) at ambient temperature (~ 23 °C)
- 4 sterile bowls (≥ 500 ml, ≥ 7 cm depth, plastic)
- 1 large sterile bowl (≥ 2 L, ≥ 10 cm depth, plastic)
- 1 scalpel, no. 11 scalpel blade
- 1 luer locking syringe (≥ 20 cc)
- Gauze pads
- Blunt tip forceps
- Blunt tip scissors
- Sterile towels

9.2 Equipment for Access, Procedure, and Monitoring

- Standard cardiac catheterization lab equipment
- Femoral vessel introducer sheath
- Fluoroscopy (fixed, mobile, or semi-mobile fluoroscopy systems appropriate for use in percutaneous coronary interventions)
- Transesophageal echocardiography capabilities
- Steerable introducer sheath
- Exchange length 0.035 inch (0.89 mm) max guidewire
- Extra small curve 0.035 inch (0.89 mm) max guidewire
- Right coronary arterial catheter and guidewire
- Sterile table for EVOQUE valve and device preparation

9.3 Standby Equipment

- Arterial bypass cannula (~18 F)
- Cardiopulmonary bypass machine
- Compliant balloon (> 20 mm diameter, 9 cc contrast volume)
- Diluted radiopaque contrast medium (15:85 medium to saline dilution)
- High pressure contrast injector
- Intra-aortic balloon pump and appropriately sized balloon
- Pigtail angiographic catheter
- Venous return bypass cannula (~18 F)
- Transthoracic echocardiographic (TTE) equipment
- Vascular access lubricant
- Temporary pacing equipment

10.0 Directions for Use

10.1 Prior to Use Inspection

Before using the EVOQUE system, visually examine each element and accessory for evidence of gross damage (e.g., a cracked jar or lid, leakage, broken or missing seals) that may have compromised the packaging sterility (if applicable) or functionality of the components.

WARNING: Do not mishandle the delivery system or use the delivery system and accessory devices if the packaging and/or sterile barriers and any components have been opened or damaged, or the expiration date has elapsed, as sterility and/or function may be compromised.

WARNING: Do not mishandle the EVOQUE valve or use device/container if found to be damaged, leaking, or without adequate sterilant (not fully submerged in glutaraldehyde, or missing intact seals). The EVOQUE valve must not be used for implantation, as sterility may be compromised.

WARNING: Do not use the EVOQUE valve if the expiration date has elapsed, as either sterility or valve function may be compromised.

WARNING: Do not use the EVOQUE valve if the temperature indicator has been activated, as valve function may be compromised.

WARNING: Do not use the EVOQUE valve if the tamper evident seal is broken, as sterility may be compromised.

10.2 Accessories Setup

10.2.1 Accessories Set 1 Setup

Step	Procedure
1	Place the plate on the operating table beneath the patient's leg to support the base during the procedure.
2	After the patient has been positioned on the operating table, place single-use base over the patient's leg, on top of the plate, at the desired distance from the mid-sternum.
3	Establish sterile barrier.
4	After sterile draping, place single-use base adapter in-line with the access site and attached to the front of the base using a clamp (Figure 8).

Note: In the Accessories set 1 configuration, the base adapter and clamp are both supplied with the stabilizer.

10.2.2 Accessories Set 2 Setup

For the Accessories set 2 configuration utilizing reusable accessories (Figure 9), refer to the Edwards Reusable Accessories IFU for set up of the platform and plate. If reusable rail is non-sterile or if unpackaging for the first time, refer to Edwards Reusable Rail Set IFU. Once reusable rail is sterile, refer to below instructions.

Step	Procedure
1	Remove Edwards reusable rail from sterilization wrap (blue wrap) and inspect for damage.
2	Prior to sterile draping the patient, assemble and position the reusable plate and reusable platform around the legs of patient, adjusting the height and angle of the platform as needed. Refer to the Edwards Reusable Accessories IFU.
3	Establish sterile barrier.
4	After sterile draping, assemble and attach Edwards reusable rail and stabilizer to the reusable platform.
5	Following the procedure, remove the reusable rail from the reusable platform. Perform standard wipe down of reusable rail before sending for reprocessing. Refer to the Edwards Reusable Rail Set IFU.

10.3 Device Handling and Preparation

Follow sterile technique during device preparation and implantation. Preparation to be performed by two operators, an implant operator (operating the distal section of the delivery system) and a handle operator (operating the proximal section of the delivery system). Edwards personnel will always serve as implant operator. Handle operator can be an Edwards personnel or hospital staff. The handle operator is to follow instructions below:

WARNING: Do not mishandle the EVOQUE valve. EVOQUE valve leaflets mishandled or damaged during any part of the loading process will require replacement of the EVOQUE valve.

WARNING: The EVOQUE valve should not remain fully crimped for a period of time longer than 120 minutes, as it may impair valve functionality.

CAUTION: Do not place the jar or the pouch of the delivery system into the sterile field. The outside of the jar and the pouch are not sterile, and the contents within the jar and pouch should be handled using standard aseptic techniques to prevent contamination.

CAUTION: To reduce the risk of contamination, do not open the EVOQUE valve jar until implantation is certain.

CAUTION: Ensure that the entire suture is removed when removing the serial number tag from the EVOQUE valve, as it may lead to emboli.

CAUTION: Do not allow the EVOQUE valve to come in contact with any sharp instrument, as it may impair valve function.

WARNING: Adequate rinsing with normal saline must be performed before implantation to reduce glutaraldehyde concentration, as it may result in glutaraldehyde toxicity.

CAUTION: Avoid contact of the leaflet tissue or the rinse solution with towels, linens, or other sources of lint or particulate matter that could be transferred to the leaflet tissue, as it may lead to emboli.

10.3.1 Delivery System Preparation

Follow sterile technique during device preparation and implantation. Edwards personnel will direct the handle operator to do the following:

Step	Procedure
1	Wipe only the handle of the delivery system using gauze soaked in saline via syringe.
2	Remove stylets from proximal and distal end of the delivery system, then flush the guidewire lumen (Figure 4(3)) with heparinized saline as the instructed amount by Edwards personnel.
3	Flush the handle flush port (Figure 3(4)) then sheath port (Figure 3(1)) with heparinized saline as the instructed amount by Edwards personnel.
4	Retract outer capsule: Rotate the white knob (Figure 3(2)) in the direction of the arrows until it comes to a hard stop to ensure outer capsule (Figure 4(8)) is fully retracted.
5	Retract inner capsule: Rotate the blue knob (Figure 3(3)) in the direction of the arrows until it comes to a hard stop to ensure inner capsule (Figure 4(6)) is fully retracted.
6	Ensure primary and secondary knobs (Figure 3(5 and 6)) are at 0 (zero). Ensure black depth knob (Figure 3(7)) is at ½. (if not, rotate to ½ or instructed by Edwards personnel).
7	Fully advance tapered tip: Press tapered tip locking button and advance the tapered tip slider (Figure 3(8)), releasing tapered tip locking button when complete.

10.3.2 Implant Preparation

Authorized Edwards personnel will perform the necessary steps to ensure the implant is ready for loading.

10.3.3 Implant Locking and Loading

Loading system components will be attached to the implant and delivery system by authorized Edwards personnel serving as the implant operator.

Edwards personnel will direct the handle operator to:

Step	Procedure
1	Slowly turn the white knob (Figure 3(2)) counterclockwise in the opposite direction of the arrows to advance the outer capsule (Figure 4(8)), stopping as indicated by Edwards personnel.
2	Rotate white knob (Figure 3(2)) in the direction of the arrows to retract outer capsule until the knob hard-stops (Figure 4(8)).
3	Rotate the blue knob (Figure 3(3)) in the opposite direction of the arrows to advance the inner capsule (Figure 4(6)), stopping when indicated by Edwards personnel. **Note: Edwards personnel will remove the lock driver and prepare the implant for loading then direct the handle operator to do the following:**
4	Rotate the white knob (Figure 3(2)) in the opposite direction of the arrows to continuously advance the outer capsule (Figure 4(8)), stopping at several stages as indicated by Edwards personnel until the guidewire shield and the implant anchors are at the appropriate position.
5	Fully advance inner capsule (Figure 4(6)) by rotating the blue knob (Figure 3(3)) in the opposite direction of the arrows until it hard-stops.
6	Fully advance outer capsule (Figure 4(8)) by rotating the white knob (Figure 3(2)) in the opposite direction of the arrows until it hard-stops. **Note: Edwards personnel will remove loader funnel and direct the handle operator to do the following:**
7	Relieve tension in the outer and inner capsule. **Note: Edwards personnel will pull tension on the support tube assembly to fully seat valve, while simultaneously directing the handle operator to do the following:**
8	Pull tension on delivery system handle while rotating white knob (Figure 3(2)) in the opposite direction of the arrows to relieve tension. **Note: Edwards personnel will perform final preparations steps to trim the capsule and direct the handle operator to do the following:**
9	Flush the handle flush port (Figure 3(4)) with the instructed amount of saline until the capsule is filled.
10	Slowly retract the tapered tip (Figure 4(1)) by pressing tapered tip button and retracting tapered tip slider (Figure 3(8)) until it contacts capsule.

Step	Procedure
11	Rotate the black depth knob (Figure 3(7)) counterclockwise in the opposite direction of the arrows until depth knob hard-stops.
12	Flush the handle flush port (Figure 3(4)) with the instructed amount of saline.
13	Flush the sheath port (Figure 3(1)) with the instructed amount to eliminate air and advance the sheath distally until mated flush to capsule.
14	Remove stylets from ends of the delivery system.
15	Flush the handle flush port (Figure 3(4)) and guidewire lumen (Figure 4(3)) with the instructed amount of heparinized saline.
16	Wipe the coated components (sheath, capsule, and tapered tip) using heparinized saline-soaked gauze.

10.4 EVOQUE Valve Implant

10.4.1 Guidewire Placement

Prepare femoral venous access using standard interventional techniques.

WARNING: Do not use excessive force and/or manipulation during advancement and positioning of the guidewire, as it may result in perforation/dissection of arteries, veins, and/or other cardiac structures. This may also result in cardiac arrhythmias and conduction disturbances.

Step	Procedure
1	Advance steerable sheath into the right atrium at the exit of the IVC.
2	Insert a guidewire through the steerable sheath.
3	Advance the guidewire across the tricuspid valve. **Note: Other interventional devices and techniques (e.g., guide catheters) may be used to assist the guidewire in crossing the tricuspid valve.**
4	Establish proper guidewire path and confirm no entanglement with cardiac structures.

10.4.2 EVOQUE Valve Delivery

WARNING: Avoid excessive movement of the delivery system while executing the procedure to protect vasculature or cardiac structures. Avoid excessive rotation of the delivery system to maintain functionality of the delivery system.

Note: Flush the delivery system with heparinized saline as needed throughout the procedure.

Step	Procedure
1	Ensure the hydrophilic coating on dilators and delivery system is activated prior to use. Dilate access site. An Edwards EVOQUE dilator kit should be used as needed.
2	Insert the delivery system over the guidewire.
3	Advance the delivery system until the distal end of the tapered tip is positioned at the junction between IVC and right atrium.
4	Using fluoroscopy, ensure the delivery system is oriented in the proper orientation. **WARNING: The primary flex on the delivery system flexes in the direction of the flush ports; care should be taken to ensure that the delivery system is orientated correctly at this point.**
5	Retract the sheath.
6	Flex and orient the delivery system towards the tricuspid valve.
7	Advance the delivery system to cross the tricuspid valve. **Note: Delivery system flex, delivery system rotation, and guidewire position may be adjusted during valve crossing to optimize crossing position.**
8	Using echocardiography and fluoroscopic guidance, verify that the delivery system has crossed through the tricuspid valve into the right ventricle.
9	If using the Accessories set 1 configuration, dock the stabilizer onto the base adapter and secure it to the base. If using the Accessories set 2 configuration, dock the rail onto the platform and secure it. Next, dock the stabilizer onto the rail and secure it.
10	Attach the delivery system and sheath to the stabilizer.

Step	Procedure
11	Adjust the delivery system as needed to ensure hemodynamic stability.
12	Using pre-operative CT data (if available), position the C-arm at the optimal viewing projection.
13	Position the delivery system to be coaxial to the tricuspid annulus while minimizing contact with the native anatomy.
14	Using echocardiography and fluoroscopic guidance, confirm that the EVOQUE valve is positioned at the appropriate depth and coaxiality with relation to the native valve. **CAUTION: Once the capsule is retracted to expose the EVOQUE valve anchors, the valve is unable to be retrieved or recaptured into the delivery system.** **WARNING: Maintain central position of the delivery system within the native valve during deployment to ensure proper positioning of the valve.**
15	Retract the outer capsule until the anchors are exposed.
16	Adjust the position of the EVOQUE valve so that the anchors are positioned within native leaflets as dictated by patient anatomy.
17	Retract the outer and inner capsule until the desired EVOQUE valve diameter is achieved.
18	Engage the leaflets.
19	Confirm positioning of the EVOQUE valve by using echo imaging to assess engagement of the leaflets. Adjust the EVOQUE valve positioning as needed.
20	Using echo imaging, observe the motion of the native leaflets and adjust the position of the EVOQUE valve as required to fully engage native tricuspid valve leaflets.
21	Once full engagement has been confirmed, ensure that the EVOQUE valve is perpendicular to the tricuspid annular plane.
22	Retract the tapered tip until it is positioned within the EVOQUE valve.
23	Retract the inner capsule until the EVOQUE valve is released from the delivery system. **CAUTION: Care should be taken during final release of the EVOQUE valve using the release knob, as premature release may impact performance of the EVOQUE valve.**
24	Using echo and fluoroscopic imaging, assess final position and functionality of the EVOQUE valve.

10.4.3 Delivery System Removal

WARNING: Take care to maintain position of delivery system central within the EVOQUE valve during delivery system removal, as failure to do so may impact valve functionality or lead to dislodgement of the valve.

Note: Delivery system can be removed from the stabilizer at any point during removal, if applicable.

Step	Procedure
1	Fully retract the tapered tip.
2	Unflex and retract delivery system as needed until the tapered tip is above the locking tabs of the EVOQUE valve. Adjust the guidewire as needed to maintain a central position relative to the EVOQUE valve. Ensure that the locking ring is free from the EVOQUE valve.
3	Rotate the release knob so that the inner capsule is in contact with the tapered tip.
4	Unflex and retract the delivery system as needed.
5	Rotate the capsule retraction knob until the outer capsule is in contact with the inner capsule.
6	Ensure the delivery system is fully unflexed and remove the delivery system from the access site. **Note: A sheath may be used to seal the femoral vein following system removal.**
7	Perform femoral closure as applicable using standard interventional techniques.
8	Perform a ventriculogram if needed to assess final position of the EVOQUE valve.

11.0 How Supplied

11.1 Sterilization and Packaging

The EVOQUE valve is provided sterile by terminal liquid sterilization and is non-pyrogenic. It is packaged and sterilized in a glutaraldehyde solution inside a jar to which a seal has been applied. The outer surface of the jar is not sterile and must not be placed in the sterile field. The EVOQUE valve is supplied with a temperature indicator and should not be used if the indicator has been activated.

The delivery system, dilator kit, and loading system are supplied sterilized by ethylene oxide and provided non-pyrogenic. The components are secured on a card and packaged in a pouch and shelf box.

The stabilizer is provided ethylene oxide sterilized. The components are secured on a card and packaged in a pouch and shelf box.

The single-use base and plate or the reusable rail, platform, and plate are provided non-sterile.

The components are packaged in individual shipper boxes.

11.2 Storage

The EVOQUE valve should be stored between 10 °C and 25 °C (50 °F and 77 °F). Stock inspection and rotation at regular intervals are recommended so that the EVOQUE valve with an earlier expiration date is used first.

The delivery system, dilator kit, loading system, single-use stabilizer/base/plate and reusable platform/plate should be stored in a cool, dry place that is contamination free. Refer to the Edwards Reusable Rail Set IFU for storage of the reusable rail.

12.0 Magnetic Resonance (MR) Safety Information

MR

Non-clinical testing has demonstrated that the Edwards EVOQUE valve is MR Conditional. A patient with the valve can be safely scanned in an MR system meeting the following conditions:

- Static magnetic field of 1.5 and 3 T only
- Maximum spatial gradient magnetic field of 3000 gauss/cm (30.0 T/m) or less
- Maximum MR system-reported, whole body averaged specific absorption rate (SAR) of 2.0 W/kg
- Normal operating mode of the MR system for both gradients and SAR

Under the scan conditions defined above, the EVOQUE valve is expected to produce a maximum temperature rise of 4 °C after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the EVOQUE valve extends approximately 0.8 cm from the device when imaged with a gradient echo or spin echo pulse sequence and a 3 T MRI system.

13.0 Patient Information

Patient education brochures are provided to each site and should be given to the patient to inform them of the risks and benefits of the procedure and alternatives in adequate time before the procedure to be read and discussed with their physician. A copy of this brochure may also be obtained from Edwards Lifesciences by calling 1.888.713.1564.

A patient implant card request form is provided with each transcatheter heart valve. After implantation, all requested information should be completed on this form. The serial number may be found on the package and on the identification tag attached to the transcatheter heart valve. The original form should be returned to the Edwards Lifesciences address indicated on the form and upon receipt, Edwards Lifesciences will provide an identification card to the patient.

14.0 Recovered Implant and Device Disposal

Edwards Lifesciences is interested in obtaining recovered clinical specimens of the EVOQUE valve for analysis. A written report summarizing our findings will be provided upon completion of our evaluation. Please contact Edwards for return of the recovered valve.

If you do decide to return any of the devices, please follow the following instructions:

- **Unopened Package with Sterile Barrier Intact:** If the pouches have not been opened, return the device in its original packaging.
- **Package Opened but Not Implanted:** If a pouch is opened, the device is no longer sterile. Please return the device in its original packaging.
- **Explanted Implant:** The explanted implant should be placed into a suitable histological fixative such as 10% formalin or 2% glutaraldehyde. Refrigeration is not necessary under these circumstances. Contact Edwards Lifesciences to request an Explant Kit for return to Edwards.

14.1 Disposal

Use universal precautions for biohazards and sharps to avoid user injury. Used devices (includes all devices that come in contact with patients) should be handled and disposed of in accordance with institutional guidelines on biohazardous materials and hospital waste to avoid possible cross-contamination. For disposal of the reusable platform and plate accessories, refer to the Edwards Reusable Accessories IFU.

15.0 Clinical Data

The EVOQUE system was studied in the TRISCEND II pivotal trial.

A. Study Design

The TRISCEND II pivotal trial was a prospective, multicenter, randomized study designed to demonstrate the safety and effectiveness of transcatheter tricuspid valve replacement with optimal medical therapy (OMT) compared to OMT alone in patients with severe TR. Eligible patients were randomized 2:1 into either the EVOQUE system with OMT ("Device Group") or OMT alone ("Control Group").

The TRISCEND II pivotal trial enrolled 400 patients and used two primary analysis phases. The trial evaluated 30-day safety and 6-month effectiveness endpoints for the first 150 randomized patients ("Breakthrough Pathway Cohort") and a 1-year safety and effectiveness endpoint for the full cohort of 400 patients ("Full Cohort") in the second phase.

The TRISCEND II pivotal trial employed a Central Screening Committee (CSC) that ensured patient appropriateness for enrollment, an independent Data Safety Monitoring Board (DSMB) that was instructed to notify the applicant of any safety or compliance issues, a Clinical Events Committee (CEC) that was responsible for adjudicating endpoint related events reported during the trial, and an echocardiographic core laboratory (ECL) for independently analyzing all echocardiograms.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the TRISCEND II pivotal 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 pivotal 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).
- 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, 6 months, and 1 year, following the procedure with the EVOQUE system (Device patients) or randomization (Control patients) and continue annually through 5 years. Patients randomized to device were also assessed on the day of their procedure and at discharge. Follow-up assessments included physical assessments and changes in medical history, laboratory measurements, imaging tests, and health status/quality-of-life (QOL) surveys. Adverse events and complications were recorded at all visits.

3. Statistical Analysis Populations

The analysis populations used for analyses of patients enrolled and randomized in the TRISCEND II pivotal trial are shown in Table 1.

Table 1: Statistical Analysis Populations

Analysis Population	Definition
Intent-to-Treat (ITT)	All patients randomized to a treatment group

Analysis Population	Definition
Modified ITT (mITT) Safety	ITT patients who either had a study procedure attempted (skin incision to access the femoral vein) in the device group or were randomized to the control group
mITT Effectiveness	mITT Safety patients who either had a study device attempted (insertion of guide sheath into femoral vein) in the device group or were randomized to the control group
As-Treated (AT)	mITT Effectiveness patients who either 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

4. Clinical Endpoints

Primary Safety Endpoint – Breakthrough Pathway Cohort

The primary safety endpoint assessed in 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 null and alternative hypotheses for the primary safety endpoint were as follows:

$$H_0: P(MAE) \geq 70\%$$

$$H_a: P(MAE) < 70\%$$

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 Endpoints – Breakthrough Pathway Cohort

There were two co-primary effectiveness endpoints assessed 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-OS) of ≥ 10 points
  - New York Heart Association (NYHA) functional class improvement of ≥ 1 class
  - 6-minute walk distance (6MWD) improvement of ≥ 30 meters

The null and alternative hypotheses for co-primary effectiveness endpoint #1 were as follows:

$$H_0: P_D(\mathrm{TR}) - P_C(\mathrm{TR}) \leq 0$$

$$H_a: P_D(\mathrm{TR}) - P_C(\mathrm{TR}) > 0$$

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 null and alternative hypotheses for co-primary effectiveness endpoint #2 were as follows:

H_0: None of the components is improved in the device group

H_a: At least one component is improved in the device group

The alternative hypothesis for 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 method was used to evaluate the treatment effect of the composite endpoint. In this 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:

1. All-cause mortality
2. Right ventricular assist device (RVAD) implantation or heart transplant
3. Tricuspid valve surgical or percutaneous intervention
4. Annualized rate of heart failure hospitalizations
5. KCCQ-OS score improvement of ≥ 10 points
6. NYHA functional class improvement of ≥ 1 class
7. 6MWD improvement of ≥ 30 meters

The null and alternative hypotheses for the primary safety and effectiveness endpoint were as follows:

H_0: None of the components is improved in the device group

H_a: At least one component is improved in the device group

The alternative hypothesis that the device group was superior to the control group in at least one component of the primary safety and effectiveness endpoint was tested using the Finkelstein-Schoenfeld method at a one-sided significance level of 0.025. As a supplementary analysis, the unmatched win ratio method was used to evaluate the treatment effect of 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.

It was determined that a sample size of 400 patients would provide adequate power to test the hypothesis for the primary safety and effectiveness endpoint of the Full Cohort. Study success of the Full Cohort was defined as meeting the primary safety and effectiveness endpoint.

Secondary Effectiveness Endpoint - Full Cohort

After the extended phase primary safety and effectiveness endpoint claimed success, the following endpoints and hypotheses were tested using the hierarchical testing method in the Full Cohort at 1 year.

1. Reduction in TR grade by at least one grade

Null and alternative hypotheses:

$$H_0: P_D - P_C \leq 0$$
$$H_a: P_D - P_C > 0$$

Where P_D and P_C represent the proportion of patients with at least one grade reduction in the device and control groups at 1 year. This endpoint was evaluated at the 2.5% level of significance in the mITT (effectiveness) analysis population.

2. Reduction in NYHA functional class by at least one class

Null and alternative hypotheses:

$$H_0: P_{D,NYHA} - P_{C,NYHA} \leq 0$$
$$H_a: P_{D,NYHA} - P_{C,NYHA} > 0$$

Where $P_{D,NYHA}$ and $P_{C,NYHA}$ present the proportion of patients with at least one class reduction in the device and control groups at 1 year, respectively. This endpoint was evaluated at the 2.5% level of significance in the mITT (effectiveness) analysis population.

3. Change in QoL (KCCQ-OS) from baseline

Null and alternative hypotheses:

$$H_0: \mu_{D,\Delta KCCQ} - \mu_{C,\Delta KCCQ} \leq 0$$
$$H_a: \mu_{D,\Delta KCCQ} - \mu_{C,\Delta KCCQ} > 0$$

Where $\mu_{D,\Delta KCCQ}$ and $\mu_{C,\Delta KCCQ}$ represent the mean change in KCCQ-OS between 1 year and baseline in the device and control groups respectively.

A one-sided t-test at the 2.5% level of significance was used to compare the mean changes in the two groups. The analysis was performed in patients with matched KCCQ-OS data at baseline and 1 year.

Based upon the N=400 (267 device vs. 133 control group patients), alpha=0.025, Std=22 and superiority margin=0, the lowest observed mean difference in KCCQ-OS at 1 year was 4.6 to claim superiority. This endpoint was tested in the mITT (effectiveness) analysis population.

4. Death and heart failure hospitalization

Null and alternative hypotheses:

$$H_0: \lambda_{D,Death} - \lambda_{C,Death} \geq 0 \text{ AND } \lambda_{D,HFH} - \lambda_{C,HFH} \geq 0$$

$$H_a: \lambda_{D,Death} - \lambda_{C,Death} < 0 \text{ OR } \lambda_{D,HFH} - \lambda_{C,HFH} < 0$$

Where $\lambda_{D,Death}$ and $\lambda_{C,Death}$ represented the rate of all-cause mortality in the Device and Control groups respectively

$\lambda_{D,HFH}$ and $\lambda_{C,HFH}$ represented the rate of recurrent HF hospitalizations in the Device and Control groups, respectively

The composite endpoint was analyzed at the 2.5% level of significance using the Finkelstein and Schoenfeld method with death higher in the hierarchy than recurrent HF. This endpoint was tested in the mITT (safety) analysis population.

5. All-cause hospitalizations through 1 year

Null and alternative hypotheses:

$$H_0: HR \geq 1.0$$

$$H_a: HR < 1.0$$

Where HR was the hazard ratio of recurrent hospitalizations due to treatment with the EVOQUE device.

All available follow-up through 1 year at the time of data cut-off was to be included in the analysis. Patients who did not experience any hospitalizations were to be censored on their data cut-off date. Patients who died were to be censored on the date of death. Patients who withdrew from the trial without hospitalization were to be censored on the date of withdrawal. This endpoint was to be evaluated at the 2.5% level of significance in the mITT (safety) analysis population.

6. All-cause mortality at 1 year

Null and alternative hypotheses:

$$H_0: HR \geq 1.0$$

$$H_a: HR < 1.0$$

Where HR was the hazard ratio of all-cause mortality at 1 year between the device and control groups. Follow-up was to be truncated at 1 year. A Cox regression model with only treatment effect as covariate was to be used to estimate the hazard ratio. This endpoint was to be evaluated at the 2.5% level of significance in the mITT (safety) analysis population.

7. Change in 6-minute walk distance (6MWD) from baseline to 1 year

Null and alternative hypotheses:

$$H_0: \mu_{D,\Delta 6MWD} - \mu_{C,\Delta 6MWD} \leq 0$$

$$H_a: \mu_{D,\Delta 6MWD} - \mu_{C,\Delta 6MWD} > 0$$

Where $\mu_{D,\Delta 6MWD}$ and $\mu_{C,\Delta 6MWD}$ represented the mean change in 6MWD between 1 year and baseline in the device and control groups, respectively. A one-sided t-test at the 2.5% level of significance was to be used to compare the mean changes in the two groups. The analysis was to be performed in patients with matched 6MWD data at baseline and 1 year. This endpoint was to be tested in the mITT (effectiveness) analysis population.

Additional Outcomes – Full Cohort

Additional outcomes assessed included the following:

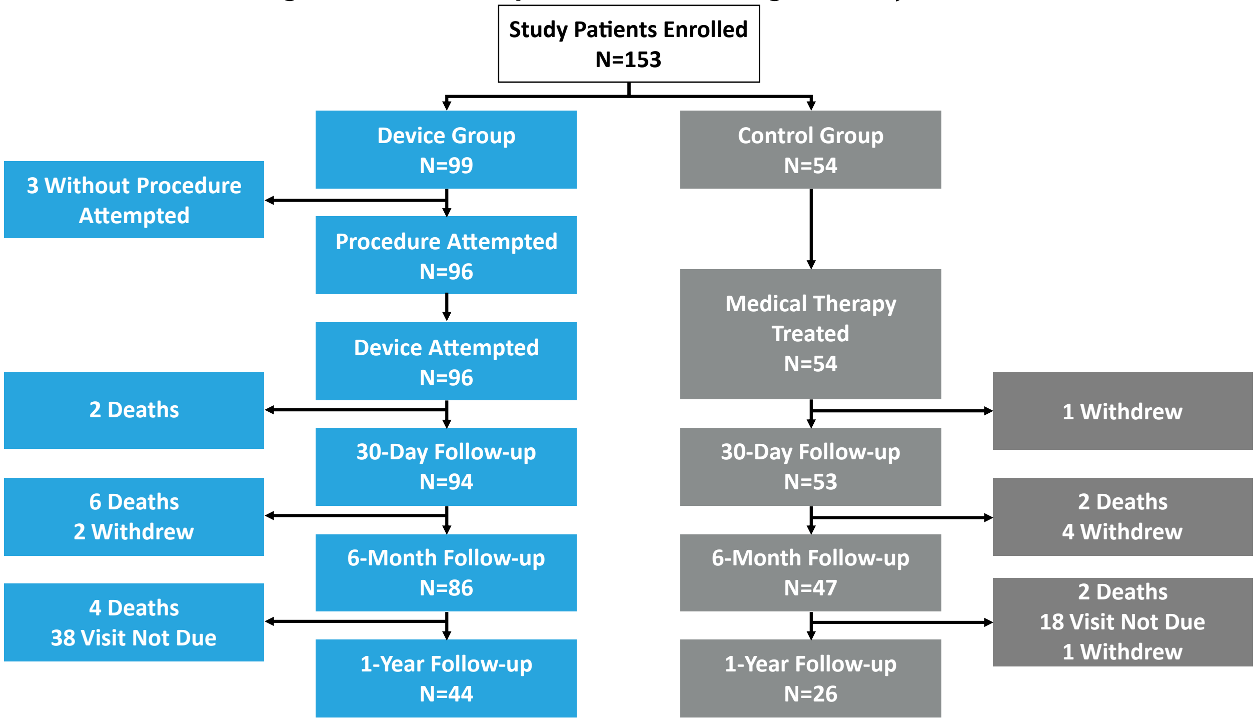
- Echocardiographic parameters by echocardiogram core laboratory assessment
- Clinical and functional parameters

B. Accountability of Breakthrough Pathway Cohort

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

The disposition of patients in the Breakthrough Pathway Cohort as are detailed in Figure 10.

Figure 10: Patient Disposition - Breakthrough Pathway Cohort



The analysis populations for the Breakthrough Pathway Cohort are defined in Table 2. The primary safety and effectiveness analyses were performed on the mITT Safety and mITT Effectiveness Populations, respectively.

Table 2: 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 procedure 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 3.

Table 3: 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)

Visit Status	30 Days		6 Months	
	Device Group (N=96)	Control Group (N=54)	Device Group (N=96)	Control Group (N=54)
* 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 - Breakthrough Pathway Cohort

The demographics and baseline characteristics of the study population in the Breakthrough Pathway Cohort are summarized in Table 4, which are typical for a TR study performed in the U.S. A majority of the study patients were female. 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 open-heart surgeries (31.2% vs. 42.6%).

Table 4: Patient Demographics and Baseline Characteristics – Breakthrough Pathway Cohort, 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/m^2)	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)

Demographics and Baseline Characteristics	Summary Statistics* (N=150)	
	Device Group (N=96)	Control Group (N=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	50% (48/96)	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 - Breakthrough Pathway Cohort

This section summarizes the results of the Breakthrough Pathway Cohort from the initial phase of the TRISCEND II pivotal trial.

1. Primary Safety Endpoint - Breakthrough Pathway Cohort

The primary safety endpoint results are presented in Table 5. 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 5: 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).

2. Primary Effectiveness Endpoints - Breakthrough Pathway Cohort

Co-primary Effectiveness Endpoint #1:

The primary analysis result of co-primary effectiveness endpoint #1 is shown in Table 6. 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 6: Co-Primary Effectiveness Endpoint #1 Result – Breakthrough Pathway Cohort, 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 echocardiogram (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 Effectiveness Endpoint #2:

The primary analysis result of co-primary effectiveness endpoint #2 is shown in Table 7. 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.

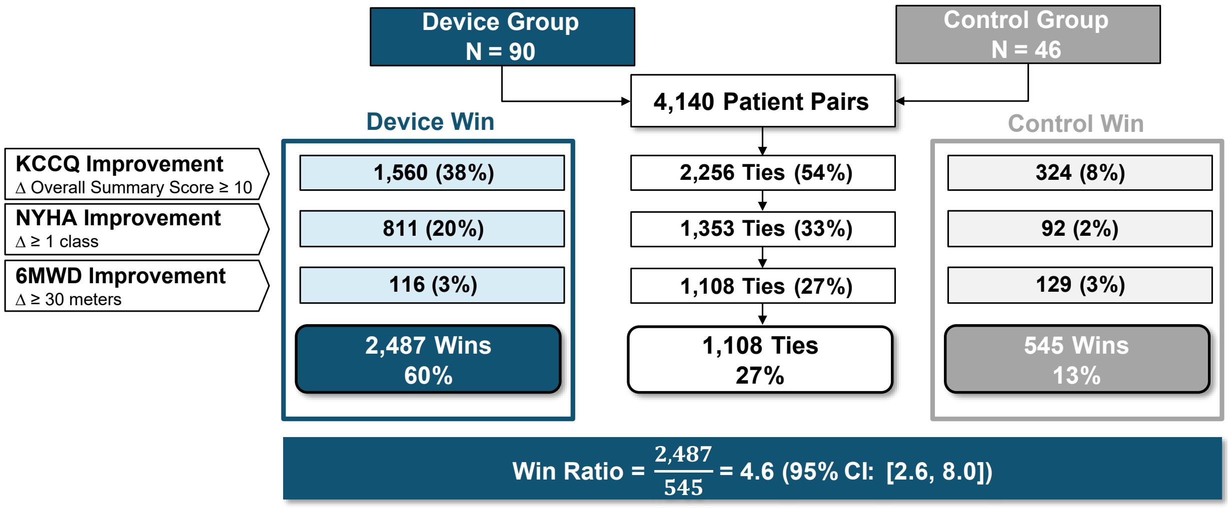
Table 7: Co-Primary Effectiveness Endpoint #2 Result – Breakthrough Pathway Cohort, mITT (Effectiveness) Population

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 11. The win ratio of the device group vs. the control group was 4.6 (95% confidence interval: [2.6, 8.0]).

Figure 11: Win Ratio Analysis of Co-Primary Effectiveness Endpoint #2 Result - Breakthrough Pathway Cohort, mITT (Effectiveness) Population.

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

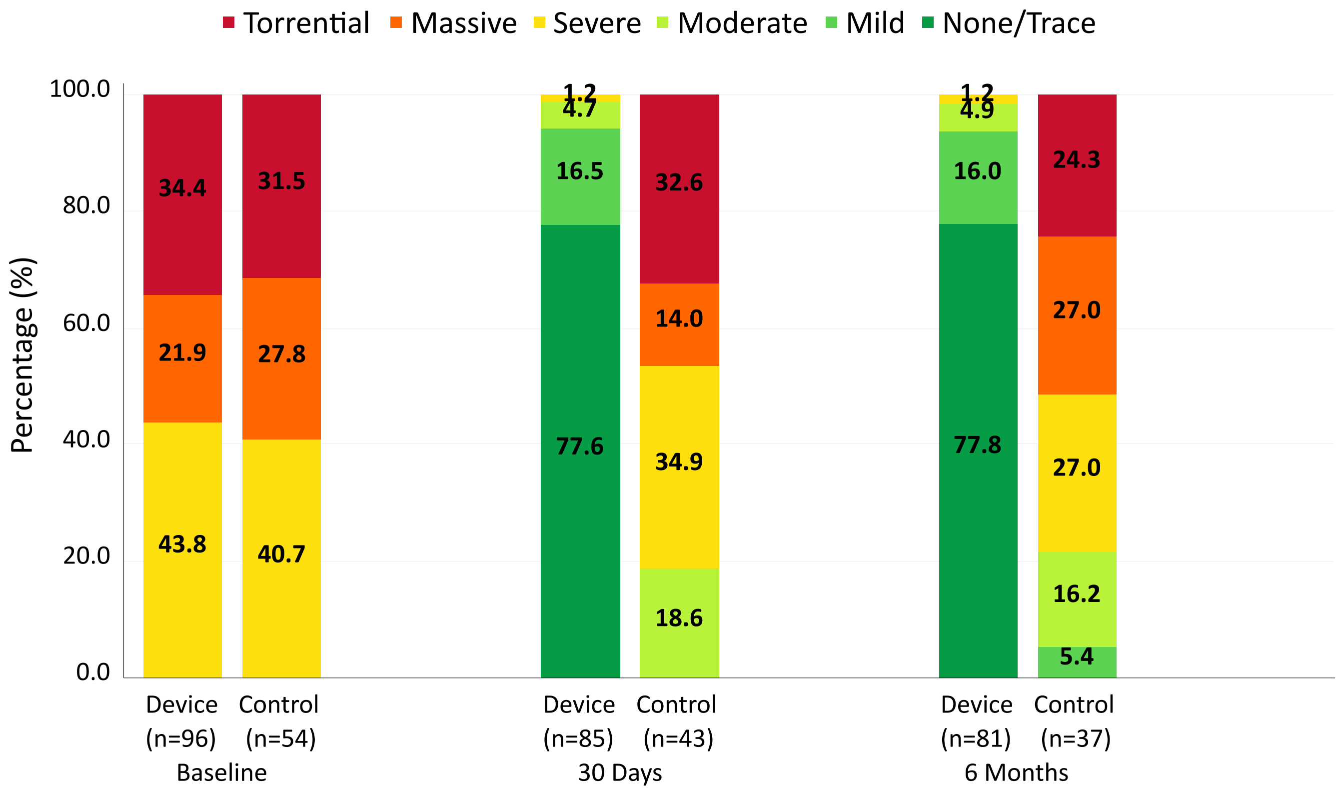


3. Other Study Observations - Breakthrough Pathway Cohort

TR Severity Grade - Breakthrough Pathway Cohort:

The TR severity grades by visit are presented in Figure 12. 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 12: TR Severity Grade by Visit - Breakthrough Pathway Cohort, mITT (Effectiveness) Population

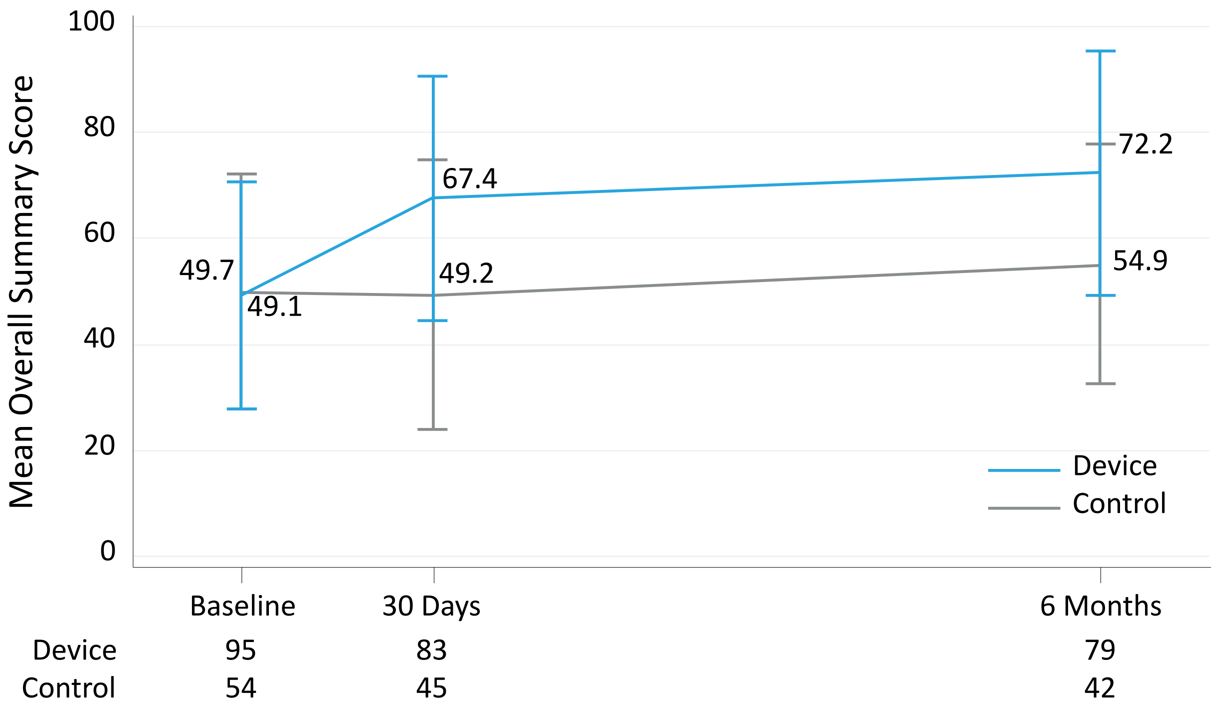


KCCQ Score - Breakthrough Pathway Cohort:

The results for the KCCQ score are presented in Figure 13. 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 13: KCCQ Overall Summary Score by Visit - Breakthrough Pathway Cohort, mITT (Effectiveness) Population.

The error bars represent standard deviations.

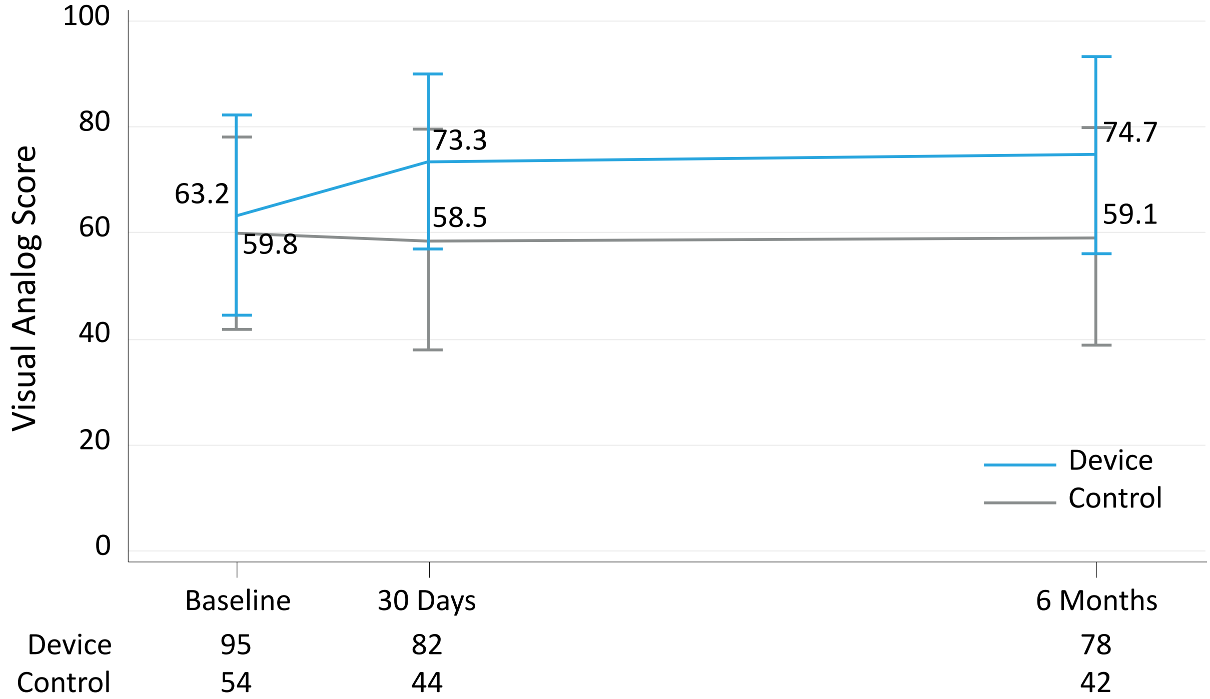


EQ-5D-5L Score - Breakthrough Pathway Cohort:

The results for the EQ-5D-5L visual analog score (VAS) are presented in Figure 14. 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 14: EQ-5D-5L Visual Analog Score by Visit - Breakthrough Pathway Cohort, mITT (Effectiveness) Population.

The error bars represent standard deviations.



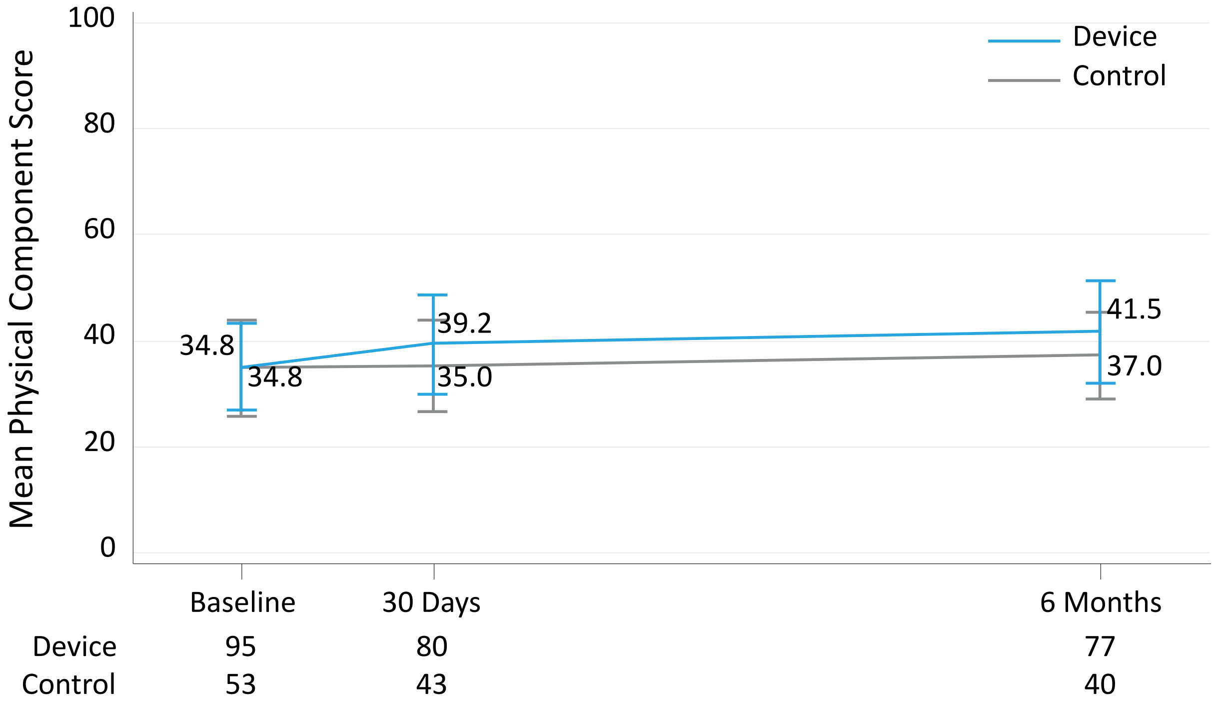
SF-36 Score - Breakthrough Pathway Cohort:

The results for the SF-36 physical component summary score and mental component summary score are presented in Figure 15. 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.

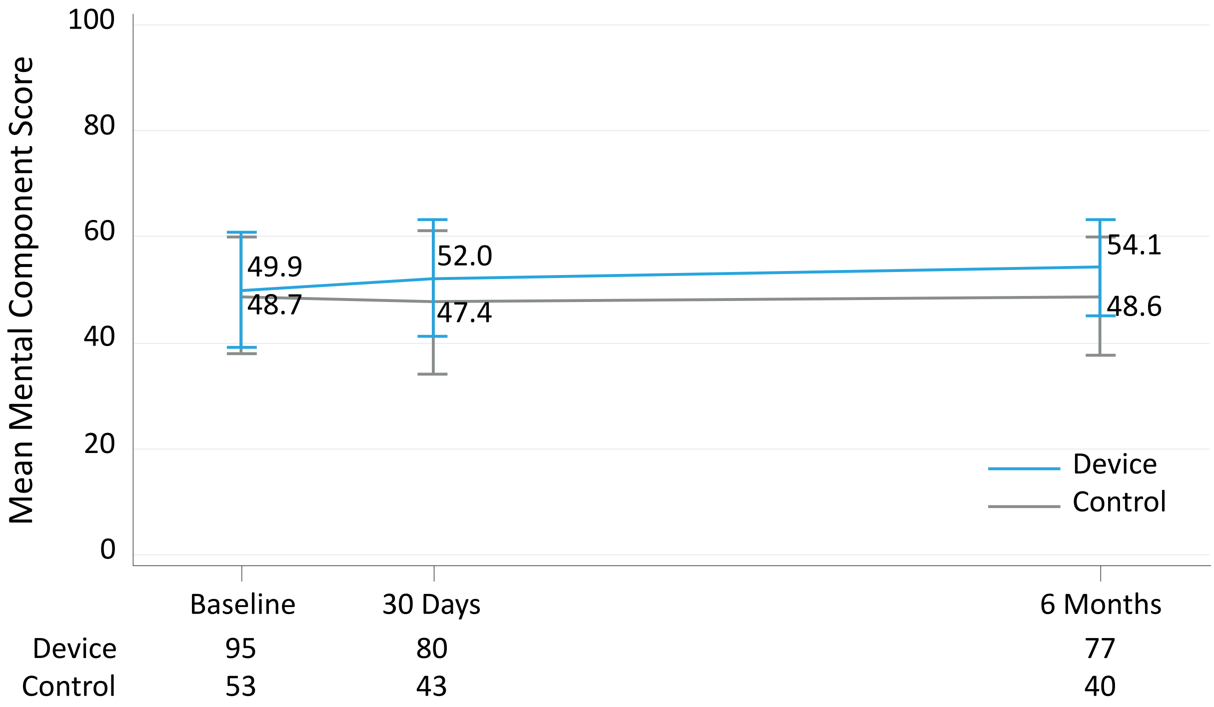
Figure 15: SF-36 Score by Visit - Breakthrough Pathway Cohort, mITT (Effectiveness) Population.

The error bars represent standard deviations.

A. Physical Component Summary Score



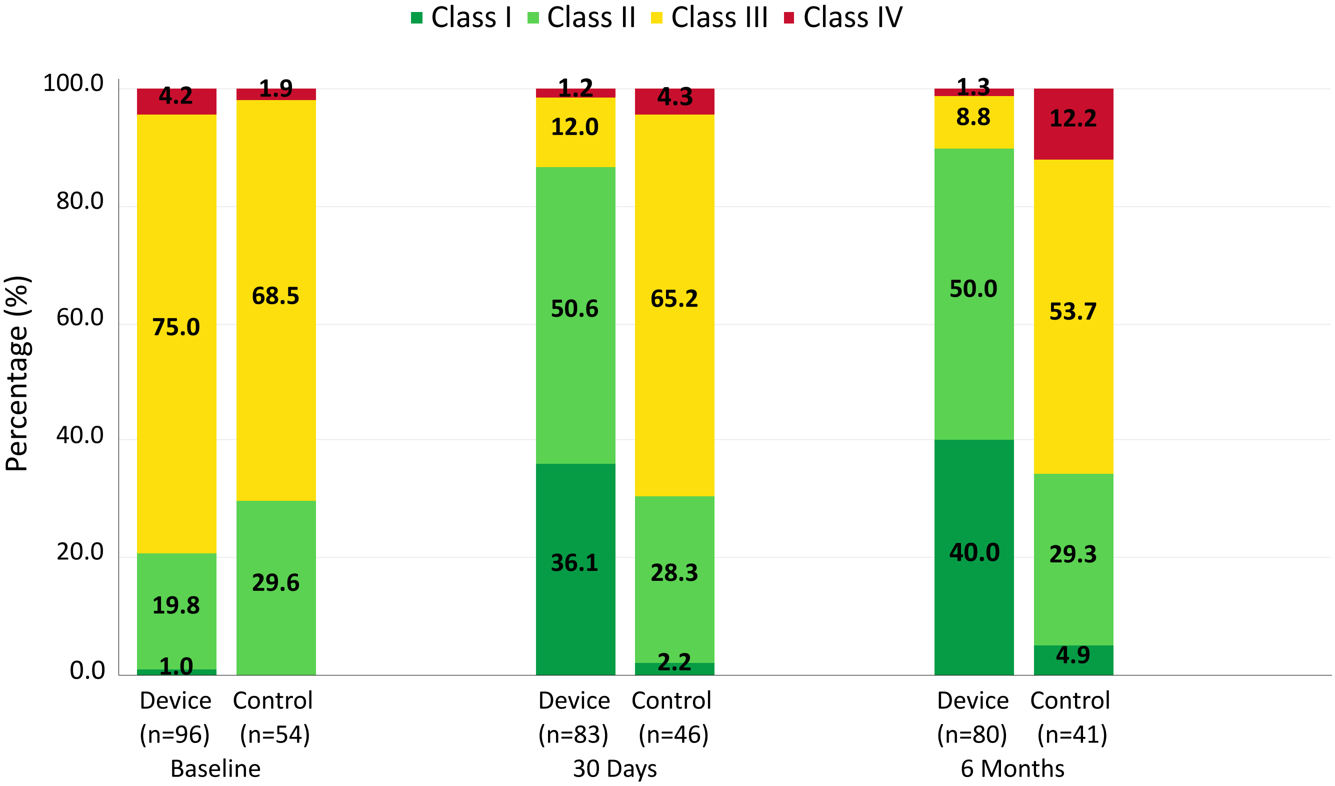
B. Mental Component Summary Score



NYHA Functional Class - Breakthrough Pathway Cohort:

The NYHA functional class by visit are presented in Figure 16. 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 16: NYHA Functional Class by Visit - Breakthrough Pathway Cohort, mITT (Effectiveness) Population

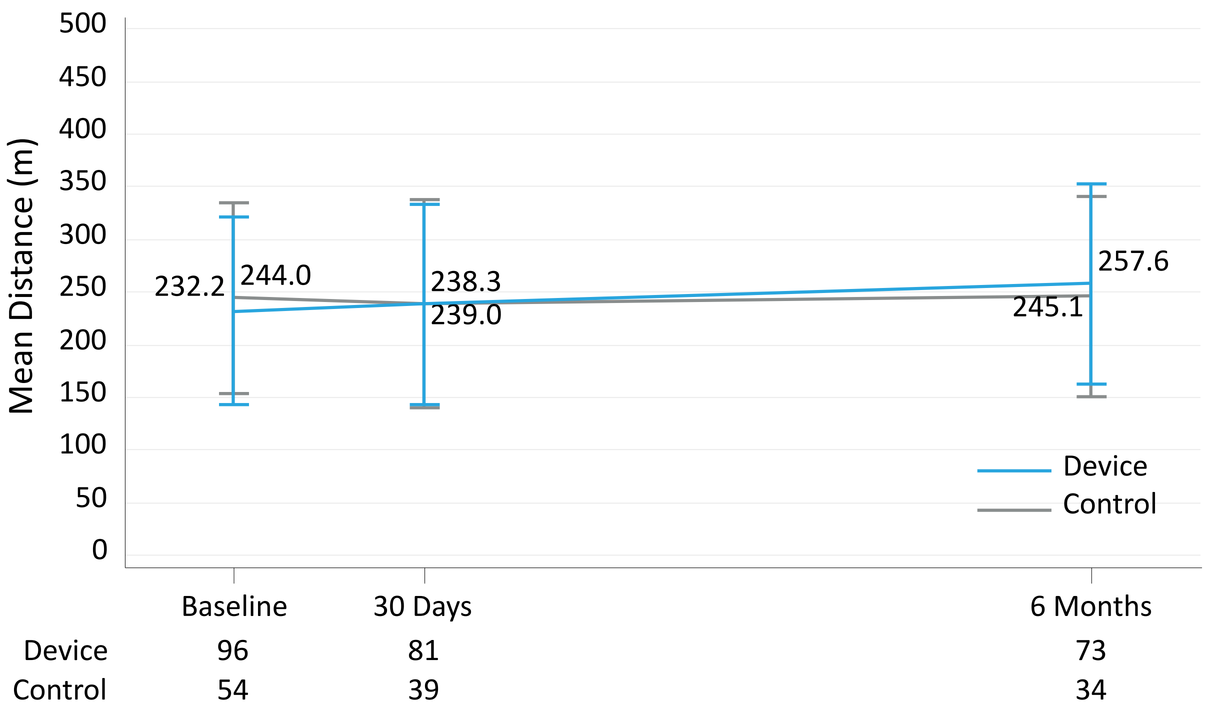


6MWD - Breakthrough Pathway Cohort:

The 6MWD results are presented in Figure 17. 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 17: 6MWD by Visit - Breakthrough Pathway Cohort, mITT (Effectiveness) Population.

The error bars represent standard deviations.



Echocardiographic Parameters - Breakthrough Pathway Cohort:

Key echocardiographic (TTE) parameters for the mITT Effectiveness population at baseline, 30 days, and 6 months are presented in Table 8.

Table 8: Echocardiographic Parameters – Breakthrough Pathway Cohort, 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 - Breakthrough Pathway Cohort:

The general procedural data for the randomized cohort are summarized in Table 9.

Table 9: General Procedure Data - Breakthrough Pathway Cohort, 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)

Variable	Result* (N=92)
*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.	

Adverse Events - Breakthrough Pathway Cohort

The site-reported device-or procedure-related serious adverse events that occurred through 6 months in the Breakthrough Pathway Cohort are presented in Table 10.

Table 10: Site-Reported Device- or Procedure-Related Serious Adverse Events - mITT (Safety) Population

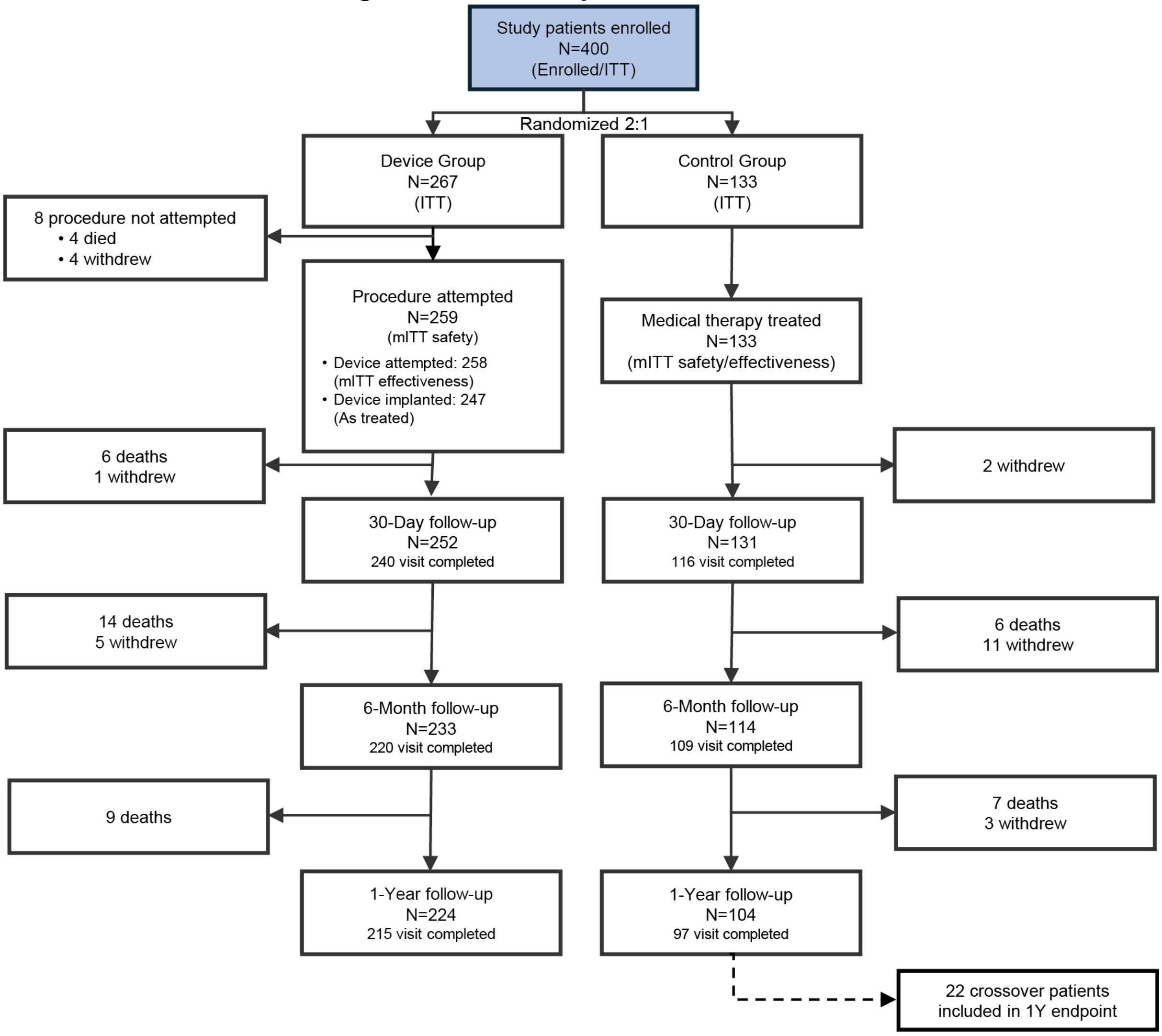
Event	Device Group (N=96)			
	30 Days		6 Months	
	No. Events	Event Rate*	No. Events	Event Rate*
Acute kidney injury	4	4.2% (4/96)	4	4.2% (4/96)
Acute left ventricular failure	0	0.0% (0/96)	1	1.0% (1/96)
Acute respiratory distress syndrome	1	1.0% (1/96)	1	1.0% (1/96)
Acute respiratory failure	1	1.0% (1/96)	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)

Event	Device Group (N=96)			
	30 Days		6 Months	
	No. Events	Event Rate*	No. Events	Event Rate*
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.)				

E. Accountability of the Full Cohort

Enrollment and randomization of all patients into the TRISCEND II pivotal trial took place between May 2021 and April 2023. A total of 400 patients were randomized at 45 investigational sites in the United States and Germany. The disposition of patients in the Full Cohort as of June 28, 2024 are detailed in Figure 18.

Figure 18: Patient Disposition – Full Cohort



The analysis populations for the Full Cohort are defined in Table 11. The primary safety and effectiveness analyses were performed on the mITT Safety and mITT Effectiveness Populations, respectively.

Table 11: Analysis Populations – Full Cohort

Analysis Population	**Definition**	**Number of Patients**	
		Device Group	**Control Group**
Intent-to-Treat (ITT)	All patients randomized to each treatment group.	267	133
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.	259	133
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.	258	133
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.	247*	133
*Eleven (11) patients had aborted procedure due to challenging anatomy or imaging.			

At the time of database lock, of the randomized patients eligible for the 1-year visit, 96.0% in the device group and 93.3% in the control group completed the visit, as shown in Table 12.

Table 12: Visit Compliance – Full Cohort, mITT (Safety) Population

Visit Status	30 Days		6 Months		1 Year	
	Device Group (N=259)	Control Group (N=133)	Device Group (N=259)	Control Group (N=133)	Device Group (N=259)	Control Group (N=133)
Ineligible for visit	7	2	26	19	35	29
Eligible for visit*	252	131	233	114	224	104
Follow-up visit completed†	95.2% (240/252)	88.5% (116/131)	94.4% (220/233)	95.6% (109/114)	96.0% (215/224)	93.3% (97/104)

* 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.)

F. Study Population Demographics and Baseline Characteristics – Full Cohort

Patient demographics and baseline characteristics for the Full Cohort are provided in Table 13. Patients were older (median age 80 years in both treatment groups), mostly female (75.5%, 296/392), and had multiple co-morbidities. Over 70% (281/392) of patients were classified as NYHA class III/IV. Baseline KCCQ-OS averaged ≤ 53 points in both groups. The device and control groups were well-balanced in their demographics and baseline characteristics.

Table 13: Patient Demographics and Baseline Characteristics – mITT (Safety) Population

Demographics and Baseline Characteristics	Summary Statistics* (N=392)	
	Device Group (N=259)	Control Group (N=133)
Age (years)	79.3 ± 7.42 (259)	79.1 ± 7.83 (133)
Female	74.9% (194/259)	76.7% (102/133)
Race		
American Indian or Alaskan Native	0.8% (2/259)	0.0% (0/133)
Asian	5.4% (14/259)	6.0% (8/133)
Black or African American	4.6% (12/259)	3.8% (5/133)
Native Hawaiian or Other Pacific Islander	0.0% (0/259)	0.8% (1/133)
White	75.3% (195/259)	73.7% (98/133)
Not available	8.9% (23/259)	8.3% (11/133)
Other	5.0% (13/259)	7.5% (10/133)
Body mass index (BMI, kg/m^2)	26.8 ± 5.93 (259)	27.0 ± 5.49 (133)
New York Heart Association (NYHA) functional class		
Class I	0.8% (2/259)	0.0% (0/133)
Class II	26.3% (68/259)	30.8% (41/133)
Class III	69.1% (179/259)	65.4% (87/133)
Class IV	3.9% (10/259)	3.8% (5/133)
Left ventricular ejection fraction (LVEF, %)	54.4 ± 9.91 (259)	54.3 ± 11.07 (133)
Society of Thoracic Surgeons (STS) Mortality Score - mitral valve replacement (%)	9.6 ± 5.08 (259)	10.0 ± 5.20 (133)
STS Mortality Score - mitral valve repair (%)	6.7 ± 4.75 (259)	7.0 ± 4.39 (133)
European System for Cardiac Operative Risk Evaluation (EuroSCORE) II (%)	5.4 ± 4.09 (259)	5.6 ± 4.27 (133)
Katz Activities of Daily Living Score	5.8 ± 0.47 (258)	5.9 ± 0.38 (132)
Canadian Study of Health and Aging (CSHA) Clinical Frailty Score		

Demographics and Baseline Characteristics	Summary Statistics* (N=392)	
	Device Group (N=259)	**Control Group (N=133)**
Non-frail to mildly frail (1-5)	89.5% (230/257)	91.7% (121/132)
Moderate-to-severely frail (6-9)	10.5% (27/257)	8.3% (11/132)
Cardiomyopathy	13.1% (34/259)	15.0% (20/133)
Dilated	9.3% (24/259)	13.5% (18/133)
Restrictive	1.2% (3/259)	0.0% (0/133)
Hypertrophic	1.2% (3/259)	0.8% (1/133)
Coronary artery disease (≥ 50% stenosis)	25.9% (67/259)	30.1% (40/133)
Hypertension	90.7% (235/259)	91.7% (122/133)
Pulmonary Hypertension	69.5% (180/259)	75.9% (101/133)
Myocardial infarction	11.2% (29/259)	14.3% (19/133)
Stroke	15.1% (39/259)	9.0% (12/133)
Atrial fibrillation	96.1% (249/259)	92.5% (123/133)
Pacemaker/implantable cardioverter defibrillator	38.2% (99/259)	39.8% (53/133)
Percutaneous coronary intervention (PCI)/stent	16.6% (43/259)	17.3% (23/133)
Total number of prior open-heart surgeries (valve or coronary artery bypass grafting)		
0	61.0% (158/259)	64.7% (86/133)
1	29.7% (77/259)	30.1% (40/133)
≥ 2	7.7% (20/259)	5.3% (7/133)
Number of hospitalizations for heart failure in the last 12 months prior to consent	1.9 ± 1.54 (88)	1.5 ± 0.71 (48)
Total number of days hospitalized for heart failure in the last 12 months (for those who had heart failure hospitalization)	10.6 ± 10.13 (83)	10.4 ± 7.84 (47)
Diabetes	22.0% (57/259)	24.8% (33/133)
Chronic obstructive pulmonary disease (COPD)	15.4% (40/259)	19.5% (26/133)
Renal insufficiency or failure	54.1% (140/259)	59.4% (79/133)
Stage I (eGFR ≥ 90)	0.0% (0/259)	0.0% (0/133)
Stage II (eGFR 60-89)	6.2% (16/259)	6.8% (9/133)
Stage III (eGFR 30-59)	42.9% (111/259)	45.9% (61/133)
Stage IV (eGFR 15-29)	5.0% (13/259)	6.8% (9/133)
Stage V (eGFR < 15)	0.0% (0/259)	0.0% (0/133)
History of renal replacement therapy (e.g., dialysis)	1.2% (3/259)	0.8% (1/133)
Baseline KCCQ Overall Summary Score	52.8 ± 21.98 (258)	50.6 ± 21.39 (133)
Baseline 6MWD (meter)	236.4 ± 92.82 (259)	240.8 ± 87.71 (133)
TR severity (severe or greater)[†]		
Severe	47.1% (122/259)	37.6% (50/133)
Massive	23.2% (60/259)	25.6% (34/133)
Torrential	29.7% (77/259)	36.8% (49/133)
Pulmonary arterial systolic pressure (PASP; mmHg)	38.6 ± 10.85 (249)	37.6 ± 11.25 (133)
TAPSE (mm)	16.3 ± 4.45 (231)	15.6 ± 4.24 (117)

Demographics and Baseline Characteristics	Summary Statistics* (N=392)	
	Device Group (N=259)	Control Group (N=133)
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).		

G. Safety and Effectiveness Results – Full Cohort

This section summarizes the results and outcomes for the Full Cohort, from the second analysis phase of the TRISCEND II pivotal trial.

1. Primary Safety and Effectiveness Endpoint – Full Cohort

The primary safety and effectiveness endpoint analysis result for the Full Cohort is presented in Table 14. The Finkelstein-Schoenfeld test statistic result was 5.283 with a one-sided p-value of < 0.001, which is less than the pre-specified one-sided significance level of 0.025. Thus, the primary safety and effectiveness endpoint was met indicating the device group was superior to the control group.

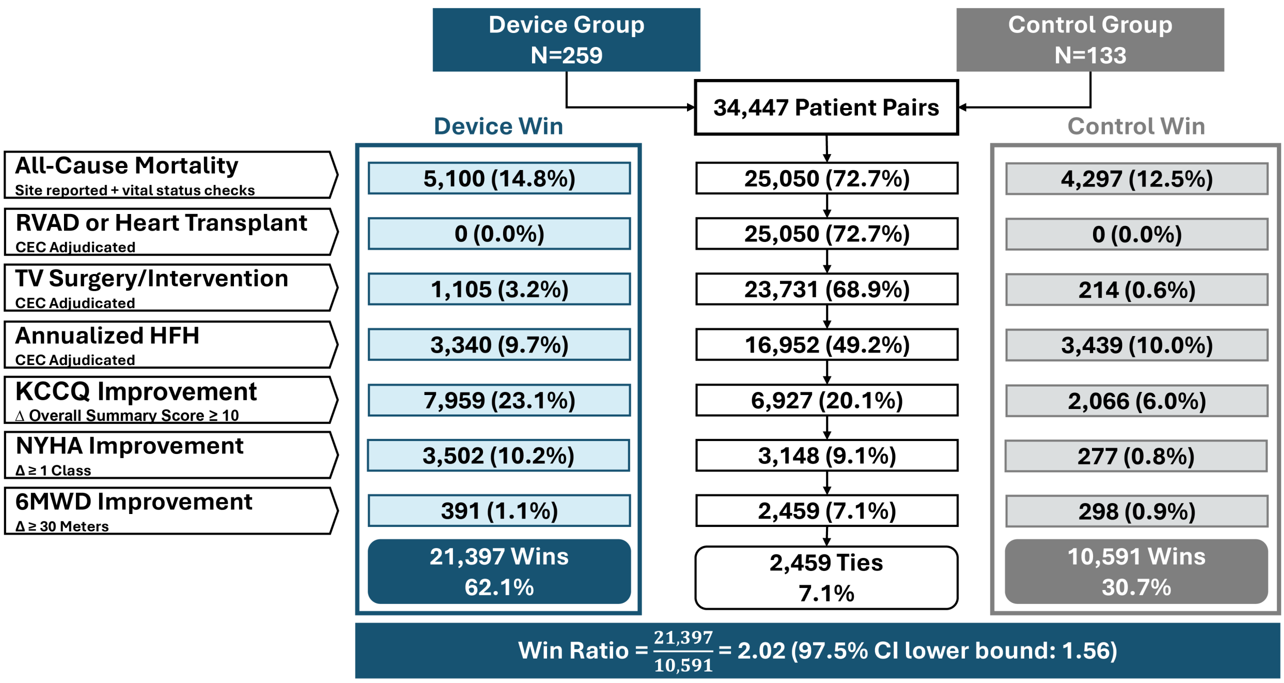
Table 14: Primary Safety and Effectiveness Endpoint Result - Full Cohort, mITT (Safety) Population

Primary Endpoint	Test Statistic	p-Value*	Result
Finkelstein-Schoenfeld analysis	5.283	< 0.001	Superiority 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 the primary safety and effectiveness endpoint is shown in Figure 19. The win ratio of the device group vs. the control group was 2.02 (97.5% confidence interval: 1.56 lower bound).

Figure 19: Win Ratio Analysis of the Primary Safety and Effectiveness Endpoint Result - Full Cohort, mITT (Safety) Population.

RVAD: Right Ventricular Assist Device; TV: Tricuspid Valve; HFH: Heart Failure Hospitalization; KCCQ: Kansas City Cardiomyopathy Questionnaire; NYHA: New York Heart Association; 6MWD: 6-minute walk distance; CI: confidence interval.



2. Secondary Effectiveness Endpoint (Hierarchical Hypothesis Testing) – Full Cohort

The secondary effectiveness endpoint analysis results are presented in Table 15. Hierarchical hypothesis testing was successful for the first 3 outcomes. Treatment with the EVOQUE system was superior to OMT alone for TR grade reduction (p<0.001), NYHA functional class reduction by ≥ 1 class (p<0.001), and improvement in KCCQ-OS at 1 year (p<0.001). Although the device group had a greater number of "wins" for the composite of death and heart failure hospitalization compared to the control group (9,163 device vs. 7,737 control), the win ratio for the composite of death and heart failure hospitalization did not meet statistical significance and the endpoint was not met.

Table 15: Secondary Effectiveness Endpoint Result – Full Cohort, mITT (Effectiveness) Population

Secondary Endpoint*	Device	Control	Difference	p-value	Hierarchical Outcome
Reduction in TR grade by at least one grade†	210/212 (99.1%)	35/87 (40.2%)	58.8% [47.6%]	< 0.001	SUCCESS
Reduction in NYHA functional class by at least one grade†	168/212 (79.2%)	23/96 (24.0%)	55.3% [44.4%]	< 0.001	SUCCESS
Change in quality of life (KCCQ Overall Summary Scores) from baseline‡	18.4 ± 22.07 (211)	2.8 ± 24.28 (96)	15.6 [10.1]	< 0.001	SUCCESS
Death and heart failure hospitalization§	9163	7737	1.2 [0.8]	0.198	FAILURE
All-cause hospitalization‖	–	–	1.2 [1.6]	–	–
All-cause mortality#	13.2% [9.6%, 17.9%]	16.8% [11.4%, 24.4%]	0.8 [1.4]	–	–
Change in 6MWD from baseline‡	23.2 ± 95.39 (185)	-14.8 ± 95.00 (88)	38.0 [13.8]	–	–

*mITT effectiveness for TR grade, NYHA, KCCQ and 6MWD and mITT safety for death/heart failure hospitalization and all-cause hospitalization.

†n/Total N (%); difference in proportions [97.5% lower bound]; pooled Z-Test with continuity correction to be compared with one-sided significance level of 0.025.

‡Mean ± SD (n); mean difference ± STD, [97.5% lower bound]; t-test to be compared with one-sided significance level of 0.025.

§Number of wins; Win Ratio [97.5% lower bound]; One-sided p-value using Finkelstein-Schoenfeld method to be compared with a one-sided significance level of 0.025.

‖Hazard Ratio [97.5% upper bound]; p-value using joint frailty model to be compared with one-sided significance level of 0.025.

#Kaplan-Meier estimates [95% CI]; Hazard Ratio [97.5% upper bound]; p-value using Cox Proportional Hazards model. 6MWD entries of 0 m are considered missing values.

3. Adverse Events – Full Cohort

CEC-adjudicated safety events for the Full Cohort through 1 year are shown in Table 16. The device group had higher rates during the first 30 days of follow-up due to periprocedural complications. Both treatment groups had similar rates with onset between Day 31 through Day 365 of follow-up.

Table 16: CEC-Adjudicated Safety Events Through 1 Year - Full Cohort, mITT Safety Population

	Early Events (≤ 30 Days)				Late Events (30 < Days ≤ 365)*			
	Device (N=259)		Control (N=133)		Device (N=259)		Control (N=133)	
Event	No. Event	Patients	No. Event	Patients	No. Event	Patients	No. Event	Patients
Cardiovascular mortality	8	8/259 (3.1%)	0	0/133 (0.0%)	14	14/247 (5.7%)	10	10/128 (7.8%)
Myocardial infarction	2	2/259 (0.8%)	0	0/133 (0.0%)	3	3/247 (1.2%)	10	1/128 (0.8%)
Stroke	1	1/259 (0.4%)	0	0/133 (0.0%)	3	3/247 (1.2%)	0	0/128 (0.0%)

	Early Events (≤ 30 Days)				Late Events (30 < Days ≤ 365)*			
	Device (N=259)		Control (N=133)		Device (N=259)		Control (N=133)	
Event	No. Event	Patients	No. Event	Patients	No. Event	Patients	No. Event	Patients
New need for renal replacement therapy	4	4/259 (1.5%)	NA	NA	4	4/247 (1.6%)	NA	NA
Severe bleeding†	27	27/259 (10.4%)	2	2/133 (1.5%)	15	13/247 (5.3%)	6	6/128 (4.7%)
Non-elective tricuspid valve re-intervention, percutaneous or surgical	2	2/259 (0.8%)	1	1/133 (0.8%)	0	0/247 (0.0%)	3	3/128 (2.3%)
Major access site and vascular complications	8	8/259 (3.1%)	NA	NA	0	0/247 (0.0%)	NA	NA
Major cardiac structural complications	3	3/259 (1.2%)	NA	NA	0	0/247 (0.0%)	NA	NA
Device-related pulmonary embolism	2	2/259 (0.8%)	NA	NA	1	1/247 (0.4%)	NA	NA
New Pacemaker/ Implantable Cardioverter Defibrillator	40	40/162‡ (24.7%)	0	0/80‡ (0.0%)	5	5/118§ (4.2%)	3	3/76§ (3.9%)

*For Late Events, patients must have at least 31 days in study follow-up to count in denominator. Numerator for Late Events includes events with start date after day 30.

†Fatal, life-threatening, extensive, or major bleeding, as defined by MVARC.

‡Patients who have a pre-existing pacemaker/defibrillator are excluded from both numerator and denominator.

§Patients who have a pre-existing pacemaker/defibrillator or had one placed in the first 30 days are excluded from both the numerator and denominator. Patients must also have at least 31 days in follow-up to count in the denominator.

NA = Event Not Applicable for control patients.

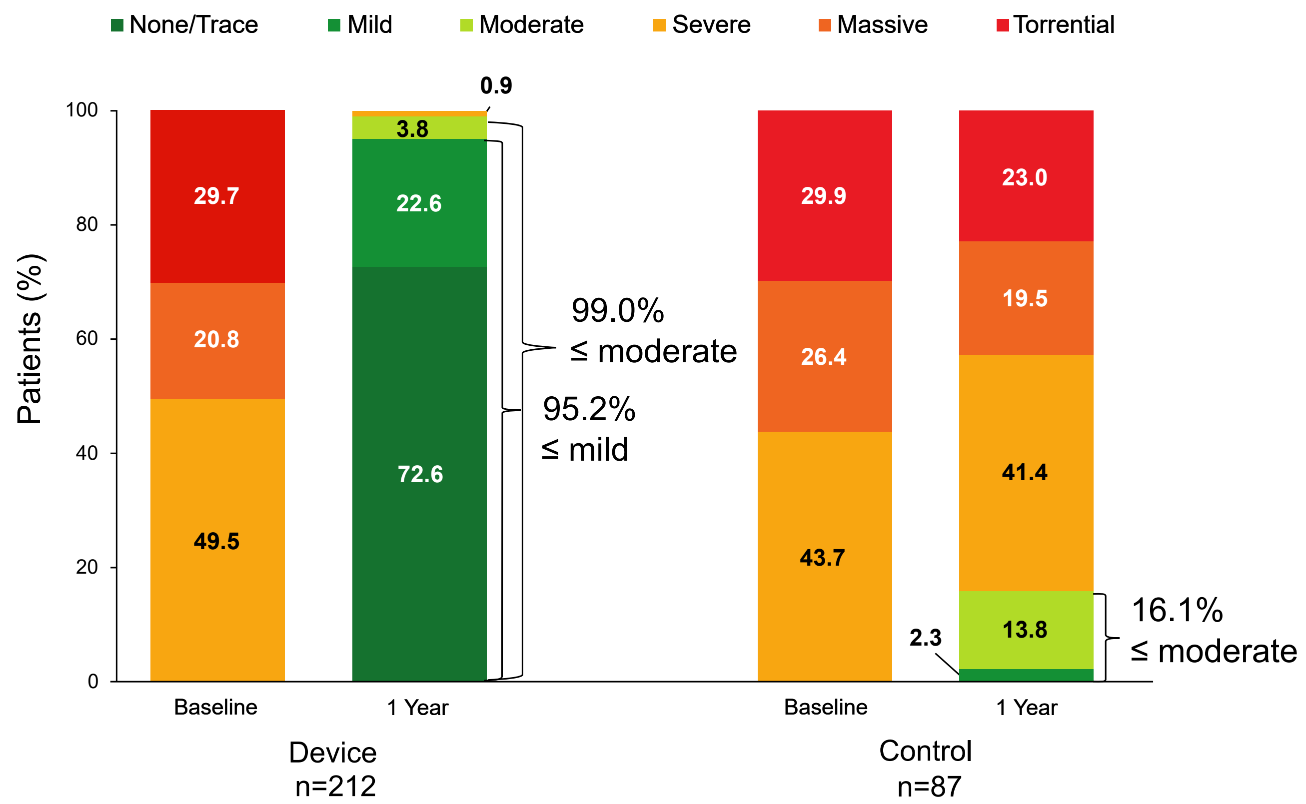
Categorical variables: n/Total N (%)

4. Other Study Observations – Full Cohort

TR Severity Grade - Full Cohort:

The TR severity grades at baseline and 1 year are presented in Figure 20. Patients with severe or greater TR decreased from 100% at baseline in both groups to 0.9% in the device group compared to 83.9% in the control group at 1 year.

Figure 20: TR Severity Grade at Baseline and 1 Year - Full Cohort, mITT (Effectiveness) Population

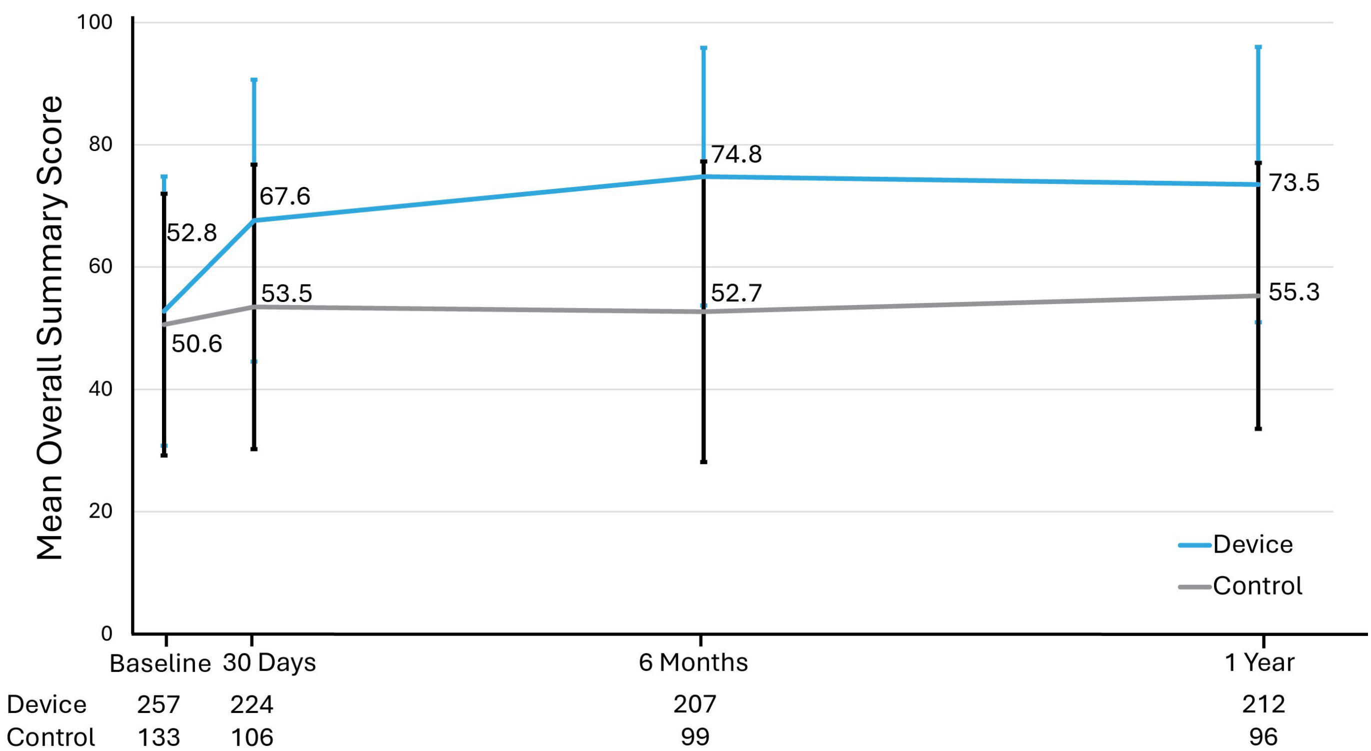


KCCQ-OS Score - Full Cohort:

The results for the KCCQ-OS score are presented in Figure 21. The mean score in the device group increased from 52.8 at baseline to 67.6 at 30 days, 74.8 at 6 months, and mostly sustained at 1 year (73.5). In contrast, the mean score in the control group remained largely unchanged from baseline (50.6) to 30 days (53.5), 6 months (52.7), and 1 year (55.3).

Figure 21: KCCQ Overall Summary Score by Visit - Full Cohort, mITT (Effectiveness) Population.

The error bars represent standard deviations.

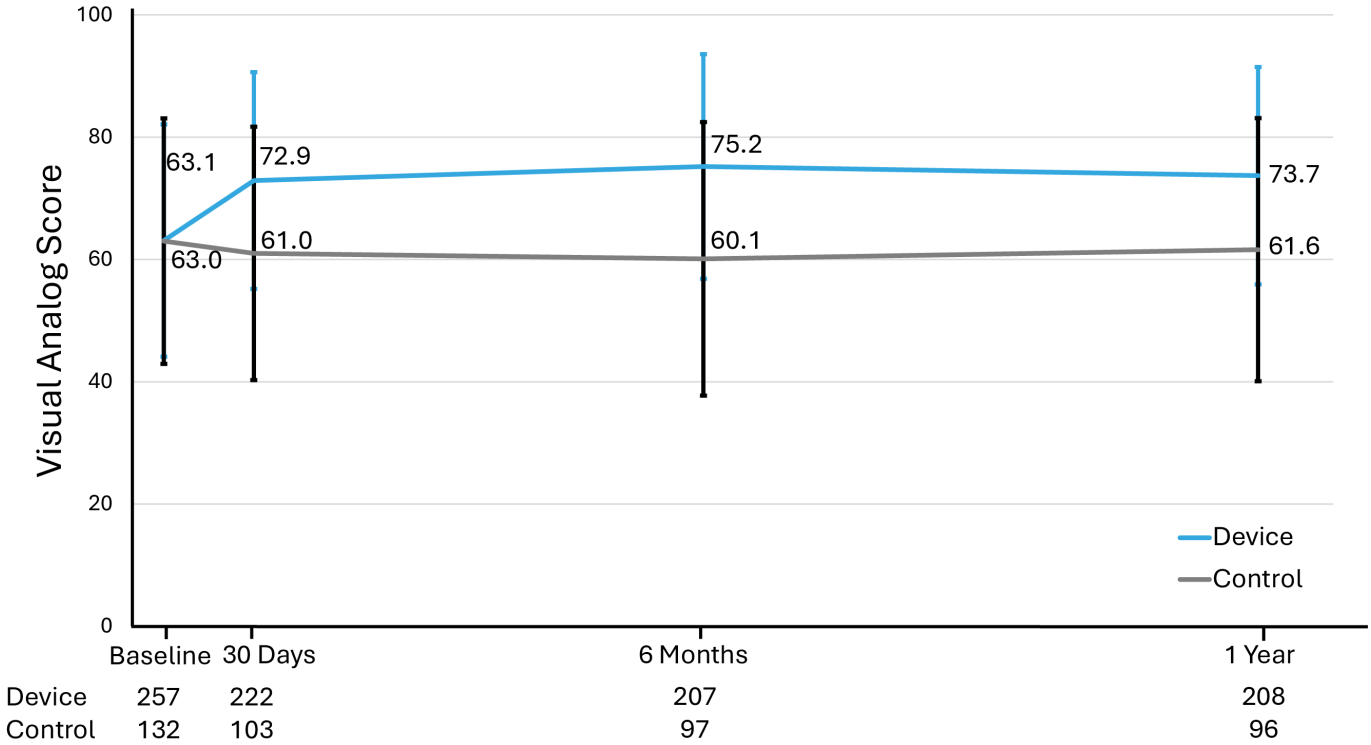


EQ-5D-5L Score:

The results for the EQ-5D-5L visual analog score (VAS) are presented in Figure 22. The mean score in the device group increased from 63.1 at baseline to 72.9 at 30 days, 75.2 at 6 months, and mostly sustained at 1 year (73.7). In contrast, the mean score in the control group remained largely unchanged from baseline (63.0) to 30 days (61.0), to 6 months (60.1), and to 1 year (61.6).

Figure 22: EQ-5D-5L Visual Analog Score by Visit - Full Cohort, mITT (Effectiveness) Population.

The error bars represent standard deviations.



SF-36 Score - Full Cohort:

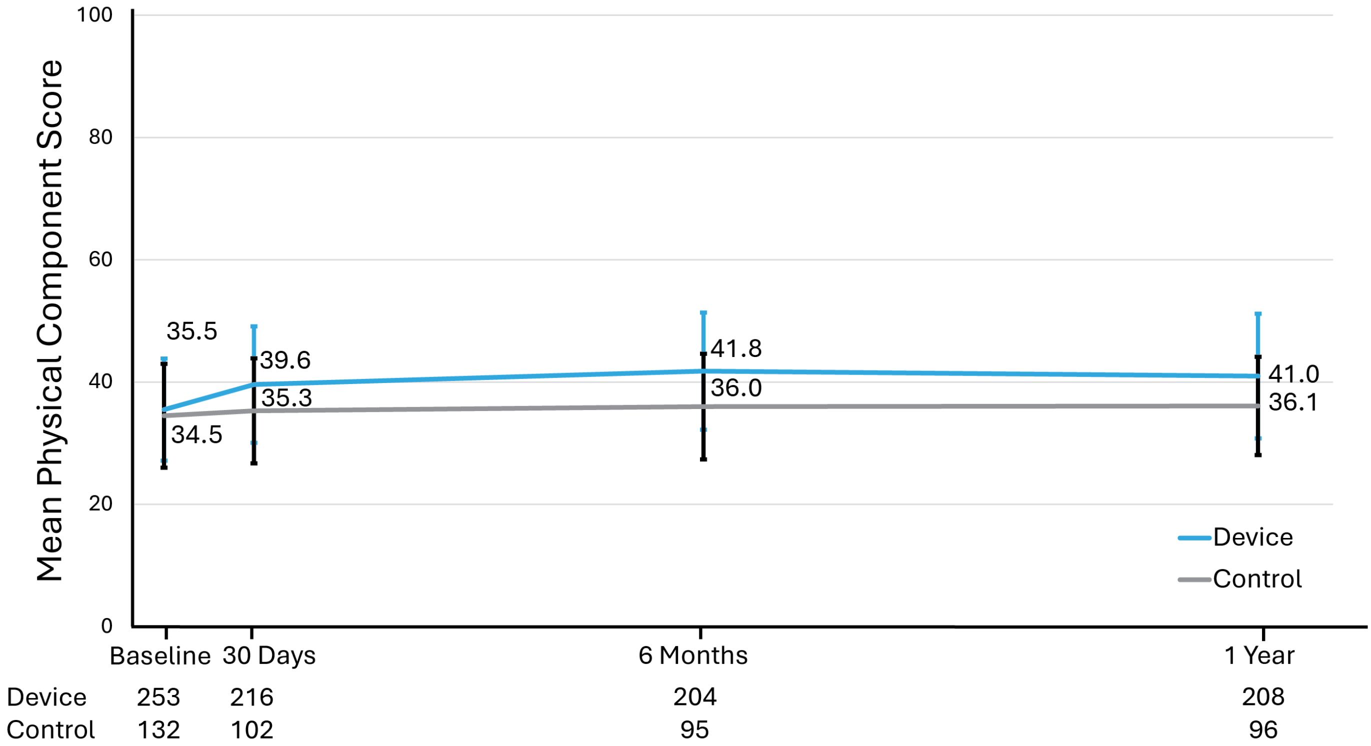
The results for the SF-36 physical component summary score and mental component summary score outcomes are presented in Figure 23 A and B. In the device group, the mean SF-36 physical component score increased from baseline by 4.1 points at 30 days and 6.3 points at 6 months; this increase was sustained through 1 year. In the control group, the mean SF-36 physical component score remained mostly unchanged from baseline (34.5) to 30 days (35.3), to 6 months (36.0), and to 1 year (36.1).

In the device group, the mean SF-36 mental component score increased from baseline by 1.8 points at 30 days and 4.8 points at 6 months; this increase was mostly sustained through 1 year. In contrast, the mean SF-36 mental component score remained largely unchanged through 1 year.

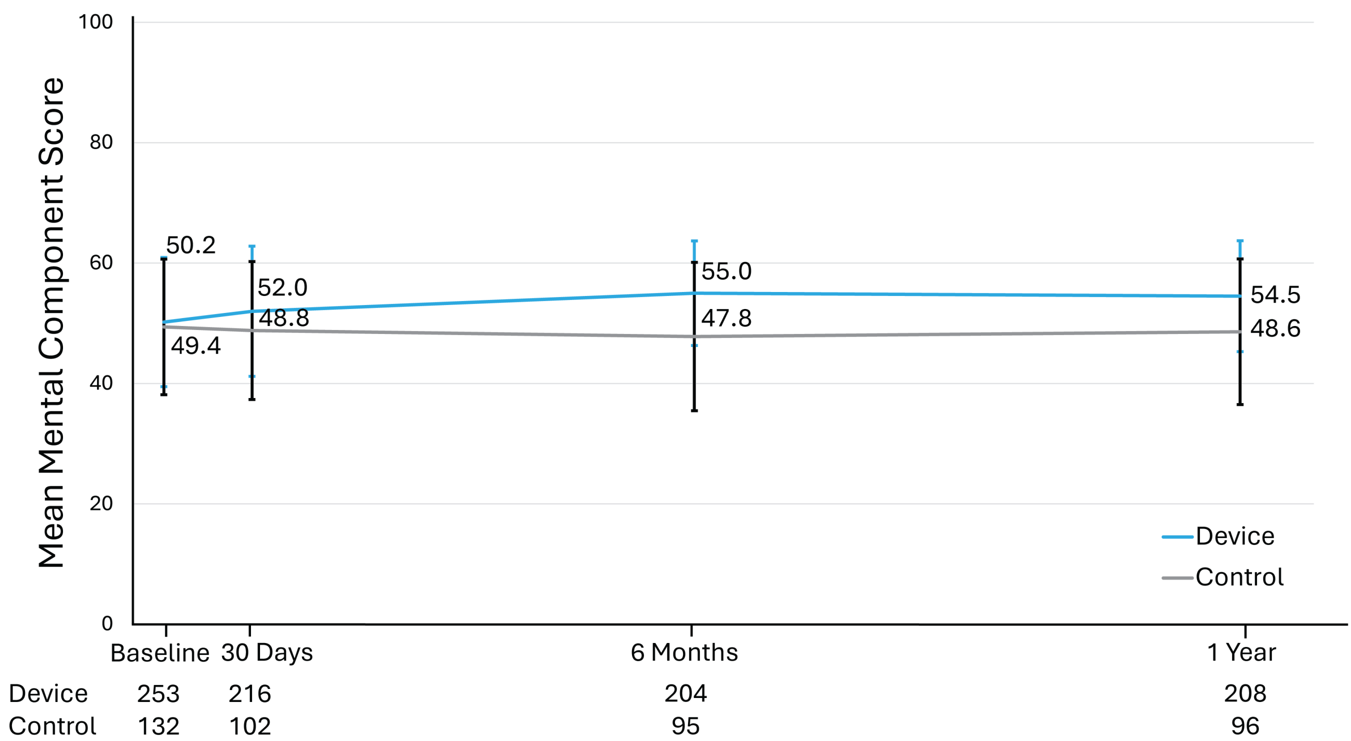
Figure 23: SF-36 Score by Visit - Full Cohort, mITT (Effectiveness) Population.

The error bars represent standard deviations.

A. Physical Component Summary Score



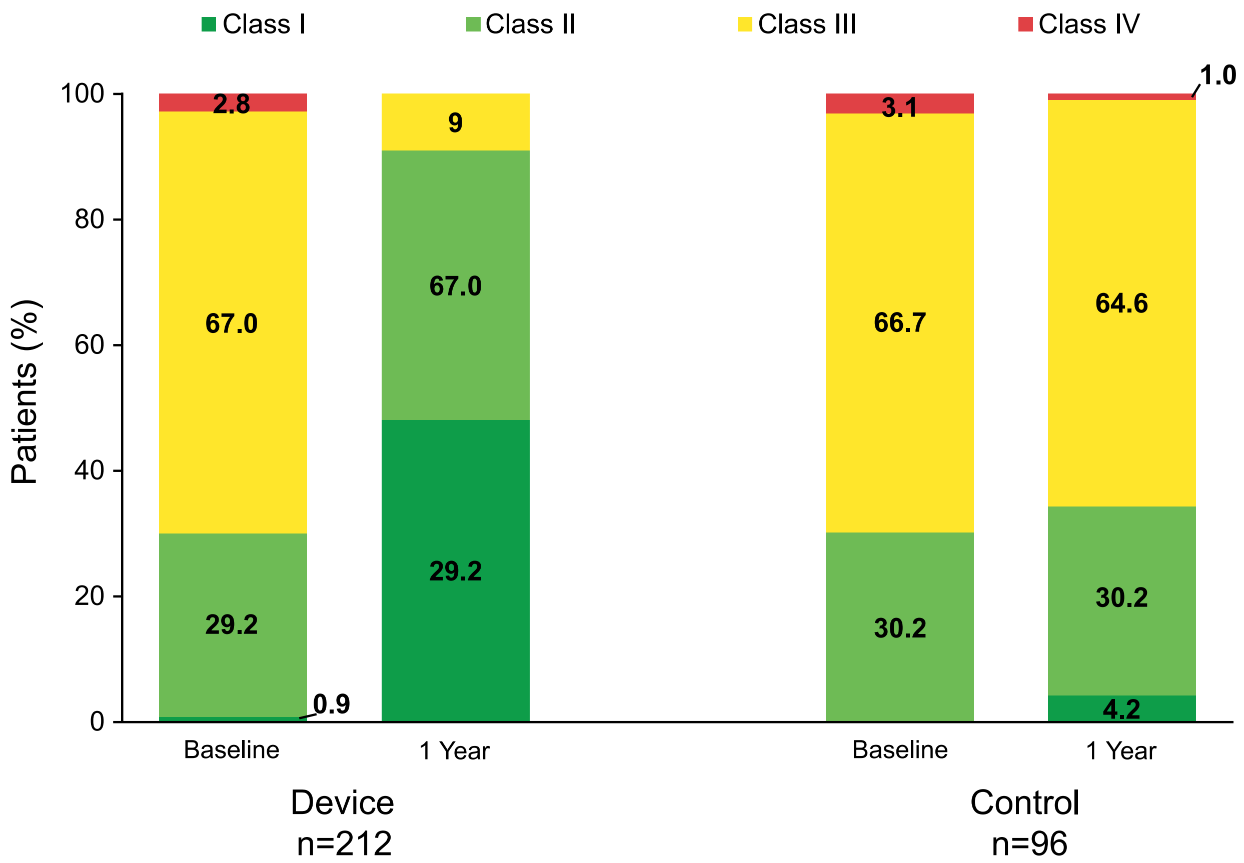
B. Mental Component Summary Score



NYHA Functional Class - Full Cohort:

NYHA functional class by visit are presented in Figure 24. At baseline, 69.8% of device patients and 69.8% of control patients were in NYHA class III/IV. At 1 year, the percent of patients in NYHA class III/IV decreased to 9% in the device group compared to 65.6% in the control group at 1 year.

Figure 24: NYHA Functional Class by Visit - Full Cohort, mITT (Effectiveness) Population

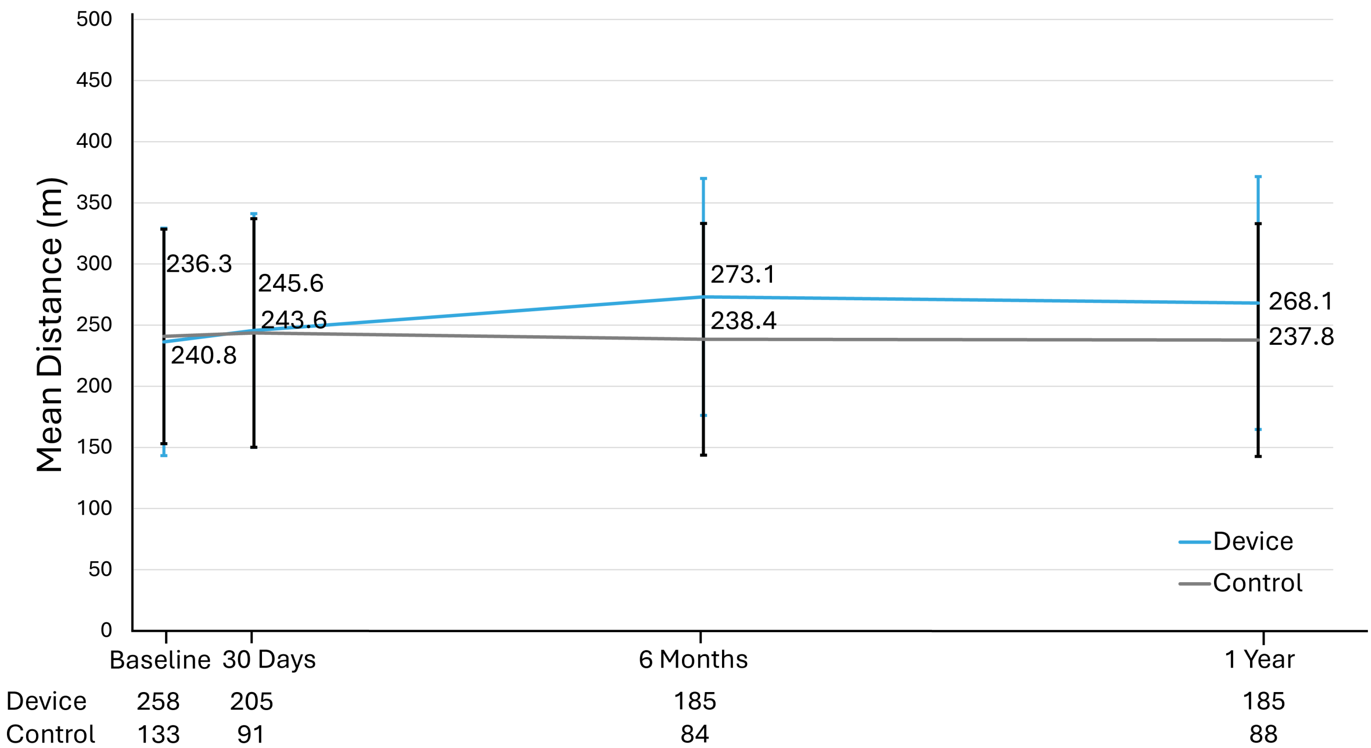


6MWD - Full Cohort:

The 6MWD results are presented in Figure 25. The mean 6MWD increased by about 31.8 meters from baseline to 1 year in the device group compared to a reduction by about 3 meters in the control group.

Figure 25: 6MWD by Visit - Full Cohort, mITT (Effectiveness) Population.

The error bars represent standard deviations.



Echocardiographic Parameters - Full Cohort:

Key echocardiographic (TTE) parameters for the mITT Effectiveness population at baseline and 1 year are presented in Table 17.

Table 17: Echocardiographic Parameters at Baseline vs. at 1 Year - Full Cohort, mITT Effectiveness Population (Paired)

Variable	Summary Statistics*					
	Baseline		1 Year		Change from Baseline	
	Device Group (N=213)	Control Group (N=93)	Device Group (N=213)	Control Group (N=93)	Device Group (N=213)	Control Group (N=93)
Cardiac output (LVOT; L/min)	4.1 ± 1.68 (195)	4.0 ± 1.54 (88)	4.6 ± 1.50 (195)	4.2 ± 1.45 (88)	0.43 ± 1.869 (195)	0.27 ± 1.627 (88)
CW TV mean gradient (mmHg)	1.7 ± 1.07 (204)	1.7 ± 1.10 (84)	3.2 ± 1.36 (204)	1.7 ± 1.21 (84)	1.5 ± 1.63 (204)	0.03 ± 0.800 (84)
RV fractional area change (%)	39.5 ± 8.10 (149)	41.4 ± 8.68 (80)	30.2 ± 9.02 (149)	37.5 ± 9.38 (80)	-9.3 ± 10.63 (149)	-3.9 ± 10.21 (80)
RV end diastolic mid diameter (mm)	39.2 ± 8.37 (175)	38.0 ± 6.60 (88)	33.4 ± 7.28 (175)	38.0 ± 9.15 (88)	-5.8 ± 10.13 (175)	0.00 ± 8.636 (88)
RVOT VTI (cm)	11.1 ± 3.45 (193)	11.1 ± 3.98 (83)	13.2 ± 4.68 (193)	11.6 ± 3.34 (83)	2.1 ± 5.09 (193)	0.50 ± 3.435 (83)
RVOT stroke volume (mL)	63.0 ± 28.42 (116)	55.3 ± 32.16 (56)	72.6 ± 26.85 (116)	66.0 ± 20.42 (56)	9.6 ± 36.58 (116)	10.8 ± 34.53 (56)
RV free wall longitudinal strain (3D only; %)	-22.3 ± 5.87 (40)	-24.7 ± 11.03 (20)	-13.3 ± 4.05 (40)	-24.0 ± 5.25 (20)	9.0 ± 6.34 (40)	0.70 ± 11.196 (20)
IVC diameter (expiration; mm)	25.3 ± 6.33 (198)	24.1 ± 7.19 (91)	20.5 ± 5.35 (198)	23.8 ± 8.05 (91)	-4.8 ± 6.82 (198)	-0.27 ± 6.054 (91)
PASP (mmHg)	38.9 ± 11.59 (93)	38.0 ± 11.16 (88)	32.7 ± 11.68 (93)	39.7 ± 11.86 (88)	-6.3 ± 14.09 (93)	1.7 ± 10.57 (88)
TAPSE (mm)	16.2 ± 4.74 (151)	15.8 ± 4.63 (70)	12.0 ± 3.71 (151)	15.6 ± 4.63 (70)	-4.2 ± 4.95 (151)	-0.19 ± 5.005 (70)

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 - Full Cohort:

The general procedural data for the randomized cohort are summarized in Table 18.

Table 18: General Procedure Data - Full Cohort, AT Population

Variable	Result* (N=247)
General anesthesia	100.0% (247/247)
Implant rate†	(246/247) 99.6%
Total procedure time (min)‡	106.0 ± 42.27 (247) 98.0 (50.0, 351.0)
Device time (min)§	61.5 ± 27.45 (243) 56.0 (16.0, 189.0)
Fluoroscopy duration (min)	29.7 ± 13.24 (247) 27.0 (10.0, 74.1)
Total length of stay in days for the index hospitalization (from procedure date)	5.4 ± 6.32 (247) 3.0 (1.0, 46.0)

Variable	Result* (N=247)
*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.	

Adverse Events - Full Cohort:

The site-reported device-or procedure-related serious adverse events that occurred through 1 year in the Full Cohort are presented in Table 19.

Table 19: Site-Reported Device- or Procedure-Related Serious Adverse Events - Full Cohort, mITT (Safety) Population

Event	Device Group (N=259)					
	30 Days		6 Months		1 Year	
	No. Events	Event Rate*	No. Events	Event Rate*	No. Events	Event Rate*
Acute kidney injury	14	5.0% (13/259)	14	5.0% (13/259)	15	5.4% (14/259)
Acute left ventricular failure	1	0.4% (1/259)	2	0.8% (2/259)	2	0.8% (2/259)
Acute respiratory distress syndrome	2	0.8% (2/259)	2	0.8% (2/259)	2	0.8% (2/259)
Acute respiratory failure	2	0.8% (2/259)	2	0.8% (2/259)	2	0.8% (2/259)
Altered mental status	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Anemia	3	1.2% (3/259)	3	1.2% (3/259)	3	1.2% (3/259)
Angina	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Arrhythmia	4	1.5% (4/259)	5	1.9% (5/259)	5	1.9% (5/259)
Arterial repair	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Ascites	0	0.0% (0/259)	0	0.0% (0/259)	1	0.4% (1/259)
Atrial fibrillation	5	1.9% (5/259)	6	2.3% (6/259)	7	2.7% (7/259)
Atrial septal defect	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Atrioventricular block complete	25	9.7% (25/259)	26	10.0% (26/259)	26	10.0% (26/259)
Bradycardia	10	3.9% (10/259)	11	4.2% (11/259)	12	4.6% (12/259)
Cardiac arrest	2	0.8% (2/259)	2	0.8% (2/259)	2	0.8% (2/259)
Cardiac failure	14	5.0% (13/259)	19	6.6% (17/259)	23	7.7% (20/259)
Cardiac pacemaker insertion	0	0.0% (0/259)	1	0.4% (1/259)	1	0.4% (1/259)
Cardiac perforation	3	1.2% (3/259)	3	1.2% (3/259)	3	1.2% (3/259)
Cardiogenic shock	6	2.3% (6/259)	6	2.3% (6/259)	6	2.3% (6/259)
Cerebrovascular accident	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Chest pain	2	0.8% (2/259)	2	0.8% (2/259)	3	1.2% (3/259)
Compartment syndrome	0	0.0% (0/259)	0	0.0% (0/259)	1	0.4% (1/259)
Decubitus ulcer	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Deep vein thrombosis	2	0.8% (2/259)	2	0.8% (2/259)	2	0.8% (2/259)
Device electrical impedance issue	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Device lead damage	1	0.4% (1/259)	1	0.4% (1/259)	2	0.8% (2/259)
Dysphagia	3	1.2% (3/259)	3	1.2% (3/259)	3	1.2% (3/259)
Electrolyte imbalance	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Encephalopathy	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)

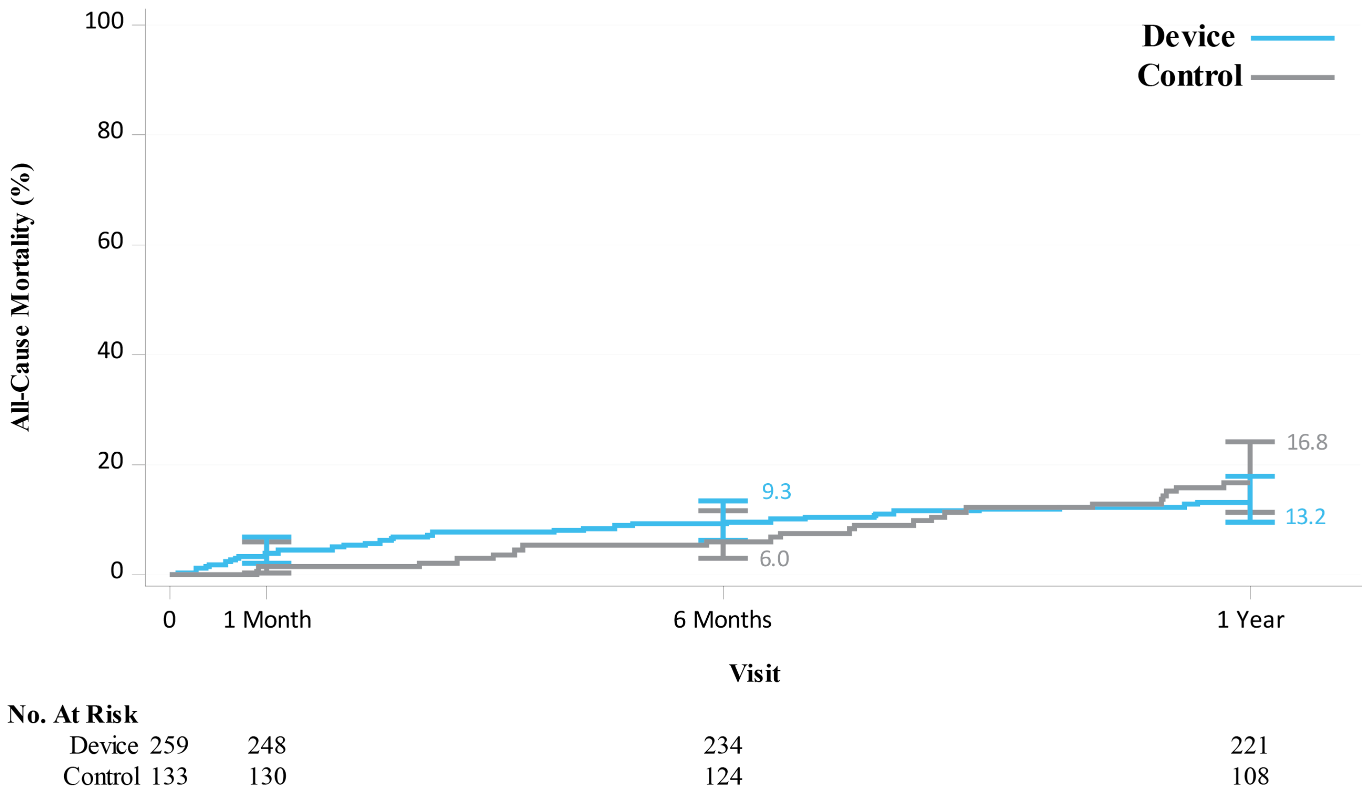
Event	Device Group (N=259)					
	30 Days		6 Months		1 Year	
	No. Events	Event Rate*	No. Events	Event Rate*	No. Events	Event Rate*
Fall	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Fever	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Gastrointestinal bleeding	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Hematoma	1	0.4% (1/259)	1	0.4% (1/259)	2	0.8% (2/259)
Hematuria	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Hemorrhagic shock	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Heparin-induced thrombocytopenia	2	0.8% (2/259)	2	0.8% (2/259)	2	0.8% (2/259)
Hepatic congestion	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Hepatic function abnormal	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Hyperkalemia	0	0.0% (0/259)	0	0.0% (0/259)	1	0.4% (1/259)
Hypervolemia	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Hyponatremia	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Hypotension	7	2.7% (7/259)	7	2.7% (7/259)	7	2.7% (7/259)
Hypothermia	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Hypovolemic shock	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Ileus paralytic	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Infection	3	1.2% (3/259)	3	1.2% (3/259)	3	1.2% (3/259)
Inflammatory marker increased	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Infusion site extravasation	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Intracardiac thrombus	1	0.4% (1/259)	2	0.8% (2/259)	2	0.8% (2/259)
Junctional rhythm	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Leukocytosis	4	1.5% (4/259)	4	1.5% (4/259)	4	1.5% (4/259)
Low cardiac output syndrome	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Mallory-Weiss tear	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Metabolic encephalopathy	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Mitral valve incompetence	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Mouth bleeding	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Pleural effusion	4	1.5% (4/259)	4	1.5% (4/259)	5	1.9% (5/259)
Pneumonia	4	1.5% (4/259)	4	1.5% (4/259)	4	1.5% (4/259)
Procedural pain	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Prosthetic cardiac valve malfunction	1	0.4% (1/259)	3	1.2% (3/259)	3	1.2% (3/259)
Prosthetic cardiac valve regurgitation	2	0.8% (2/259)	2	0.8% (2/259)	3	1.2% (3/259)
Prosthetic cardiac valve thrombosis	4	1.5% (4/259)	7	2.7% (7/259)	8	3.1% (8/259)
Prosthetic valve endocarditis	1	0.4% (1/259)	2	0.8% (2/259)	2	0.8% (2/259)
Pulmonary edema	6	2.3% (6/259)	6	2.3% (6/259)	7	2.7% (7/259)
Pulmonary embolism	2	0.8% (2/259)	2	0.8% (2/259)	2	0.8% (2/259)
Respiratory failure	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Respiratory insufficiency	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Retroperitoneal bleeding	4	1.5% (4/259)	4	1.5% (4/259)	4	1.5% (4/259)
Right bundle branch block	4	1.5% (4/259)	4	1.5% (4/259)	4	1.5% (4/259)
Right ventricular dysfunction	11	4.2% (11/259)	11	4.2% (11/259)	11	4.2% (11/259)
Right ventricular failure	3	1.2% (3/259)	3	1.2% (3/259)	4	1.5% (4/259)
Sepsis	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Septic shock	2	0.8% (2/259)	2	0.8% (2/259)	2	0.8% (2/259)

Event	Device Group (N=259)					
	30 Days		6 Months		1 Year	
	No. Events	Event Rate*	No. Events	Event Rate*	No. Events	Event Rate*
Shock	1	0.4% (1/259)	1	0.4% (1/259)	3	1.2% (3/259)
Sinus arrest	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Sinus node dysfunction	0	0.0% (0/259)	1	0.4% (1/259)	1	0.4% (1/259)
Supraventricular tachycardia	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Syncope	3	1.2% (3/259)	3	1.2% (3/259)	3	1.2% (3/259)
Thrombocytopenia	2	0.8% (2/259)	2	0.8% (2/259)	2	0.8% (2/259)
Thrombosis	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Traumatic bleeding	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Traumatic hematoma	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Ureteric obstruction	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Urinary retention postoperative	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Urosepsis	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Vascular access site bleeding	5	1.9% (5/259)	5	1.9% (5/259)	5	1.9% (5/259)
Vascular access site complication	3	1.2% (3/259)	3	1.2% (3/259)	3	1.2% (3/259)
Vascular access site hematoma	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Vascular access site infection	0	0.0% (0/259)	1	0.4% (1/259)	1	0.4% (1/259)
Ventricular extrasystoles	1	0.4% (1/259)	1	0.4% (1/259)	1	0.4% (1/259)
Ventricular tachycardia	3	1.2% (3/259)	3	1.2% (3/259)	3	1.2% (3/259)
*% (no./total no.)						

All-Cause Mortality - Full Cohort:

The Kaplan-Meier curves for All-Cause Mortality are shown in Figure 26 for the Full Cohort.

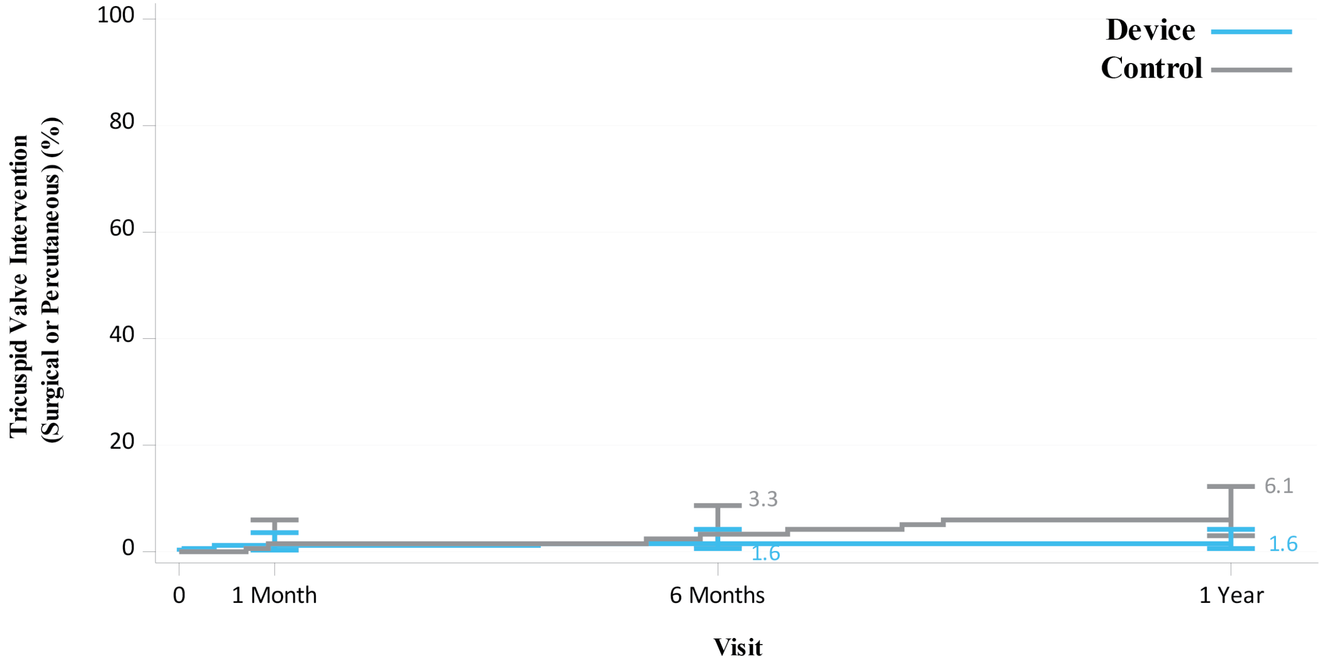
Figure 26: Kaplan-Meier Analysis of Site-Reported All-Cause Mortality - Full Cohort, mITT Safety Population



Tricuspid Valve Surgical or Percutaneous Intervention - Full Cohort:

The Kaplan-Meier curves for Tricuspid Valve Surgical of Percutaneous Intervention are shown in Figure 27 for the Full Cohort.

Figure 27: Kaplan-Meier Analysis of Site-Reported All-Cause Mortality - Full Cohort, mITT Safety Population



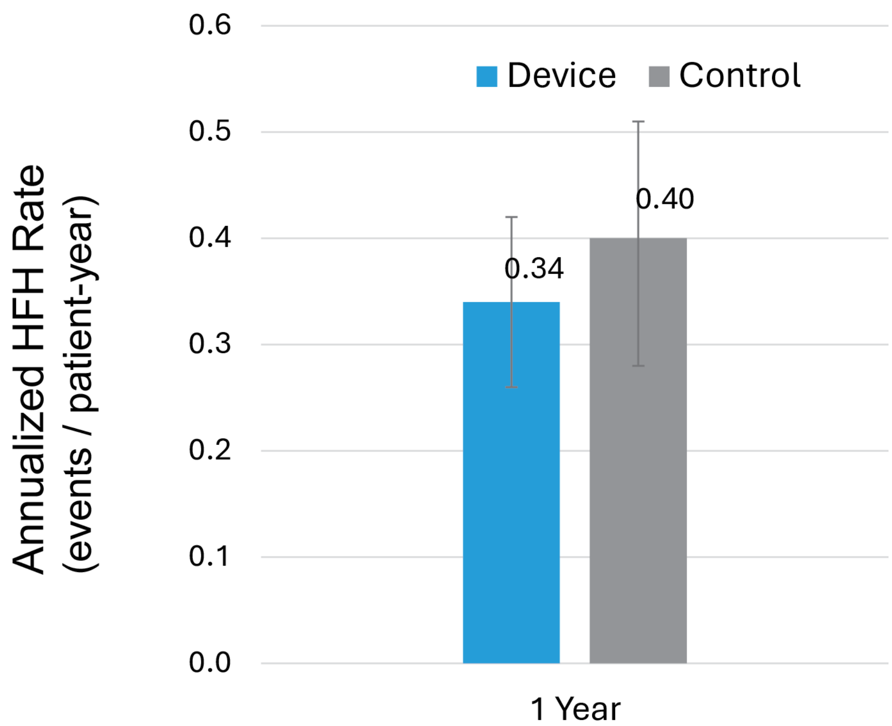
No. At Risk	0	1 Month	6 Months	1 Year
Device	259	243	229	215
Control	133	121	109	93

Annualized Heart Failure Rehospitalization Rate - Full Cohort:

The Annualized Heart Failure Hospitalization Rates (events/patient/year) are shown in Figure 28 for the Full Cohort.

Figure 28: Annualized HF Hospitalization Rate - 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.

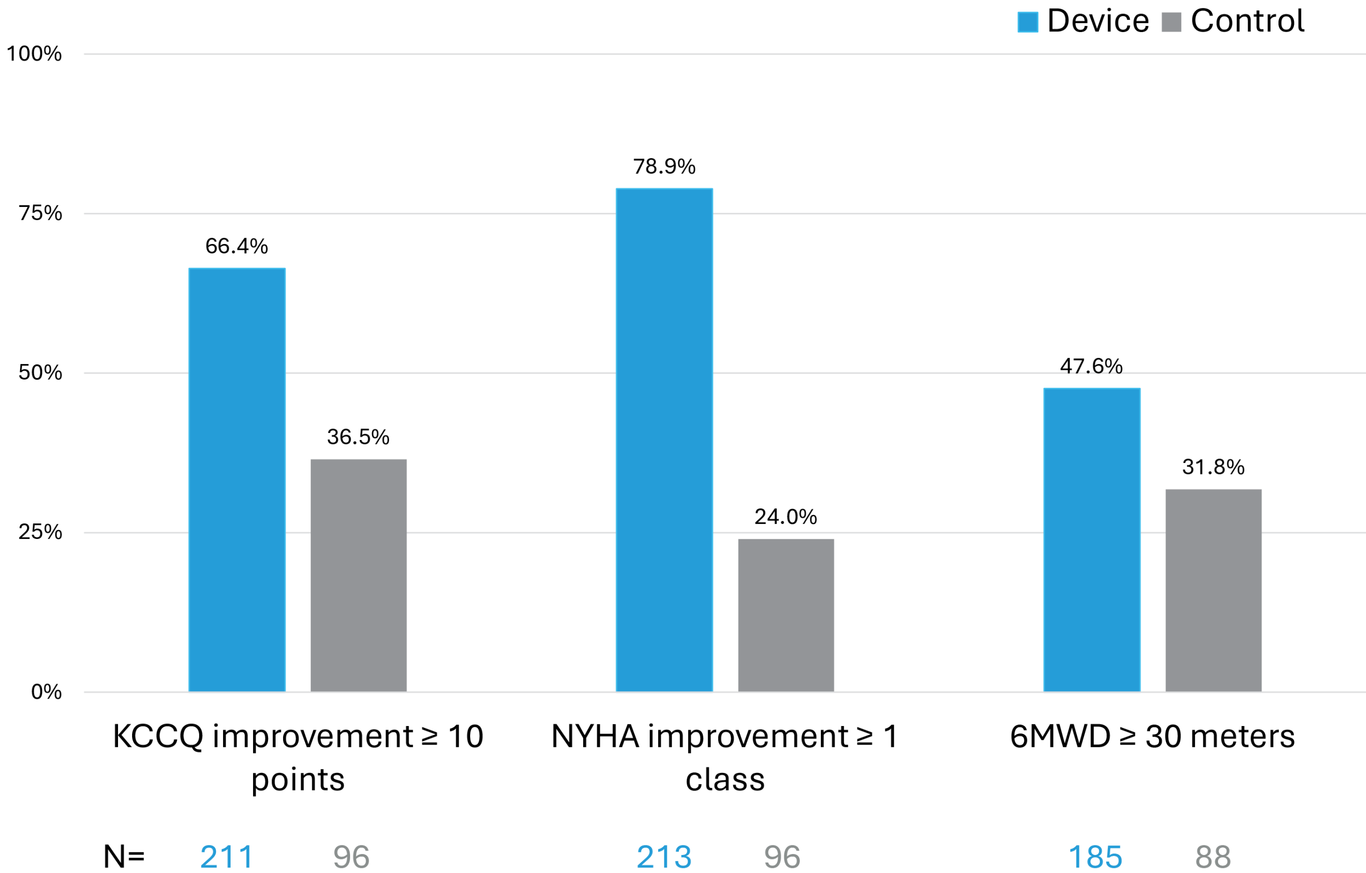


KCCQ-OS, NYHA, and 6MWD - Full Cohort:

The improvements in KCCQ-OS, NYHA, and 6MWD are shown in Figure 29 for the Full Cohort.

Figure 29: KCCQ-OS, NYHA, and 6MWD Improvements at 1 Year - Full Cohort, mITT Safety Population.

KCCQ-OS: Kansas City Cardiomyopathy Questionnaire Overall Summary Score; NYHA: New York Heart Association; 6MWD: 6-minute walk distance



Figures

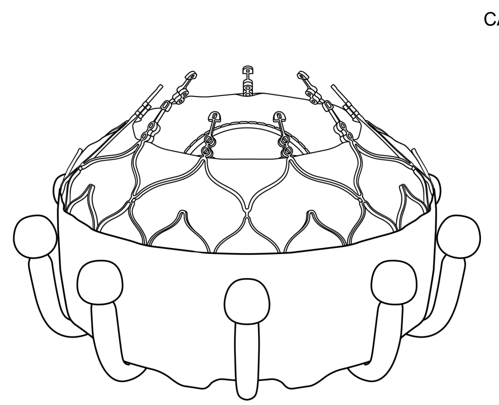


Figure 1: Edwards EVOQUE Valve

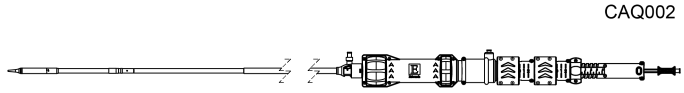
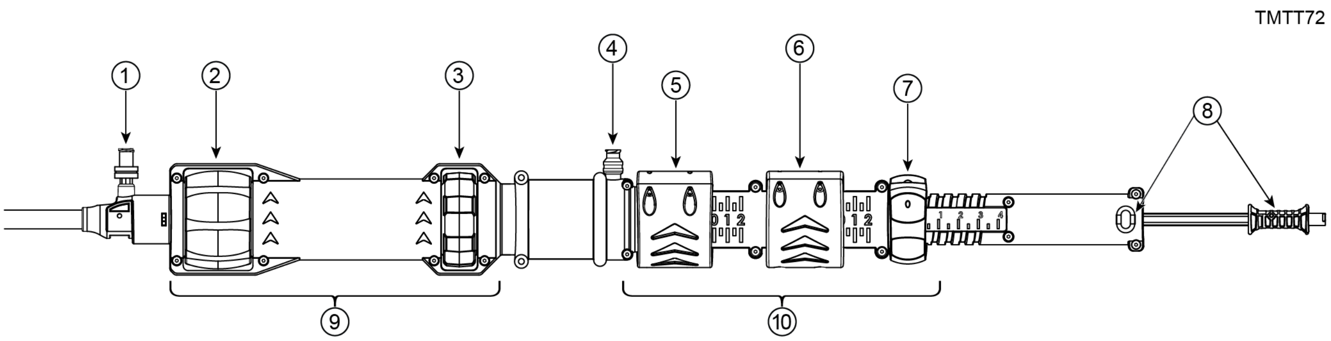
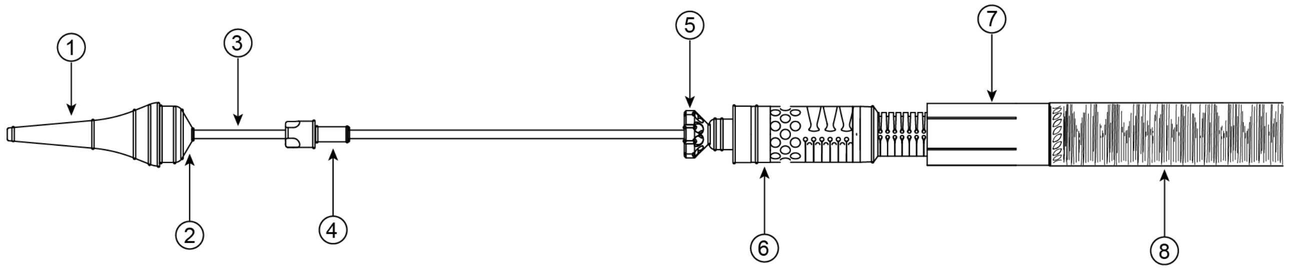


Figure 2: Edwards EVOQUE Tricuspid Delivery System



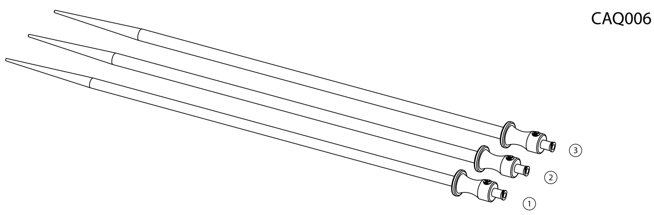
1. Sheath port
2. White knob (advances/retracts outer capsule)
3. Blue knob (advances/retracts inner capsule)
4. Handle flush port
5. Primary flex
6. Secondary flex
7. Depth
8. Tapered tip button and slider
9. Implant release knob
10. Implant positioning knob

Figure 3: Edwards EVOQUE Tricuspid Delivery System – Close Up of Proximal End



1. Tapered tip
2. Guidewire shield stopper
3. Guidewire lumen
4. Guidewire shield
5. Locking ring
6. Inner capsule
7. Tabs
8. Outer capsule

Figure 4: Edwards EVOQUE Tricuspid Delivery System – Close Up of Distal End



1. 24 F Dilator
2. 28 F Dilator
3. 33 F Dilator

Figure 5: Edwards EVOQUE Dilator Kit

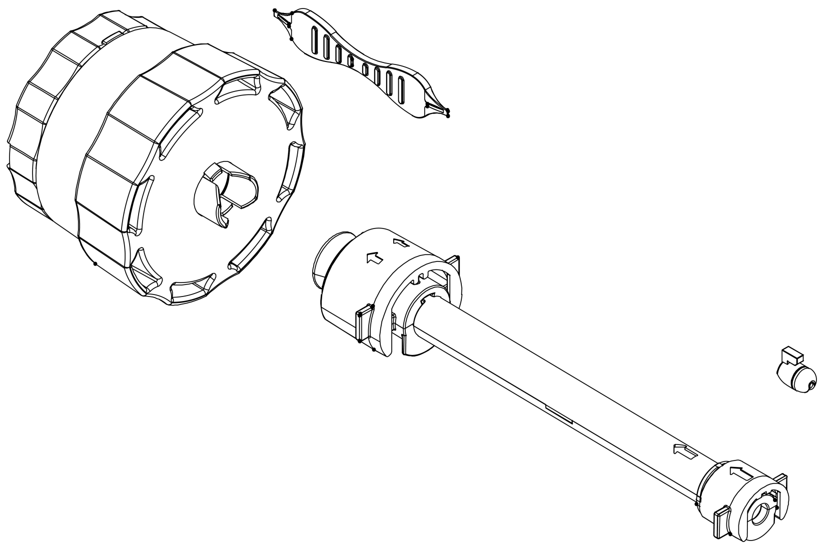


Figure 6: Edwards EVOQUE Loading System

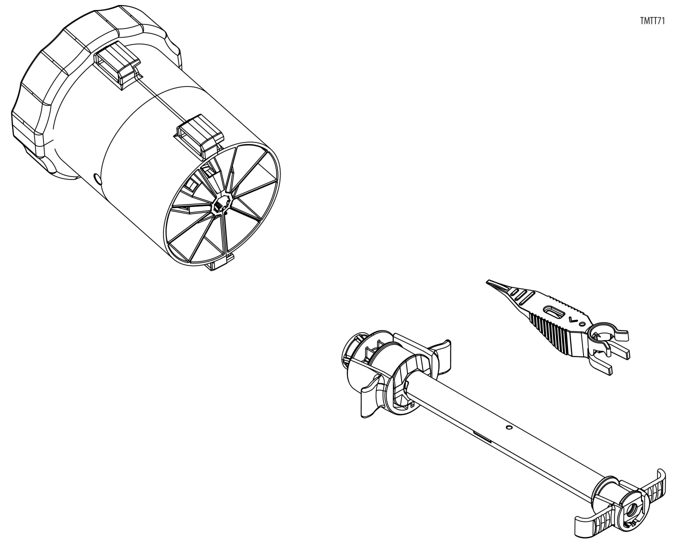


Figure 7: Edwards EVOQUE Loading System and Trimmer

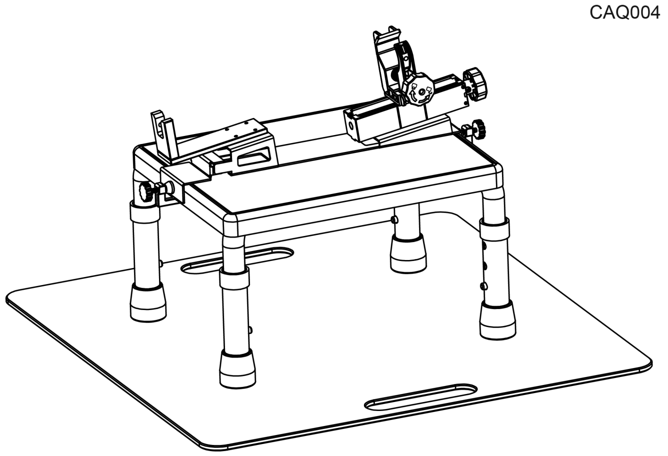


Figure 8: Edwards EVOQUE System Accessories Set 1

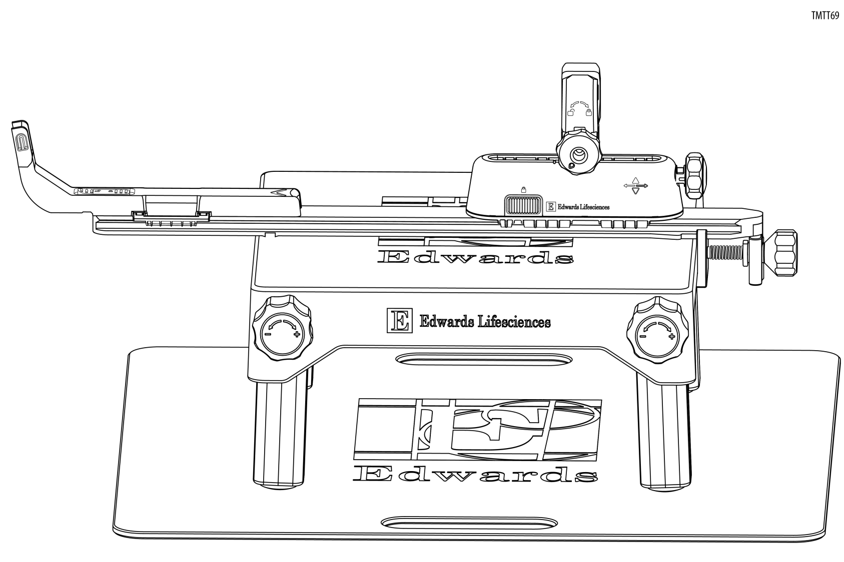


Figure 9: Edwards EVOQUE System Accessories Set 2

Symbol Legend

	English
#	Model Number
REF	Catalogue Number
LOT	Lot Number
QTY	Quantity
	Contents
cm	Usable length
	Do not re-use
	Caution
	Consult instructions for use or consult electronic instructions for use
	Do not use if package is damaged and consult instructions for use
Do Not Use	Do not use product if indication is shown
Use OK	Use product if indication is shown
	Store in a cool, dry place
	Keep away from sunlight
	Keep dry
eifu.edwards.com + 1 888 570 4016	Consult instructions for use on the website
Rx only	Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.

	English
STERILE EO	Sterilized using ethylene oxide
STERILE R	Sterilized using irradiation
STERILE LC	Sterilized using liquid chemical
STERILIZE	Do not resterilize
NON STERILE	Non-sterile
	Non-pyrogenic
DEHP	Non-DEHP
	Use-by date
SN	Serial Number
EC REP	Authorized representative in the European Community/ European Union
	Manufacturer
	Date of manufacture
44 mm	For use with size 44 mm Edwards transcatheter heart valve
48 mm	For use with size 48 mm Edwards transcatheter heart valve
52 mm	For use with size 52 mm Edwards transcatheter heart valve
56 mm	For use with size 56 mm Edwards transcatheter heart valve

	English
	Temperature limit
MD	Medical device
	Exterior diameter
	Inner diameter
	Recommended guidewire length
GW	Recommended guidewire size
GWC	Guidewire compatibility
SZ	Size
Catheter	Catheter shaft size
	Balloon diameter
	Balloon working length
MR	MR Conditional
MR	MR Unsafe
UDI	Unique device identifier
	Contains hazardous substances
	Single sterile barrier system
BIO	Contains biological material of animal origin

Note: The labeling of this product may not contain every symbol depicted in this legend.

Edwards

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