Rx ONLY

TriClip™ G4 SYSTEM

TriClip™ G4 Delivery System REF TCDS0301
TriClip™ Steerable Guide Catheter REF TSGC0201

MitraClip™and TriClip™ Accessories
Stabilizer SZR01ST / SZR07
Lift LFT01ST/ LFT07
Support Plate PLT01ST / PLT07

INSTRUCTIONS FOR USE

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1.0 DEVICE DESCRIPTION

The TriClip™ G4 System is comprised of the TriClip™ Steerable Guide Catheter (TSGC), the TriClip™ G4 Delivery System (TDS), and the MitraClip™ and TriClip™ Accessories listed in **Table 1** below:

Table 1: TriClip G4 System model numbers

Product name	Part number
TriClip Steerable Guide Catheter	TSGC0201
TriClip G4 Delivery System	TCDS0301
Lift	LFT01ST or LFT07
Plate	PLT01ST or PLT07
Stabilizer	SZR01ST or SZR07

TriClip Steerable Guide Catheter

The TriClip Steerable Guide Catheter's primary function is to access the right atrium, maneuver to the target location above the tricuspid valve and position the TriClip G4 Delivery System.

TriClip G4 Delivery System

The TriClip G4 Delivery System (TDS) is used to deliver, position, and place the Implant of the TriClip G4 System on the tricuspid valve leaflets. The TDS is comprised of the Delivery Catheter, the Steerable Sleeve, a handle, and the TriClip™ G4 Implant. The TDS user interface allows for the adjustment of the Implant to the desired position for implantation which are open, closed or inverted.

The Delivery Catheter controls the actuation and deployment of the TriClip G4 Implant. The Delivery Catheter is controlled using the Arm Positioner, Gripper Levers, Actuator Knob, and Lock Lever.

The Steerable Sleeve facilitates the navigation and positioning of the TriClip G4 Implant in the appropriate location above the tricuspid valve.

The Implant grasps and coapts the tricuspid valve leaflets resulting in fixed approximation of the leaflets throughout the cardiac cycle. It is available in four sizes (NT, XT, NTW, XTW) and can be locked, unlocked, and repeatedly opened and closed to allow for repositioning of the Implant to the target location.

Accessories

The Accessories are intended to support the TriClip G4 System during the procedure. The Accessories consist of the Stabilizer, the Support Plate, and the Lift. The Lift and the Support Plate are used outside of the sterile field to provide a stable platform during the procedure. The Stabilizer is used in the sterile field to support and position the TriClip Steerable Guide Catheter and the TriClip G4 Delivery System during the procedure.

Figure 1 shows the TriClip G4 Implant Positions. **Table 2** lists the TriClip G4 System Dimensions.

Figure 1: TriClip™ G4 Implant Positions

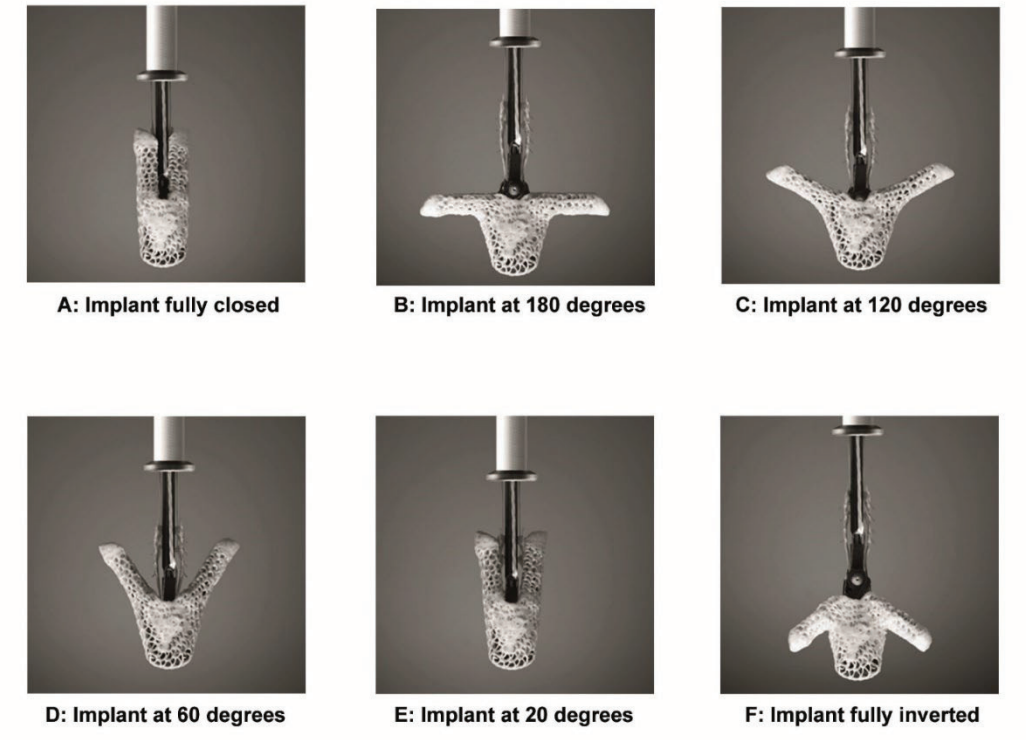


Table 2: TriClip™ G4 System Dimensions

Component	*Dimension*			
Delivery Catheter				
Extended Length, *minimum* mm (from Sleeve curved at 90 degrees)	*56 mm*			
Steerable Sleeve				
Working Length	*109.5 cm*			
Catheter Distal Shaft Outer Diameter	*5.3 mm (16 Fr)*			
Implant Sizes	*NT*	*NTW*	*XT*	*XTW*
Grasping Width at 120 degrees, *minimum* mm	*17 mm*		*22 mm*	
Implant Width at 180 degrees, *nominal* mm	*20 mm*		*25 mm*	
Arm Width, *maximum* mm	*4 mm*	*6 mm*	*4 mm*	*6 mm*
Maximum Arm (Coaptation) Length, *maximum* mm	*9 mm*		*12 mm*	
TriClip™ Steerable Guide Catheter				
Working Length	*80.0 cm*			
Catheter Shaft Outer Diameter	*8.4 mm (25 Fr)*			
Dilator				
Working Length	*122.0 cm*			
Shaft Inner Diameter	*1.0 mm (3 Fr)*			
Shaft Outer Diameter	*5.4 mm (16 Fr)*			
Distal Tip Outer Diameter	*1.5 mm (4 Fr)*			

2.0 INDICATIONS

The TriClip™ G4 System is indicated for improving quality of life and functional status in patients with symptomatic severe tricuspid regurgitation despite optimal medical therapy, who are at intermediate or greater risk for surgery and in whom transcatheter edge-to-edge valve repair is clinically appropriate and is expected to reduce tricuspid regurgitation severity to moderate or less, as determined by a multidisciplinary heart team.

3.0 CONTRAINDICATIONS

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

- Intolerance, including allergy or untreatable hypersensitivity, to procedural anticoagulation
- Untreatable hypersensitivity to Implant components (nickel-titanium alloy, cobalt-chromium alloy)
- Active endocarditis or other active infection of the tricuspid valve

4.0 WARNINGS

- The TriClip™ Steerable Guide Catheter and TriClip™ G4 Delivery System are designed, intended, and distributed for single use only. Cleaning, re-sterilization and/or reuse may result in infection, malfunction of the device and other serious injury or death.
- The Stabilizer, Lift, and Support Plate are non-sterile and must be cleaned, disinfected, and/or sterilized prior to each use. Follow the cleaning, disinfection, and sterilization instructions provided with these accessories.
- The devices should be handled using standard sterile technique to prevent infection.
- Do not use the devices if the “Use by” date specified on the package has elapsed.
- Do not use the devices if the package is damaged or the packing seal is broken.
- Inspect all reusable accessories prior to use. Do not use if the devices are damaged or mishandled.
- Read all instructions carefully. Use universal precautions for biohazards and sharps while handling the TriClip G4 System to avoid user injury.
- Failure to prepare the device as stated in these instructions and failure to handle the device with care might result in damage to the device coating, which may lead to additional intervention or serious adverse event.
- Failure to follow these instructions, warnings and precautions may lead to device damage, user injury, or patient injury including:
    - Failure to deliver the TriClip™ G4 Implant to the intended site
    - Difficulty or failure to retrieve TriClip G4 System components

5.0 PRECAUTIONS

- The TriClip G4 System should be implanted with sterile techniques using fluoroscopy and transoesophageal echocardiography in a facility with immediate access to cardiovascular surgery.
- Echocardiographic images should be carefully assessed to ensure they are of adequate quality to allow successful implantation of the TriClip G4 Implant.
- The TriClip G4 Procedure should be considered with caution in patients with rheumatic disease who have significant leaflet thickening and small annular dimensions considering the risk of iatrogenic tricuspid stenosis.
- Patients with pre-existing cardiac leads should be assessed to ensure placement of the TriClip Implant is possible.
- The safety and effectiveness of the TriClip G4 System has not been established in the following patient populations:
    - Pregnant or lactating women
    - Pediatric patients less than 18 years old

- Patients with systolic pulmonary artery pressure (sPAP) >70 mmHg or fixed pre-capillary pulmonary hypertension as assessed by right heart catheterization (RHC)
- Patients with severe uncontrolled hypertension defined as systolic blood pressure SBP) ≥180 mmHg and/or diastolic blood pressure (DBP) ≥110 mm Hg)

6.0 POTENTIAL ADVERSE EVENTS

The following events have been identified as possible complications of the TriClip G4 Procedure.

Allergic reactions or hypersensitivity to latex, contrast agent, anaesthesia, device materials and drug reactions to anticoagulation, or antiplatelet drugs Additional treatment/surgery from device-related complications Bleeding Blood disorders (including coagulopathy, hemolysis, and heparin induced thrombocytopenia (HIT)) Cardiac arrhythmias (including conduction disorders, atrial arrhythmias, ventricular arrhythmias) Cardiac ischemic conditions (including myocardial infarction, myocardial ischemia, unstable angina, and stable angina) Cardiac perforation Cardiac tamponade Chest pain Death Dyspnea Edema Embolization (device or components of the device) Endocarditis Fever or hyperthermia Fluoroscopy and transesophageal echocardiogram (TEE) related complications: • Skin injury or tissue changes due to exposure to ionizing radiation • Esophageal irritation • Esophageal perforation • Gastrointestinal bleeding Hypotension/hypertension Infection including: • Septicemia	Nausea or vomiting Pain Pericardial effusion Stroke/cerebrovascular accident (CVA) and transient ischemic attack (TIA) System organ failure: • Cardio-respiratory arrest • Worsening heart failure • Pulmonary congestion • Respiratory dysfunction or failure or atelectasis • Renal insufficiency or failure • Shock (including cardiogenic and anaphylactic) Thrombosis Tricuspid valve complications, which may complicate or prevent later surgical repair, including: • Chordal entanglement/rupture • Single leaflet device attachment (SLDA) • Dislodgement of previously implanted devices • Tissue damage • Tricuspid valve stenosis • Worsening, persistent or residual regurgitation Vascular access complications which may require additional intervention, including: • Wound dehiscence • Bleeding of the access site • Arteriovenous fistula pseudoaneurysm, aneurysm, dissection, perforation (rupture), vascular occlusion • Embolism (air, thrombus) • Peripheral nerve injury Venous thrombosis (including deep vein thrombosis) and thromboembolism (including pulmonary embolism)

7.0 MRI SAFETY INFORMATION

A patient with the TriClip™ G4 Implant may be safely scanned under the following conditions. Failure to follow these conditions may result in injury to the patient.

Name/Identification of the Device	TriClip G4 Implant
Nominal Value(s) of Static Magnetic Field [T]	1.5T or 3.0T
Maximum Spatial Field Gradient [T/m and gauss/cm]	40 T/m (4,000 gauss/cm)
RF Excitation	Circularly Polarized (CP)
Operating Mode	Normal Operating Mode
Maximum Whole Body SAR [W/kg]	2W/kg
Limits on Scan Duration	2 W/kg whole body average SAR for 60 minutes of continuous RF (a sequence or back-to-back series/scan without breaks) (Under these scan conditions, the implants are expected to produce a maximum temperature rise of less than or equal to 2.7°C after 15 minutes of continuous scanning.)
MR Image Artifact	In non-clinical testing, the image artifact caused by a pair of implants extends approximately 40 mm beyond the implants when imaged with a spin echo or gradient echo pulse sequence in a 3 T magnetic resonance imaging system. The presence of additional implants in a patient's valve may increase the image artifact size when imaged in an MRI system.
If information about a specific parameter is not included, there are no conditions associated with the parameter.	

8.0 PATIENT SELECTION

Patient selection should be performed by a multi-disciplinary heart team. It is advised that the heart team assess whether the use of TriClip™ G4 System is preferable to surgery or other available treatment options. It is advised that the heart team specifically consider the following when assessing patients for the use of the TriClip G4 System:

- The patient is at intermediate or greater risk for surgical tricuspid valve repair or replacement
- The patient has anatomy suitable for use of TriClip™ Implant. Tricuspid valve leaflet anatomy which may preclude clip implantation, proper clip positioning on the leaflets, or reduction in tricuspid regurgitation to moderate or less include:
  - Evidence of calcification in the grasping area
  - Presence of a severe coaptation defect (>2 cm) of the tricuspid leaflets
  - Severe leaflet defect(s) preventing proper device placement
  - Ebstein Anomaly - Identified by having a normal annulus position while the valve leaflets are attached to the walls and septum of the right ventricle
- The patient's current quality of life or functional status

Patients with the following conditions may have an increased risk of serious adverse events:

- Known or suspected unstable angina or myocardial infarction within the last 12 weeks
- Recent cerebrovascular events
- Persistent bacteremia despite antibiotic treatment

9.0 INFORMATION TO BE SUPPLIED TO THE PATIENT

Physicians should consider the following information when counseling patients about the TriClip G4 Implant and procedure:

- The potential benefits and risks of the TriClip G4 System.
- Alternative therapies available to the patients and their advantages and disadvantages.
- Patients who have good baseline quality of life and functional status may not experience further improvement in these attributes following treatment with the TriClip G4 System. Patients on average are unlikely to experience any survival benefit or a reduced rate of heart failure-related hospitalization.

The following are measures that the patient may have to take following the TriClip G4 Procedure:

- Patients undergoing procedures known to potentially be associated with bacteremia should be prescribed prophylactic antibiotic therapy prior to such procedures.
- Anticoagulation and other medical therapy should be prescribed per institutional guidelines.
- Patients should be advised to limit strenuous physical activity for at least the first month post-procedure or longer if warranted.

After placement of a TriClip G4 Implant, the Patient Implant Card should be filled out, and the patient should be instructed to carry it at all times.

Patient Guides are available to each site and should be given to the patient to inform them of the risks and benefits of the procedure and alternative treatments. Additional counseling information can be found in the Patient Guide and in the Clinical Data section.

10.0 STERILIZATION AND PACKAGING

- The TriClip™ G4 Delivery System and TriClip™ Steerable Guide Catheter are individually packaged and sterilized with ethylene oxide gas.
- The Silicone Pad and Fasteners are single use components and are provided sterile with the TSGC packaging.
- The Stabilizer, Lift, and Support Plate are provided separately as non-sterile and must be cleaned, disinfected, and/or sterilized prior to each use. Follow the cleaning, disinfection, and sterilization instructions provided with these accessories.

11.0 STORAGE

Handle with care. Store in original packaging. Keep dry. Keep away from sunlight.

12.0 ADDITIONAL REQUIRED EQUIPMENT NOT INCLUDED

Exchange length supportive guidewire
High-pressure three-way stopcocks (5)
Arterial high-pressure extension tubing (3)
50-60 cc syringes with luer fitting (2)
1000 ml pressure bags (2)
Sterile IV tubing with thumbwheel occluders (2)
Heparinized sterile saline solution (2, 1-liter bags)
Rolling IV Pole
Sterile Basin

13.0 PATIENT PREPARATION

13.1 Prepare the patient per institution's standard practice for transfemoral catheterization.

13.2 Place Support Plate under patient's leg in the region between the area of the upper leg and the knee and place the Lift over the ipsilateral lower extremity prior to draping the patient.

13.3 Place the Lift on the Support Plate such that the front edge (i.e., the edge that corresponds with the shorter legs of the Lift) is approximately 85 cm from the patient's mid sternum.

13.4 Adjust the height of the Lift so that the front edge of the Lift is close to the patient's leg but is not impinging on it. Adjust the back legs to be 2 or 3 notches above the front legs (i.e., the back legs of the Lift are taller than the front legs).

CAUTION: Ensure the Lift and Support Plate are covered completely by sterile drape during the procedure. Use towels as necessary to minimize direct contact between the patient and all surfaces of both the Lift and Support Plate.

13.5 Prepare the patient for invasive hemodynamic monitoring.

14.0 TRICLIP™ G4 SYSTEM PREPARATION BEFORE USE

WARNING: DO NOT use the TriClip G4 System after the "Use By" date stated on the package label, and never reuse or re-sterilize the system. Use of expired, reused, or re-sterilized devices may result in infection.

WARNING: Always inspect the TriClip G4 System and its packaging to verify no damage has occurred as a result of shipping and handling and that the sterile barrier has not been compromised. DO NOT use the device if damage is detected. Use of product with a compromised sterile barrier may result in infection. Use of damaged product may result in patient injury.

- DO NOT remove the protective cover placed over the Implant.

WARNING: DO NOT handle the Implant directly; leave it in the protective cover to avoid potential contamination. Removal of the protective cover may result in infection. Removal of the protective cover may result in damaged product which may result in patient injury.

- The preparation is most easily accomplished with the aid of an assistant.

14.1 TriClip™ Steerable Guide Catheter Preparation

WARNING: All lumens contain air when shipped. Use proper de-airing techniques before and during use to minimize the risk of air embolism.

14.1.1 Carefully remove the white Guide tip shape retainer and transparent protective tubing from the Guide tip.

14.1.2 Inspect Guide and Dilator to verify they are undamaged.

WARNING: DO NOT use if damage is detected. Use of damaged product may result in air embolism, vascular and/or cardiac injury.

14.1.3 Remove the sterile package containing Fasteners and Silicone Pad from the Guide tray.

14.1.4 Fill a basin with heparinized saline.

14.1.5 Flush and de-air the Guide and Dilator with heparinized saline:

14.1.5.1 Connect 3-way stopcocks to the Guide and Dilator flush ports, de-air the Dilator and then close the stopcock and the Rotating Hemostatic Valve.

14.1.5.2 Hydrate 5-10 cm of the distal end of the Dilator with heparinized saline and insert the Dilator approximately 10 cm into Guide then remove.

14.1.5.3 Connect high pressure tubing and a 50-60 cc syringe filled with heparinized saline to the Guide flush port.

14.1.5.4 De-air the Guide.

14.1.5.4.1 With the tip raised, displace all air from the Guide while tapping along the length of the catheter shaft.

14.1.5.4.2 Cover the Guide tip with finger once heparinized saline exits the Guide.

14.1.5.4.3 Close the Guide stopcock.

14.1.6 Submerge the Guide tip in the basin of heparinized saline.

14.1.7 While the Guide tip is submerged in the basin of heparinized saline, remove finger from Guide tip and check the Guide valve for leaks by raising the handle to a vertical position for a minimum of 30 seconds.

14.1.8 Hydrate 5-10 cm of the distal end of the Dilator with heparinized saline.

14.1.9 Cover the Guide tip with finger and insert the Dilator into the Guide while Guide tip remains submerged in the basin of heparinized saline.

14.1.9.1 While advancing the Dilator, continually watch for air in the Guide Hemostasis Valve housing. If needed, remove finger from Guide tip and aspirate while assuring the Guide tip is submerged.

14.1.10 Remove finger from tip of Guide when the Dilator tip approaches the Guide tip.

14.1.11 Position the Dilator to create a smooth transition.

14.2 Stabilizer Preparation

14.2.1 Assemble the sterilized Stabilizer. Set the Stabilizer aside in a protected sterile environment for later use.

14.3 TriClip™ G4 Delivery System Preparation

14.3.1 Release the DC Fastener and rotate the DC Handle 90 degrees clockwise when the TDS is removed from packaging. Secure the DC Fastener.

14.3.2 Inspect all TriClip™ G4 Delivery System parts, including the TriClip™ G4 Implant, DC shaft, and Sleeve to verify they are undamaged.

WARNING: DO NOT use the device if damage is detected. Use of damaged product may result in air embolism, Implant or device component embolization, vascular and/or cardiac injury.

Sleeve Preparation

14.3.3 Connect 3-way stopcocks to the Sleeve flush port and bottom DC flush port.

14.3.4 Remove the cap from the Introducer and place the cap on the top flush port of the DC Handle.

14.3.5 Connect a 3-way stopcock to the Introducer flush port.

14.3.6 Attach a 50-60 cc syringe filled with heparinized saline to the 3-way stopcock on the Introducer, de-air the Introducer, and close the stopcock.

14.3.7 Connect one high pressure tube to each drip line from the pressurized bags with sterile heparinized saline; flush and de-air the lines.

14.3.8 Connect one high pressure tube to the 3-way stopcock on the bottom flush port of the DC Handle and one high pressure tube to the 3-way stopcock on the flush port of the Sleeve Handle.

14.3.9 Flush and de-air the Sleeve with heparinized saline.

14.3.9.1 While flushing, release the DC Fastener, retract and advance the DC Handle to remove residual air from the lumen.

WARNING: DO NOT use excessive force when pulling the DC (Delivery Catheter) Radiopaque Ring against the Sleeve tip, while translating the DC shaft. It may result in device damage including distal tip embolization.

14.3.10 Secure the DC Fastener with DC Handle fully advanced.

Delivery Catheter Preparation

CAUTION: DO NOT handle the TriClip™ G4 Implant directly; leave in the protective cover to avoid potential contamination. Removal of the protective cover may result in damaged product which may result in patient injury.

14.3.11 Temporarily remove the cap from top flush port of the DC Handle to flush and de-air DC Handle and all lumens of the DC with heparinized saline.

14.3.12 After de-airing the DC Handle chamber, replace the cap to close off top flush port of the DC Handle.

14.3.13 Retract and advance the Lock Lever several times to remove residual air from the lumens.

WARNING: DO NOT retract the Lock Lever forcefully. It may result in the inability to lock or unlock the Implant. Damage could occur causing the Implant to not unlock or open. Inability to open the Implant may result in valve injury or lead to deployment of the Implant in an unintended location.

14.3.14 Loosen the Lock Lever Cap to de-air. DO NOT turn Lock Lever cap more than 1/2 turn in the “Open” direction. After de-airing, tighten the Lock Lever cap.

14.3.15 With the tip raised and the shaft held taut, displace all air from the DC and Sleeve while tapping along the length of the catheter shaft.

14.3.16 Confirm continuous flow from the distal end of the DC and Sleeve.

Delivery Catheter and TriClip™ G4 Implant Inspection

WARNING: DO NOT handle the Implant directly, leave in the protective cover to avoid potential contamination. Removal of the protective cover may result in infection. Removal of the protective cover may result in damaged product which may result in patient injury.

14.3.17 *Raise the Gripper(s), Unlock the Implant,* and confirm the Implant is at *Grasping Arm Angle*.

NOTE: If *Implant Arm Angle* is greater than *Grasping Arm Angle*, close the Implant to *Grasping Arm Angle*; if *Implant Arm Angle* is less than *Grasping Arm Angle*, *Open the Implant Arms* to *Grasping Arm Angle*.

14.3.18 *Lower the Gripper(s)* once to de-air the lumens.

14.3.19 Close the Implant Arms to approximately 60 degrees and *Lock the Implant.*

14.3.20 Close the Implant Arms to approximately 20 degrees and *Establish Final Arm Angle.*

WARNING: DO NOT turn the Arm Positioner more than 1 turn in the "Open" direction from neutral. Failure to stop turning the Arm Positioner at 1 turn in the "Open" direction past neutral may result in Implant opening or device damage which could cause the Implant to become non-functional and lead to embolization and/or conversion to surgical intervention.

14.3.21 Return the *Arm Positioner to Neutral.*

14.3.22 *Raise the Gripper(s), Unlock the Implant,* and *Invert the Implant Arms.*

WARNING: DO NOT retract the Lock Lever forcefully. It may result in the inability to lock or unlock the Implant. Damage could occur causing the Implant to not unlock or open. Inability to open the Implant may result in valve injury or lead to deployment of the Implant in an unintended location.

WARNING: Turning the Arm Positioner in the "Open" direction more than 1 full turn past an *Implant Arm Angle* of 180° or turning past when resistance is first noted may result in device damage which could cause the Implant to become non-functional and lead to embolization, and/or conversion to surgical intervention.

14.3.23 *Lock the Implant, Fully Close the Implant Arms, and Lower the Gripper(s)*

14.3.24 Release the DC Fastener and torque the DC Handle clockwise and counter-clockwise ¼ turn while translating the DC Shaft.

14.3.25 Retract the DC fully against the Sleeve and secure the DC Fastener.

WARNING: Do not use excessive force when pulling the DC (Delivery Catheter) Radiopaque Ring against the Sleeve tip while translating the DC shaft, it may result in device damage including distal tip embolization.

14.3.26 Without removing the protective cover, carefully slide the Introducer over the Implant and stop when the tip of the Implant is just proximal to the tip of the Introducer.

WARNING: DO NOT compress the Implant Arms. Compressing the Implant Arms may result in inability to open the Implant. Inability to open the Implant may result in valve injury or lead to deployment of the Implant in an unintended location.

WARNING: *Fully Close the Implant Arms*, before insertion or retraction into the Introducer. Failure to do so may result in difficulty or inability to advance or retract the Implant, which may result in vascular and/or cardiac injury, air embolism, and/or the need for surgical intervention.

14.3.27 Return the *Arm Positioner to Neutral*

14.3.28 Temporarily discontinue heparinized saline flushes.

14.3.29 Re-start heparinized saline flushes just before the use of the Delivery System.

WARNING:

- **Heparinized saline flush should be continuous throughout the procedure.**
- **Discontinuing flush may result in air embolism and/or thrombus formation.**
- **Ensure flow is visible through the drip chamber and that the tubing is free from kinks and/or obstruction.**
- **Ensure pressure of 300 mmHg is maintained.**

15.0 ACCESS TO THE TRICUSPID VALVE

NOTE: This is a suggested sequence for the procedure. Variations may be used based upon patient anatomy.

15.1 Access the RA to accommodate the Guide tip using transvenous techniques and equipment.

15.2 Heparinize the patient.

WARNING: Failure to administer heparin may result in thrombus formation.

15.3 Carefully place an exchange length supportive guidewire in the superior vena cava. Dilate the subcutaneous tissue and femoral vein to accommodate the Guide shaft using standard dilation technique.

16.0 TRICLIP™ STEERABLE GUIDE CATHETER INSERTION

WARNING: Confirm a smooth transition between the Dilator and the tip of the Guide to minimize the risk of vascular and/or cardiovascular injury.

CAUTION: Always use pressure monitoring, echocardiography and fluoroscopy for guidance and observation during use of the TriClip™ G4 System.

WARNING: Always use a careful, deliberate, and iterative approach to positioning the TriClip G4 System. It is recommended to make multiple small adjustments rather than single large adjustments. Large adjustments may result in vascular and/or cardiac injury.

16.1 Rotate the +/- Knob in the "-" direction until the Guide curve is substantially straightened.

16.2 Wet the surface of the Guide shaft with sterile saline.

16.3 Insert the Guide-Dilator assembly over the stationary guidewire into the femoral vein.

WARNING: DO NOT use excessive force to advance or manipulate the Guide-Dilator assembly. If resistance is encountered, use echocardiography and/or fluoroscopy to assess before proceeding. Use of excessive force may result in arrhythmias, vascular and/or cardiac injury.

16.4 Advance the Guide-Dilator assembly to the RA maintaining the Guide in a straightened position.

16.5 Adjust Guide torque to position the tip away from adjacent tissues.

16.6 Place the Silicone Pad on the sterile drape over the Lift. Place the Stabilizer onto the Silicone Pad.

16.7 Secure the Guide in the Stabilizer slot using the Fastener. Ensure the Fastener engages the metallic tube on the Guide shaft. The Guide handle should be immediately adjacent to the Stabilizer, such that they are in contact with each other.

16.8 Retract the Dilator approximately 5 cm into the Guide, leaving the guide wire in the superior vena cava.

CAUTION: Always loosen the Fastener before torquing the Guide to prevent stripping the screw.

16.9 Retract the guidewire into the tip of the Dilator. Remove the Dilator and guidewire while gently aspirating the Guide (starting when the Dilator is approximately halfway retracted into the Guide, approximately 40 cm) using a 50-60 cc syringe. Cover Guide Hemostasis Valve with finger upon Dilator removal.

NOTE: Avoid contacting tissue or creating a vacuum in the Guide lumen. If necessary, position the Guide handle below the level of the RA to allow blood to fill the Guide lumen.

WARNING: DO NOT create a vacuum while removing the dilator from the Guide; air may enter the lumen of the Guide which may result in air embolism.

WARNING: Failure to fully retract guidewire into the Dilator may result in air embolism.

17.0 TRICLIP™ G4 DELIVERY SYSTEM INSERTION

17.1 Confirm the Guide lumen is completely de-aired.

WARNING: To minimize the potential of air embolism, DO NOT introduce the Delivery System into the Guide until the Guide lumen has been completely de-aired.

17.2 Confirm there is a slow, continuous heparinized saline flush through both the Sleeve and the DC and that the tip of the Implant is just proximal to the tip of the Introducer.

WARNING: Failure to continuously flush the Delivery System with heparinized saline may reduce device performance.

WARNING:

- **Heparinized saline flush should be continuous throughout the procedure.**
- **Discontinuing flush may result in air embolism and/or thrombus formation. Ensure flow is visible through the drip chamber and that tubing is free from kinks and/or obstruction.**
- **Ensure pressure of 300 mmHg is maintained.**

17.3 Carefully remove the protective cover surrounding the Implant and the Introducer.

17.4 Confirm that the stopcock on the Introducer flush port is closed and that the Introducer is de-aired.

17.5 While flushing heparinized saline on the Guide Hemostasis Valve, place the tip of the Introducer against the Guide Hemostasis Valve and advance the Introducer straight into the valve in a continuous motion while rotating the Introducer in small clockwise and counterclockwise motions until the Implant can be observed distal to the valve.

WARNING: DO NOT continue to advance the Introducer if resistance is felt; the Guide Hemostasis Valve, Introducer or the Implant may be damaged. Damage to these components may result in air embolism, vascular or cardiac injury.

WARNING: To minimize the potential of air embolism, ensure proper de-airing when inserting the Introducer into the Guide Hemostasis Valve.

17.6 Leave the Introducer fully inserted in the Guide Hemostasis Valve throughout the procedure.

17.7 Align the Longitudinal Alignment Marker on the Sleeve shaft with the Alignment Marker on the Guide Hemostasis Valve.

17.8 Confirm that the Guide is substantially straightened prior to advancing the Delivery System.

17.9 Carefully advance the Delivery System through the Guide under fluoroscopic guidance. Stop when tip of the Implant is even with the tip of the Guide.

WARNING: Failure to confirm Guide is substantially straightened prior to advancing the Delivery System may result in damage to the Delivery System or the Implant. Damage to these components may result in vascular or cardiac injury.

17.10 Under echocardiographic and fluoroscopic guidance, advance the Delivery System until the Implant Arms exit slightly beyond the Guide RO Tip Ring. The Guide may be placed in a neutral position by rotating the '+/-' Knob in the '+' direction. Confirm that the Implant is free from the right atrial wall and valve tissue.

17.11 Under echocardiographic guidance, advance the Delivery System and retract the Guide iteratively as needed while maintaining the Guide in the RA. Stop when the Guide RO Tip Ring is between the RO Alignment Markers of the Sleeve, as confirmed under fluoroscopic guidance.

17.12 Position the Sleeve Handle in the Stabilizer slot.

17.13 Confirm that the Implant is free from the right atrial wall and valve tissue.

WARNING: Failure to confirm that the Implant is free from the right atrial wall and valve tissue may result in cardiac injury.

18.0 INITIAL TRICLIP™ G4 SYSTEM POSITIONING IN THE RIGHT ATRIUM

NOTE: Positioning is achieved with iterative adjustments of the Guide and Delivery System using torque, translation, and knob adjustments. The goals of positioning are:

A. Positioning the TriClip G4 System centrally over the valve with respect to aortic-posterior and septal-lateral directions.

B. Aligning the Implant so the DC Shaft is perpendicular to the plane of the tricuspid valve.

C. Positioning the distal tip of the Implant above the leaflets.

WARNING: Excessive torque on the Guide and translation of the TriClip G4 System may inadvertently displace the tip of the Guide from the RA, which may result in arrhythmias or cardiac injury.

WARNING: DO NOT continue to rotate or manipulate any of the handle knobs if significant resistance is noted; device damage may occur and result in cardiac injury.

18.1 Adjust the Guide position as necessary to maintain that the Implant is free from adjacent tissue.

18.2 Adjust Implant height above the leaflets as necessary using the Guide +/- Knob.

18.3 Adjust Sleeve deflection using the F/E Knob to deflect the Implant towards the apex. Retract the DC Radiopaque Ring against the Sleeve tip as necessary.

18.4 During Sleeve deflections confirm that the Guide RO Tip Ring is between the RO Alignment Markers of the Sleeve prior to making maximum Sleeve deflections.

WARNING: DO NOT deflect the Sleeve tip more than 90 degrees as device damage may occur. Use of damaged product may result in cardiac injury.

18.5 Secure the Sleeve handle in the Stabilizer using the Fastener.

18.6 To reposition the TriClip G4 System, adjust the Stabilizer and the system together until positioning is adequate.

18.7 Adjust the Implant position to maintain adequate height above the tricuspid valve in the RA.

WARNING: Maintain the Implant above the leaflets until ready to grasp to minimize the risk of Implant entanglement in the chordal apparatus. Implant entanglement may result in cardiac injury, worsening tricuspid regurgitation, difficulty or inability to remove the Implant and conversion to surgical intervention.

19.0 FINAL TRICLIP™ G4 SYSTEM POSITIONING

19.1 *Raise the Gripper(s)*

CAUTION: Raising the Grippers more often than needed, retracting the Gripper Levers forcefully may damage the Gripper cover and impair Delivery System performance.

19.2 *Unlock the Implant* and *Open the Implant Arms* to approximately 180 degrees.

WARNING: DO NOT RETRACT THE LOCK LEVER FORCEFULLY. Retracting the Lock Lever forcefully may result in the inability to unlock Implant. Inability to open the Implant may result in valve injury or lead to deployment of the Implant in an unintended location.

19.3 Adjust the TriClip G4 System to reposition the Implant as necessary. Confirm that the distal tip of the Implant is above the leaflets.

19.4 Rotate the DC handle to align the Implant Arms perpendicular to the line of coaptation. DO NOT rotate the Implant more than 90 degrees in each direction.

19.5 Carefully translate the DC shaft multiple times to release stored torque. Fully retract the DC.

WARNING: Fully release stored torque. If not done, it may result in unwanted Implant Arm orientation changes during grasping. Torque of the DC Handle more than 180 degrees may result in DC damage and cardiac injury.

19.6 *Identify Gripper Orientation*

19.7 Close the Implant to an *Implant Arm Angle* of approximately 60 degrees.

19.8 Complete final TriClip G4 System positioning in the RA using multiple imaging planes. Re-secure the Guide and Sleeve Fasteners as appropriate.

20.0 GRASPING THE LEAFLETS AND VERIFYING THE GRASP

20.1 Advance the DC distally to position the Implant below the valve. Ensure that the Implant Arms are oriented perpendicular to the line of coaptation.

WARNING: Do confirm that the Implant Arms are perpendicular to the line of coaptation. Failure to do so may result in loss of leaflet capture and insertion. Loss of leaflet capture and insertion may result in inadequate reduction of tricuspid regurgitation and may result in a single leaflet device attachment (SLDA).

WARNING: DO NOT make substantial Implant Arm orientation adjustment in the RV. Implant entanglement in sub-valvular apparatus may result in cardiac injury and worsening tricuspid regurgitation; and may result in difficulty or inability to remove the Implant, and conversion to surgical intervention.

WARNING: Always ensure that either the Grippers are raised or that the Implant is closed while in the RV to avoid potential cardiac injury.

20.2 *Open the Implant Arms* to the *Grasping Arm Angle*.

20.3 Without using excessive force, retract the DC to grasp both leaflets.

WARNING: An improper grasp will allow one or both leaflets to move freely. Closing and deploying the Implant in this situation may result in loss of leaflet capture and insertion. Loss of leaflet capture and insertion may result in inadequate reduction of tricuspid regurgitation and may result in a single leaflet device attachment (SLDA).

20.4 If the grasp appears satisfactory, *Lower the Gripper(s)* onto the leaflets.

NOTE: Simultaneous leaflet capture with both Grippers should be attempted first. If unsuccessful, *Raise the Gripper(s)* to release leaflet capture and *Lower the Gripper(s)* again to capture leaflets. Raising and lowering the Gripper(s) can be done simultaneously or independently.

WARNING: DO NOT advance the DC handle or adjust the position of the TriClip™ G4 System in a way that increases tension on the leaflets after grasping the leaflets, as valve injury may occur.

20.4.1 If both Grippers have not lowered:
- 20.4.1.1 *Lock the Implant*.
- 20.4.1.2 Confirm both Grippers have lowered.
- 20.4.1.3 *Unlock the Implant*.

WARNING: Failure to confirm that both Grippers have been lowered onto the leaflets prior to closing the Implant may result in loss of leaflet capture and insertion. Loss of leaflet capture and insertion may result in inadequate reduction of tricuspid regurgitation and may result in a single leaflet device attachment (SLDA).

20.5 Close the Implant until the *Implant Arm Angle* is approximately 60 degrees. Release tension on the DC and secure the DC Fastener.

20.6 Use echocardiographic imaging to verify insertion of both leaflets and satisfactory grasp by observation of:

- Leaflet immobilization
- Single or multiple valve orifice(s)
- Limited leaflet mobility relative to the tips of both Implant Arms
- Adequate TR reduction.

20.6.1 If grasping fails to hold both leaflets and the Implant retracts to the RA, reposition the Implant.

- 20.6.1.1 *Open the Implant Arms* and reorient the Implant Arms in the RA, as needed, then repeat grasping steps (refer to Section 19.0 and 20.0).
  - 20.6.1.1.1 If significant repositioning is necessary, *Fully Close the Implant Arms* and *Lower the Gripper(s)* then repeat positioning and grasping steps.

20.6.2 If the Sleeve limits DC travel during grasping, an inadequate grasp may require repositioning of the Implant.

- 20.6.2.1 *Raise the Gripper(s)* and *Open the Implant Arms* to approximately 180 degrees *and* advance the DC handle. Repeat positioning and grasping steps as necessary (refer to Section 19.0 and 20.0).

21.0 CLOSING THE TRICLIP™ G4 IMPLANT AND EVALUATING IMPLANT POSITION

21.1 *Lock the Implant.*

WARNING: Failure to *Lock the Implant* may result in loss of leaflet capture and insertion. Loss of leaflet capture and insertion may result in inadequate reduction of tricuspid regurgitation and may result in a single leaflet device attachment (SLDA).

21.2 Slowly close the Implant just until the leaflets are coapted and TR is sufficiently reduced. The Implant should maintain a distinct "V" shape.

WARNING: DO NOT use excessive force to close the Implant further than is necessary to adequately reduce TR. Leaflet injury may occur. DO NOT close the Implant too tightly as it may result in inability to deploy the Implant. Inability to deploy the Implant may result in worsening tricuspid regurgitation, cardiac injury, a single leaflet device attachment (SLDA), and/or conversion to surgical intervention.

WARNING: Failure to turn the Arm Positioner at least ½ turn in the "Close" direction after locking the Implant may result in loss of leaflet capture and insertion. Loss of leaflet capture and insertion may result in inadequate reduction of tricuspid regurgitation and may result in a single leaflet device attachment (SLDA).

21.3 Use echocardiographic imaging to verify valve function, satisfactory coaptation, and insertion of both leaflets by observation of:

- Leaflet immobilization
- Single or multiple valve orifice(s)
- Limited leaflet mobility relative to the tips of both Implant Arms
- Adequate TR reduction.

21.3.1 If the Implant position is not satisfactory, *Raise the Gripper(s), Unlock the Implant,* and *Invert the Implant Arms*.

WARNING: Turning the Arm Positioner in the "Open" direction more than 1 full turn past an *Implant Arm Angle* of 180° or turning past when resistance is first noted may result in device damage which could cause the Implant to become non-functional and lead to embolization, and/or conversion to surgical intervention.

21.3.2 Retract the inverted Implant into the RA.

21.3.3 Confirm both leaflets move freely.

21.3.4 Repeat positioning steps, as necessary, then repeat grasping steps.

22.0 TRICLIP™ G4 SYSTEM PRE-DEPLOYMENT IMPLANT ASSESSMENT

22.1 Confirm DC Handle is secure.

WARNING: Do secure the DC Handle. If not done, it may result in leaflet injury or loss of leaflet insertion with resultant worsening tricuspid regurgitation, single leaflet device attachment (SLDA), and/or conversion to surgical intervention.

22.2 *Establish Final Arm Angle*.

WARNING: DO NOT turn the Arm Positioner more than 1 turn in the "Open" direction from neutral. Failure to stop turning the Arm Positioner at 1 turn in the "Open" direction past neutral may result in Implant opening or device damage which could cause the Implant to become non-functional and lead to embolization and/or conversion to surgical intervention.

22.3 Turn the Arm Positioner to the "closed" side of the neutral position.

22.4 Perform mean pressure gradient assessment prior to proceeding to deployment.

23.0 TRICLIP™ G4 IMPLANT DEPLOYMENT

23.1 Deployment Step 1: Lock Line Removal

23.1.1 While holding the ends of the Lock Line remove the Lock Lever Cap and “O” ring. Unwrap the two ends of the Lock Line in a counterclockwise direction. Separate the ends of the Lock Line and remove the plastic cover from the lines so that no twists or knots are present.

WARNING: Do not let Line unravel freely. Do not remove Lock Line or plastic covers if line is bunched. Letting Line unravel freely may result in knots in the line. Removing Line if it is bunched may result in difficulty or inability to remove line due to knots or twists.

23.1.2 Grasp one of the free ends of the Lock Line, confirm the line moves freely, and slowly remove the Lock Line. Pull the Lock Line coaxial to the Lock Lever. If resistance is noted, stop and pull on the other free end to remove the Lock Line.

23.1.3 *Establish Final Arm Angle*.

NOTE: The Implant Arms may open slightly (~5°) and then remain in a stable position. If Arms open more than slightly, close the Implant to the desired Arm position and re-*Establish Final Arm Angle*.

WARNING: DO NOT turn the Arm Positioner more than 1 turn in the “Open” direction from neutral. Failure to stop turning the Arm Positioner at 1 turn in the “Open” direction past neutral may result in Implant opening or device damage which could cause the Implant to become non-functional and lead to embolization and/or conversion to surgical intervention.

23.1.4 Turn the *Arm Positioner to Neutral*.

23.2 Deployment Step 2: Delivery Catheter Shaft Detachment

23.2.1 Confirm that the Arm Positioner is Neutral. Remove the Release Pin from the DC Handle.

23.2.2 Turn the Arm Positioner in the “Open” direction until the Release Pin groove is fully exposed.

NOTE: After the Release Pin is removed, turning the Arm Positioner in the “Open” direction will not open the Implant Arms.

23.2.3 Turn the Actuator Knob of the DC approximately 8 turns in the direction of the arrow printed on the Actuator Knob.

If it is difficult to turn the Actuator Knob, STOP and confirm that the Arm Positioner has been turned in the “Open” direction, such that the Release Pin groove is fully exposed.

WARNING: Stop turning the Actuator Knob when resistance is felt, otherwise it may result in inability to deploy the Implant. Inability to deploy the Implant may result in worsening tricuspid regurgitation, cardiac injury, a single leaflet device attachment (SLDA), and/or conversion to surgical intervention.

23.2.4 Retract the Actuator Knob approximately 0.5 cm after it is fully unthreaded.

23.2.5 Fully retract the Gripper Levers

WARNING: Do retract the Gripper Levers fully prior to retracting the DC Handle. Failure to retract the Gripper Levers may result in higher forces to deploy the Implant. This may result in worsening tricuspid regurgitation, cardiac injury or a single leaflet device attachment (SLDA).

23.2.6 Release the DC Fastener, and slowly retract the DC Handle until the DC Radiopaque Ring is against the tip of the Sleeve.

23.2.6.1 If resistance is felt during DC Detachment and Implant separation from the DC can be confirmed by fluoroscopy, confirm the Gripper Levers are fully retracted. If resistance is still felt, access the Gripper Lines.

23.2.6.2 If resistance is still felt during DC Detachment and Implant separation from the DC cannot be confirmed by fluoroscopy:

23.2.6.2.1 Confirm that the Actuator Knob is retracted approximately 0.5 cm beyond the fully exposed Release Pin Groove and the Gripper Levers are fully retracted.

23.2.6.2.2 If resistance is still felt during DC Detachment, confirm by fluoroscopy that the DC Shaft and the Implant are coaxially aligned. If they are not aligned, secure the DC fastener and slowly translate the Stabilizer and/or rotate the Guide until the angulation between the DC Shaft and the Implant is reduced or eliminated (as observed under fluoroscopic imaging).

23.2.6.2.3 If resistance is still felt, release the DC Fastener, retract the Actuator Knob an additional 0.5 cm.

23.2.6.2.4 If resistance is still felt, secure the DC Fastener and fully advance both Gripper Levers.

23.2.6.2.5 If resistance is still felt, access the Gripper Lines.

23.2.6.2.6 If resistance is still felt, secure the DC Fastener and repeat alignment steps to reduce / eliminate the angulation between the DC shaft and the Implant (as observed under fluoroscopic imaging).

23.2.7 Confirm that the DC Fastener is secure.

23.2.8 **Confirm that the Implant position is stable**

23.2.9 Use echocardiographic imaging to verify valve function, satisfactory coaptation, and insertion of both leaflets by observation of:

- Leaflet immobilization
- Single or multiple valve orifice s)
- Limited leaflet mobility relative to the tips of both Implant Arms
- Adequate TR reduction.

23.2.10 **If placing an additional Implant proceed to Section 24.0 If not placing an additional Implant proceed to section 25.0.**

24.0 ADDITIONAL TRICLIP™ G4 IMPLANT PLACEMENT

WARNING: Use caution not to displace or dislodge an implanted Implant when placing an additional Implant; Implant detachment from leaflet(s) may occur which may result in a single leaflet device attachment (SLDA) or Implant embolization.

24.1 When placing an additional Implant, the following are recommended:

24.1.1 In the RA, ensure Implant Arms are oriented perpendicular to the line of coaptation and Grippers are raised.

24.1.2 Use both fluoroscopy and echocardiography when crossing into the RV and during grasping.

24.1.3 Cross into the RV with an *Implant Arm Angle* of < 60 degrees.

WARNING: DO NOT use excessive force or retraction distance during grasping. This may compromise leaflet capture and insertion. Loss of leaflet capture and insertion may result in inadequate reduction of tricuspid regurgitation and may result in a single leaflet device attachment (SLDA).

25.0 TRICLIP™ G4 DELIVERY SYSTEM REMOVAL

WARNING: During Implant removal always retract the Delivery System by pulling only on the Sleeve Handle. Retracting the Delivery System by pulling on the DC Handle may result in device damage and/or device or component embolization, and may result in vascular and/or cardiac injury.

WARNING: Do release the DC Fastener before releasing Sleeve curves, otherwise it may result in device damage and/or device or component embolization.

WARNING: Use echocardiographic guidance while releasing Sleeve deflection. Failure to do so may result in cardiac injury.

25.1 TriClip™ G4 Delivery System Removal After Implant Deployment

25.1.1 Removal of the Delivery System While Leaving the Guide in Place.

25.1.1.1 Release the DC Fastener.

25.1.1.2 Slowly release Sleeve deflection by rotating the F/E Knob to neutral.

25.1.1.3 Secure DC Fastener once Sleeve curves are released.

25.1.1.4 Straighten the Guide with the +/- Knob and turn the S/L Knob to neutral when the Delivery Catheter tip is free from the right atrial wall and the tricuspid valve.

25.1.1.5 Release the Sleeve Fastener and retract the Delivery System approximately 10 cm into the Guide by pulling only on the Sleeve Handle.

25.1.1.6 Confirm that the Introducer is still fully advanced in the Guide Hemostasis Valve.

25.1.1.7 Retract the Delivery System by pulling only on the Sleeve Handle and position the Delivery Catheter tip inside the Introducer. Begin gently aspirating the Guide (starting when the Delivery System is approximately halfway into the Guide, approximately 40 cm retracted) using a 50-60 cc syringe.

25.1.1.8 Remove the Delivery System and the Introducer simultaneously from the Guide by pulling on the Sleeve shaft and Introducer. Ensure the Delivery Catheter tip is inside the Introducer by visualizing the Proximal Sleeve alignment marker just outside the Introducer. Aspirate the Guide during removal of the Delivery System and Introducer. Cover Guide Hemostasis Valve with finger upon Delivery System removal. If necessary, position the Guide Handle below the level of the RA to allow blood to fill the Guide Lumen.

WARNING: DO NOT remove the tip of the Delivery System from the Guide without removing the Introducer simultaneously. Failure to remove the Introducer simultaneously may result in air embolism.

WARNING: DO NOT create a vacuum while removing the Delivery System from the Guide; air may enter the lumen of the Guide which may result in air embolism.

25.1.1.9 Aspirate using a 50-60 cc syringe to remove any remaining air from the Guide.

25.1.2 Removal of the Delivery System and Guide simultaneously.

25.1.2.1 Release the DC Fastener.

25.1.2.2 Slowly release Sleeve curves by rotating the F/E Knob to neutral.

25.1.2.3 Secure the DC Fastener once Sleeve curves are released.

25.1.2.4 Straighten the Guide with the +/- Knob and turn the S/L Knob to neutral when the Delivery Catheter tip is free from the right atrial wall and the tricuspid valve.

25.1.2.5 Release the Sleeve Fastener and retract the Delivery System approximately 10 cm into the Guide by pulling only on the Sleeve Handle.

25.1.2.6 Carefully retract the Guide tip into the RA/IVC junction. The Guide may be straightened further with the +/- Knob if desired.

25.1.2.7 Remove the TriClip™ G4 System from the femoral vein, while providing hemostasis.

25.2 TriClip™ G4 Delivery System Removal With TriClip™ G4 Implant Attached

25.2.1 **Removal of the Delivery System while leaving the Guide in place.**

25.2.1.1 Confirm Implant is locked.

25.2.1.2 *Fully Close the Implant Arms* and continue to turn the Arm Positioner until it is no longer possible to rotate the Arm Positioner. Return the Arm Positioner to Neutral.

WARNING: Failure to follow Step 25.2.1.2 prior to retraction into the Guide may result in device damage, inability to remove the Delivery System and/or vascular and cardiac injury.

25.2.1.3 *Lower the Gripper(s)*.

25.2.1.4 Release the DC Fastener and retract the DC Handle until the DC Radiopaque Ring is fully against the tip of the Sleeve.

25.2.1.5 Slowly release Sleeve deflection by rotating the F/E Knob to neutral.

25.2.1.6 Rotate DC handle such that the Implant arms are perpendicular to the guide curve plane.

25.2.1.7 Secure the DC Fastener once Sleeve curves are released.

25.2.1.8 Straighten the Guide with the +/- Knob and turn the S/L Knob to neutral when the tip of the Implant is free from the right atrial wall and the tricuspid valve.

WARNING: Straighten the Guide prior to retracting the Implant into the Guide. If not done, it may result in device damage, inability to remove the Delivery System and/or vascular and cardiac injury.

25.2.1.9 Release the Sleeve Fastener and retract the Delivery System into the Guide by retracting only on the Sleeve Handle.

NOTE: If resistance is noted, advance and rotate the Implant by rotating the DC Handle then retract the Delivery System into the Guide. The Guide and/or Sleeve position may also be adjusted to facilitate Implant entry into the Guide. If necessary, retract the Sleeve or advance the Implant to create a 2-3 cm separation to facilitate Implant entry into the Guide.

WARNING: Use fluoroscopic guidance while retracting the Delivery System into the Guide. Failure to do so may result in device damage, inability to remove the Delivery System and/or vascular and cardiac injury.

25.2.1.10 Confirm that the Introducer is still fully advanced in the Guide Hemostasis Valve.

25.2.1.11 Retract the Delivery System by pulling only on the Sleeve Handle and position the Implant inside the Introducer. Begin gently aspirating the Guide (starting when the Delivery System is approximately halfway into the Guide, approximately 40 cm retracted) using a 50-60 cc syringe.

25.2.1.12 Remove Delivery System and Introducer simultaneously from the Guide by pulling on the Sleeve shaft and Introducer. Ensure the Implant is inside the Introducer by visualizing the Proximal Sleeve alignment marker just outside the Introducer. Aspirate the Guide during removal of the Delivery System and Introducer. If necessary, position the Guide Handle below the level of the RA to allow blood to fill the Guide lumen.

WARNING: DO NOT remove the tip of the Delivery System from the Guide without removing the Introducer simultaneously and with the Implant inside the Introducer. Failure to remove the Introducer simultaneously may result in air embolism.

WARNING: DO NOT create a vacuum while removing the Delivery System from the Guide; air may enter the lumen of the Guide which may result in air embolism.

WARNING: DO NOT re-use the Delivery System after removal. Replace the Delivery System with a new device. Reinserting the Delivery System after removal may result in inability to open the Implant. Inability to open the Implant may result in valve injury or lead to deployment of the Implant in an unintended location.

25.2.1.13 Aspirate using a 50-60 cc syringe to remove any remaining air from the Guide.

25.2.2 **Simultaneous removal of Delivery System and Guide.**

25.2.2.1 Confirm Implant is locked.

25.2.2.2 *Fully Close the Implant Arms* and continue to turn the Arm Positioner until it is no longer possible to rotate the Arm Positioner. Return the Arm Positioner to Neutral.

WARNING: Failure to follow Step 25.2.2.2 prior to retraction into the Guide may result in device damage, inability to remove the Delivery System, and/or vascular and cardiac injury.

25.2.2.3 *Lower the Gripper(s)*.

25.2.2.4 Release the DC Fastener and retract the DC Handle until the DC Radiopaque Ring is fully against the tip of the Sleeve.

25.2.2.5 Slowly release Sleeve deflection by rotating the F/E Knob to neutral.

25.2.2.6 Rotate DC handle such that the Implant Arms are perpendicular to the guide curve plane.

25.2.2.7 Secure the DC Fastener once Sleeve curves are released.

25.2.2.8 Straighten the Guide with the +/- Knob and turn the S/L Knob to neutral when the tip of the Implant is free from the right atrial wall and the tricuspid valve.

WARNING: Straighten the Guide prior to retracting the Implant into the Guide. Failure to do so may result in device damage, inability to remove the Delivery System and/or vascular and cardiac injury.

25.2.2.9 Release the Sleeve Fastener and retract the Delivery System approximately 10 cm into the Guide by retracting only on the Sleeve Handle.

NOTE: If resistance is noted, advance and rotate the Implant by rotating the DC Handle then retract the Delivery System into the Guide. The Guide and/or Sleeve position may also be adjusted to facilitate Implant entry into the Guide. If necessary, retract the Sleeve or advance the Implant to create a 2-3 cm separation to facilitate Implant entry into the Guide.

WARNING: Use fluoroscopic guidance while retracting the Delivery System into the Guide. Failure to do so may result in device damage, inability to remove the Delivery System and/or vascular and cardiac injury.

25.2.2.10 Carefully retract the Guide tip into the RA/IVC junction. The Guide may be straightened further with the +/- Knob if desired.

25.2.2.11 Remove the TriClip™ G4 System from the femoral vein, while providing hemostasis.

26.0 DISPOSAL

After use, these devices and packaging should be appropriately classified for disposal, e.g., biohazard, sharps, non-hazardous waste etc., and carefully disposed of in compliance with facility procedures and applicable laws and regulations.

27.0 CLINICAL DATA

27.1 TRILUMINATE™ Pivotal Trial

The TRILUMINATE Pivotal Trial was performed to establish safety and effectiveness of transcatheter edge-to-edge repair with the TriClip G4 System for subjects with symptomatic severe tricuspid regurgitation (TR) despite optimal medical therapy (OMT) who were at intermediate or greater estimated risk for mortality or morbidity with tricuspid valve surgery in the US, European Union, and Canada under IDE #G170118 (“TRILUMINATE Pivotal”). A summary of the clinical study is presented below.

The TriClip System and TriClip G4 System (a next-generation system) were used in the pivotal trial. Minor design changes were made to the TriClip G4 Delivery System compared to the TriClip Delivery System, but the same TriClip Steerable Guide Catheter was used with both generations. The TriClip G4 System added two additional clip sizes compared to the TriClip System, resulting in a total of four clip length and width options with similar designs and no difference in materials or principle of operation. The minor changes and additional implant sizes were not anticipated to impact TRILUMINATE Pivotal Trial outcomes.

27.2 Study Design

The TRILUMINATE Pivotal Trial was a prospective, multicenter, randomized (1:1), controlled clinical trial designed to test the superiority of transcatheter tricuspid repair using the TriClip device plus OMT (device group) vs. OMT alone (control group) in subjects with severe, symptomatic TR who were determined by the site’s local heart team to be at intermediate or greater risk for mortality or morbidity with open heart surgery. In addition to the Randomized Cohort, the trial also included a Single-Arm Cohort. After being enrolled into the trial, subjects were assigned to a cohort based on the following criteria:

- Randomized Cohort: High likelihood that the TriClip could reduce TR to moderate or less (i.e., less than or equal to grade 2).
- Single-Arm Cohort: High likelihood that the TriClip could reduce TR by at least 1 grade but a low likelihood that TR will be reduced to moderate or less.

This determination was based on multiple considerations, including but not limited to:

- Baseline TR severity
- The presence of cardiovascular implantable electronic device (CIED) leads across the tricuspid valve
- The coaptation gap width

A Cardiac Computed Tomography/Magnetic Resonance Imaging (CT/MRI) imaging sub-study (referred to as imaging sub-study) was conducted for a maximum of 100 subjects to provide insights into cardiac reverse remodeling and quantitative “gold standard” measurements to assess TR severity and the effect of changes in TR on clinical endpoints.

The TRILUMINATE™ Pivotal Trial utilized: an independent Eligibility Committee (EC), which confirmed that the subject met enrollment criteria, assessed anatomic suitability for the TriClip device, and assigned eligible patients to the Randomized or Single-Arm Cohort; an Echocardiography Core Laboratory (ECL), which reviewed screening echocardiography images to confirm patient eligibility and assessed TR severity, right ventricular measurements, and other measures at baseline and follow-up; a Clinical Events Committee (CEC), which adjudicated all adverse events per pre-established definitions; and a Data Monitoring Committee (DMC), which monitored the safety of subjects throughout trial. The study was unblinded except for the research staff administering Kansas City Cardiomyopathy Questionnaire (KCCQ), 6-minute walk test, SF-36, and New York Heart Association (NYHA) functional classification assessments.

The trial was to enroll up to 550 patients in the Randomized Cohort and up to 200 patients in the Single-Arm Cohort. Up to 3 roll-in patients per implanter were to be enrolled at sites with implanters who did not have prior or recent experience using the TriClip device.

27.2.1 Inclusion and Exclusion Criteria

Enrollment in the TRILUMINATE Pivotal Trial was limited to patients who met the inclusion criteria listed in **Table 3.**

Table 3. Inclusion and Exclusion Criteria

Inclusion Criteria
1. In the judgment of the site local heart team, subject has been adequately treated per applicable standards (including medical management) and stable for at least 30 days as follows: • Optimized medical therapy for treatment of TR (e.g., diuretics) • Medical and/or device therapy, for mitral regurgitation, atrial fibrillation, coronary artery disease and heart failure The EC will confirm that the subject has been adequately treated medically. 2. Subject is symptomatic with Severe TR despite being optimally treated. TR severity is determined by the assessment of a qualifying transthoracic echocardiogram (TTE) and confirmed by the ECL. The ECL will also request a transesophageal echocardiogram (TEE) to confirm TR etiology. Note: If any cardiac procedure(s) occur after eligibility was determined, TR severity will need to be re-assessed 30 days after the cardiac procedure(s). 3. The cardiac surgeon of the site local heart team concur that the patient is at intermediate or greater estimated risk for mortality or morbidity with tricuspid valve surgery. 4. New York Heart Association (NYHA) Functional Class II, III or ambulatory class IV 5. In the judgment of the TriClip implanting Investigator, femoral vein access is determined to be feasible and can accommodate a 25 Fr catheter. 6. Age ≥18 years at time of consent. 7. Subject must provide written informed consent prior to any trial related procedure.
Exclusion Criteria
1. Systolic pulmonary artery pressure (sPAP) > 70 mmHg or fixed pre-capillary pulmonary hypertension as assessed by right heart catheterization (RHC). 2. Severe uncontrolled hypertension Systolic Blood Pressure (SBP) ≥ 180 mmHg and/or Diastolic Blood Pressure (DBP) ≥ 110 mm Hg 3. Any prior tricuspid valve procedure that would interfere with placement of the TriClip device 4. Indication for left-sided (e.g. severe aortic stenosis, severe mitral regurgitation) or pulmonary valve correction prior 60 days. Note: Patients with concomitant Mitral and tricuspid valve disease will have the option of getting their MR treated, and wait 60 days prior to being reassessed for the trial. 5. Pacemaker or ICD leads that would prevent appropriate placement of the TriClip device. 6. Tricuspid valve stenosis - Defined as a tricuspid valve orifice of ≤ 1.0 cm^2 and/or mean gradient ≥5 mmHg as measured by the ECL 7. Left Ventricular Ejection Fraction (LVEF) ≤20% 8. Tricuspid valve leaflet anatomy which may preclude clip implantation, proper device positioning on the leaflets or sufficient reduction in TR. This may include: a. Evidence of calcification in the grasping area b. Presence of a severe coaptation defect (> 2cm) of the tricuspid leaflets. c. Severe leaflet defect(s) preventing proper device placement

d. Ebstein Anomaly - Identified by having a normal annulus position while the valve leaflets are attached to the walls and septum of the right ventricle.

9. Tricuspid valve anatomy not evaluable by TTE and TEE
10. Active endocarditis or active rheumatic heart disease or leaflets degenerated from rheumatic disease (i.e. noncompliant, perforated).
11. MI or known unstable angina within prior 30 days
12. Percutaneous coronary intervention within prior 30 days
13. Hemodynamic instability defined as SBP < 90 mmHg with or without afterload reduction, cardiogenic shock or the need for inotropic support or intra-aortic balloon pump or other hemodynamic support device.
14. Cerebrovascular Accident (CVA) within prior 90 days
15. Chronic dialysis
16. Bleeding disorders or hypercoagulable state
17. Active peptic ulcer or active gastrointestinal (GI) bleeding
18. Contraindication, allergy or hypersensitivity to dual antiplatelet and anticoagulant therapy
    Note: Contraindication to either antiplatelet or anticoagulant therapy (individually not both therapies) is not an exclusion criterion.
19. Ongoing infection requiring current antibiotic therapy (if temporary illness, patients may enroll 30 days after discontinuation of antibiotics with no active infection).
20. Known allergy or hypersensitivity to device materials
21. Evidence of intracardiac, inferior vena cava (IVC), or femoral venous mass, thrombus or vegetation.
22. Life expectancy of less than 12 months
23. Subject is currently participating in another clinical trial that has not yet completed its primary endpoint.
24. Subject is currently participating in another clinical investigation for valvular heart disease(s).
25. Pregnant or nursing subjects and those who plan pregnancy during the clinical investigation follow-up period. Female subjects of child-bearing potential are required to have a negative pregnancy test done within 7 days of the baseline visit per site standard test. Female patients of childbearing potential should be instructed to use safe contraception (e.g., intrauterine devices, hormonal contraceptives: contraceptive pills, implants, transdermal patches hormonal vaginal devices, injections with prolonged release.) It is accepted, in certain cases, to include subjects having a sterilized regular partner or subjects using a double barrier contraceptive method.
26. Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results.

27.2.2 Follow-Up Schedule

All subjects were required to have a Treatment visit within 14 days of randomization (within 14 days of the baseline visit for single-arm subjects). At this visit, Device subjects underwent the TriClip™ Procedure, and Control subjects were seen by a heart failure specialist and underwent a physical exam, including vital signs, cardiac health status and evaluation of heart failure medications.

The follow-up time points included 30 days, 6 months, and 12 months from the date of the treatment visit and will continue annually through 5 years. The device group patients were also assessed at discharge.

Follow-up visit assessments included physical assessment and patient interview, laboratory measurements, imaging tests, and health status/quality-of-life questionnaire. Adverse events and complications were recorded at all visits.

27.2.3 Statistical Analysis Population

The analysis populations for the TRILUMINATE™ Pivotal Trial are shown in **Table 4**.

Table 4. Statistical Analysis Populations

Analysis Population	Definition
Randomized Cohort	
Intent-to-Treat (ITT)	All patients randomized in the trial.
As-Treated (AT)	ITT patients grouped by treatment received.*
Per Protocol (PP)	ITT patients who received assigned randomized treatment according to protocol and followed all major study requirements.
Attempted Procedure (AP)	Patients randomized to the device group with an attempted TriClip™ Procedure (i.e., femoral vein puncture performed).
Single-Arm Cohort	
Attempted Procedure (AP)	Patients with an attempted TriClip procedure (i.e., femoral vein puncture performed).
*Patients randomized to device group who died or had heart failure hospitalization prior to the TriClip™ Procedure are considered to be in the Control group regardless of randomization. Patients randomized to device group who died or had heart failure hospitalization after (but not prior to) a TriClip procedure are considered to be in the device group regardless of randomization. Patients who did not experience death or heart failure hospitalization at any time during follow-up were assigned to the group that constituted >50% of their follow-up duration.	

27.2.4 Randomized Cohort Clinical Endpoints

Primary Endpoint

The primary endpoint was a hierarchical composite of the following components at 12 months:
1. Time to all-cause death or tricuspid valve surgery
2. Number of Heart Failure (HF) Hospitalizations
3. An Improvement of ≥15 points in KCCQ from baseline

The hypothesis for the primary endpoint was as follows:
H_0: None of the components are different between the Treatment and Control group
H_1: At least one component is different between the Treatment and Control group

The alternative hypothesis that the device group was superior to the control group in at least one component of the primary endpoint was tested using the Finkelstein-Schoenfeld methodology (Finkelstein et al. 1999) at a two-sided significance level of 5%. A sample size of 350 randomized patients was simulated to provide approximately 83% power to reject the null hypothesis at a two-sided significance level of 5%. The 350 randomized ITT patients was defined as the Primary Analysis Population.

As a supplementary analysis, the win-ratio method (Pocock et al. 2012) 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 hierarchy defined above, and the win ratio was defined as the number of winners divided by the number of losers in the device group.

An adaptive design with sample size re-estimation was planned when the first 150 randomized patients completed the 12-month follow-up visit. At that time, an independent statistician was unblinded to the interim data and calculated the conditional power for the primary endpoint. The interim analysis concluded that the original 350-patient sample size would provide adequate power to assess the primary endpoint.

Secondary Endpoints

Four powered secondary endpoints were assessed hierarchically at 12 months (see **Table 5**).

Table 5. Ordered List of Secondary Endpoints for Hierarchical Testing (Randomized Cohort)

Order	Secondary Endpoint	Null and Alternative Hypotheses	Analysis Population	Significance Level
1	Freedom from MAEs at 30 days post-procedure	$H_0: P_D(MAEs) \leq 90\%$ $H_1: P_D(MAEs) > 90\%$	AP	2.5% (one-sided)
2	Change in KCCQ score at 12 months over baseline	$H_0: \mu_D(\Delta KCCQ) - \mu_C(\Delta KCCQ) = 0$ $H_1: \mu_D(\Delta KCCQ) - \mu_C(\Delta KCCQ) \neq 0$	ITT	5% (two-sided)
3	TR reduction to moderate or less at 30-day visit	$H_0: P_D(TR \leq 2) - P_C(TR \leq 2) = 0$ $H_1: P_D(TR \leq 2) - P_C(TR \leq 2) \neq 0$	ITT	5% (two-sided)
4	Change in 6MWD at 12 months over baseline	$H_0: \mu_D(\Delta 6MWD) - \mu_C(\Delta 6MWD) = 0$ $H_1: \mu_D(\Delta 6MWD) - \mu_C(\Delta 6MWD) \neq 0$	ITT	5% (two-sided)

MAEs: major adverse events, including cardiovascular mortality, new onset renal failure, endocarditis requiring surgery, and non-elective cardiovascular surgery for TriClip device-related adverse events post-index procedure; KCCQ: Kansas City Cardiomyopathy Questionnaire; 6MWD: 6-minute walk distance; AP: attempted procedure; ITT: intent-to-treat; H_0: null hypothesis; H_1: alternative hypothesis; P_D(MAEs): proportion of TriClip patients free from MAEs; μ_D(ΔKCCQ) and μ_C ΔKCCQ): mean KCCQ score change in TriClip and control patients; P_D(TR≤2) and P_C TR≤2 : proportion of TriClip and control patients with ≤moderate TR; μ_D(Δ6MWD : mean 6MWD change in TriClip and control patients.

Additional Outcomes

Additional outcomes assessed for the Randomized Cohort included the following:

- Technical success at exit from procedure room: alive with successful access, delivery and retrieval of the device delivery system, and deployment and correct positioning of a clip, and no need for additional unplanned or emergency surgery or re-intervention related to the device or access procedure
- Device success at 30-days post-procedure: alive with original intended clip(s) in place, and no additional surgical or interventional procedures related to access or device since completion of the original procedure, and intended performance of the clip(s) (i.e., ≥1 grade improvement in TR severity, no embolization, single leaflet device attachment, absence of para-device complications)
- Procedural success at 30-days post-procedure: device success, and no device- or procedure-related serious adverse event
- Echocardiographic parameters of tricuspid valve and cardiac function
- Clinical and functional parameters

27.2.5 Single-Arm Cohort Clinical Endpoints

Primary Endpoint

The primary endpoint was survival at 12 months plus a KCCQ score improvement of≥10 points compared to baseline, tested in the AP population.

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

H_0: $P(12M) \leq 30\%$

H_1: $P(12M) > 30\%$

Where 30% was a performance goal based on the expected TriClip patient survival rate and the KCCQ result observed in the COAPT trial control group (NCT01626079; Stone et al. 2018). A sample size of 100 patients was estimated to provide 90% power to reject the null hypothesis at a one-sided significance level of 2.5%.

Secondary Endpoints

Five powered secondary endpoints were assessed hierarchically at 12 months (see **Table 6**)

Table 6. Ordered List of Secondary Endpoints for Hierarchical Testing (Single-arm Cohort)

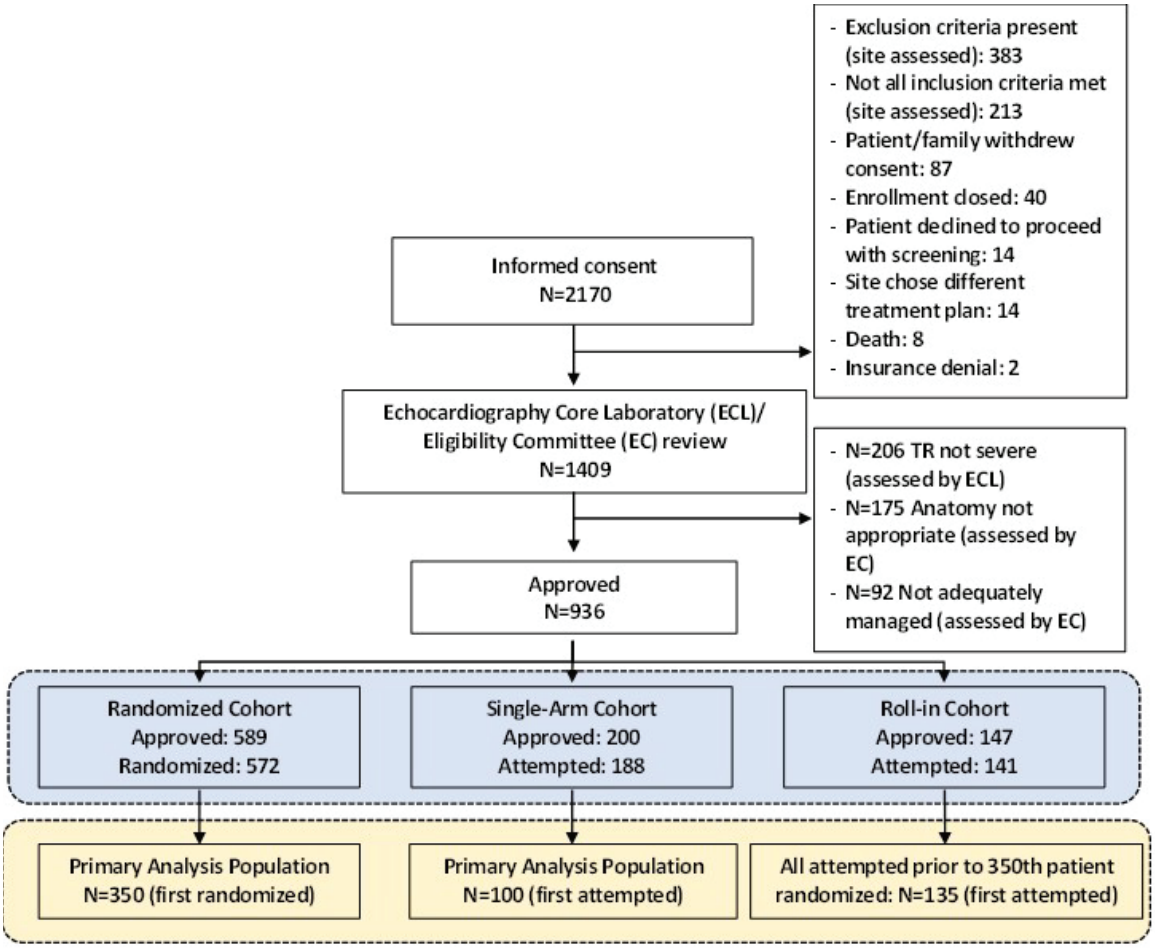
Order	Secondary Endpoint	Null and Alternative Hypotheses	Analysis Population	Significance Level
1	TR reduction by at least one grade at 30 days post-procedure	$H_0: P_D(\Delta TR \geq 1) \leq 50\%$ $H_1: P_D(\Delta TR \geq 1) > 50\%$	AP	2.5% (one-sided)
2	Freedom from MAEs at 30 days post-procedure	$H_0: P_D(MAEs) \leq 80\%$ $H_1: P_D(MAEs) > 80\%$	AP	2.5% (one-sided)
3	Change in 6MWD at 12 months over baseline	$H_0: \mu_D(\Delta 6MWD) \leq 0$ $H_1: \mu_D(\Delta 6MWD) > 0$	AP	2.5% (one-sided)
4	Freedom from all-cause mortality and tricuspid valve surgery at 12 months	$H_0: P_D(Survival) \leq 65\%$ $H_1: P_D(Survival) > 65\%$	AP	2.5% (one-sided)
5	Recurrent HF hospitalizations at 12 months	$H_0: \lambda_D(PRE) \leq \lambda_D(POST)$ $H_1: \lambda_D(PRE) > \lambda_D(POST)$	AP	2.5% (one-sided)

TR: tricuspid regurgitation; MAEs: major adverse events, including cardiovascular mortality, new onset renal failure, endocarditis requiring surgery, and non-elective cardiovascular surgery for TriClip device-related adverse events post-index procedure; 6MWD: 6-minute walk distance; AP: attempted procedure; HF: heart failure; H_0: null hypothesis; H_1: alternative hypothesis; $P_D(\Delta TR \geq 1)$: proportion of TriClip patients with TR reduction by at least 1 grade; P_D(MAEs): probability of freedom from any MAE; $\mu_D(\Delta 6MWD$: mean 6MWD change; λ_D(PRE) and λ_D(POST): annualized event rates for recurrent HF hospitalizations within 12 months pre- and post-procedure.

27.3 Accountability Of The PMA Cohort

The database for this PMA reflected data collected through April 24, 2023. A total of 936 eligible patients were enrolled between August 21, 2019 and June 29, 2022 at 68 sites in the US, Canada, and Europe. Of these patients, 901 were approved by the Eligibility Committee and were randomized or had an attempted procedure, including 141 in the Roll-in Cohort, 572 in the Randomized Cohort, and 188 in the Single-Arm Cohort. Patient accountability is shown in **Figure 2**. As planned, the primary endpoint analysis was performed on the first 350 patients (296 in the US, 38 in Canada, and 16 in Europe) in the Randomized Cohort and the first 100 patients with an attempted procedure in the Single-Arm Cohort (**Figure 3**).

Figure 2: Patient Accountability.



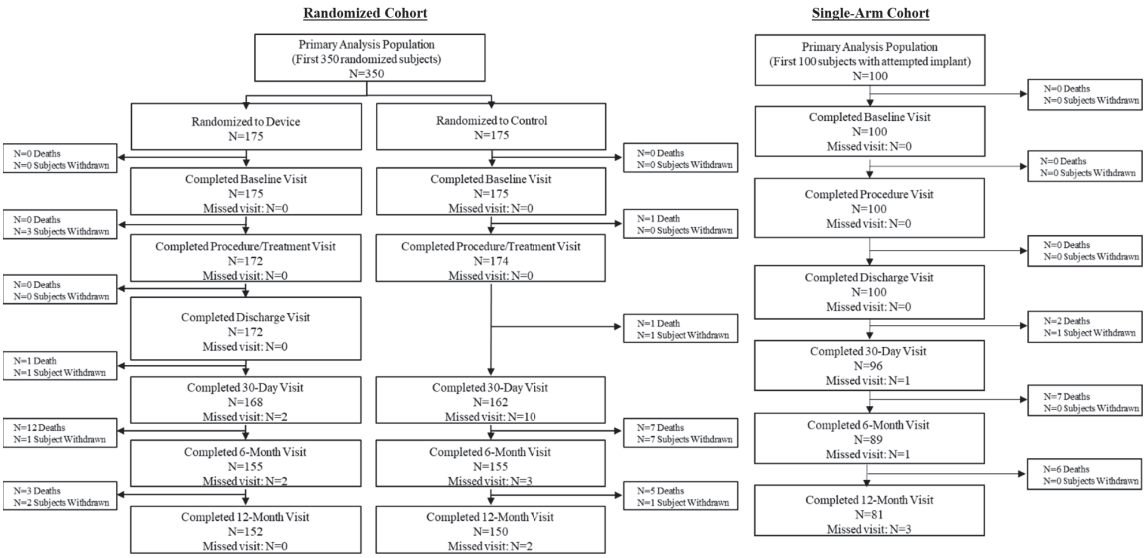
At the time of database lock, of the randomized patients eligible for the for the 1-year visit, 100% in the device group, 99% in the control group, and 96% in the single-arm cohort completed the visit, as shown in **Table 7**.

Table 7: Visit Compliance

	Device Group			Control Group			Single-Arm Cohort		
Visit	**Expected Visits**	**Actual Visits**	**Compliance[1]**	**Expected Visits**	**Actual Visits**	**Compliance[1]**	**Expected Visits**	**Actual Visits**	**Compliance[1]**
Baseline	175	175	N/A	175	175	N/A	100	100	N/A
Index Procedure or Treatment Visit	172	172	100%	174	174	100%	100	100	100%
Discharge (Device group only)	172	172	100%	-	-	-	100	100	100%
30-Day Visit	170	168	99%	172	162	94%	97	96	99%
6-Month Visit	157	155	99%	158	155	98%	90	89	99%
12-Month Visit	152	152	100%	152	150	99%	84	81	96%
Overall Follow-up[2]	**823**	**819**	**99%**	**656**	**641**	**98%**	**471**	**466**	**99%**

[1]Compliance calculated as Actual/Expected, where Expected excludes subject withdrawal.
[2]Overall follow-up includes discharge through 12-month visit (excludes baseline visit).

Figure 3: Disposition of Subjects



27.4 Study Population Demographics And Baseline Characteristics

Patient demographics and baseline characteristics for the primary analysis population of the Randomized Cohort and Single-Arm Cohort are shown in **Table 8**.

In both the randomized and single-arm cohorts, the majority of patients were Caucasian and just over half were female. Over 90% of Randomized Cohort patients had functional TR and atrial fibrillation and most patients were in NYHA functional class II/III with an average KCCQ score in the mid-50s. Torrential TR was present in approximately half of the patients in both the device and control groups. Medication use at baseline was similar between the two randomized groups. In all, demographics and baseline characteristics were similar between Randomized Cohort Device and Control groups.

Compared to the Randomized Cohort, a higher proportion of Single-Arm Cohort patients had torrential TR (74.0% vs. 50.9% , CIED-related TR (5.1% vs. 0%), had a pacemaker or defibrillator (35.0% vs. 16.0%), and had larger coaptation gaps 7.4 ± 2.7 vs. 5.5 ± 1.8 mm). Baseline covariate differences were expected between the Randomized and Single-Arm cohorts as TR severity and complex tricuspid anatomy were considered when assigning patients to each cohort.

Table 8. Baseline Characteristics (Randomized Cohort, *Primary Analysis Population)*

Demographics and Baseline Characteristics	Summary Statistic*		
	Randomized Cohort (N=350)		Single-Arm Cohort (N=100)
	Device (N=175)	Control (N=175)	
Demographics			
Age	78.0 ± 7.4 (175)	77.8 ± 7.2 (175)	80.4 ± 6.2 (100)
Sex			
Male	44.0% (77/175)	46.3% (81/175)	47.0% (47/100)
Female	56.0% (98/175)	53.7% (94/175)	53.0% (53/100)
Race			
Caucasian	85.1% (149/175)	81.7% (143/175)	87.0% (87/100)
Black/African American	4.0% (7/175)	5.7% (10/175)	7.0% (7/100)
Asian	4.0% (7/175)	4.0% (7/175)	3.0% (3/100)
American Indian/Alaska Native	0.6% (1/175)	0.0% (0/175)	0.0% (0/100)
Native Hawaiian/Pacific Islander	0.0% (0/175)	0.0% (0/175)	0.0% (0/100)
Declined or unable to disclose	6.3% (11/175)	8.6% (15/175)	3.0% (3/100)
Ethnicity			
Hispanic or Latino	2.9% (5/175)	5.1% (9/175)	4.0% (4/100)
Not Hispanic or Latino	93.1% (163/175)	87.4% (153/175)	94.0% (94/100)
Declined/unknown	4.0% (7/175)	7.4% (13/175)	2.0% (2/100)
Body mass index (BMI, kg/m^2)	27.0 ± 5.8 (175)	26.9 ± 5.2 (175)	26.3 ± 5.3 (100)
Medical history			
Atrial fibrillation	87.4% (153/175)	93.1% (163/175)	93.0% (93/100)
Chronic obstructive pulmonary disease	10.9% (19/175)	13.7% (24/175)	22.0% (22/100)
CRT/CRT-D/ICD/permanent pacemaker	16.0% (28/175)	13.7% (24/175)	35.0% (35/100)
Dyslipidemia	66.9% (117/175)	52.6% (92/175)	64.0% (64/100)
Hypertension	81.1% (142/175)	80.6% (141/175)	83.0% (83/100)
Liver disease	6.3% (11/175)	9.1% (16/175)	3.0% (3/100)

Demographics and Baseline Characteristics	Summary Statistic*		
	Randomized Cohort (N=350)		Single-Arm Cohort (N=100)
	Device (N=175)	Control (N=175)	
Renal disease	35.4% (62/175)	35.4% (62/175)	36.0% (36/100)
Peripheral vascular disease	9.1% (16/175)	10.3% (18/175)	11.0% (11/100)
Prior aortic valve intervention	15.4% (27/175)	15.4% (27/175)	11.0% (11/100)
Prior mitral valve intervention	25.7% (45/175)	24.0% (42/175)	36.0% (36/100)
Echocardiography measurements			
TR severity			
Trace	0.0% (0/173)	0.0% (0/165)	0.0% (0/96
Mild	0.0% (0/173)	0.0% (0/165)	0.0% (0/96
Moderate	2.3% (4/173)	1.2% (2/165)	0.0% (0/96
Severe grade 3 (severe)	25.4% (44/173)	29.7% (49/165)	9.4% (9/96
Severe grade 4 (massive)	21.4% (37/173)	18.2% (30/165)	16.7% (16/96)
Severe grade 5 (torrential)	50.9% (88/173)	50.9% (84/165)	74.0% (71/96)
TR etiology			
Functional	94.8% (165/174)	92.9% (158/170)	85.9% (85/99)
Degenerative	2.3% (4/174)	1.2% (2/170)	5.1% (5/99
Mixed	2.9% (5/174)	5.9% (10/170)	4.0% (4/99
Pacer-related	0.0% (0/174)	0.0% (0/170)	5.1% (5/99
Coaptation gap (mm)	5.5 ± 1.8 (137)	5.2 ± 1.7 (142)	7.4 ± 2.7 (75)
Health status			
KCCQ overall summary score	56.0 ± 23.4 (175)	54.1 ± 24.2 (174)	54.5 ± 22.6 (99)
6MWD (m)	240.5 ± 117.1 (164)	253.6 ± 129.1 (169)	237.7 ± 120.4 (97)
NYHA functional class			
Class I	0.0% (0/175)	0.0% (0/175)	0.0% (0/100)
Class II	40.6% (71/175)	44.6% (78/175)	41.0% (41/100)
Class III	57.1% (100/175)	52.0% (91/175)	53.0% (53/100
Class IV	2.3% (4/175)	3.4% (6/175)	6.0% (6/100)
Medication use			
Beta-blockers	72.6% (127/175)	73.1% (128/175)	74.0% (74/100)
ACE-I or ARBs	42.3% (74/175)	45.1% (79/175)	41.0% (41/100)
Vasodilators	10.9% (19/175)	12.0% (21/175)	12.0% (12/100)
Diuretics	97.1% (170/175)	98.9% (173/175)	98.0% (98/100)

CRT: cardiac resynchronization therapy; CRT-D: cardiac resynchronization therapy defibrillator; ICD: implantable cardioverter-defibrillator; KCCQ: Kansas City Cardiomyopathy Questionnaire; 6MWD: 6-minute walk distance; NYHA: New York Heart Association; ACE-I: angiotensin-converting enzyme 1; ARBs: angiotensin receptor blockers.
*Continuous measures – Mean ± standard deviation total no. ; Categorical measures - % no./total no.)

27.5 Safety And Effectiveness Results

27.5.1 Primary Endpoint- Randomized Cohort

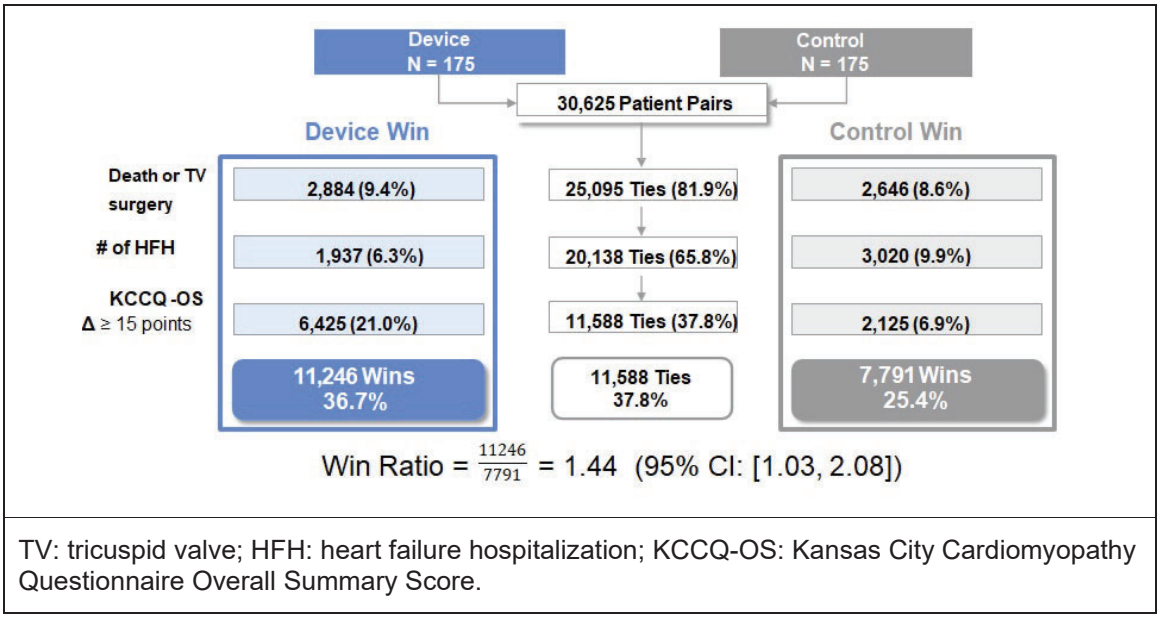
The Randomized Cohort primary endpoint analysis results are shown in **Table 9**. The Finkelstein-Schoenfeld test statistic result was 2.16 with a 2-sided p-value of 0.0311, which is less than the pre-specified two-sided significance level of 0.05. Thus, the primary endpoint was met indicating the device group was superior to the control group.

Table 9. Primary Analysis Result – Randomized Cohort ITT Population

Primary Endpoint	Test Statistic	p-Value (2-sided)	Significance Level (2-sided)	Result
Finkelstein-Schoenfeld analysis	2.16	0.0311	0.05	Superiority endpoint met

The supplemental win ratio analysis is shown in **Figure 4**. The win ratio of the device group vs. the control group was 1.44 (95% confidence interval of 1.03 - 2.08). The number of wins in the device group and control group were similar for death or TV surgery, and there were slightly more wins in the control group for heart failure hospitalization (6% in the device group vs 10% in the control group). The primary endpoint success was driven by KCCQ score improvement of at least 15 points, which had 21% wins in the device group and 7% wins in the control group.

Figure 4: Win Ratio Analysis of the Randomized Cohort Primary Endpoint – ITT Population



TV: tricuspid valve; HFH: heart failure hospitalization; KCCQ-OS: Kansas City Cardiomyopathy Questionnaire Overall Summary Score.

27.5.2 Secondary Endpoint- Randomized Cohort

The results of the powered secondary endpoints are shown in **Table 10**. The endpoints of freedom from major adverse events (MAEs) at 30 days post-procedure, change in KCCQ score at 12 months vs. baseline, and TR reduction to moderate or less at 30 days were met. There was a numerically smaller reduction in 6MWD at 12 months in the device group vs. the control group (-8.12 vs. -25.17 meters), but the difference was not statistically significant, and standard deviations were large. Therefore, the 6MWD endpoint was not met.

Table 10. Summary of Powered Secondary Endpoint Results – Randomized Cohort ITT Population (Paired)

Order	Secondary Endpoint	Summary Statistics		p-Value	Result
		Device Arm	Control Arm		
1	Freedom from MAEs at 30 days post-procedure	98.3% [96.3%, 100%][*]	-	< 0.0001	Endpoint met
2	Change in KCCQ score at 12 months over baseline	12.34 (1.75)[†]	0.61 (1.75)[†]	< 0.0001	Endpoint met
3	TR reduction to moderate or less at 30-day visit	87.0% (141/162)[‡]	5.4% (8/147)[‡]	<0.0001	Endpoint met
4	Change in 6MWD at 12 months over baseline[‖] (meters)	-8.12 (10.50)[†]	-25.17 (10.31)[†]	0.2482	**Endpoint not met**

MAEs: major adverse events, including cardiovascular mortality, new onset renal failure, endocarditis requiring surgery, and non-elective cardiovascular surgery for TriClip device-related adverse events post-index procedure; TR: tricuspid regurgitation; KCCQ: Kansas City Cardiomyopathy Questionnaire; 6MWD: 6-minute walk distance.
[*]Kaplan-Meier estimate [95% confidence interval]
[†]Least square means (standard error) from analysis of covariance (ANCOVA) model
[‡]% (no./total no.
[‖]A KCCQ overall score of 0 and a 6MWD of 0 meter were imputed for subjects who had a heart failure related cardiovascular death or tricuspid valve surgery prior to 12 months.

The individual MAE component rates are shown in **Table 11**. Of the MAEs, one case of new onset renal failure was adjudicated as procedure-related but not device-related. A second new onset renal failure case and the one cardiovascular mortality were adjudicated as neither procedure- nor device-related.

Table 11. Results of Individual MAE Components at 30 Days – Randomized Cohort AP Population.

MAE Component	Event Rate at 30 Days
Cardiovascular mortality	0.6% (1/172)
New onset renal failure	1.2% (2/172)
Endocarditis requiring surgery	0% (0/172)
Non-elective cardiovascular surgery for TriClip™ Implant-related AE post-index procedure	0% (0/172)

[*]% no./total no.

27.5.3 Adverse Events- Randomized Cohort

CEC-adjudicated adverse events through 12 months (unless otherwise noted) are shown in **Table 12** for the Randomized Cohort. Rates of HF hospitalizations, cardiovascular mortality, and tricuspid valve reintervention at 12 months as well as major bleeding and new onset renal failure at 30 days were numerically higher in the device group vs. the control group.

Table 12. CEC-Adjudicated Adverse Events through 12 Months – Randomized Cohort ITT Population.

Event	Summary Statistics	
	Device Arm* (N=175)	Control Arm† (N=175)
All-cause mortality	8.6% (15, 15, 0, 0, 1	7.4% (13, 13, 0)
Cardiovascular (VARC II definition)	6.3% (11, 11, 0, 0, 0	4.6% (8, 8, 0)
Heart failure-related	4.0% (7, 7, 0, 0, 0)	2.9% (5, 5, 0)
Non-heart failure-related	2.3% (4, 4, 0, 0, 0)	1.7% (3, 3, 0)
Non-cardiovascular (VARC II definition)	2.3% (4, 4, 0, 0, 1)	2.9% (5, 5, 0)
Hospitalization	36.0% (111, 63, 2, 7, 2)	34.3% (100, 60, 0)
Heart failure hospitalization	14.9% (35, 26, 1, 2, 0	11.4% (8, 20, 0)
Other cardiovascular hospitalization	9.1% (17, 16, 1, 5, 0	9.1% (21, 16, 0)
Non-cardiovascular hospitalization	21.7% (59, 38, 0, 0, 2	21.1% (51, 37, 0
Tricuspid valve surgery	1.7% (3, 3, 2, 2, 0)	3.4% (6, 6, 0)
Tricuspid valve intervention‡	2.3% (4, 4, 3, 4, 0)	1.7% (3, 3, 0)
Major bleeding (≥BARC 3a)‖	5.7% (10, 10, 0, 3, 0	1.7% (3, 3, 0)
New onset renal failure‖	2.3% (4, 4, 0, 1, 0)	0.6% (1, 1, 0)
Transient ischemic attack (TIA)	0.6% (1, 1, 0, 0, 0)	0.0% (0, 0, 0)
Stroke (VARC II definition)	1.7% (3, 3, 0, 0, 0)	1.7% (4, 3, 0)
Myocardial infarction (VARC II definition)‖	0.0% (0, 0, 0, 0, 0)	0.0% (0, 0, 0)
Endocarditis requiring surgery‖	0.0% (0, 0, 0, 0, 0)	0.0% (0, 0, 0)
Non-elective cardiovascular surgery for TriClip-related adverse event post index procedure‖	0.0% (0, 0, 0, 0, 0)	0.0% (0, 0, 0)
Cardiogenic shock	0.0% (0, 0, 0, 0, 0)	0.6% (1, 1, 0)

VARC: Valve Academic Research Consortium; BARC: Bleeding Academic Research Consortium; TIA: transient ischemic attack.
*Event rate (no. of events, no. of subjects, no. of device-related events, number of procedure-related events, number of COVID-19-related events); event rate = no./total no. Number of COVID-19-related events includes related or possibly related events; this excludes events with unknown relatedness.
†Event rate (no. of events, no. of subjects, number of COVID-19-related events).
‡Tricuspid valve intervention includes reintervention for device group and first intervention for control group.
‖Per the study CEC charter, myocardial infarction, bleeding, new onset renal failure, endocarditis requiring surgery, and non-elective cardiovascular surgery for TriClip-related adverse event post index procedure were adjudicated up to 30 days post treatment visit for the device and control groups.

Table 13 provides site-reported procedure- or device-related serious adverse events from treatment visit through 1 year. Procedure- or device-related serious adverse events occurred in 3.5% (6/172) of subjects.

Table 13: Listing of Site-reported Procedure/Device Related Serious Adverse Events from treatment visit through 1 Year (Primary Analysis Population) (Attempted Procedure Population, n=172)

Subject	Description
1	Access site bleeding
	Hypotension with tachycardia secondary to acute blood loss
2	Access site complication
3	Access site complication – thrombin injection for pseudoaneurysm
	Access site complication – surgical repair of pseudoaneurysm
4	TV surgery due to unsuccessful TriClip™ Procedure
5	Re-intervention due to SLDA
6	Heart failure due to volume overload

27.5.4 Other Randomized Cohort Observations

Procedural endpoints:

Technical success was achieved in 98.8% of TriClip subjects, device success in 88.9%, and procedural success in 87.0% (see **Table 14**).

Table 14: Results of Procedural Endpoints – Randomized Cohort AP Population.

Endpoints	Results
Technical success (at exit from procedure room)	98.8% (170/172)
Device success (at 30 days post-procedure)	88.9% (144/162)
Procedural success (at 30 days post-procedure)	87.0% (141/162)

Technical success was not achieved in 2 subjects due to inability to successfully deploy the TriClip device. Device success could not be evaluated in 10 subjects due to missing TR grade assessment. In addition, device success was not achieved in 18 subjects due to single leaflet device attachment (n=11), no reduction in TR (n=3), surgery/intervention within 30 days post procedure (n=3), and death within 30 days post procedure (n=1). Procedural success was not achieved in the same 18 subjects in whom device success was not achieved and in 3 additional subjects who experienced a device- or procedure-related site-reported serious adverse event: single leaflet device attachment (n=1; not confirmed by the ECL), ruptured chordae (n=1), and access site complication (n=1).

Procedural Data:

The TriClip procedure was performed under general anesthesia with echocardiographic (TEE) and fluoroscopic guidance. Procedural data for the Randomized Cohort AP Population is shown in **Table 15**. TriClip was successfully implanted in 170 of the 172 (98.8%) subjects with an attempted procedure in the Randomized Cohort, with approximately 85% of subjects receiving two or three TriClip devices.

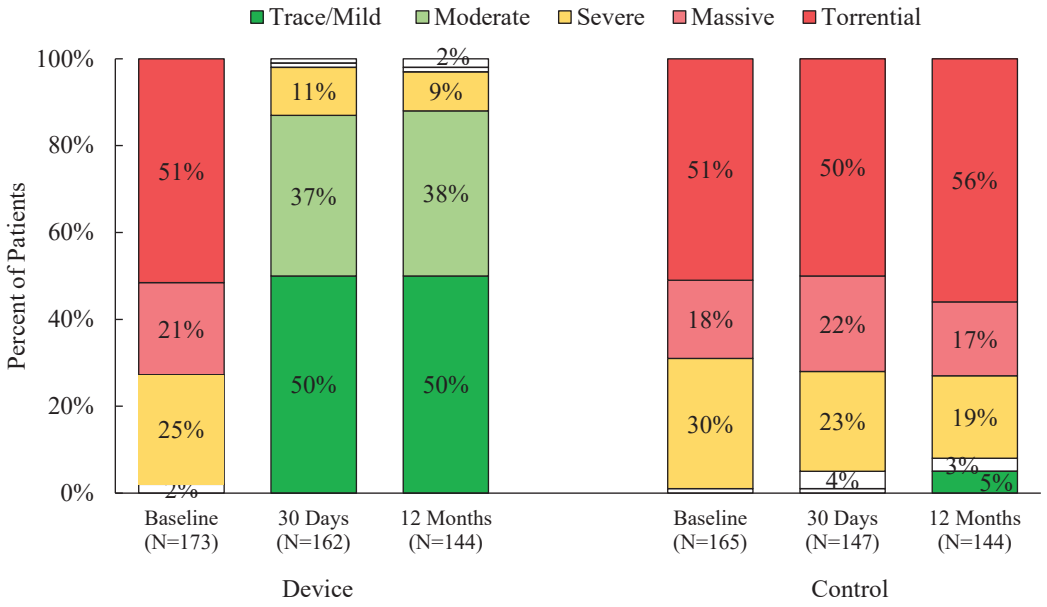
Table 15. Procedural Data – AP Population.

Number of clips implanted	2.2 ± 0.7 (172)
0 clips	1.2% (2/172)
1 clip	10.5% (18/172)
2 clips	61.0% (105/172)
3 clips	24.4% (42/172)
4 clips	2.9% (5/172)
TriClip (first-generation)	47.1% (81/172)
TriClip G4	52.9% (91/172)
Total procedure time (min)	151.0 ± 71.7 (171)
Device time (min)	89.7 ± 66.4 (168)
Fluoroscopy exposure (min)	31.9 ± 23.5 (171)
*Continuous measures – Mean ± standard deviation (total no.); Categorical measures - % (no./total no.)	

TR Severity:

TR severity for the Randomized Cohort ITT Population is shown in **Figure 5**. In the device group, the proportion of subjects with greater than moderate TR was 97% at baseline, which decreased to 13% at 30 days and 12% at 12 months. In the control group, TR severity was greater than moderate in 99% of subjects at baseline and remained greater than moderate in 95% of subjects at 30 days and 92% at 12 months.

Figure 5. TR Severity Visit – Randomized Cohort ITT Population (Unpaired).

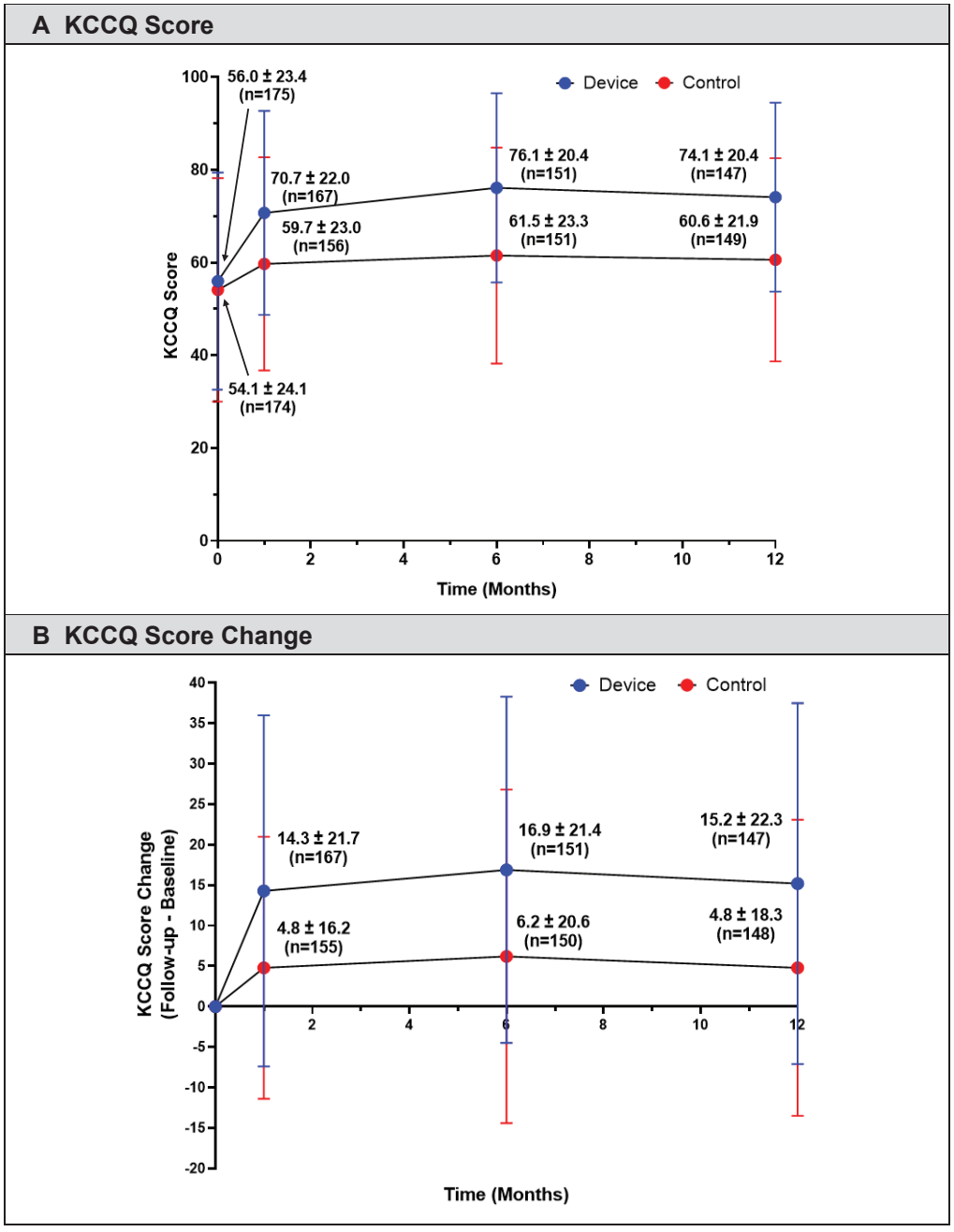


Note: Values ≤ 1% are not labeled.

KCCQ Score:

KCCQ scores and score changes through 12 months are shown in **Figure 6** for the Randomized Cohort ITT Population. On average, the KCCQ score increased by 15.2 points in the device group vs. 4.8 points in the control group through 12 months.

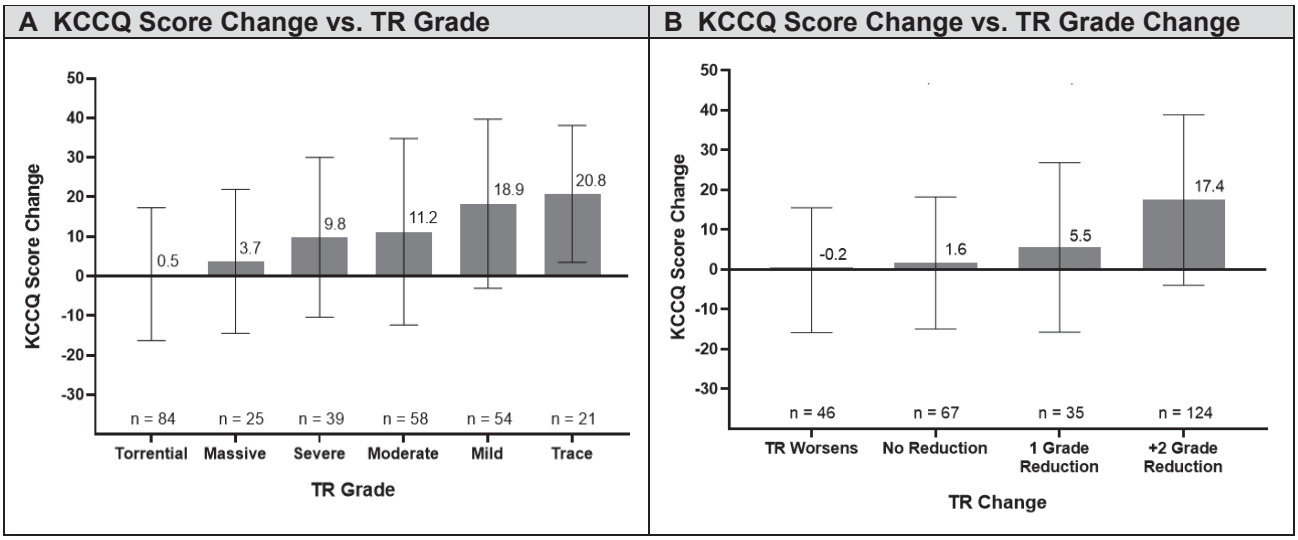
Figure 6. KCCQ Score by Visit – Randomized Cohort ITT Population (Unpaired).
The error bars are standard deviations.



Association between KCCQ Score and TR:

Post hoc analyses were performed to investigate the associations between KCCQ score changes and TR severity and between KCCQ score changes and TR severity changes at 12 months. These analyses were conducted to provide evidence that the KCCQ score improvement observed in the study was not solely the result of a placebo effect. The associations are shown in **Figure 7** Lower TR severity and greater TR severity reductions were generally associated with greater KCCQ score improvements.

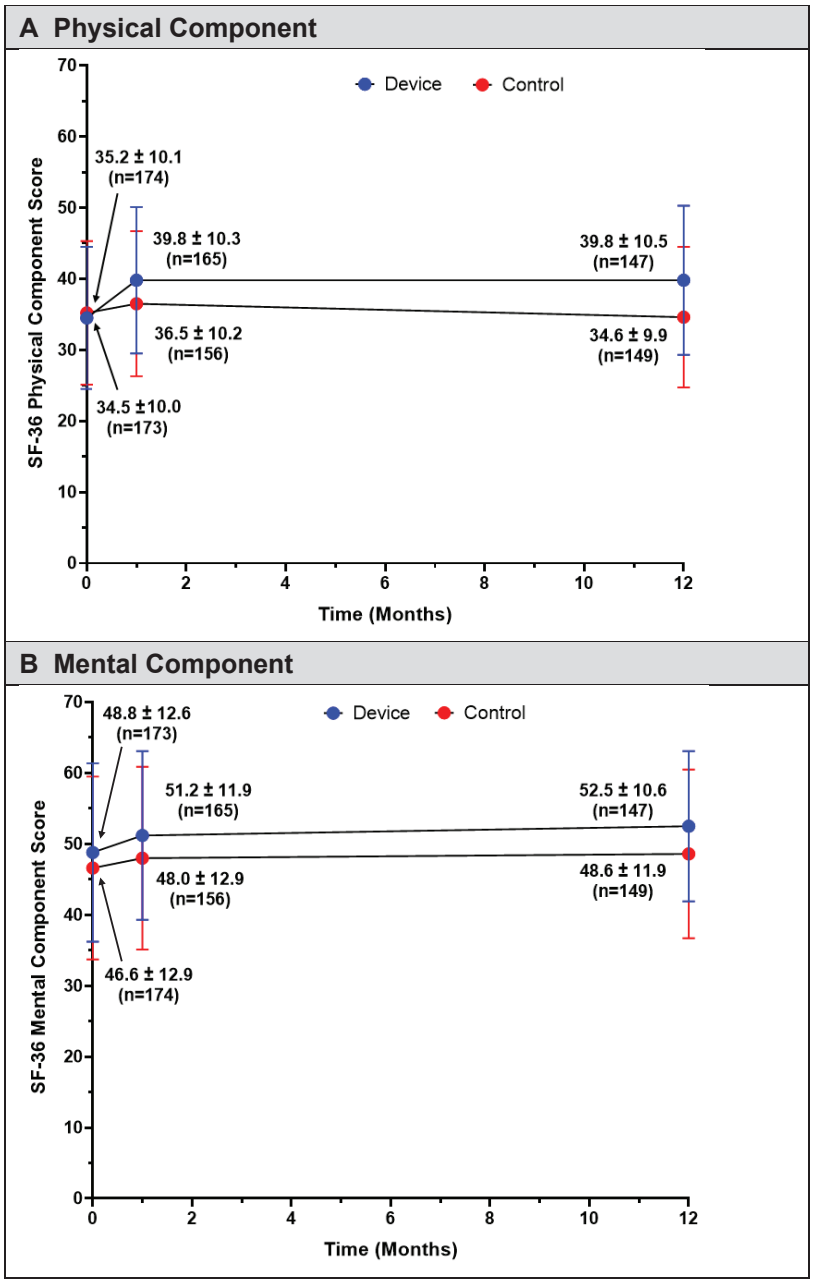
Figure 7. Association between KCCQ Score and TR at 12 Months.
The error bars are standard deviations.



SF-36 Score:

SF-36 scores through 12 months are shown in **Figure 8** for the Randomized Cohort ITT Population. The mean physical component score increased by about 5 points through 12 months compared to the baseline in the device group, while remaining mostly unchanged from baseline through 12 months in the control group. A similar trend was seen in the mental component score. In some studies, SF-36 score changes similar to the changes observed in the device group have been interpreted as clinically significant.

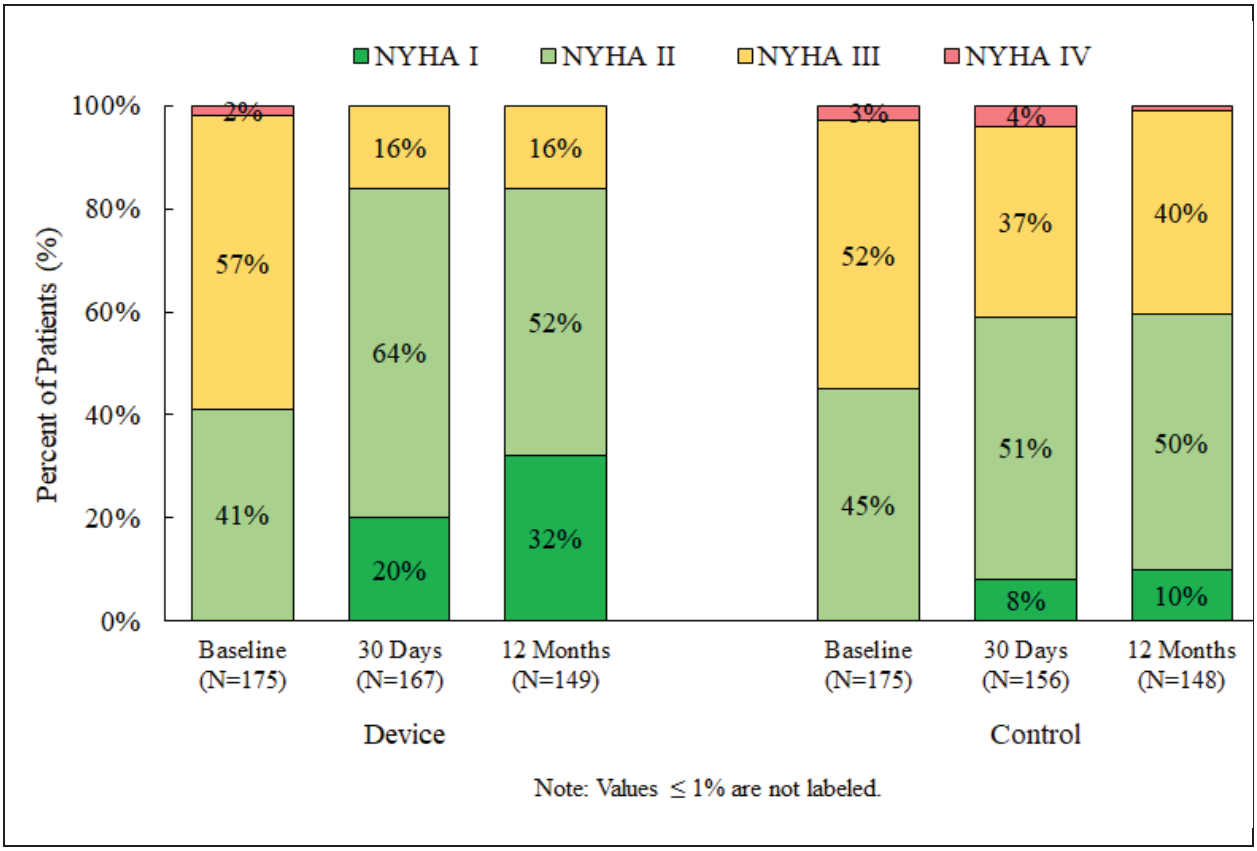
Figure 8. SF-36 Score by Visit – Randomized Cohort ITT Population (Unpaired).
The error bars are standard deviations.



NYHA Functional Class:

The results for NYHA classifications by visit are shown in **Figure 9** for the Randomized Cohort ITT Population. At baseline, 59% of subjects in the device group and 55% in the control group were in NYHA III/IV. At 12 months, fewer device subjects were in NYHA III/IV than the control subjects (16% vs. 40%).

Figure 9. NYHA Functional Class by Visit – Randomized Cohort ITT Population (Unpaired).



Echocardiographic Parameters:

PISA EROA, PISA regurgitant volume, and vena contracta width all showed substantial decreases from baseline to 12 months in the device group and were minimally changed in the control group (**Table 16**). There were no notable changes in cardiac size or function in either treatment group at 12 months. Right atrial volume, which would be expected to decrease as a result of reduced TR due to reverse remodeling, showed an unexpected small increase in the device group.

Table 16. Results of Echocardiographic Endpoints – Randomized Cohort ITT Population (Paired Analysis).

Echocardiographic Endpoint Change from Baseline to 12 Months	Device Arm (N=175)	Control Arm (N=175)	Difference [95% CI]*
ΔTricuspid annulus diameter (end-diastole, apical 4Ch, cm)			
Mean ± SD (n	-0.09 ± 0.64 (140)	-0.11 ± 0.74 (135)	0.02 [-0.14, 0.19]
Median (Q1, Q3)	-0.10 (-0.50, 0.30)	-0.17 (-0.50, 0.30)	
Range (min, max)	(-1.46, 1.39)	(-3.90, 2.02)	
ΔPISA EROA (cm^2)			
Mean ± SD (n	-0.44 ± 0.33 (115)	-0.04 ± 0.31 (127)	-0.40 [-0.48, -0.32]
Median (Q1, Q3)	-0.42 (-0.56, -0.26)	0.00 (-0.16, 0.12)	
Range (min, max)	(-2.33, 0.25)	(-1.25, 0.80)	
ΔPISA regurgitant volume calculation (mL)			
Mean ± SD (n	-33.84 ± 20.48 (115)	-1.99 ± 23.56 (127)	-31.85 [-37.43, -26.28]
Median (Q1, Q3)	-33.20 (-44.90, -21.40)	-1.30 (-12.40, 10.21)	
Range (min, max)	(-105.20, 12.11)	(-115.90, 67.80)	
ΔVena contracta width (SL, 4Ch view, cm)			
Mean ± SD (n	-0.52 ± 0.48 (139)	0.03 ± 0.44 (136)	-0.54 [-0.65, -0.43]
Median (Q1, Q3)	-0.48 (-0.77, -0.26)	0.00 (-0.30, 0.32)	
Range (min, max)	(-3.00, 0.97)	(-1.10, 1.40)	
ΔRV end diastolic diameter – mid (4Ch, cm)			
Mean ± SD (n	-0.18 ± 0.73 (140)	-0.02 ± 0.85 (134)	-0.17 [-0.36, 0.02]
Median (Q1, Q3)	-0.20 (-0.60, 0.20)	0.10 (-0.50, 0.50)	
Range (min, max)	(-1.90, 2.80)	(-2.20, 2.90)	
ΔRV end diastolic diameter – base (4Ch, cm)			
Mean ± SD (n	-0.21 ± 0.71 (142)	-0.12 ± 0.76 (134)	-0.09 [-0.26, 0.08]
Median (Q1, Q3)	-0.15 (-0.70, 0.20)	-0.10 (-0.60, 0.40)	
Range (min, max)	(-2.40, 2.70)	(-2.00, 1.90)	
ΔRight atrial volume (single plane Simpson's, mL)			
Mean ± SD (n	7.78 ± 55.92 (140	-2.13 ± 54.14 (136)	9.91 [-3.13, 22.95]
Median (Q1, Q3)	8.17 (-22.48, 28.25)	-4.35 (-29.90, 21.90)	
Range (min, max)	(-122.03, 276.20)	(-154.44, 181.20)	
ΔRV fractional area change (%)			
Mean ± SD (n	-0.73 ± 8.16 (133)	-0.52 ± 7.38 (125)	-0.21 [-2.12, 1.69]
Median (Q1, Q3)	-0.50 (-6.40, 3.90)	-1.00 (-5.80, 3.90)	
Range (min, max)	(-27.90, 21.22)	(-18.70, 23.00)	

Echocardiographic Endpoint Change from Baseline to 12 Months	Device Arm (N=175)	Control Arm (N=175)	Difference [95% CI]*
ΔLV end diastolic volume (mL)			
Mean ± SD (n	3.91 ± 25.02 (129	-4.80 ± 23.49 (114)	8.70 [2.57, 14.84]
Median (Q1, Q3)	3.30 (-12.90, 16.30)	-4.98 (-16.80, 9.70)	
Range (min, max)	(-70.30, 94.50)	(-83.20, 52.70)	
ΔLV end systolic volume (mL)			
Mean ± SD (n	2.31 ± 15.28 (129	-2.93 ± 12.52 (114)	5.24 [1.72, 8.75]
Median (Q1, Q3)	0.82 (-4.80, 8.80)	-2.95 (-9.50, 4.20)	
Range (min, max)	(-37.00, 85.50)	(-65.34, 23.80)	
ΔRV TAPSE (cm)			
Mean ± SD (n	-0.13 ± 0.45 (141)	0.00 ± 0.48 (132)	-0.13 [-0.24, -0.02]
Median (Q1, Q3)	-0.10 (-0.43, 0.10)	0.01 (-0.20, 0.30)	
Range (min, max)	(-1.40, 1.00)	(-2.27, 1.00)	
ΔCardiac output (L/min)			
Mean ± SD (n	-0.05 ± 1.89 (136)	0.03 ± 1.40 (131)	-0.07 [-0.47, 0.33]
Median (Q1, Q3)	-0.14 (-0.98, 0.63)	-0.04 (-0.88, 0.86)	
Range (min, max)	(-4.98, 14.95)	(-3.42, 4.10)	
ΔLVOT Doppler stroke volume (mL)			
Mean ± SD (n	-1.58 ± 17.62 (138	-1.93 ± 16.48 (133	0.35 [-3.73, 4.43]
Median (Q1, Q3)	-2.04 (-11.00, 7.80)	-1.50 (-11.73, 4.40)	
Range (min, max)	(-49.50, 65.00)	(-40.60, 51.70)	
ΔInferior vena cava diameter (cm)			
Mean ± SD (n	-0.09 ± 0.56 (135)	-0.01 ± 0.56 (136)	-0.08 [-0.21, 0.05]
Median (Q1, Q3)	-0.04 (-0.48, 0.34)	0.00 (-0.34, 0.32)	
Range (min, max)	(-1.80, 1.16)	(-1.90, 1.80)	
ΔTricuspid valve diastolic mean gradient (CW, mmHg)			
Mean ± SD (n	1.15 ± 1.28 (136)	0.07 ± 0.58 (126)	1.08 [0.84, 1.32]
Median (Q1, Q3)	0.86 (0.32, 1.89)	0.02 (-0.31, 0.43)	
Range (min, max)	(-2.80, 7.32)	(-1.11, 1.60)	

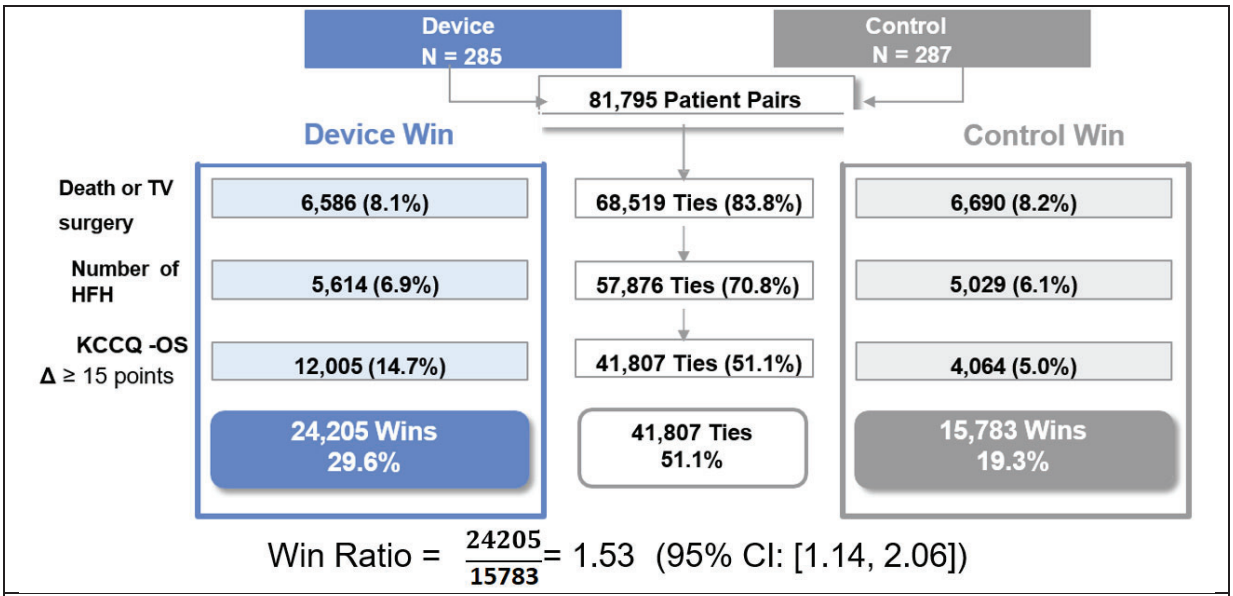
PISA: proximal isovelocity surface area (a method for estimating regurgitant volume); EROA: effective regurgitant orifice area; RV: right ventricular; LV: left ventricular: TAPSE: tricuspid annular plane systolic excursion (a measure of the RV apex to-base shortening and RV systolic function); LVOT: left ventricular outflow tract.
SD: standard deviation; CI: confidence interval. The CIs were calculated without multiplicity adjustment. The adjusted CIs could be wider than presented here.
*By normal approximation.

27.5.5 1-Year Outcomes for All Available Subjects in the Randomized Cohort

The trial used an adaptive design with sample size re-estimation for the Randomized cohort. The pre-specified sample size re-estimation occurred once the first 150 randomized subjects completed 12-month follow-up, while the trial was still enrolling. The trial continued to randomize subjects until the sample size re-estimation analysis was completed, by which point a total of 572 subjects were randomized at 68 sites. Fifty-six subjects (29 Device, 26 Control) were pending 12-month follow-up visits at the time of data analysis.

The win ratio analysis result for all available randomized subjects was 1.53 (**Figure 10**), which is slightly greater than the win-ratio result for the primary analysis cohort. The number of device wins and control wins for death or TV surgery continued to be similar. While there were more control wins for heart failure hospitalizations in the primary win ratio analysis, the number of device wins and control wins for heart failure hospitalizations were similar for all available subjects. The win ratio continued to be driven by KCCQ score improvement, and the data for all available subjects support the conclusion of the primary analysis.

Figure 10. Win Ratio Analysis for All Available Subjects – Randomized Cohort ITT Population.



HFH: heart failure hospitalization; KCCQ-OS: Kansas City Cardiomyopathy Questionnaire overall summary score; CI: confidence interval. The CI was calculated without multiplicity adjustment. The adjusted CI could be wider than presented here.

Components of the primary endpoint for the Primary Analysis Population and Full Randomized Cohort are provided in **Table 17**.

Table 17. Primary Endpoint Components (Primary Analysis Population and Full Randomized Cohort)

Component	Primary Analysis Population (N=350)		Full Randomized Cohort (N=572)	
	Device (N=175)	Control (N=175)	Device (N=285)	Control (N=287)
All-cause mortality or TV surgery at 12 months, Kaplan-Meier (%)[1]	9.4%	10.6%	9.9%	9.7%
Rate of heart failure hospitalizations, per patient-year[2]	0.22	0.17	0.17	0.19
Proportion with KCCQ-OS improvement ≥15 points at 12 months	50%	26%	50%	26%

[1]Kaplan-Meier estimate with Log-rank test
[2]Normal approximation for differences in Binomial proportions

Secondary endpoints were consistent in the Primary Analysis Population and Full Randomized cohorts as summarized in **Table 18**. Device subjects experienced a larger improvement in 6MWD than Control subjects in the Full Randomized Cohort than in the Primary Analysis Population.

Table 18. Secondary Endpoints (Primary Analysis Population and Full Randomized Cohort)

Secondary Endpoints	Primary Analysis Population (N=350)		Full Randomized Cohort (N=572)	
	Device (N=175)	Control (N=175)	Device (N=285)	Control (N=287)
Freedom from MAE at 30 days	98.3%	-	98.9%	-
Moderate or less TR at 30 days	87.0%	5.4%	88.9%	5.3%
Change from Baseline to 12 months				
KCCQ-OS (imputed , ANCOVA), Mean ± SE	12.3 ± 1.8	0.6 ± 1.8	11.5 ± 1.6	-0.5 ± 1.6
Between-group difference, Mean [95% CI]	11.7 [6.9, 16.6]		11.9 [7.4, 16.4]	
KCCQ-OS (complete-case paired), Mean ± SD	15.2 ± 22.3	4.8 ± 18.3	15.2 ± 22.8	4.2 ± 18.9
Between-group difference, Mean [95% CI]	10.4 [5.7, 15.1]		11.0 [6.9, 15.2]	
6MWD (imputed[a], ANCOVA), Mean ± SE	-8.1 ± 10.5	-25.2 ± 10.3	-5.0 ± 8.7	-29.8 ± 8.4
Between-group difference, Mean [95% CI]	17.1 [-12.0, 46.1]		24.8 [1.1, 48.6]	
6MWD (complete-case paired), Mean ± SD	11.5 ± 111.4	-8.7 ± 109.7	15.1 ± 103.4	-12.1 ± 102.0
Between-group difference, Mean [95% CI]	20.3 [-7.2, 47.7]		27.2 [5.5, 48.9]	

[a] Subjects who experienced HF-related death or had TV surgery prior to 12-month visit were assigned 12-month KCCQ-OS or 6MWD of 0. Subjects who were unable to exercise due to cardiac reasons were also assigned a 6MWD of 0 meters at 12-month follow-up.
Subjects who experienced hospitalization related to COVID-19 had their follow-up information following the COVID-19 related hospitalization excluded.

CEC-adjudicated adverse event rates through 12 months (unless otherwise noted) were also consistent in the Primary Analysis Population and Full Randomized cohorts as summarized in **Table 19**.

Table 19. Selected CEC-Adjudicated Adverse Events through 12 Months – Full Randomized Cohort ITT Population.

Event	Summary Statistics	
	Device Arm (N=285)*	Control Arm (N=287)†
All-cause mortality	8.1% (23, 23, 0, 0, 1	7.0% (20, 20, 0)
Cardiovascular (VARC II definition)	5.3% (15, 15, 0, 0, 0	3.8% (11, 11, 0)
Heart failure-related	3.9% (11, 11, 0, 0, 0	2.8% (8, 8, 0)
Non-heart failure-related	1.4% (4, 4, 0, 0, 0)	1.0% (3, 3, 0)
Non-cardiovascular (VARC II definition)	2.8% (8, 8, 0, 0, 1)	3.1% (9, 9, 0)
Hospitalization	33.7% (161, 96, 2, 7, 9)	31.0% (155, 89, 0)
Heart failure hospitalization	11.2% (44, 32, 1, 2, 0	11.8% (48, 34, 0
Other cardiovascular hospitalization	7.7% (23, 22, 1, 5, 0	7.0% (25, 20, 0)
Non-cardiovascular hospitalization	22.8% (94, 65, 0, 0, 9	19.5% (82, 56, 0
Tricuspid valve surgery	1.8% (5, 5, 2, 2, 0)	2.4% (7, 7, 0)
Tricuspid valve intervention‡	2.5% (7, 7, 5, 7, 0)	1.0% (3, 3, 0)
Major bleeding (≥BARC 3a)‖	3.2% (9, 9, 0, 3, 0)	1.7% (5, 5, 0)
New onset renal failure‖	0.7% (2, 2, 0, 1, 0)	0.3% (1, 1, 0)

*Event rate (no. of events, no. of subjects, no. of device-related events, number of procedure-related events, number of COVID-19-related events); event rate = no./total no. Number of COVID-19-related events includes related or possibly related events; this excludes events with unknown relatedness.

†Event rate (no. of events, no. of subjects, number of COVID-19-related events).

‡Tricuspid valve intervention includes reintervention for device group and first intervention for control group.

‖Per the study CEC charter bleeding and new onset renal failure were adjudicated up to 30 days post treatment visit for the device and control groups.

VARC: Valve Academic Research Consortium; BARC: Bleeding Academic Research Consortium

27.5.6 Single-Arm Cohort Results

Primary Endpoint:

There were 100 subjects with an attempted TriClip™ Procedure in the Single-Arm Cohort. The primary analysis was performed on 91 subjects, which excluded subjects who withdrew (n=1), died or were hospitalized due to COVID-19 (n=2), or missed the 12-month visit or did not complete the 12-month KCCQ assessment (n=6). The results of the primary analysis are shown in **Table 20**. Fifteen (15) subjects died prior to 12 months, 34 had a KCCQ score improvement of <10 points, and 42 survived with a KCCQ score improvement of ≥10 points at 12 months. The proportion of subjects who survived and experienced at least a 10-point improvement in KCCQ score at 12 months from baseline was 46.2%, with a lower 98.75% confidence limit of 34.3%, which exceeded the performance goal of 30%. Thus, the primary endpoint was met.

Table 20. Primary Analysis Results – Single-Arm Cohort.

Primary Endpoint	Rate	Lower 98.75% Confidence Limit	Performance Goal	P-value	Result
Survival with ≥10 point improvement vs. baseline in KCCQ score at 12 months	46.2% (42/91)	34.3%	30%	0.008	Endpoint Met

Secondary Endpoint:

The results of the powered secondary endpoints for the Single-Arm Cohort are summarized in **Table 21**. TR reduction by at least one grade at 30 days post-procedure occurred in 98.9% of subjects, and freedom from MAEs at 30 days post-procedure occurred in 100% of subjects; these endpoints were met. However, the improvement in 6MWD at 12 months from baseline (13.7±92.7) did not meet the performance goal, so the endpoint was not met. As a result, the subsequent endpoints in the pre-defined hierarchy (freedom from all-cause mortality or tricuspid valve surgery and recurrent HF hospitalizations at 12 months post-procedure) were not hypothesis-tested. Descriptively, the annualized HF hospitalization rates pre- and post- TriClip™ Procedure were generally similar.

Table 21. Summary of Powered Secondary Endpoints – Single-Arm Cohort AP Population.

Order	Secondary Endpoint	Summary Statistics	p-Value	Result
1	TR reduction by at least one grade at 30 days post-procedure	98.9% (87/88)*	< 0.0001	Endpoint met
2	Freedom from MAEs at 30 days post-procedure	100% (99/99)*	<0.0001	Endpoint met
3	Change in 6MWD at 12 months from baseline (m)	13.7±92.7 (71)† 95% CI: [-8.3, 35.6]	0.1090	**Endpoint not met**
4	Freedom from all-cause mortality and tricuspid valve surgery at 12 months	83.7% (3.7%)‡	-	Not tested
5	Recurrent HF hospitalizations at 12 months (events/patient-year)	Pre-procedure: 0.33 [0.23, 0.46]‖ Post-procedure: 0.36 [0.26, 0.51]‖	-	Not tested

TR: tricuspid regurgitation; MAEs: major adverse events, including cardiovascular mortality, new onset renal failure, endocarditis requiring surgery, and non-elective cardiovascular surgery for TriClip device-related adverse events post-index procedure; 6MWD: 6-minute walk distance; HF: heart failure.
CI: confidence interval. The CIs were calculated without multiplicity adjustment. The adjusted CIs could be wider than presented here.
*% no./total no.
†Mean ± standard deviation (total no.
‡Kaplan-Meier estimate (standard error)
‖Annualized event rate [95% CI].

Safety Results:

CEC-adjudicated adverse event rates through 12 months are shown in **Table 22**. The rates of all-cause mortality, cardiovascular mortality, and heart failure hospitalization were approximately two-fold higher in the Single-Arm Cohort than in the device group of the Randomized Cohort. Other event rates were comparable to the device group of the Randomized Cohort.

Table 22. CEC-Adjudicated Adverse Events through 12 Months – Single-Arm Cohort AP Population.

Event	Summary Statistics* N=100
All-cause mortality	15% (15, 15, 0, 0, 1)
Cardiovascular (VARC II definition)	11% (11, 11, 0, 0, 0)
Heart failure-related	10% (10, 10, 0, 0, 0)
Non-heart failure-related	1% (1, 1, 0, 0, 0)
Non-cardiovascular (VARC II definition)	4% (4, 4, 0, 0, 1)
Hospitalization	50% (85, 50, 5, 4, 1)
Heart failure hospitalization	24% (33, 24, 1, 0, 0)
Other cardiovascular hospitalization	14% (17,14, 4, 3, 0)
Non-cardiovascular hospitalization	26% (35, 26, 0, 1, 1)
Tricuspid valve surgery	2% (2, 2, 1, 0, 0)
Tricuspid valve intervention	7% (7, 7, 5, 4, 0)
Major bleeding (greater than BARC 3a)‖	5% (5, 5, 0, 1, 0)
New onset renal failure‖	0% (0, 0, 0, 0, 0)
Transient ischemic attack (TIA)	1% (1, 1, 0, 0, 0)
Stroke (VARC II)	0% (0, 0, 0, 0, 0)
Myocardial infarction (VARC II definition)‖	0% (0, 0, 0, 0, 0)
Endocarditis requiring surgery‖	0% (0, 0, 0, 0, 0)
Non-elective cardiovascular surgery for TriClip-related adverse event post index procedure‖	0% (0, 0, 0, 0, 0)
Cardiogenic shock	1% (1, 1, 0, 1, 0)

VARC: Valve Academic Research Consortium; BARC: Bleeding Academic Research Consortium; TIA: transient ischemic attack.
*Event rate (no. of events, no. of subjects, no. of device-related events, number of procedure-related events, number of COVID-19-related events); event rate = no./total no. Number of COVID-19-related events includes related or possibly related events; this excludes events with unknown relatedness.
‖Per the study CEC charter, myocardial infarction, bleeding, new onset renal failure, endocarditis requiring surgery, and non-elective cardiovascular surgery for TriClip-related adverse event post index procedure were adjudicated up to 30 days post treatment visit for the device and control groups.

Imaging Sub-study

A pre-planned exploratory imaging sub-study was conducted on a subset of all available subjects to further investigate changes in TR, right ventricular size, and right ventricular function and to gain additional insights into cardiac reverse remodeling. Ten (10) sites participated, and site selection was based on MRI/CT imaging expertise, adequate imaging equipment, and study enrollment. The imaging sub-study was to enroll 100 subjects. A total of 82 subjects enrolled and completed baseline imaging as of April 23, 2023, with 44 subjects enrolled at a single site.

MRI and CT were performed at baseline and 30 days, and CT was performed at 12 months. TR parameters were only assessed with MRI. The 30-day cardiac MRI results (**Table 23**) showed TR reduction in TriClip subjects consistent with the echocardiogram results. In addition, there were general trends in right ventricular reverse remodeling in TriClip subjects. However, the sample sizes were small and there was large patient-to-patient variability in the results. The long-term prognostic values of the observed changes are unknown.

Table 23. Imaging Sub-Study: 30-Day Cardiac MRI Results.

Endpoint Change from Baseline to 30 Days	Randomized Cohort		Single-Arm & Roll-in Cohorts (N=12)
	Device Arm (N=27)	Control Arm (N=26)	
ΔTR volume (mL)			
Mean ± SD (n)	-34.1 ± 28.2 (27)	3.2 ± 22.1 (24)	-39.0 ± 16.3 (10)
Median (Q1, Q3)	-28.0 (-52.0, -10.0)	2.0 (-13.0, 11.5)	-43.0 (-46.0, -28.0)
Range (min, max)	(-100.0, 4.0)	(-20.0, 84.0)	(-62.0, -9.0)
ΔTR fraction (%)			
Mean ± SD (n)	-27.8 ± 16.0 (27)	-2.3 ± 21.2 (24)	-29.1 ± 14.6 (10)
Median (Q1, Q3)	-28.0 (-45.0, -13.8)	0.5 (-8.4, 6.0)	-29.5 (-37.0, -18.0)
Range (min, max)	(-52.9, 9.4)	(-66.4, 60.2)	(-56.3, -9.0)
ΔRight atrial end diastolic volume (RAEDV, mL)			
Mean ± SD (n)	-8.7 ± 23.1 (27)	-4.0 ± 38.5 (26)	-29.6 ± 27.8 (12)
Median (Q1, Q3)	-9.0 (-21.0, 8.0)	-3.0 (-16.0, 22.0)	-17.5 (-51.0, -5.5)
Range (min, max)	(-64.0, 37.0)	(-113.0, 63.0)	(-83.0, -2.0)
ΔRight ventricular mass (g)			
Mean ± SD (n)	-4.7 ± 5.2 (27)	0.0 ± 6.0 (25)	-7.2 ± 8.7 (11)
Median (Q1, Q3)	-5.0 (-9.0, 0.0)	1.0 (-4.0, 5.0)	-5.0 (-9.0, -1.0)
Range (min, max)	(-16.0, 4.0)	(-13.0, 10.0)	(-32.0, -1.0)
ΔRight ventricular ejection fraction (RVEF, %)			
Mean ± SD (n)	-5.6 ± 6.6 (27)	0.6 ± 6.1 (25)	-9.2 ± 5.6 (11)
Median (Q1, Q3)	-6.0 (-11.0, 1.0)	1.0 (-1.0, 2.0)	-10.0 (-15.0, -6.0)
Range (min, max)	(-17.0, 5.0)	(-15.0, 17.0)	(-16.0, 2.0)
ΔCorrected RVEF (%)*			
Mean ± SD (n)	8.4 ± 7.6 (27)	-0.2 ± 4.5 (24)	7.1 ± 9.3 (10)
Median (Q1, Q3)	8.1 (4.0, 15.0)	0.0 (-2.6, 2.5)	8.5 (-1.0, 14.0)
Range (min, max)	(-8.2, 20.3)	(-12.0, 8.8)	(-10.9, 18.5)

Endpoint Change from Baseline to 30 Days	Randomized Cohort		Single-Arm & Roll-in Cohorts (N=12)
	Device Arm (N=27)	Control Arm (N=26)	
ΔRight ventricular free wall strain (%)			
Mean ± SD (n)	-2.0 ± 4.5 (27)	1.2 ± 6.1 (25)	-2.7 ± 4.8 (10)
Median (Q1, Q3)	-1.0 (-5.0, 1.0)	0.0 (-3.0, 3.0)	-2.0 (-6.0, 2.0)
Range (min, max)	(-12.0, 6.0)	(-8.0, 16.0)	(-12.0, 3.0)
ΔPulmonary forward flow (mL)			
Mean ± SD (n)	5.2 ± 13.0 (27)	0.3 ± 9.1 (24)	-1.8 ± 27.5 (11)
Median (Q1, Q3)	5.0 (-4.0, 14.0)	1.0 (-4.0, 5.0)	4.0 (-5.0, 10.0)
Range (min, max)	(-19.0, 41.0)	(-22.0, 19.0)	(-79.0, 29.0)

*Corrected RVEF: provides a more accurate measurement of forward flow by subtracting regurgitant volume from the total stroke volume for a regurgitant valve.

The 12-month cardiac CT results are shown in **Table 24**. Similar to the cardiac MRI results, general trends of right ventricular reverse remodeling were observed in TriClip subjects. However, sample sizes were small, and there was large patient-to-patient variability in the results. The long-term prognostic values of the observed changes are unknown.

Table 24. Imaging Sub-Study: 12-Month Cardiac CT Results.

Endpoint Change from Baseline to 12 Months	Randomized Cohort		Single-Arm & Roll-In Cohorts (N=7)
	Device Group (N=20)	Control Group (N=20)	
ΔRight atrial end diastolic volume (RAEDV, mL)			
Mean ± SD (n)	-19.5 ± 34.2 (20)	4.4 ± 35.5 (20)	-3.3 ± 23.6 (7)
Median (Q1, Q3)	-18.0 (-31.5, -4.0)	5.0 (-14.0, 23.0)	4.0 (-28.0, 21.0)
Range (min, max)	(-83.0, 45.0)	(-70.0, 99.0)	(-33.0, 23.0)
ΔTricuspid valve annular area (mm^2)			
Mean ± SD (n)	-195.0 ± 197.1 (20)	-3.0 ± 142.8 (20)	-194.3 ± 119.7 (7)
Median (Q1, Q3)	-205.0 (-305.0, -60.0)	-20.0 (-70.0, 60.0)	-160.0 (-300.0, -130.0)
Range (min, max)	(-690.0, 90.0)	(-240.0, 390.0)	(-360.0, 0.0)
ΔRight ventricular end diastolic volume (RVEDV, mL)			
Mean ± SD (n)	-35.8 ± 26.4 (20)	-1.0 ± 38.1 (20)	-42.4 ± 33.5 (7)
Median (Q1, Q3)	-38.0 (-58.5, -18.5)	-3.5 (-22.5, 12.5)	-37.0 (-56.0, -16.0)
Range (min, max)	(-74.0, 8.0)	(-61.0, 68.0)	(-103.0, 0.0)
ΔRight ventricular mass (g)			
Mean ± SD (n)	-4.7 ± 4.9 (20)	1.4 ± 6.5 (20)	-3.6 ± 5.7 (7
Median (Q1, Q3)	-3.5 (-6.5, -1.0)	1.5 (-4.5, 5.0)	-5.0 (-7.0, -2.0)
Range (min, max)	(-16.0, 2.0)	(-10.0, 13.0)	(-10.0, 8.0)
ΔRight ventricular ejection fraction (%)			
Mean ± SD (n)	-6.9 ± 6.2 (20)	0.9 ± 5.2 (20)	-2.1 ± 7.0 (7
Median (Q1, Q3)	-9.0 (-11.0, -2.0)	0.5 (-2.0, 4.0)	-2.0 (-8.0, 7.0)
Range (min, max)	(-16.0, 5.0)	(-10.0, 11.0)	(-11.0, 7.0)

Endpoint Change from Baseline to 12 Months	Randomized Cohort		Single-Arm & Roll-In Cohorts (N=7)
	Device Group (N=20)	Control Group (N=20)	
ΔRight ventricular free wall strain (%)			
Mean ± SD (n)	-4.2 ± 7.2 (18)	-1.3 ± 5.4 (19)	-1.3 ± 6.5 (7
Median (Q1, Q3)	-3.5 (-8.0, 2.0)	-2.0 (-5.0, 3.0)	2.0 (-8.0, 3.0)
Range (min, max)	(-20.0, 5.0)	(-14.0, 10.0)	(-13.0, 4.0)
SD: standard deviation;			

Subgroup Analyses

Pre-specified subgroup analyses were performed on the primary endpoint components at 12 months by sex (male vs. female), baseline TR grade (severe vs. greater than severe), baseline NYHA functional class (I/II vs. III/IV), and TR etiology (primary vs. secondary). Outcomes for each component of the primary endpoint were generally consistent across subgroups except KCCQ score change by TR etiology. However, this is not considered a qualitative interaction, as the device group had a higher proportion of subjects with a KCCQ improvement of ≥15 points vs. the control group for both the primary and secondary TR etiology subgroups.

A subgroup analysis was also performed to investigate potential differences in outcomes based on race. The number of non-Caucasians is too small to draw any conclusions (see **Table 25**).

Table 25. Primary Endpoint Components of Safety and Effectiveness by Race

Race	All-Cause Mortality or TV Surgery§		Heart Failure Hospitalization§		ΔKCCQ ≥15 Points §	
	Device	Control	Device	Control	Device	Control
American Indian or Alaskan Native	0/1	0/0	0/1	0/0	0/1	0/0
Asian	0/7	1/7	1/7	0/7	2/7	4/9
Black or African American	2/7	2/7	2/7	1/10	1/4	4/9
Native Hawaiian or Other Pacific Islander*	0/0	0/0	0/0	0/0	0/0	0/0
White	13/149	15/143	20/149	19/143	67/127	28/120
Not available†	1/11	0/15	3/11	0/15	3/8	5/13

KCCQ: Kansas City Cardiomyopathy
*No subjects in the race category enrolled.
†Europeans regulations did not allow the race information to be collected for subjects enrolled in Germany.
§ The numbers shown were no. of patients with events/total no. of patients.

28.0 TRICLIP G4 PROCEDURE ACRONYMS AND DEFINITIONS OF TERMS.

28.1 Glossary Of Acronyms

DC:	Delivery Catheter	RA:	Right Atrium
TDS or Delivery System:	TriClip™ G4 Delivery System	RV:	Right Ventricle
TSGC or Guide:	TriClip™ Steerable Guide Catheter	RO:	Radiopaque
Sleeve:	Steerable Sleeve	TR:	Tricuspid Regurgitation
Clip or Implant:	TriClip™ G4 Implant		

28.2 Definition Of Terms

Defined Terms are in italics throughout document.

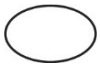
TERM	DEFINITION AND RELATED TECHNIQUE
Lock the Implant	1. Rotate the Lock Lever outward. 2. Fully advance the Lock Lever. 3. Rotate the Lock Lever inward to engage the lever.
Unlock the Implant	1. Rotate the Lock Lever outward and then retract the lever until the mark on the lever is fully exposed. 2. Rotate the Lock Lever inward to engage the lever.
Open the Implant Arms	1. Confirm the Implant is unlocked. 2. Turn the Arm Positioner at least 1/2 turn in the “Close” (clockwise) direction. 3. Turn the Arm Positioner in the “Open” (counter-clockwise) direction until the desired *Implant Arm Angle* is achieved. **NOTE 1**: If the Implant does not open smoothly, retract the Lock Lever farther, then repeat steps 2 – 3. **NOTE 2**: If the Implant Arms fail to open visibly (as observed under fluoroscopic guidance), use the following techniques in the order provided, as needed: A. Stop and return *Arm Positioner to Neutral*. Retract Lock Lever farther, then turn the Arm Positioner farther in the “Close” direction before turning in the “Open” direction. Advance the lock lever just enough so that the mark on the lever is still fully exposed. B. Turn the *Arm Positioner to Neutral*, then incrementally iterate the amount of Arm Positioner rotation in the “Close” direction followed by rotation in the “Open” direction. Iterate until the Implant opens or until it is no longer possible to rotate the Arm Positioner in the “Close” direction. Advance the lock lever just enough so that the mark on the lever is still fully exposed. C. Turn the *Arm Positioner to Neutral*, iterate the amount of Lock Lever retraction past the mark in 5 mm increments, and rotate the Arm Positioner fully in the “Close” direction, before rotating in the “Open” direction, until Implant opens. Advance the lock lever just enough so that the mark on the lever is still fully exposed.

TERM	DEFINITION AND RELATED TECHNIQUE
	D. Advance the Gripper Lever and repeat NOTE 2, Step C. Retract the Gripper Lever after Implant opens. E. If in the RA and free of tissue, release the DC Fastener, then release the Sleeve curves and repeat NOTE 2, Step C. **WARNING: Do release the DC Fastener before releasing Sleeve curves, otherwise it may result in device damage and/or device or component embolization.** F. If the Implant does not open after performing all steps in NOTE 2, DO NOT use the device.
Arm Positioner to Neutral	Turn the Arm Positioner in the "Close" or "Open" direction until no resistance to turning is noted.
Invert the Implant Arms	1. Confirm the Implant is unlocked. 2. Turn the Arm Positioner at least 1/2 turn in the "Close" direction. 3. Turn the Arm Positioner in the "Open" direction until an *Implant Arm Angle* of 180° is observed under fluoroscopic guidance. Note the orientation of the blue line on the Arm Positioner. 4. Continue turning the Arm Positioner in the "Open" direction until the Implant Arms invert, no more than 1 full turn from 180°. DO NOT over-invert the Implant Arms. DO NOT turn Arm Positioner more than 1 full turn past an *Implant Arm Angle* of 180° or past when resistance is first noted. **WARNING: Turning the Arm Positioner in the "Open" direction more than 1 full turn past an *Implant Arm Angle* of 180° or turning past when resistance is first noted may result in device damage which could cause the Implant to become non-functional and lead to embolization, and/or conversion to surgical intervention.**
Raise the Gripper(s)	(a) Simultaneously- Confirm Gripper Levers are latched. Slowly retract the Gripper Levers until a hard stop is reached (under fluoroscopic and echocardiographic observation). **or** (b) Independently- Unlatch the Gripper Levers and slowly retract the desired Gripper Lever until a hard stop is reached (under fluoroscopic and echocardiographic observation). Re-latch the Gripper Levers.
Lower the Gripper(s)	(a) Simultaneously- Confirm the Gripper Levers are latched and fully advance the Gripper Levers. **or** (b) Independently- Unlatch the Gripper Levers and fully advance the desired Gripper Lever(s). Re-latch the Gripper Levers.

TERM	DEFINITION AND RELATED TECHNIQUE
Identify Gripper Orientation	1. Unlatch the Gripper Levers. 2. Advance and retract the Gripper Lever with the tactile marker under imaging (echocardiography) to identify Gripper Lever to the corresponding leaflet. 3. Once Gripper(s) are identified, *Raise the Gripper(s)* and re-latch the Gripper Levers until ready for leaflet capture.
Implant Arm Angle	• Angle between the inner edges of both Implant Arms. • All *Implant Arm Angle*s are measured using fluoroscopy with optimal view allowing clear observation of the tip of the Implant and both arms in the same plane so they appear as a "V" (see **Figure 1**).
Grasping Arm Angle	A *Implant Arm Angle* of approximately 120 degrees.
Fully Close the Implant Arms	Turn the Arm Positioner in the "Close" direction until the Implant Arms contact the DC. • Under direct visualization, the Implant is fully closed when the Implant Covering contacts the DC. • Under fluoroscopic observation, the Implant is fully closed when the inner edges of the Implant Arms are parallel.
Establish Final Arm Angle	Verification step to confirm that the pre-deployment *Implant Arm Angle* will reflect the *Implant Arm Angle* post-deployment. 1. With the Lock Lever fully advanced, and *the Arm Positioner to Neutral* (note the orientation of the blue line on the Arm Positioner), turn the Arm Positioner 1 turn in the "Open" direction (confirm blue line has returned to the original orientation). The Implant Arms may open slightly (~5°) and then remain in a stable position. **NOTE:** If continued opening of the Implant Arms is noted, reconfirm that the Lock Lever is completely advanced. Close the Implant Arms, and *Establish Final Arm Angle*. **WARNING: DO NOT turn the Arm Positioner more than 1 turn in the "Open" direction from neutral. Failure to stop turning the Arm Positioner at 1 turn in the "Open" direction past neutral may result in Implant opening or device damage which could cause the Implant to become non-functional and lead to embolization and/or conversion to surgical intervention.**

GRAPHICAL SYMBOLS FOR MEDICAL DEVICE LABELING:

Source reference for recognized symbols retained at the manufacturer in the Medical Device File.

LOT	Batch code		Do not resterilize
REF	Catalogue number		Do not re-use
	Use-by date		Non-pyrogenic
STERILE EO	Sterilized using ethylene oxide.		Do not use if package is damaged and consult instructions for use
	Single sterile barrier system		Manufacturer
	Consult instructions for use or consult electronic instructions for use		Date of manufacture
	Refer to instruction manual/booklet (Symbol Color: Blue)		Packaging unit
	MR Conditional		Keep away from sunlight
UDI	Unique device identifier		Keep dry
MD	Medical device	Rx ONLY	CAUTION: Federal law restricts this device to sale by or on the order of a physician.

Abbott Medical
177 County Road B East
St. Paul, MN 55117 USA
TEL: +1 855 478 5833
FAX: +1 651 756 5833
Outside USA TEL: +1 855 478 5833
Outside USA FAX: +1 651 756 5833

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