Edwards Lifesciences

Edwards SAPIEN XT

Transcatheter Heart Valve with the NovaFlex+ Delivery System

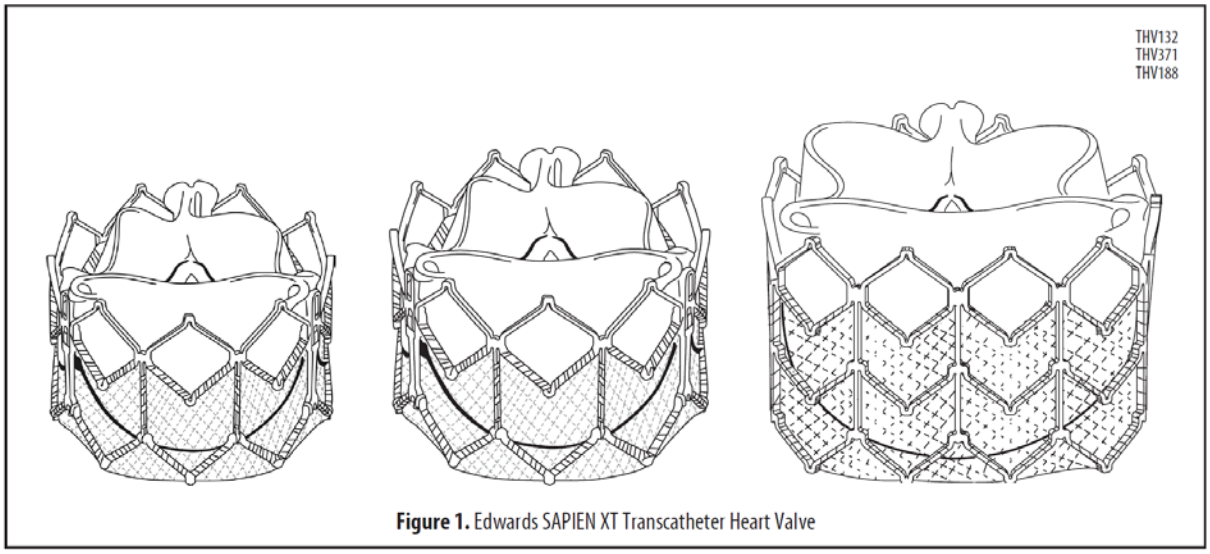


Figure 1. Edwards SAPIEN XT Transcatheter Heart Valve

Instructions for Use – Pulmonic

CAUTION: Federal (USA) law restricts these devices to sale by or on the order of a physician.

Implantation of the Transcatheter Heart Valve (THV) should be performed only by physicians who have received Edwards Lifesciences training. The implanting physician should be experienced in balloon valvuloplasty.

Please verify that you have the latest version of the instructions for use prior to using the device by visiting http://THVIFU.edwards.com or by calling 1.800.822.9837. In order to access the instructions for use, an IFU Code will be required.

STERILE: The THV is supplied sterilized with glutaraldehyde solution. The delivery system is supplied sterilized with ethylene oxide gas.

1.0 Device Description

Edwards SAPIEN XT Transcatheter Heart Valve- Model 9300TFX (Figure 1)

The Edwards SAPIEN XT Transcatheter Heart Valve (THV) is comprised of a balloon-expandable, radiopaque, cobalt-chromium frame, trileaflet bovine pericardial tissue valve, and polyethylene terephthalate (PET) fabric skirt. The leaflets are treated according to the Carpentier-Edwards ThermaFix process.

Table 1

THV Size	Height
23 mm	14.3 mm
26 mm	17.2 mm
29 mm	19.1 mm

The following table identifies the sizing recommendations for the intended location within the non-compliant Right Ventricular Outflow Tract (RVOT) conduit:

Table 2

Diameter	THV Size
20-23 mm	23 mm
23-26 mm	26 mm
26-29 mm	29 mm

NovaFlex+ Delivery System (Figures 2a, 2b, 2c)

The NovaFlex+ delivery system (usable length 105 cm) is used for delivery of the Edwards SAPIEN XT THV. The delivery system includes a flex wheel for articulation of the flex catheter, a tapered tip at the distal end of the delivery system to facilitate advancing to the RVOT, and a balloon catheter for deployment of the THV. The handle also contains a flex indicator depicting articulation of the flex catheter, a valve alignment wheel for fine adjustment of the THV during valve alignment, a button that enables movement between handle positions, and a flush port to flush the flex catheter. The balloon catheter has radiopaque markers defining the valve alignment position and the working length of the balloon. A radiopaque double marker proximal to the balloon indicates flex catheter position during deployment.

Figure 2a. NovaFlex+ Delivery System

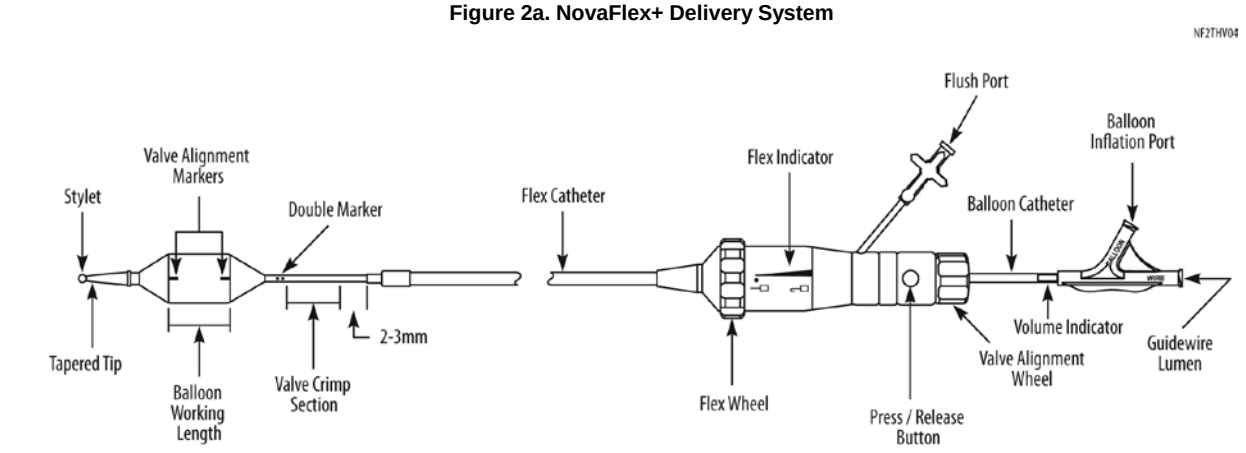


Figure 2b. Default Position

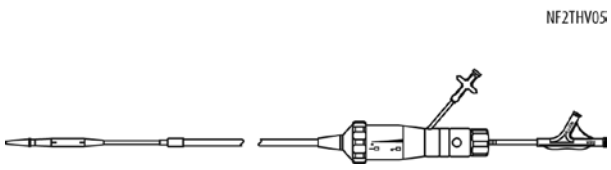
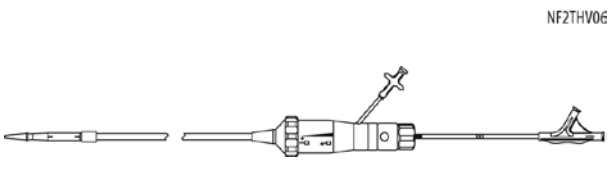


Figure 2c. Valve Alignment Position



The inflation parameters for THV deployment are:

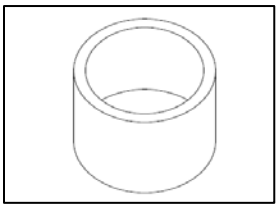
Table 3

Model	Nominal Balloon Diameter	Nominal Inflation Volume	Rated Burst Pressure (RBP)
9355FS23	23 mm	17 mL	7 atm
9355FS26	26 mm	22 mL	7 atm
9355FS29	29 mm	33 mL	7 atm

Qualcrimp Crimping Accessory (Figure 3)

The laminated Qualcrimp crimping accessory (packaged with the NovaFlex+ delivery system and manufactured in foam) is used during crimping of the THV.

Figure 3



Laminated Qualcrimp

2.0 Indications

The Edwards SAPIEN XT Transcatheter Heart Valve (THV) Systems are indicated for use in pediatric and adult patients with a dysfunctional, non-compliant Right Ventricular Outflow Tract (RVOT) conduit with a clinical indication for intervention and:

- pulmonary regurgitation ≥ moderate and/or
- mean RVOT gradient ≥ 35 mmHg.

3.0 Contraindications

The THV and delivery systems are contraindicated in patients with:

- Inability to tolerate an anticoagulation/antiplatelet regimen
- Active bacterial endocarditis

4.0 Warnings

- The devices are designed, intended, and distributed for single use only. **Do not resterilize or reuse the devices.** There are no data to support the sterility, nonpyrogenicity, and functionality of the devices after reprocessing.
- Assessment for coronary compression risk prior to valve implantation is essential to prevent the risk of severe patient harm.
- Incorrect sizing of the THV may lead to paravalvular leak, migration, embolization and/or RVOT rupture.
- Accelerated deterioration of the THV may occur in patients with an altered calcium metabolism.
- Prior to delivery, the THV must remain hydrated at all times and cannot be exposed to solutions other than its shipping storage solution and sterile physiologic rinsing solution. THV leaflets mishandled or damaged during any part of the procedure will require replacement of the THV.
- Do not use the THV if the tamper evident seal is broken, the storage solution does not completely cover the THV, the temperature indicator has been activated, the THV is damaged, or the expiration date has elapsed.
- Do not mishandle the NovaFlex+ delivery system or use it if the packaging or any components are not sterile, have been opened or are damaged (e.g. kinked or stretched), or the expiration date has elapsed.

- Use of excessive contrast media may lead to renal failure. Measure the patient's creatinine level prior to the procedure. Contrast media usage should be monitored.
- Patient injury could occur if the delivery system is not un-flexed prior to removal.
- Care should be exercised in patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/or polymeric materials.
- The procedure should be conducted under fluoroscopic guidance. Some fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. These injuries may be painful, disfiguring, and long-lasting.
- THV recipients should be maintained on anticoagulant/antiplatelet therapy as determined by their physician. This device has not been tested for use without anticoagulation.
- Do not add or apply antibiotics to the storage solution, rinse solutions, or to the THV.

5.0 Precautions

- Safety, effectiveness, and durability of the THV have not been established for implantation within a previously placed surgical or transcatheter pulmonic valve.
- Long-term durability has not been established for the THV. Regular medical follow-up is advised to evaluate THV performance.
- Glutaraldehyde may cause irritation of the skin, eyes, nose and throat. Avoid prolonged or repeated exposure to, or breathing of, the solution. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water; in the event of contact with eyes, immediately flush the affected area with water and seek immediate medical attention. For more information about glutaraldehyde exposure, refer to the Material Safety Data Sheet available from Edwards Lifesciences.
- Patient anatomy should be evaluated to prevent the risk of access that would preclude the delivery and deployment of the device.
- To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon.
- Appropriate antibiotic prophylaxis is recommended post-procedure in patients at risk for prosthetic valve infection and endocarditis.
- Safety and effectiveness have not been established for patients with the following characteristics/comorbidities:
    - Echocardiographic evidence of intracardiac mass, thrombus, or vegetation
    - A known hypersensitivity or contraindication to aspirin, heparin or sensitivity to contrast media, which cannot be adequately premedicated
    - Pregnancy
    - Patients under the age of 10 years

6.0 Potential Adverse Events

Potential risks associated with the overall procedure including potential access complications associated with standard cardiac catheterization, balloon valvuloplasty, the potential risks of conscious sedation and/or general anesthesia, and the use of angiography:

- Death
- Respiratory insufficiency or respiratory failure
- Hemorrhage requiring transfusion or intervention
- Cardiovascular injury including perforation or dissection of vessels, ventricle, myocardium or valvular structures that may require intervention
- Pericardial effusion or cardiac tamponade
- Embolization including air, calcific valve material or thrombus
- Infection including septicemia and endocarditis
- Heart failure
- Myocardial infarction

- Renal insufficiency or renal failure
- Conduction system defect Arrhythmia
- Arteriovenous fistula
- Reoperation or reintervention
- Ischemia or nerve injury
- Pulmonary edema
- Pleural effusion
- Bleeding
- Anemia
- Abnormal lab values (including electrolyte imbalance)
- Hypertension or hypotension
- Allergic reaction to anesthesia, contrast media, or device materials
- Hematoma or ecchymosis
- Syncope
- Pain or changes at the access site
- Exercise intolerance or weakness
- Inflammation
- Angina
- Fever

Additional potential risks associated with the use of the THV, delivery system, and/or accessories include:

- Cardiac arrest
- Cardiogenic shock
- Emergency cardiac surgery
- Coronary flow obstruction/transvalvular flow disturbance
- Device thrombosis requiring intervention
- Valve thrombosis
- Device embolization
- Device malposition requiring intervention
- Valve deployment in unintended location
- Structural valve deterioration (wear, fracture, calcification, leaflet tear/tearing from the stent posts, leaflet retraction, suture line disruption of components of a prosthetic valve, thickening, stenosis)
- Paravalvular or transvalvular leak
- Valve regurgitation
- Hemolysis
- Device explants
- Nonstructural dysfunction
- Mechanical failure of delivery system, and/or accessories

7.0 Directions for Use

7.1 Required Equipment

Table 4

Product Name	23 mm System (9355NF23A)	26 mm System (9355NF26A)	29 mm System (9355NF29A)
	Model		
Edwards SAPIEN XT Transcatheter Heart Valve	9300TFX (23 mm)	9300TFX (26 mm)	9300TFX (29 mm)
NovaFlex+ Delivery System*	9355FS23	9355FS26	9355FS29
Edwards Expandable Introducer Sheath Set**	916ES23	918ES26	920ES29
Edwards Dilator Kit	9100DKS		
Edwards Balloon Catheter (optional)	9350BC20 (or equivalent)	9350BC23 (or equivalent)	9350BC25 (or equivalent)
Inflation devices provided by Edwards Lifesciences			
Edwards Crimper	9350CR		

* Includes the Qualcrimp Crimping Accessory and 2-piece Crimp Stopper

** Or other compatible sheath provided by Edwards Lifesciences

Additional Equipment:

- 20 cc syringe or larger (x2)
- 50 cc syringe or larger
- High-pressure 3-way stopcock (x2)
- Standard cardiac catheterization lab equipment
- Fluoroscopy (fixed, mobile or semi-mobile fluoroscopy systems appropriate for use in percutaneous coronary interventions)
- Exchange length 0.035 inch (0.89 mm) extra-stiff guidewire
- Sterile rinsing basins, physiological saline, heparinized saline, 15% diluted radiopaque contrast medium
- Sterile table for THV and device preparation

7.2 THV Handling and Preparation

Follow sterile technique during device preparation and implantation.

7.2.1 THV Rinsing Procedure

Before opening the valve jar, carefully examine for evidence of damage (e.g. a cracked jar or lid, leakage, or broken or missing seals).

CAUTION: THVs from containers found to be damaged, leaking, without adequate sterilant, or missing intact seals must not be used for implantation.

Step	Procedure
1	Set up two (2) sterile bowls with at least 500 mL of sterile physiological saline to thoroughly rinse the glutaraldehyde sterilant from the THV.
2	Carefully remove the THV/holder assembly from the jar without touching the tissue. Verify the THV serial identification number with the number on the jar lid and record in the patient information documents. Inspect the THV for any signs of damage to the frame or tissue.

Step	Procedure
3	Rinse the THV as follows: Place the THV in the first bowl of sterile, physiological saline. Be sure the saline solution completely covers the THV and holder. With the THV and holder submerged, slowly agitate (to gently swirl the THV and holder) back and forth for a minimum of 1 minute. Transfer the THV and holder to the second rinsing bowl of physiological saline and gently agitate for at least one more minute. Ensure the rinse solution in the first bowl is not used. The THV should be left in the final rinse solution until needed to prevent the tissue from drying. **CAUTION: Do not allow the THV to come into contact with the bottom or sides of the rinse bowl during agitation or swirling in the rinse solution. Direct contact between the identification tag and THV is also to be avoided during the rinse procedure. No other objects should be placed in the rinse bowls. The THV should be kept hydrated to prevent the tissue from drying.**

7.2.2 Prepare the Components

Refer to the Edwards Dilator Kit, Edwards Expandable Introducer Sheath Set, Edwards Crimper and Edwards Balloon Catheter instructions for use for device preparation.

Step	Procedure
1	Visually inspect all components for damage. Ensure the NovaFlex+ delivery system is fully unflexed and the valve alignment wheel is adjacent to the handle.
2	Flush the flex catheter.
3	Carefully remove the distal balloon cover from the delivery system.
4	Remove the stylet from the distal end of the guidewire lumen and set aside. Flush the guidewire lumen with heparinized saline and insert the stylet back into the distal end of the guidewire lumen. Note: Failure to insert the stylet back into the guidewire lumen may result in damage to the lumen during crimping process.
5	Place the delivery system into the default position and make sure that the flex catheter tip is covered by the proximal balloon cover. Unscrew the loader cap from the loader tube and flush the loader cap. Place the loader cap over the proximal balloon cover and onto the flex catheter with the inside of the cap oriented towards the distal tip.
6	Press button on handle and bring the device handle adjacent to the Y-connector. Peel off the proximal balloon cover over the blue section of the balloon shaft.
7	Attach a 3-way stopcock to the balloon inflation port. Partially fill a 50 cc or larger syringe with 15-20 mL diluted contrast medium and attach to the 3-way stopcock.
8	Fill the inflation device provided by Edwards Lifesciences with excess volume relative to the indicated inflation volume. Lock the inflation device and attach to the 3-way stopcock.
9	Close the 3-way stopcock to the Inflation device provided by Edwards Lifesciences and de-air the system using the 50 cc or larger syringe. Slowly release the plunger and leave zero-pressure in the system.
10	Close the stopcock to the delivery system. By rotating the knob of the inflation device provided by Edwards Lifesciences, transfer the contrast medium into the syringe to achieve the appropriate volume required to deploy the THV, per the following:
11	Close the stopcock to the 50 cc or larger syringe. Remove the syringe. Verify that the inflation volume is correct and lock the Inflation device provided by Edwards Lifesciences. **CAUTION: Maintain the Inflation device provided by Edwards Lifesciences in the locked position until THV deployment.**

Delivery System	THV Size	Inflation Volume
Model 9355FS23	23 mm	17 mL
Model 9355FS26	26 mm	22 mL
Model 9355FS29	29 mm	33 mL

7.2.3 Mount and Crimp the THV on the Delivery System

Step	Procedure
1	Set up two (2) additional sterile bowls with at least 100 mL of sterile physiological saline to thoroughly rinse the Qualcrimp crimping accessory.

2	Completely submerge the Qualcrimp crimping accessory in the first bowl and gently compress it to ensure complete saline absorption. Slowly swirl the Qualcrimp crimping accessory for a minimum of 1 minute. Repeat this process in the second bowl.
3	Remove the THV from the holder and remove the ID tag.
4	Attach the 2-piece crimp stopper to the base of the crimper and click into place.
5	With the crimper in the open position, gently place the THV into the crimper aperture. Gradually crimp the THV until it fits into the Qualcrimp crimping accessory.
6	Place the Qualcrimp crimping accessory over the THV making sure the THV is parallel to the edge of the Qualcrimp.
7	Place the THV and Qualcrimp crimping accessory in crimper aperture. Insert the delivery system coaxially within the THV on the Valve Crimp Section (2-3 mm distal to the balloon shaft) with the inflow (fabric cuff end) of the THV towards the proximal end of the delivery system.
8	Crimp the THV until it reaches the Qualcrimp Stop located on the 2-piece Crimp Stopper.
9	Gently remove the Qualcrimp crimping accessory from the THV. Remove the Qualcrimp Stop from the Final Stop, leaving the Final Stop in place.
10	Fully crimp the THV until it reaches the Final Stop. **NOTE: Ensure that the Valve Crimp Section remains coaxial within the THV.**
11	Repeat the full crimp of the THV for a total of two full crimps.
12	Pull the balloon shaft until it is locked in the default position.
13	Flush the loader with heparinized saline. Immediately advance the THV into the loader until the tapered tip of the delivery system is exposed. **CAUTION: To prevent possible leaflet damage, the THV should not remain fully crimped and/or in the loader for over 15 minutes.**
14	Attach the loader cap to the loader, re-flush the delivery system through the flush port and close the stopcock to the delivery system. Remove the stylet and flush the guidewire lumen of the delivery system. **CAUTION: Keep the THV hydrated until ready for implantation.** **CAUTION: The physician must verify correct orientation of the THV prior to its implantation; its inflow (fabric cuff end) should be oriented towards the proximal end of the delivery system.**

7.3 Valvuloplasty and THV Delivery

Valvuloplasty and THV delivery should be performed under conscious sedation and/or general anesthesia with hemodynamic monitoring in a catheterization lab/hybrid operating room with fluoroscopic capabilities.

Administer heparin to maintain the ACT at ≥ 250 sec during the procedure.

CAUTION: Use of excessive contrast media may lead to renal failure. Measure the patient's creatinine level prior to the procedure. Contrast media usage should be monitored.

CAUTION: Procedure may require venous cut-down with surgical closure of the puncture site due to the size of the venotomy.

7.3.1 Valvuloplasty

Refer to Edwards Balloon Catheter Instructions for Use (IFU) for information on device preparation and handling.

7.3.2 THV Delivery

Step	Procedure
1	Dilate the access site using the Edwards Dilator Kit, if needed. Refer to the Edwards Dilator Kit IFU for information on device preparation and handling.
2	Ensure the guidewire placement is via the left pulmonary artery, unless precluded by patient anatomy.
3	Prepare and insert the Edwards Expandable Introducer Sheath Set. Refer to the Edwards Expandable Introducer Sheath Set IFU for information on device preparation and handling.
4	Insert the loader into the sheath until the loader stops.
5	Advance the NovaFlex+ delivery system through the sheath until the THV exits the sheath. Retract the loader to the proximal end of the delivery system. **CAUTION: If accessing femorally or via the iliac, the THV should not be advanced through the sheath if the sheath tip is not past the IVC.** **CAUTION: To prevent possible leaflet damage, the THV should not remain in the sheath for over 2 minutes.**
6	In a straight section of the vena cava, initiate valve alignment by pressing the button, begin pull back of the balloon catheter, and release the button. Continue pulling back the balloon catheter until the delivery system locks into the valve alignment position (Refer to **Figure 2c**). Use the Valve Alignment Wheel to position the THV between the valve alignment markers. **CAUTION: Deployment should be within a non-compliant pulmonic conduit (stented or calcific).** **CAUTION: Do not turn the Valve Alignment Wheel if the delivery system is not locked in the Valve Alignment Position.** **WARNING: Do not position the THV past the distal Valve Alignment Marker. This will prevent proper valve deployment.** **CAUTION: Maintain guidewire position in the pulmonary artery during valve alignment.**
7	Advance the catheter and use the flex wheel, if needed, to advance to the RVOT. **NOTE: The delivery system articulates in a direction opposite from the flush port.**
8	If additional working length is needed, remove the loader by unscrewing the loader cap and peeling the loader tubing from the delivery system.
9	Press the button and retract the Flex Catheter to the Double Marker and position the THV within the RVOT.
10	Verify the correct position of the THV with respect to the RVOT.
11	Begin THV deployment: • Unlock the Inflation device provided by Edwards Lifesciences. • Slowly deploy the THV by inflating the balloon with the entire volume in the Inflation device provided by Edwards Lifesciences. • Assess and reposition the THV as necessary. • Hold inflation for 3 seconds and confirm that the barrel of the inflation device is empty to ensure complete inflation of the balloon. • Deflate the balloon. **Caution: If resistance is experienced during the inflation of the delivery system balloon, do not force the inflation of the balloon. If the delivery system was rotated during tracking, rotate back to a neutral position and attempt re-inflation.**

7.3.4 System Removal

Step	Procedure
1	Unflex the delivery system while retracting the device, if needed. Retract the flex catheter until it locks in the default position and remove it from the sheath. **CAUTION: Patient injury could occur if the delivery system is not unflexed prior to removal.**
2	Remove all devices when the ACT level is appropriate. Refer to the Edwards Expandable Introducer Sheath Set instructions for use for device removal.
3	Close the access site.

8.0 How Supplied

STERILE: The THV is supplied sterilized with glutaraldehyde solution. The delivery system is supplied sterilized with ethylene oxide gas.

8.1 Storage

The THV must be stored at 10 °C to 25 °C (50 °F to 77 °F). Each jar is shipped in an enclosure containing a temperature indicator to detect exposure of the THV to extreme temperature.

The delivery system should be stored in a cool, dry place.

9.0 MR Safety

MR Conditional

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

- Static magnetic field of 1.5 tesla or 3 tesla.
- Maximum spatial gradient field of 2500 gauss/cm (25 T/m) or less.
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2 W/kg (Normal Operating Mode).

Under the scan conditions defined above, the SAPIEN XT THV is expected to produce a maximum temperature rise of 2.6 °C after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends as far as 14.5 mm from the implant for spin echo images and 30 mm for gradient echo images when scanned in a 3.0 T MRI system. The implant has not been evaluated in MR systems other than 1.5 or 3.0 T.

10.0 Patient Information

Patient education brochures are provided to each site and should be given to the patient to inform them of the risks and benefits of the procedure and alternatives in adequate time before the procedure to be read and discussed with their physician. A copy of this brochure may also be obtained from Edwards Lifesciences by calling 1.800.822.9837. A patient implant card request form is provided with each THV. After implantation, all requested information should be completed on this form. The serial number may be found on the package and on the identification tag attached to the THV. The original form should be returned to the Edwards Lifesciences address indicated on the form and upon receipt, Edwards Lifesciences will provide an identification card to the patient.

11.0 Recovered THV and Device Disposal

The explanted THV should be placed into a suitable histological fixative such as 10% formalin or 2% glutaraldehyde and returned to the company. Refrigeration is not necessary under these circumstances. Contact Edwards Lifesciences to request an Explant Kit.

Used delivery system may be disposed of in the same manner that hospital waste and biohazardous materials are handled. There are no special risks related to the disposal of these devices.

12.0 Clinical Studies

The COMPASSION trial was conducted using the SAPIEN THV, Edwards' first generation THV, which is no longer available for distribution. There were no clinical data collected on SAPIEN XT, Edwards' second generation THV, in the COMPASSION trial. However, there is extensive clinical evidence on Edwards SAPIEN and SAPIEN XT THVs in the aortic position from the PARTNER I and II trials. Information on the PARTNER I and II trials may be found on the FDA website:
SAPIEN: http://www.accessdata.fda.gov/cdrh_docs/pdf10/P100041b.pdf
SAPIEN XT: http://www.accessdata.fda.gov/cdrh_docs/pdf13/p130009s034b.pdf

COMPASSION Clinical Trial

The COMPASSION trial was a prospective, non-randomized multi-center study to assess the safety and effectiveness of pulmonic implantation of the SAPIEN THV in patients with dysfunctional RVOT conduits requiring treatment for moderate or severe pulmonary regurgitation (PR) by transthoracic echocardiography (TTE) and/or RVOT conduit obstruction with a mean gradient of ≥ 35 mmHg by TTE.

The valve sizes used in the COMPASSION trial included the 23 and 26 mm sizes, which were the only available sizes for the SAPIEN THV. The majority of the data (68.6%) were derived from patients who received a 23 mm THV.

Enrollment is complete. A total of 81 patients were enrolled into the study. Two enrolled patients were screen failures and did not undergo the index procedure; therefore, there were 79 patients in the safety population. An Edwards device was not used nor inserted into the vascular system in 9 patients in the safety population; therefore, there were 70 patients in the attempted implant population. Only one patient did not have a SAPIEN THV implanted in the target location; therefore, there were 69 patients in the valve implant population.

Patient follow-up was performed at one day post-procedure, discharge, 30 days, 6 months, 12 months, and annually thereafter for 5 years post procedure. Clinical Table 1 shows the time on study for the Safety Population.

Clinical Table 1: Total Study Follow-up Time (Safety Population, N=79)

Summary Statistic	Results
Total Follow-up Time (years)	2.78±1.74 (79) 3.04 (0.00, 5.31)
Total Patient Years [1]	219.8

Summary statistics:
Continuous measures- Mean ± SD (N); Median (Min, Max)
[1] Total patient years is the sum of the time on study for all patients

COMPASSION Clinical Data

The demographics and baseline characteristics of the safety population are summarized in Clinical Table 2.

Clinical Table 2: Demographics and Baseline Characteristics (Safety Population, N=79)	
Characteristic	**Statistic**
Age - yr	28.0 ± 13.97 (79)
	25.0 (10.0, 72.0)
<12 Years(Child)	3 / 79 (3.8%)
12-21 Years (Adolescent)	26 / 79 (32.9%)
>=22 Years (Adult)	50 / 79 (63.3%)
Male sex	52 / 79 (65.8%)
NYHA class	
I	18 / 79 (22.8%)
II	36 / 79 (45.6%)
III	23 / 79 (29.1%)
IV	2 / 79 (2.5%)
Primary Indication	
Pulmonary Stenosis	7 / 79 (8.9%)
Pulmonary Regurgitation	10 / 79 (12.7%)
Both	62 / 79 (78.5%)
Any Stent Placed (Prior to Study or During Study Procedure)	71 / 78 (91.0%)
Valve size (mm)	
23	48 / 70 (68.6%)
26	22 / 70 (31.4%)
Pulmonary Stenosis	
None	10 / 79 (12.7%)
Mild	13 / 79 (16.5%)
Moderate	25 / 79 (31.6%)
Severe	31 / 79 (39.2%)
Pulmonary Regurgitation by TTE	
None	4 / 78 (5.1%)
Trace	2 / 78 (2.6%)
Mild	1 / 78 (1.3%)
Moderate	5 / 78 (6.4%)
Severe	66 / 78 (84.6%)

Categorical measures-No. / Total no. (%)
Continuous measures- Mean ± SD (N); Median (Min, Max)

COMPASSION Results

The primary endpoint was freedom from device- or procedure-related death and/or reintervention at 1 year for the valve implant population, which was 97.1% (Clinical Table 3) and met the prespecified performance goal of 75%. There were no device- or procedure-related patient deaths at one year, and the incidence of reinterventions solely contributed to the KM estimate.

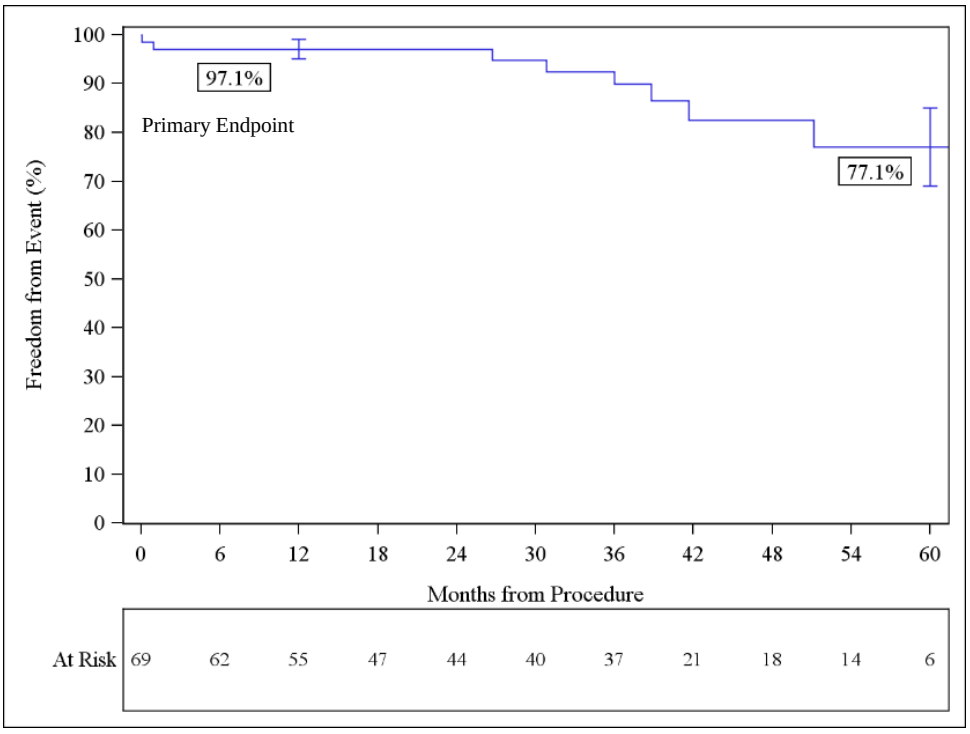
Clinical Table 3: Freedom from Device- or Procedure-Related Death and/or Reintervention at 1 Year (Valve Implant Population)

Adverse Event	Events	Patients with Event	Patients at Risk	KM Estimate [1]	Standard Error [2]	95% Confidence Interval
Device- or Procedure- Related Death and/or Reintervention	3	2	55	0.971	0.020	(0.889, 0.993)
Device- or Procedure- Related Death	0	0	57	1.000	0.000	NA
Reintervention	3	2	55	0.971	0.020	(0.889, 0.993)

[1] Kaplan-Meier survival estimates are calculated at 1 year and use the first event per patient. 1 Year is taken to mean 365.25 days. Any event occurring after 1 year is not included.
[2] Standard error of the survival estimate at 1 year.

At 5 years, the freedom from device- or procedure-related death and/or reintervention was 77.1% (Clinical Figure 1). As there were no device- or procedure-related patient deaths at 5 years, the incidence of reinterventions solely contributed to the KM estimate.

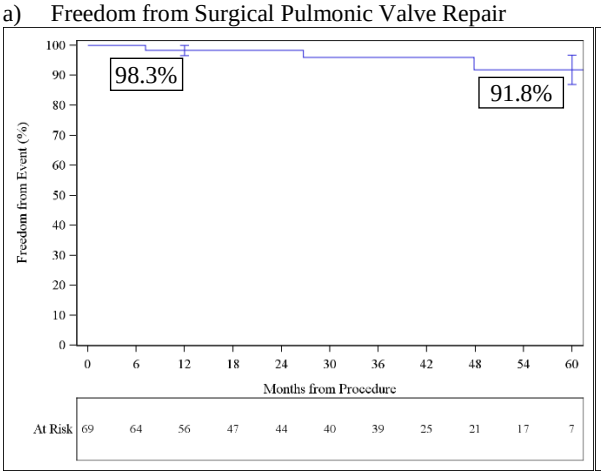
Clinical Figure 1: Freedom from Device- or Procedure-Related Death and/or Reintervention to 5 Years (Valve Implant Population)



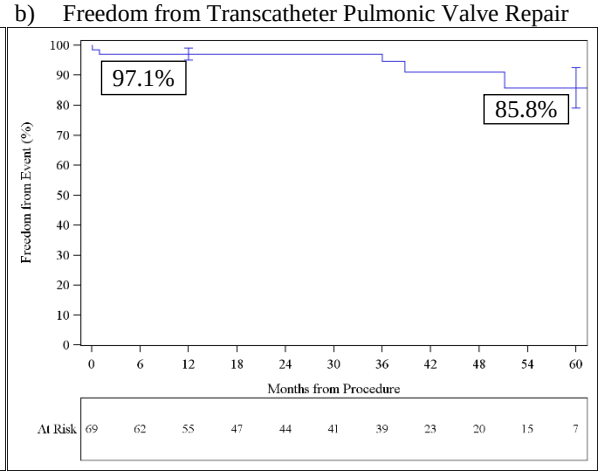
Clinical Figure 2 presents the freedom from reintervention to 5 years for the valve implant population, stratified by type of reintervention: a) freedom from surgical pulmonic valve repair was 98.3% at 1 year and 91.8% at 5 years; b) freedom from transcatheter pulmonic valve implantation was 97.1% at 1 year and 85.8% at 5 years; c) freedom from balloon valvuloplasty was 100% at 1 year and 93.7% at 5 years; and d) freedom from other types of reintervention was 100% at 1 year and 97.9% at 5 years.

Clinical Figure 2: Freedom from Reintervention by Type of Reintervention to 5 Years (Valve Implant Population)

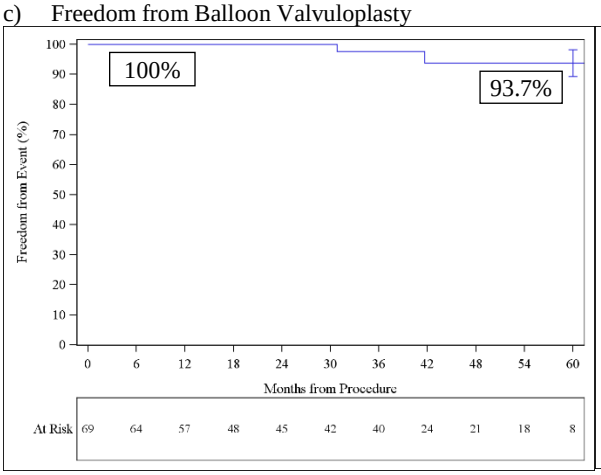
a) Freedom from Surgical Pulmonic Valve Repair



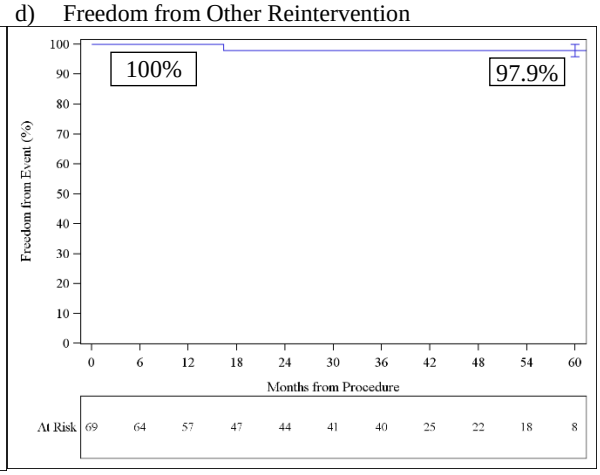
b) Freedom from Transcatheter Pulmonic Valve Repair



c) Freedom from Balloon Valvuloplasty



d) Freedom from Other Reintervention



The secondary endpoints were defined as freedom from Major Adverse Cardiac and Cerebrovascular Events (MACCE) at 6 months, and functional improvement at 6 months.

Freedom from MACCE at 6 months in the valve implant population was 94.1% (see Clinical Table 4).

Clinical Table 4: Freedom from MACCE at 6 Months (Valve Implant Population)

Adverse Event	Events	Patients with Event	Patients at Risk	KM Estimate [1]	Standard Error [2]
MACCE	4	4	60	0.941	0.028
All-cause mortality	0	0	64	1.000	0.000
Myocardial infarction	0	0	64	1.000	0.000
Reintervention	2	2	62	0.971	0.020
Vascular injury	1	1	63	0.986	0.014
Stroke	0	0	64	1.000	0.000
Pulmonary embolism	1	1	63	0.985	0.015

[1] Kaplan-Meier survival estimates are calculated at 6 months and use the first event per patient. Six months is taken to mean 180 days. Events occurring after 6 months are not included in this analysis.
[2] Standard error of the survival estimate at 6 months.

Overall functional improvement at 6 months for patients in the valve implant population was 87.9% (Clinical Table 5). A decrease in pulmonary regurgitation to mild or less was observed in 96.2%; improved pulmonary stenosis mean gradient was 93.8%; functional improvement in NYHA was 92.2%; and freedom from recurrent pulmonary stenosis was 100%.

Clinical Table 5: Overall Functional Improvement at 6 Months (Valve Implant Population)

Functional Improvement	Summary Statistics
Overall Functional Improvement [1]	51 / 58 (87.9%)
Improved Pulmonary Regurgitation [a]	51 / 53 (96.2%)
Improved Mean Gradient [b]	15 / 16 (93.8%)
Functional Improvement in NYHA [c]	47 / 51 (92.2%)
Freedom from Recurrent Pulmonary Stenosis [d]	56 / 56 (100.0%)

Summary statistics: Categorical measures-No. / Total no. (%)
[1] Overall functional improvement, as defined by the following 4 categories:
a) Improved valve function demonstrated by a decrease in PR to mild or less per TTE at 6 months for patients with moderate or more PR at baseline
b) Improved valve function demonstrated by a decrease in pulmonary stenosis mean gradient to <30mmHg for patients with pulmonary stenosis mean gradient >30mmHg at baseline.
c) Functional improvement from baseline of ≥ 1 NYHA functional class at 6 months for patients with baseline NYHA functional class ≥ 2
d) Freedom from recurrent pulmonary stenosis at 6 months
For patients with mild or less PR at baseline only categories b, c, and d were used to determine overall functional improvement. For patients with pulmonary stenosis mean gradient <30mmHg at baseline only categories a, c, and d were used for overall functional improvement. For patients with NYHA functional class of <2 at baseline only categories a, b, and d were used to determine overall functional improvement. For patients treated for indications other than pulmonary stenosis only categories a, b, and c for overall functional improvement were used.

The site-reported serious adverse events are shown in Clinical Table 6.

Clinical Table 6: Incidence of Site-Reported Serious Adverse Events by Study Visit (with CEC adjudication where available) (Safety Population, (N=79))

Adverse Event	<= 30 Days		31 – 365 Days		All Events	
	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event
Any Serious Adverse Event	29	3/ 79 (29.1%)	22	13/ 79 (16.5%)	132	38/ 79 (48.1%)
Other	2	2/ 79 (2.5%)	10	6/ 79 (7.6%)	37	13/ 79 (16.5%)
Infection (excluding endocarditis)	1	1/ 79 (1.3%)	3	3/ 79 (3.8%)	12	7/ 79 (8.9%)
CHF	1	1/ 79 (1.3%)	0	0/ 79 (0.0%)	11	4/ 79 (5.1%)
Electrolyte and/or CBC and platelet counts abnormal	1	1/ 79 (1.3%)	2	1/ 79 (1.3%)	11	2/ 79 (2.5%)
Valve stenosis	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)	9	6/ 79 (7.6%)
Arrhythmia	2	2/ 79 (2.5%)	0	0/ 79 (0.0%)	8	6/ 79 (7.6%)
Endocarditis	1	1/ 79 (1.3%)	2	2/ 79 (2.5%)	5	4/ 79 (5.1%)
Pulmonary artery perforation – rupture of RVOT conduit	5	5/ 79 (6.3%)	0	0/ 79 (0.0%)	5	5/ 79 (6.3%)
Fever	3	3/ 79 (3.8%)	0	0/ 79 (0.0%)	4	4/ 79 (5.1%)
Hemorrhage requiring transfusion	2	2/ 79 (2.5%)	1	1/ 79 (1.3%)	3	3/ 79 (3.8%)
Syncope	0	0/ 79 (0.0%)	0	0/ 79 (0.0%)	3	3/ 79 (3.8%)
Valve damage or dysfunction	2	2/ 79 (2.5%)	0	0/ 79 (0.0%)	3	3/ 79 (3.8%)
Device migration	2	2/ 79 (2.5%)	0	0/ 79 (0.0%)	2	2/ 79 (2.5%)
Hematoma	2	2/ 79 (2.5%)	0	0/ 79 (0.0%)	2	2/ 79 (2.5%)
Respiratory complication	1	1/ 79 (1.3%)	0	0/ 79 (0.0%)	2	2/ 79 (2.5%)
Anemia	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)	1	1/ 79 (1.3%)
Angina	0	0/ 79 (0.0%)	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)
Atelectasis	1	1/ 79 (1.3%)	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)
Bleeding Event	1	1/ 79 (1.3%)	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)
Dyspnea	0	0/ 79 (0.0%)	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)
Embolism: air or thrombus	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)	1	1/ 79 (1.3%)
Hemolysis	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)	1	1/ 79 (1.3%)
Hemorrhagic event	0	0/ 79 (0.0%)	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)
Hypotension	1	1/ 79 (1.3%)	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)
Ischemia	0	0/ 79 (0.0%)	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)
MI	0	0/ 79 (0.0%)	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)
Neurological Event (including TIA, stroke and psychomotor deficit)	0	0/ 79 (0.0%)	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)
Non-emergent reoperation	0	0/ 79 (0.0%)	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)
Nonstructural valve dysfunction	1	1/ 79 (1.3%)	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)
Thromboembolism	0	0/ 79 (0.0%)	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)

Summary statistics:
Categorical measures-No. / Total no. (%)
Seriousness was determined by the CEC for these events if they have been adjudicated and the site otherwise.
Note: The rates given in the All Events columns are cumulative based on all events reported by all patients up to their current follow up time including 10 patients who completed 5 year follow-up.

Two patients experienced a device migration (2/79, 2.5%) early in the trial. The instructions for use were modified; no other device migrations occurred in the trial after this modification. SAE RVOT conduit ruptures occurred in 5/79 (6.3%) patients. Please note that all 5 ruptures were related to balloon valvuloplasty or placement of a pre-stent. No ruptures occurred during placement of the SAPIEN THV.

The key CEC-adjudicated adverse events to 5 years are presented in Clinical Table 7.

Clinical Table 7: CEC-Adjudicated Endpoint Adverse Events (Valve Implant Population, N=69)

	30 Days (Patients at risk=69) [k]		1 Year (Patients at risk=57) [k]		2 Year (Patients at risk=45) [k]		3 Years (Patients at risk=41) [k]		4 Years (Patients at risk=23) [k]		5 Years (Patients at risk=9) [k]	
Outcome [a]	KM Survival Estimate [j]	Patients With Event	KM Survival Estimate [j]	Patients With Event	KM Survival Estimate [j]	Patients With Event	KM Survival Estimate [j]	Patients With Event	KM Survival Estimate [j]	Patients With Event	KM Survival Estimate [j]	Patients With Event
Valve Dysfunction [b]	0.957	3	0.942	4	0.885	7	0.772	12	0.707	14	0.657	15
MACCE [c]	0.971	2	0.941	4	0.919	5	0.825	9	0.751	11	0.697	12
Device or Procedure Related Death or Reintervention	0.971	2	0.971	2	0.971	2	0.900	5	0.826	7	0.771	8
Reintervention	0.971	2	0.971	2	0.971	2	0.900	5	0.826	7	0.771	8
Transcatheter pulmonic valve implantation (TPVI or V-in-V)	0.971	2	0.971	2	0.971	2	0.947	3	0.912	4	0.858	5
Endocarditis (site) [d]	0.986	1	0.970	2	0.970	2	0.970	2	0.933	3	0.871	4
Surgical Pulmonic Valve Repair / Replacement	1.000	0	0.983	1	0.983	1	0.960	2	0.918	3	0.918	3
Balloon valvuloplasty	1.000	0	1.000	0	1.000	0	0.976	1	0.937	2	0.937	2
Deaths	1.000	0	1.000	0	0.978	1	0.978	1	0.978	1	0.978	1
Death from cardiovascular cause [e]	1.000	0	1.000	0	0.978	1	0.978	1	0.978	1	0.978	1
Myocardial infarction	1.000	0	1.000	0	1.000	0	0.976	1	0.976	1	0.976	1
Other reintervention [f]	1.000	0	1.000	0	0.979	1	0.979	1	0.979	1	0.979	1
Vascular Injury [g]	1.000	0	0.986	1	0.986	1	0.986	1	0.986	1	0.986	1
Pulmonary embolism	1.000	0	0.985	1	0.985	1	0.985	1	0.985	1	0.985	1
Device or procedure related death	1.000	0	1.000	0	1.000	0	1.000	0	1.000	0	1.000	0
Stroke	1.000	0	1.000	0	1.000	0	1.000	0	1.000	0	1.000	0
Study Valve Stent Fracture (site) [d,h]	1.000	0	1.000	0	1.000	0	1.000	0	1.000	0	1.000	0

Summary statistics: n/N (%) of Patients
[a] CEC-adjudicated
[b] Valve Dysfunction is a non-hierarchical composite of the following events: all-cause mortality, surgical pulmonary valve replacement, valve frame fracture, recurrent pulmonary stenosis, moderate/severe regurgitation and reintervention.
[c] MACCE is a non-hierarchical composite of the following events: all-cause mortality, myocardial infarction, reintervention, vascular injury, stroke and pulmonary embolism.
[d] Site-reported events.
[e] Deaths from unknown causes were assumed to be deaths from cardiovascular causes.
[f] The other consists of a patient that underwent successful stenting of stenotic, surgically placed conduit.
[g] Vascular injury resulting in the need for an unplanned vascular intervention.
[h] A study valve fracture is a fracture of the frame of the study valve.
[j] Kaplan-Meier freedom from event rates are provided at the time point specified. Any events occurring after are not included.
[k] Patients at risk are the number of patients with at least as many days on study as the time point. 1 Year is taken to mean 365.25 days.

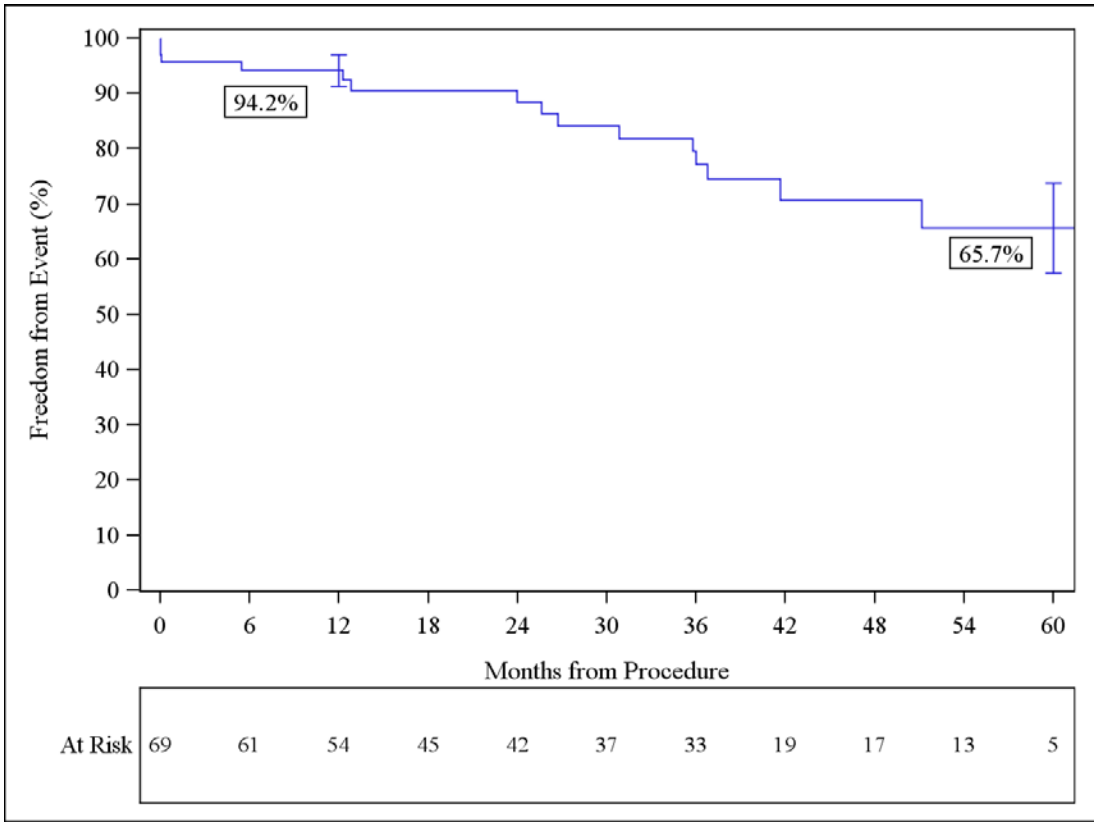
Valve Frame Fractures

No patient had a study valve frame fracture.

Valve Dysfunction

Valve dysfunction is a non-hierarchical composite of all-cause mortality, surgical pulmonary valve replacement, valve frame fracture, recurrent pulmonary stenosis, moderate/severe regurgitation and reintervention. Clinical Figure 4 presents the freedom from valve dysfunction, which was 94.2% at 1 year and 65.7% at 5 years.

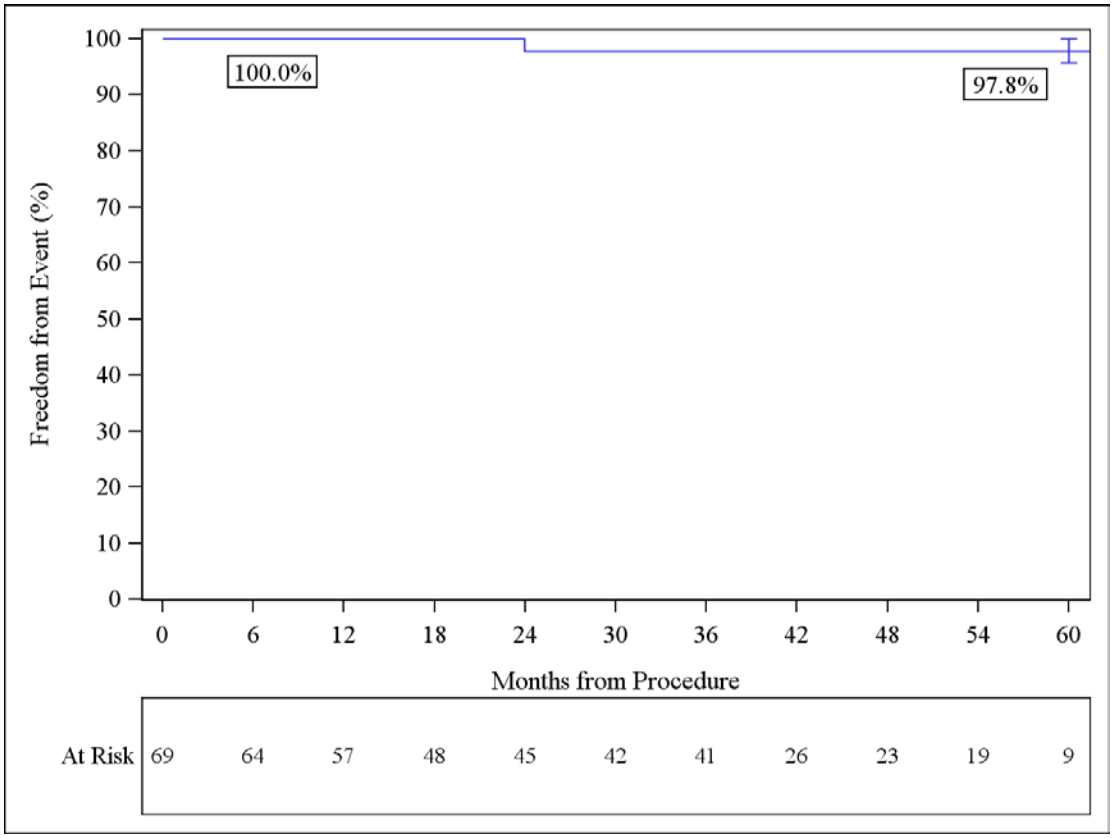
Clinical Figure 4: Freedom from Valve Dysfunction to 5 Years (Valve Implant Population)



All Cause Mortality

Clinical Figure 5 presents the freedom from all-cause mortality for the valve implant population, which was 100% at 1 year and 97.8% at 5 years.

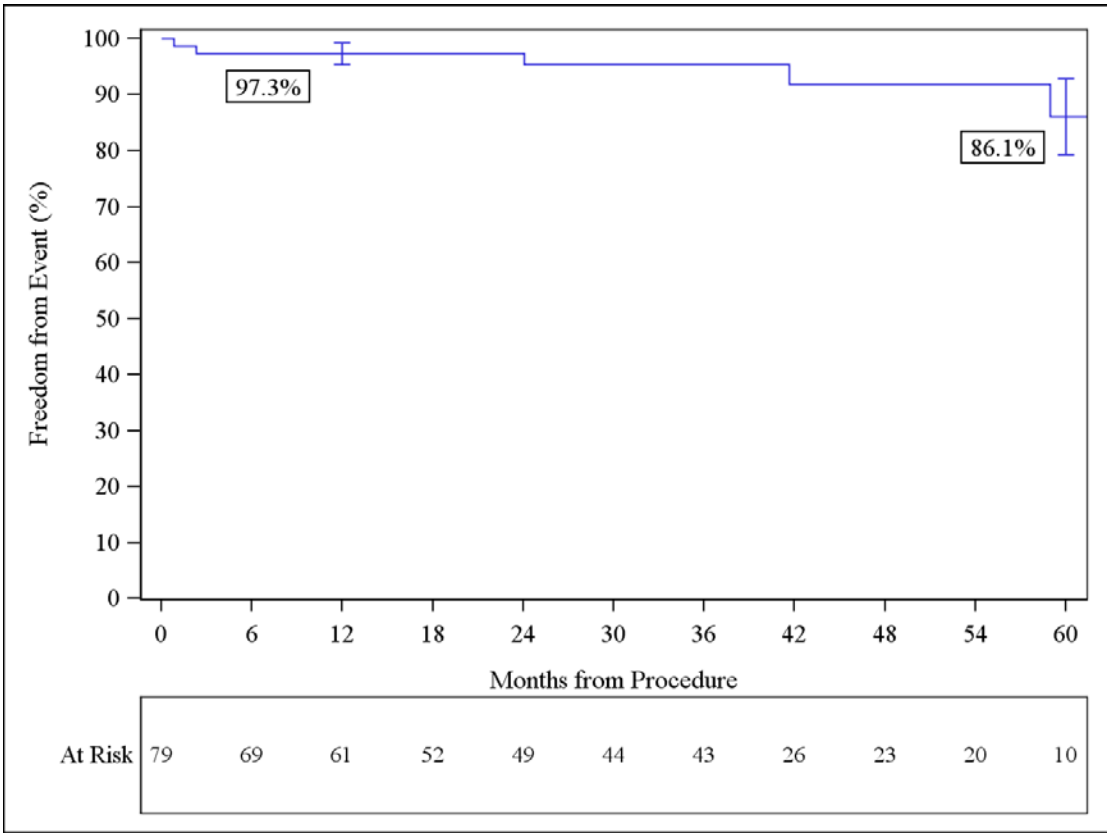
Clinical Figure 5: Freedom from All-Cause Mortality to 5 Years (Valve Implant Population)



Endocarditis

Clinical Figure 6 presents the freedom from endocarditis for the safety population, which was 97.3% at 1 year and 86.1% at 5 years. Patients that were pre-stented had an observed rate of endocarditis of 4.2% (3/71) whereas patients that were not pre-stented had no reported endocarditis (0/7). Due to the small number of patients that were not pre-stented, no statistical conclusions may be made from this data.

Clinical Figure 6: Freedom from Endocarditis at 5 Years (Safety Population, N=79)



Subgroup Analyses

By Pre-stenting

Pre-stenting of the RVOT conduit for the SAPIEN THV was performed during the IDE study, at the discretion of the treating physician. The protocol did not specify any criteria for how or when to perform the pre-stenting procedure. Therefore, the data presented below represents the outcomes of subjects who were implanted with a variety (in number and type) of stents along with the SAPIEN THV.

In total, 91.0% (71/78) of patients had pre-stenting of the RVOT conduit, either prior to or during the implant procedure. Clinical Table 8 below shows the site-reported serious adverse events from the COMPASSION trial stratified by pre-stenting status. Note that this study was not designed to investigate the differences in outcomes between patients with and without pre-stenting, nor was it designed to investigate whether stents used to pre-stent the RVOT conduit are safe and effective for this use.

Clinical Table 8: Incidence of Site-Reported Serious Adverse Events by Study Visit By Stenting (Safety Population)

	No Stent (N=7)						Stented (N=71)					
	<= 30 Days		31 – 365 Days		All Events		<= 30 Days		31 – 365 Days		All Events	
Adverse Event	**Events**	**Patients with Event**	**Events**	**Patients with Event**	**Events**	**Patients with Event**	**Events**	**Patients with Event**	**Events**	**Patients with Event**	**Events**	**Patients with Event**
Any Serious Adverse Event	1	1/7(14.3%)	0	0/7 (0.0%)	5	3/7 (42.9%)	27	21/ 71 (29.6%)	22	13/ 71 (18.3%)	125	34/ 71 (47.9%)
Other	0	0/7(0.0%)	0	0/7 (0.0%)	1	1/7 (14.3%)	1	1/ 71 (1.4%)	10	6/ 71 (8.5%)	35	11/ 71 (15.5%)
Infection (excluding endocarditis)	0	0/7(0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	1	1/ 71 (1.4%)	3	3/ 71 (4.2%)	12	7/ 71 (9.9%)
CHF	0	0/7(0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	1	1/ 71 (1.4%)	0	0/ 71 (0.0%)	11	4/ 71 (5.6%)
Electrolyte and/or CBC and platelet counts abnormal	0	0/7(0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	1	1/ 71 (1.4%)	2	1/ 71 (1.4%)	11	2/ 71 (2.8%)
Valve stenosis	0	0/7(0.0%)	0	0/7 (0.0%)	2	1/7 (14.3%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)	7	5/ 71 (7.0%)
Arrhythmia	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	2	2/ 71 (2.8%)	0	0/ 71 (0.0%)	8	6/ 71 (8.5%)
Pulmonary artery perforation – rupture of RVOT conduit	1	1/7 (14.3%)	0	0/7 (0.0%)	1	1/7 (14.3%)	4	4/ 71 (5.6%)	0	0/ 71 (0.0%)	4	4/ 71 (5.6%)
Endocarditis	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	1	1/ 71 (1.4%)	2	2/ 71 (2.8%)	4	3/ 71 (4.2%)
Fever	0	0/7(0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	3	3/ 71 (4.2%)	0	0/ 71 (0.0%)	4	4/ 71 (5.6%)
Hemorrhage requiring transfusion	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	2	2/ 71 (2.8%)	1	1/ 71 (1.4%)	3	3/ 71 (4.2%)
Syncope	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/ 71 (0.0%)	0	0/ 71 (0.0%)	3	3/ 71 (4.2%)
Valve damage or dysfunction	0	0/7 (0.0%)	0	0/7 (0.0%)	1	1/7 (14.3%)	2	2/ 71 (2.8%)	0	0/ 71 (0.0%)	2	2/ 71 (2.8%)
Device migration	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	2	2/ 71 (2.8%)	0	0/ 71 (0.0%)	2	2/ 71 (2.8%)
Hematoma	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	2	2/ 71 (2.8%)	0	0/ 71 (0.0%)	2	2/ 71 (2.8%)
Respiratory complication	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	1	1/ 71 (1.4%)	0	0/ 71 (0.0%)	2	2/ 71 (2.8%)
Anemia	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)	1	1/ 71 (1.4%)
Angina	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/ 71 (0.0%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)

Clinical Table 8: Incidence of Site-Reported Serious Adverse Events by Study Visit By Stenting (Safety Population)												
	No Stent (N=7)						Stented (N=71)					
	<= 30 Days		31 – 365 Days		All Events		<= 30 Days		31 – 365 Days		All Events	
Adverse Event	**Events**	**Patients with Event**	**Events**	**Patients with Event**	**Events**	**Patients with Event**	**Events**	**Patients with Event**	**Events**	**Patients with Event**	**Events**	**Patients with Event**
Atelectasis	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	1	1/ 71 (1.4%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)
Bleeding Event	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	1	1/ 71 (1.4%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)
Dyspnea	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/ 71 (0.0%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)
Embolism: air or thrombus	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)	1	1/ 71 (1.4%)
Hemolysis	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)	1	1/ 71 (1.4%)
Hemorrhagic event	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/ 71 (0.0%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)
Hypotension	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	1	1/ 71 (1.4%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)
Ischemia	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/ 71 (0.0%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)
MI	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/ 71 (0.0%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)
Neurological Event (including TIA, stroke and psychomotor deficit)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/ 71 (0.0%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)
Non-emergent reoperation	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/ 71 (0.0%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)
Nonstructural valve dysfunction	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	1	1/ 71 (1.4%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)
Thromboembolism	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/7 (0.0%)	0	0/ 71 (0.0%)	0	0/ 71 (0.0%)	1	1/ 71 (1.4%)

Summary statistics:
Categorical measures-No. / Total no. (%)
Seriousness was determined by the CEC for these events if they have been adjudicated and the site otherwise.
Note: The rates given in the All Events columns are cumulative based on all events reported by all patients up to their current follow up time including 10 patients reaching the 5 year follow up.

By Patient Age

Clinical Table 9 shows the site-reported serious adverse events grouped by age at baseline (≤ 21 or ≥ 22 years of age). Note that this study was not designed to investigate the differences in outcomes between age groups.

Clinical Table 9: Incidence of Site-Reported Serious Adverse Events by Study Visit by Baseline Age Group (Safety Population)

	Age 21 or Younger (N=29)						Age 22 or Older (N=50)					
	<= 30 Days		31 – 365 Days		All Events		<= 30 Days		31 – 365 Days		All Events	
Adverse Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event
Any Serious Adverse Event	11	8/29 (27.6%)	4	4/29 (13.8%)	35	15/29 (51.7%)	18	15/50 (30.0%)	18	9/50 (18.0%)	97	23/50 (46.0%)
Other	0	0/29 (0.0%)	1	1/29 (3.4%)	8	3/29 (10.3%)	2	2/50 (4.0%)	9	5/50 (10.0%)	29	10/50 (20.0%)
Infection (excluding endocarditis)	1	1/29 (3.4%)	1	1/29 (3.4%)	2	2/29 (6.9%)	0	0/50 (0.0%)	2	2/50 (4.0%)	10	5/50 (10.0%)
CHF	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	1	1/50 (2.0%)	0	0/50 (0.0%)	11	4/50 (8.0%)
Electrolyte and/or CBC and platelet counts abnormal	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	1	1/50 (2.0%)	2	1/50 (2.0%)	11	2/50 (4.0%)
Valve stenosis	0	0/29 (0.0%)	1	1/29 (3.4%)	5	4/29 (13.8%)	0	0/50 (0.0%)	0	0/50 (0.0%)	4	2/50 (4.0%)
Arrhythmia	0	0/29 (0.0%)	0	0/29 (0.0%)	1	1/29 (3.4%)	2	2/50 (4.0%)	0	0/50 (0.0%)	7	5/50 (10.0%)
Endocarditis	1	1/29 (3.4%)	1	1/29 (3.4%)	3	2/29 (6.9%)	0	0/50 (0.0%)	1	1/50 (2.0%)	2	2/50 (4.0%)
Pulmonary artery perforation – rupture of RVOT conduit	2	2/29 (6.9%)	0	0/29 (0.0%)	2	2/29 (6.9%)	3	3/50 (6.0%)	0	0/50 (0.0%)	3	3/50 (6.0%)
Fever	2	2/29 (6.9%)	0	0/29 (0.0%)	3	3/29 (10.3%)	1	1/50 (2.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)
Hemorrhage requiring transfusion	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	2	2/50 (4.0%)	1	1/50 (2.0%)	3	3/50 (6.0%)
Syncope	0	0/29 (0.0%)	0	0/29 (0.0%)	2	2/29 (6.9%)	0	0/50 (0.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)
Valve damage or dysfunction	1	1/29 (3.4%)	0	0/29 (0.0%)	2	2/29 (6.9%)	1	1/50 (2.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)
Device migration	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	2	2/50 (4.0%)	0	0/50 (0.0%)	2	2/50 (4.0%)
Hematoma	2	2/29 (6.9%)	0	0/29 (0.0%)	2	2/29 (6.9%)	0	0/50 (0.0%)	0	0/50 (0.0%)	0	0/50 (0.0%)
Respiratory complication	0	0/29 (0.0%)	0	0/29 (0.0%)	1	1/29 (3.4%)	1	1/50 (2.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)
Anemia	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)	1	1/50 (2.0%)
Angina	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/50 (0.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)
Atelectasis	1	1/29 (3.4%)	0	0/29 (0.0%)	1	1/29 (3.4%)	0	0/50 (0.0%)	0	0/50 (0.0%)	0	0/50 (0.0%)
Bleeding Event	1	1/29 (3.4%)	0	0/29 (0.0%)	1	1/29 (3.4%)	0	0/50 (0.0%)	0	0/50 (0.0%)	0	0/50 (0.0%)
Dyspnea	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/50 (0.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)
Embolism: air or thrombus	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)	1	1/50 (2.0%)
Hemolysis	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)	1	1/50 (2.0%)

Clinical Table 9: Incidence of Site-Reported Serious Adverse Events by Study Visit by Baseline Age Group (Safety Population)												
	Age 21 or Younger (N=29)						Age 22 or Older (N=50)					
	<= 30 Days		31 – 365 Days		All Events		<= 30 Days		31 – 365 Days		All Events	
Adverse Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event
Hemorrhagic event	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/50 (0.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)
Hypotension	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	1	1/50 (2.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)
Ischemia	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/50 (0.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)
MI	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/50 (0.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)
Neurological Event (including TIA, stroke and psychomotor deficit)	0	0/29 (0.0%)	0	0/29 (0.0%)	1	1/29 (3.4%)	0	0/50 (0.0%)	0	0/50 (0.0%)	0	0/50 (0.0%)
Non-emergent reoperation	0	0/29 (0.0%)	0	0/29 (0.0%)	1	1/29 (3.4%)	0	0/50 (0.0%)	0	0/50 (0.0%)	0	0/50 (0.0%)
Nonstructural valve dysfunction	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	1	1/50 (2.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)
Thromboembolism	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/29 (0.0%)	0	0/50 (0.0%)	0	0/50 (0.0%)	1	1/50 (2.0%)

Summary statistics:
Categorical measures-No. / Total no. (%)
Seriousness was determined by the CEC for these events if they have been adjudicated and the site otherwise.
Note: The rates given in the All Events columns are cumulative based on all events reported by all patients up to their current follow up time including 10 patients reaching the 5 year follow up.

Clinical Table 10 presents a summary of freedom from CEC-adjudicated MACCE by baseline age group for the VI population.

Clinical Table 10: Summary of Freedom from CEC-Adjudicated MACCE by Baseline Age Group (VI Population)

Age group	Adverse Event	Kaplan-Meier Survival Estimate [1]						
		30 Days (Patients at risk=69) [4]	6 Months (Patients at risk=64) [4]	1 Year (Patients at risk=57) [4]	2 Year (Patients at risk=45) [4]	3 Years (Patients at risk=41) [4]	4 Years (Patients at risk=23) [4]	5 Years (Patients at risk=9) [4]
Age 21 or Younger (N=27)	MACCE [2]	0.963	0.963	0.963	0.963	0.856	0.770	0.642
	All-Cause Mortality	1.000	1.000	1.000	1.000	1.000	1.000	1.000
	Myocardial infarction	1.000	1.000	1.000	1.000	1.000	1.000	1.000
	Reintervention	0.963	0.963	0.963	0.963	0.856	0.770	0.642
	Vascular Injury [3]	1.000	1.000	1.000	1.000	1.000	1.000	1.000
	Stroke	1.000	1.000	1.000	1.000	1.000	1.000	1.000
	Pulmonary embolism	1.000	1.000	1.000	1.000	1.000	1.000	1.000
Age 22 or Older (N=42)	MACCE [2]	0.976	0.928	0.928	0.891	0.806	0.744	0.744
	All-Cause Mortality	1.000	1.000	1.000	0.963	0.963	0.963	0.963
	Myocardial infarction	1.000	1.000	1.000	1.000	0.957	0.957	0.957
	Reintervention	0.976	0.976	0.976	0.976	0.934	0.871	0.871
	Vascular Injury [3]	1.000	0.976	0.976	0.976	0.976	0.976	0.976
	Stroke	1.000	1.000	1.000	1.000	1.000	1.000	1.000
	Pulmonary embolism	1.000	0.976	0.976	0.976	0.976	0.976	0.976

[1] Kaplan-Meier survival estimates are calculated at each time point and use the first event per patient. 6 months is taken to mean 180 days, and 1 year is taken to mean 365.25 days. Events occurring after the time point are not included in the analysis.

[2] MACCE is a non-hierarchical composite of the following events: All-cause mortality, myocardial infarction, reintervention, vascular injury, stroke, and pulmonary embolism

[3] Vascular injury resulting in the need for an unplanned vascular intervention

[4] Patients at risk are the number of patients with at least as many days on study as the time point. 1 Year is taken to mean 365.25 days.

Clinical Table 11 presents overall functional improvement at 6 months by baseline age group in the VI population.

Clinical Table 11: Functional Improvement at 6 Months by Baseline Age Group (VI Population)		
Functional Improvement	**Age 21 or Younger (N=27)**	**Age 22 or Older (N=42)**
Overall Functional Improvement [1]	17 / 22 (77.3%)	34 / 36 (94.4%)
Improved Valve Function [a]	19 / 20 (95.0%)	32 / 33 (97.0%)
Functional Improvement in NYHA [b]	11 / 14 (78.6%)	36 / 37 (97.3%)
Freedom from Recurrent Pulmonary Stenosis [c]	21 / 21 (100.0%)	35 / 35 (100.0%)
Improved Gradient [d]	7 / 8 (87.5%)	8 / 8 (100.0%)

Categorical measures-No. / Total no. (%)
[1] Overall functional improvement, as defined by the following 4 categories:
a) Improved valve function demonstrated by a decrease in pulmonary regurgitation (PR) to mild or less (<= 2+) per TTE at 6 months for patients with moderate or more (> 2+) PR at baseline
b) Functional improvement from baseline of >= 1 NYHA functional class at 6 months for patients with baseline NYHA functional class >= 2
c) Freedom from recurrent pulmonary stenosis at 6 months
d) Improved valve function demonstrated by a decrease in pulmonary stenosis mean gradient to <30mmHg for patients with pulmonary stenosis mean gradient >30mmHg at baseline.
Patients with mild or less (<= 2+) pulmonary regurgitation at baseline only use categories b, c, and d to determine overall functional improvement. Patients with NYHA functional class of <2 at baseline only use categories a, c, and d to determine overall functional improvement. Patients treated for indications other than pulmonary stenosis only use categories a, b, and d for overall functional improvement. Patients with pulmonary stenosis mean gradient <30mmHg at baseline only use categories a, b, and c for overall functional improvement.

Clinical Table 12 presents the improved valve function at 6 months in patients with high gradient at baseline by baseline age group for the VI population.

Clinical Table 12: Improved Valve Function at 6 Months in Patients with Mean Gradient > 30 mmHg at Baseline by Baseline Age Group (VI Population)		
Mean Gradient	**Age 21 or Younger (N=8)**	**Age 22 or Older (N=8)**
Responder at 6 months [1]	7 / 8 (87.5%)	8 / 8 (100.0%)

Categorical measures-No. / Total no. (%)
[1] Mean gradient < 30mmHg at 6 months.

Of the patients who had NYHA functional class ≥ 2 at baseline, Clinical Table 13 shows the patients with improvement of at least one NYHA functional class.

Clinical Table 13: Improved NYHA Functional Class at 6 Months in Patients with Baseline NYHA Functional Class ≥ 2 by Baseline Age Group (VI Population)		
NYHA Functional Class Change from Baseline	**Age 21 or Younger (N=16)**	**Age 22 or Older (N=38)**
Responder at 6 months [1]	11 / 14 (78.6%)	36 / 37 (97.3%)

Categorical measures-No. / Total no. (%)
[1] NYHA functional class improvement of at least 1 class at 6 months.

Clinical Table 14 presents the overall functional improvement through 5 years of follow-up by age group for the VI population.

Clinical Table 14: Functional Improvement at Follow-Up by Age Group (VI Population)								
Age Group	**Functional Improvement**	**30 Days**	**6 Months**	**1 Year**	**2 Years**	**3 Years**	**4 Years**	**5 Years**
Age 21 or Younger (N=27)	Overall Functional Improvement [1]	23 / 26 (88.5%)	17 / 22 (77.3%)	18 / 21 (85.7%)	15 / 19 (78.9%)	13 / 18 (72.2%)	4 / 7 (57.1%)	3 / 7 (42.9%)
	Improved Valve Function [a]	21 / 22 (95.5%)	19 / 20 (95.0%)	19 / 19 (100.0%)	15 / 16 (93.8%)	13 / 15 (86.7%)	5 / 5 (100.0%)	5 / 5 (100.0%)
	Functional Improvement in NYHA [b]	14 / 16 (87.5%)	11 / 14 (78.6%)	13 / 14 (92.9%)	11 / 12 (91.7%)	11 / 12 (91.7%)	3 / 3 (100.0%)	4 / 4 (100.0%)
	Freedom from Recurrent Pulmonary Stenosis [c]	24 / 24 (100.0%)	21 / 21 (100.0%)	18 / 19 (94.7%)	17 / 18 (94.4%)	16 / 18 (88.9%)	6 / 9 (66.7%)	5 / 9 (55.6%)
	Improved Gradient [d]	9 / 10 (90.0%)	7 / 8 (87.5%)	7 / 8 (87.5%)	6 / 7 (85.7%)	5 / 6 (83.3%)	3 / 3 (100.0%)	3 / 3 (100.0%)
Age 22 or Older (N=42)	Overall Functional Improvement [1]	34 / 40 (85.0%)	34 / 36 (94.4%)	29 / 33 (87.9%)	20 / 23 (87.0%)	18 / 20 (90.0%)	8 / 11 (72.7%)	5 / 8 (62.5%)
	Improved Valve Function [a]	37 / 37 (100.0%)	32 / 33 (97.0%)	28 / 30 (93.3%)	20 / 20 (100.0%)	17 / 18 (94.4%)	7 / 7 (100.0%)	6 / 6 (100.0%)
	Functional Improvement in NYHA [b]	33 / 38 (86.8%)	36 / 37 (97.3%)	32 / 33 (97.0%)	23 / 24 (95.8%)	20 / 20 (100.0%)	12 / 13 (92.3%)	8 / 8 (100.0%)
	Freedom from Recurrent Pulmonary Stenosis [c]	36 / 36 (100.0%)	35 / 35 (100.0%)	31 / 31 (100.0%)	20 / 21 (95.2%)	16 / 18 (88.9%)	8 / 11 (72.7%)	7 / 10 (70.0%)
	Improved Gradient [d]	7 / 8 (87.5%)	8 / 8 (100.0%)	7 / 8 (87.5%)	2 / 3 (66.7%)	3 / 3 (100.0%)	2 / 2 (100.0%)	2 / 2 (100.0%)

Categorical measures-No. / Total no. (%)
[1] Overall functional improvement, as defined by the following 4 categories:
a) Improved valve function demonstrated by a decrease in pulmonary regurgitation (PR) to mild or less per TTE at visit for patients with moderate or more (> 2) PR at baseline
b) Functional improvement from baseline of >= 1 NYHA functional class at visit for patients with baseline NYHA functional class >=2
c) Freedom from recurrent pulmonary stenosis at visit
d) Improved valve function demonstrated by a decrease in pulmonary stenosis mean gradient to <30mmHg for patients with pulmonary stenosis mean gradient >30mmHg at baseline.
Patients with mild or less (<= 2+) pulmonary regurgitation at baseline only use categories b, c, and d to determine overall functional improvement. Patients with NYHA functional class of <2 at baseline only use categories a, c, and d to determine overall functional improvement. Patients treated for indications other than pulmonary stenosis only use categories a, b, and d for overall functional improvement. Patients with pulmonary stenosis mean gradient <30mmHg at baseline only use categories a, b, and c for overall functional improvement.

By Valve Size

Clinical table 10 shows the site-reported serious adverse events stratified by valve size. Note that this study was not designed to investigate the differences in outcomes between valve sizes. Also note that the 29 mm valve size was not evaluated in this study.

Clinical Table 15: Incidence of Site-Reported Serious Adverse Events by Study Visit By Valve Size (Safety Population)

	23 mm Valve (N=48)						26 mm Valve (N=22)					
	<= 30 Days		31 – 365 Days		All Events		<= 30 Days		31 – 365 Days		All Events	
Adverse Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event
Any Serious Adverse Event	11	7/48 (14.6%)	9	7/48 (14.6%)	49	19/48 (39.6%)	12	10/22 (45.5%)	10	4/22 (18.2%)	72	13/22 (59.1%)
Other	0	0/48 (0.0%)	4	2/48 (4.2%)	12	5/48 (10.4%)	0	0/22 (0.0%)	5	3/22 (13.6%)	22	5/22 (22.7%)
Electrolyte and/or CBC and platelet counts abnormal	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/48 (0.0%)	1	1/22 (4.5%)	2	1/22 (4.5%)	11	2/22 (9.1%)
Infection (excluding endocarditis)	0	0/48 (0.0%)	1	1/48 (2.1%)	2	2/48 (4.2%)	1	1/22 (4.5%)	1	1/22 (4.5%)	9	4/22 (18.2%)
CHF	0	0/48 (0.0%)	0	0/48 (0.0%)	2	1/48 (2.1%)	0	0/22 (0.0%)	0	0/22 (0.0%)	7	2/22 (9.1%)
Valve stenosis	0	0/48 (0.0%)	1	1/48 (2.1%)	7	5/48 (10.4%)	0	0/22 (0.0%)	0	0/22 (0.0%)	2	1/22 (4.5%)
Arrhythmia	0	0/48 (0.0%)	0	0/48 (0.0%)	2	2/48 (4.2%)	2	2/22 (9.1%)	0	0/22 (0.0%)	6	4/22 (18.2%)
Endocarditis	1	1/48 (2.1%)	1	1/48 (2.1%)	3	2/48 (4.2%)	0	0/22 (0.0%)	1	1/22 (4.5%)	1	1/22 (4.5%)
Fever	1	1/48 (2.1%)	0	0/48 (0.0%)	2	2/48 (4.2%)	2	2/22 (9.1%)	0	0/22 (0.0%)	2	2/22 (9.1%)
Hemorrhage requiring transfusion	1	1/48 (2.1%)	1	1/48 (2.1%)	2	2/48 (4.2%)	1	1/22 (4.5%)	0	0/22 (0.0%)	1	1/22 (4.5%)
Syncope	0	0/48 (0.0%)	0	0/48 (0.0%)	2	2/48 (4.2%)	0	0/22 (0.0%)	0	0/22 (0.0%)	1	1/22 (4.5%)
Valve damage or dysfunction	2	2/48 (4.2%)	0	0/48 (0.0%)	3	3/48 (6.3%)	0	0/22 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)
Device migration	1	1/48 (2.1%)	0	0/48 (0.0%)	1	1/48 (2.1%)	1	1/22 (4.5%)	0	0/22 (0.0%)	1	1/22 (4.5%)
Hematoma	1	1/48 (2.1%)	0	0/48 (0.0%)	1	1/48 (2.1%)	1	1/22 (4.5%)	0	0/22 (0.0%)	1	1/22 (4.5%)
Pulmonary artery perforation – rupture of RVOT conduit	1	1/48 (2.1%)	0	0/48 (0.0%)	1	1/48 (2.1%)	1	1/22 (4.5%)	0	0/22 (0.0%)	1	1/22 (4.5%)
Respiratory complication	1	1/48 (2.1%)	0	0/48 (0.0%)	2	2/48 (4.2%)	0	0/22 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)
Angina	0	0/48 (0.0%)	0	0/48 (0.0%)	1	1/48 (2.1%)	0	0/22 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)
Atelectasis	1	1/48 (2.1%)	0	0/48 (0.0%)	1	1/48 (2.1%)	0	0/22 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)
Bleeding Event	1	1/48 (2.1%)	0	0/48 (0.0%)	1	1/48 (2.1%)	0	0/22 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)
Dyspnea	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)	1	1/22 (4.5%)
Embolism: air or thrombus	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/22 (0.0%)	1	1/22 (4.5%)	1	1/22 (4.5%)
Hemolysis	0	0/48 (0.0%)	1	1/48 (2.1%)	1	1/48 (2.1%)	0	0/22 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)
Hemorrhagic event	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)	1	1/22 (4.5%)

Clinical Table 15: Incidence of Site-Reported Serious Adverse Events by Study Visit By Valve Size (Safety Population)												
	23 mm Valve (N=48)						26 mm Valve (N=22)					
	<= 30 Days		31 – 365 Days		All Events		<= 30 Days		31 – 365 Days		All Events	
Adverse Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event
Hypotension	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/48 (0.0%)	1	1/22 (4.5%)	0	0/22 (0.0%)	1	1/22 (4.5%)
Ischemia	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)	1	1/22 (4.5%)
MI	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)	1	1/22 (4.5%)
Neurological Event (including TIA, stroke and psychomotor deficit)	0	0/48 (0.0%)	0	0/48 (0.0%)	1	1/48 (2.1%)	0	0/22 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)
Non-emergent reoperation	0	0/48 (0.0%)	0	0/48 (0.0%)	1	1/48 (2.1%)	0	0/22 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)
Nonstructural valve dysfunction	0	0/48 (0.0%)	0	0/48 (0.0%)	0	0/48 (0.0%)	1	1/22 (4.5%)	0	0/22 (0.0%)	1	1/22 (4.5%)
Thromboembolism	0	0/48 (0.0%)	0	0/48 (0.0%)	1	1/48 (2.1%)	0	0/22 (0.0%)	0	0/22 (0.0%)	0	0/22 (0.0%)

Summary statistics:
Categorical measures-No. / Total no. (%)
Seriousness was determined by the CEC for these events if they have been adjudicated and the site otherwise.
Note: The rates given in the All Events columns are cumulative based on all events reported by all patients up to their current follow up time including 10 patients reaching the 5 year follow up.

Clinical Table 16 presents a summary of freedom from CEC-adjudicated device- or procedure-related death and/or reintervention by valve size for the VI population.

Clinical Table 16: Summary of Freedom from CEC-Adjudicated Device- or Procedure-Related Death and/or Reintervention by Valve Size (VI Population)							
		Kaplan-Meier Survival Estimate [1]						
Valve Size	Adverse Event	30 Days (Patients at risk=69) [2]	6 Months (Patients at risk=64) [2]	1 Year (Patients at risk=57) [2]	2 Year (Patients at risk=45) [2]	3 Years (Patients at risk=41) [2]	4 Years (Patients at risk=23) [2]	5 Years (Patients at risk=9) [2]
23mm (N=47)	Device or Procedure Related Death or Reintervention	0.979	0.979	0.979	0.979	0.874	0.822	0.754
	Device or Procedure Related Death	1.000	1.000	1.000	1.000	1.000	1.000	1.000
	Reintervention	0.979	0.979	0.979	0.979	0.874	0.822	0.754
26mm (N=22)	Device or Procedure Related Death or Reintervention	0.955	0.955	0.955	0.955	0.955	0.818	0.818
	Device or Procedure Related Death	1.000	1.000	1.000	1.000	1.000	1.000	1.000
	Reintervention	0.955	0.955	0.955	0.955	0.955	0.818	0.818

[1] Kaplan-Meier survival estimates are calculated at each study visit. 6 Months is taken to be 180 days and 1 year is taken to be 365.25 days. Events that occur after the time point are not included in the analysis.
[2] Patients at risk are the number of patients with at least as many days on study as the time point. 1 Year is taken to mean 365.25 days.

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