Edwards SAPIEN 3 Transcatheter Heart Valve System
Edwards SAPIEN 3 Transcatheter Heart Valve
Edwards Commander Delivery System

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 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 valve is supplied sterilized with glutaraldehyde solution. The delivery system, sheath, and crimper are supplied sterilized with ethylene oxide gas.

1.0 Device Description

Edwards SAPIEN 3 Transcatheter Heart Valve System

The Edwards SAPIEN 3 transcatheter heart valve (THV) system, used for the pulmonic indication, consists of the Edwards SAPIEN 3 transcatheter heart valve, Edwards Commander delivery system, and accessories.

- **Edwards SAPIEN 3 Transcatheter Heart Valve (Figure 1)**

The Edwards SAPIEN 3 transcatheter heart valve (THV) is comprised of a balloon-expandable, radiopaque, cobalt-chromium frame, a trileaflet bovine pericardial tissue valve, and polyethylene terephthalate (PET) fabric skirt. The leaflets are treated according to the Carpentier-Edwards ThermaFix process.

9600TFX

Figure 1. Edwards SAPIEN 3 Transcatheter Heart Valve

Table 1

Valve Size	Valve Height
20 mm	15.5 mm
23 mm	18 mm
26 mm	20 mm
29 mm	22.5 mm

Sizing recommendations for the Edwards SAPIEN 3 transcatheter heart valve in non-compliant Right Ventricular Outflow Tract (RVOT) conduits using balloon sizing are shown in the table below:

Table 2: Valve Sizing in RVOT Conduit

Landing Zone Diameter	SAPIEN 3 Valve Size
16.5 – 20.0 mm	20 mm
20.0 – 23.0 mm	23 mm
23.0 – 26.0 mm	26 mm
26.0 – 29.0 mm	29 mm

Note: For a failing stentless bioprosthesis, consider sizing recommendations for a non-compliant Right Ventricular Outflow Tract (RVOT) conduit landing zone.

Sizing recommendations for implanting the Edwards SAPIEN 3 transcatheter heart valve for THV-in-surgical valve procedures for bioprosthesis based on a True Inner Diameter (True ID) are shown in the table below:

Table 3: Valve Sizing in Failed Bioprosthesis

Surgical Valve True ID[1]	SAPIEN 3 Valve Size
16.5 – 19.0 mm	20 mm
18.5 – 22.0 mm	23 mm
22.0 – 25.0 mm	26 mm
25.0 – 28.5 mm	29 mm

NOTE: The dimensions of the failed bioprosthesis should be determined so that the appropriate valve size can be implanted; and is best determined by using balloon sizing and/or computed tomography to perform the necessary measurements. Surgical valve 'True ID' may be smaller than the labeled valve size.

NOTE: Exact volume required to deploy the valve may vary depending on the bioprosthesis inner diameter. Factors such as calcification and pannus tissue growth may not be accurately visualized in imaging and may reduce the effective inner diameter of the failing bioprosthesis to a size smaller than the 'True ID'. These factors should be considered and assessed in order to determine the most appropriate valve size to achieve nominal valve deployment and sufficient anchoring. Do not exceed the rated burst pressure. See Table 4 for inflation parameters.

- **Edwards Commander Delivery System (Figure 2)**

The Edwards Commander delivery system facilitates the placement of the bioprosthesis. It consists of a Flex Catheter to aid in valve alignment to the balloon, tracking, and positioning of the valve. The delivery system includes a tapered tip to facilitate crossing of the valve. The handle contains a Flex Wheel to control flexing of the Flex Catheter, and a Balloon Lock and Fine Adjustment Wheel to facilitate valve alignment and positioning of the valve within the target location. A stylet is included within the guidewire lumen of the delivery system. The Balloon Catheter has radiopaque Valve Alignment Markers defining the working length of the balloon. A radiopaque Center Marker in the balloon is provided to help with valve positioning. A radiopaque Triple Marker proximal to the balloon indicates the Flex Catheter position during deployment. The inflation parameters for valve deployment are shown in the table below:

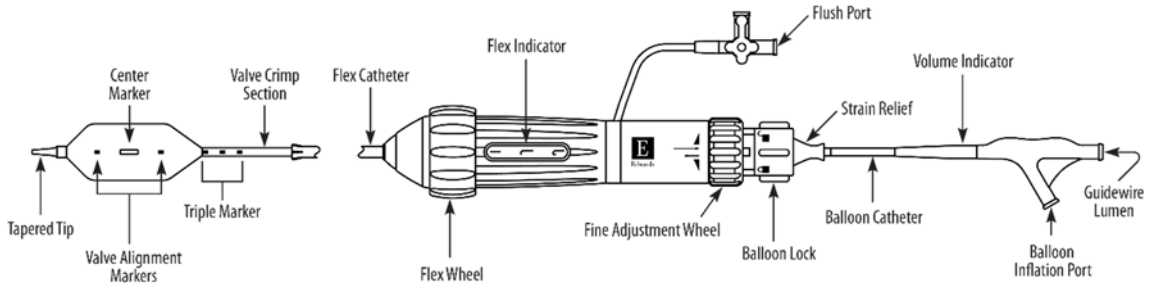


Figure 2. Edwards Commander Delivery System

Table 4

Model	Nominal Balloon Diameter	Nominal Inflation Volume	Rated Burst Pressure (RBP)
9600LDS20	20 mm	11 mL	7 atm
9600LDS23	23 mm	17 mL	7 atm
9600LDS26	26 mm	23 mL	7 atm
9600LDS29	29 mm	33 mL	7 atm

Additional Accessories

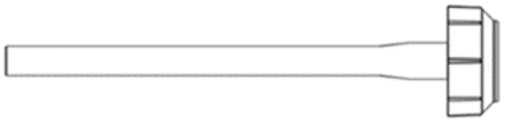


Figure 3. Loader

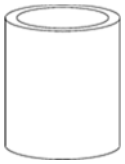


Figure 4. Qualcrimp Crimping Accessory

- **Loader**

The loader allows for the delivery of the crimped valve through the hemostasis valves of the sheath.

- **Edwards Sheath**

Refer to the provided Edwards sheath instructions for use (IFU) for device description.

- **Edwards Crimper**

Refer to the Edwards Crimper instructions for use for device description.

2.0 Indications

The Edwards SAPIEN 3 Transcatheter Heart Valve (THV) System with Edwards Commander Delivery System is indicated for use in the management of pediatric and adult patients who have a clinical indication for intervention on a dysfunctional right ventricular outflow tract (RVOT) conduit or surgical bioprosthetic valve in the pulmonic position with ≥ moderate regurgitation and/or a mean RVOT gradient of ≥ 35 mmHg.

3.0 Contraindications

The Edwards SAPIEN 3 THV System with Edwards Commander Delivery System is contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections.

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.
- Correct sizing of the valve into the non-compliant RVOT conduit or failing bioprosthesis (landing zone) is essential to minimize risks. Too small of a valve may result in paravalvular leak, migration, or valve embolization; whereas too large of a valve may result in residual gradient (patient-prosthesis mismatch) or RVOT rupture.
- Accelerated deterioration of the valve may occur in patients with an altered calcium metabolism.
- Assessment for coronary compression risk prior to valve implantation is essential to prevent the risk of severe patient harm.
- The physician must verify correct orientation of the valve prior to its implantation; the inflow (outer skirt end) of the valve should be oriented towards the proximal end (handle) of the delivery system to prevent the risk of severe patient harm.
- Prior to delivery, the valve must remain hydrated at all times and cannot be exposed to solutions other than its shipping storage solution and sterile physiologic rinsing solution. Valve leaflets mishandled or damaged during any part of the procedure will require replacement of the valve.
- Patients with pre-existing bioprostheses should be carefully assessed prior to implantation of the valve to ensure proper valve positioning and deployment.
- Do not use the valve if the tamper evident seal is broken, the storage solution does not

completely cover the valve, the temperature indicator has been activated, the valve is damaged, or the expiration date has elapsed.

- Do not mishandle the 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.
- It is recommended that all prosthetic heart valve recipients be prophylactically treated for endocarditis to minimize the possibility of prosthetic valve infection.
- Valve recipients should be maintained on anticoagulant/antiplatelet therapy, except when contraindicated, 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 valve.

5.0 Precautions

- Long-term durability has not been established for the valve. Regular medical follow-up is advised to evaluate valve 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, seek immediate medical attention. For more information about glutaraldehyde exposure, refer to the Material Safety Data Sheet available from Edwards Lifesciences.
- 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.
- Patient venous anatomy should be evaluated to prevent the risk of access that would preclude the delivery and deployment of the device.
- Patient should be heparinized to maintain the ACT at ≥ 250 sec prior to introduction of the delivery system in order to prevent thrombosis.
- Safety and effectiveness have not been established for patients with the following characteristics/comorbidities:
    - Blood dyscrasias defined as: leukopenia, acute anemia, thrombocytopenia, or history of bleeding diathesis or coagulopathy
    - A known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid™), or clopidogrel (Plavix™), or sensitivity to contrast media, which cannot be adequately premedicated
    - Positive urine or serum pregnancy test in female subjects of child-bearing potential
- Residual mean gradient may be higher in a "THV-in-failing bioprosthesis" configuration than that observed following implantation of the valve inside a native annulus using the same size device. Patients with elevated mean gradient post procedure should be carefully followed. It is important that the manufacturer, model and size of the preexisting bioprosthetic valve be determined, so that the appropriate valve can be implanted and a prosthesis-patient mismatch be avoided.

Additionally, pre-procedure imaging modalities must be employed to make as accurate a determination of the inner diameter as possible.

6.0 Potential Adverse Events

Potential risks associated with the anesthesia, interventional procedure and imaging include but are not limited to:

- Death
- Stroke/transient ischemic attack
- Respiratory insufficiency or respiratory failure
- Cardiovascular or vascular injury, such as perforation or damage (dissection) of vessels, myocardium or valvular structures including rupture of the RVOT that may require intervention
- Pericardial effusion/cardiac tamponade
- Embolic event: air, calcific material, thrombus, device fragments
- Infection including incisional site infection, septicemia and endocarditis
- Myocardial infarction
- Renal insufficiency or renal failure
- Conduction system injury
- Arrhythmia
- Arteriovenous (AV) fistula
- Systemic or peripheral nerve injury
- Systemic or peripheral ischemia
- Pulmonary edema
- Pneumothorax
- Pleural effusion
- Atelectasis
- Blood loss requiring transfusion
- Anemia
- Radiation injury
- Electrolyte imbalance
- Hypertension or hypotension
- Allergic reaction to anesthesia, contrast media, antithrombotic therapy, device materials
- Hematoma or ecchymosis
- Syncope
- Pain
- Exercise intolerance or weakness
- Inflammation
- Angina
- Fever
- Cardiac failure

Potential risks associated with the valve, delivery system and/or accessories include, but may not be limited to, the following:

- Cardiac arrest
- Cardiogenic shock
- Coronary flow obstruction/transvalvular flow disturbance
- Device thrombosis requiring intervention
- Injury to tricuspid valve
- Device embolization requiring intervention
- Device acute migration or malposition requiring intervention
- Endocarditis
- Hemolysis / hemolytic anemia
- THV dysfunction resulting in pulmonary valve symptoms
- Mechanical failure of delivery system, and/or accessories
- Emergent and non-emergent re-intervention

- Dyspnea

See Section 12 for adverse events that occurred in the clinical study.

7.0 Directions for Use

7.1 System Compatibility

Table 5

Product Name	20 mm System	23 mm System	26 mm System	29 mm System
	Model			
Edwards SAPIEN 3 Transcatheter Heart Valve	9600TFX20	9600TFX23	9600TFX26	9600TFX29
Edwards Commander Delivery System	9600LDS20	9600LDS23	9600LDS26	9600LDS29
Sheath provided by Edwards Lifesciences				
Inflation device, Qualcrimp crimping accessory, Crimp Stopper and Loader provided by Edwards Lifesciences				
Edwards Crimper	9600CR			

Additional Equipment

- Other compatible sheath:

  Valve size: 20, 23, 26 mm GORE DrySeal Flex Introducer Sheath (24F, 65 cm)
  Valve size: 29 mm GORE DrySeal Flex Introducer Sheath (26F, 65 cm)

- Balloon catheter, per the discretion of the physician
- 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) stiff guidewire
- Sterile rinsing basins; physiological saline, heparinized saline, and 15% diluted radiopaque contrast medium
- Sterile table for valve and device preparation

7.2 Valve Handling and Preparation

Follow sterile technique during device preparation and implantation.

7.2.1 Valve 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: Valves 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 valve.
2	Carefully remove the valve/holder assembly from the jar without touching the tissue. Verify the valve serial identification number with the number on the jar lid and record in the patient information documents. Inspect the valve for any signs of damage to the frame or tissue.
3	Rinse the valve as follows: Place the valve in the first bowl of sterile, physiological saline. Be sure the saline solution completely covers the valve and holder. With the valve and holder submerged, slowly agitate (to gently swirl the valve and holder) back and forth for a minimum of 1 minute. Transfer the valve 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 valve should be left in the final rinse solution until needed to prevent the tissue from drying. **CAUTION: Do not allow the valve 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 valve is also to be avoided during the rinse procedure. No other objects should be placed in the rinse bowls. The valve should be kept hydrated to prevent the tissue from drying.**

7.2.2 Prepare the System

Refer to the Edwards sheath, GORE DrySeal Flex Introducer Sheath, Edwards Crimper and Edwards Balloon Catheter instructions for use for device preparation.

Step	Procedure
1	Visually inspect all the components for damage. Ensure the Edwards Commander delivery system is fully unflexed and the balloon catheter is fully advanced in the flex catheter. **WARNING: To prevent possible damage to the balloon shaft, ensure that the proximal end of the balloon shaft is not subjected to bending.**
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 replace the stylet in 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.
6	If using the Edwards provided sheath, 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. If using the GORE DrySeal Flex Introducer Sheath, proceed to step 7.
7	Fully advance the balloon catheter in the flex catheter. Peel off the proximal balloon cover over the blue section of the balloon shaft.
8	Attach a 3-way stopcock to the balloon inflation port. Fill a 50 cc or larger syringe with 15-20 mL of diluted contrast medium and attach to the 3-way stopcock.
9	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.

Step	Procedure
10	Close 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. **WARNING: Ensure there is no residual fluid left in the balloon to avoid potential difficulty with valve alignment during the procedure.**
11	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 valve, per the inflation parameters.
12	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 valve deployment.**

7.2.3 Mount and Crimp the Valve on the Delivery System

7.2.3.1 Procedure with Edwards Provided Sheath

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 valve 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 valve into the crimper aperture. Gradually crimp the valve until it fits into the Qualcrimp crimping accessory.
6	Place the Qualcrimp crimping accessory over the valve making sure the valve is parallel to the edge of the Qualcrimp crimping accessory.
7	Place the valve and Qualcrimp crimping accessory in crimper aperture. Insert the delivery system coaxially within the valve on the Valve Crimp Section (2-3 mm distal to the balloon shaft) with the orientation of the valve on the delivery system with the Inflow (outer skirt end) of the valve towards the proximal end of the delivery system.
8	Crimp the valve until it reaches the Qualcrimp stop located on the 2-piece Crimp Stopper.
9	Gently remove the Qualcrimp crimping accessory from the valve. Remove the Qualcrimp stop from the Final Stop, leaving the Final Stop in place.
10	Fully crimp the valve until it reaches the Final Stop. **NOTE: Ensure that the Valve Crimp Section remains coaxial within the valve.**
11	Repeat the full crimp of the valve two more times for a total of three full crimps.
12	Pull the balloon shaft and lock in default position.
13	Flush the loader with heparinized saline. Immediately advance the valve into the loader until the tapered tip of the delivery system is exposed. **CAUTION: To prevent possible leaflet damage, the valve should not remain fully crimped and/or in the loader for over 15 minutes.**

Step	Procedure
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 valve hydrated until ready for implantation.** **CAUTION: The physician must verify correct orientation of the valve prior to its implantation.**

7.2.3.2 Procedure with GORE DrySeal Flex Introducer Sheath

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 valve 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 valve into the crimper aperture. Gradually crimp the valve until it fits into the Qualcrimp crimping accessory.
6	Place the Qualcrimp crimping accessory over the valve making sure the valve is parallel to the edge of the Qualcrimp crimping accessory.
7	Place the valve and Qualcrimp crimping accessory in crimper aperture. Insert the delivery system coaxially within the valve on the Valve Crimp Section (2-3 mm distal to the balloon shaft) with the orientation of the valve on the delivery system with the Inflow (outer skirt end) of the valve towards the proximal end of the delivery system**.**
8	Crimp the valve until it reaches the Qualcrimp stop located on the 2-piece Crimp Stopper.
9	Gently remove the Qualcrimp crimping accessory from the valve. Remove the Qualcrimp stop from the Final Stop, leaving the Final Stop in place.
10	Fully crimp the valve until it reaches the Final Stop. **NOTE: Ensure that the Valve Crimp Section remains coaxial within the valve.**
11	Repeat the full crimp of the valve two more times for a total of three full crimps.
12	Pull the balloon shaft and lock in default position.
13	Flush the catheter with heparinized saline. **CAUTION: To prevent possible leaflet damage, the valve should not remain fully crimped and/or in the loader for over 15 minutes.**
14	Close the stopcock to the delivery system. **CAUTION: Keep valve hydrated until ready for implantation.** **CAUTION: The physician must verify correct orientation of the valve prior to its implantation.**

Step	Procedure
15	Initiate valve alignment by disengaging the Balloon Lock and pulling the balloon catheter straight back until part of the Warning Marker is visible. Do not pull past the Warning Marker. **WARNING: To prevent possible damage to the balloon shaft, ensure that the proximal end of the balloon shaft is not subjected to bending.**
16	Open the stopcock and flush the flex catheter using heparinized saline. Close the stopcock.
17	Engage the Balloon Lock.
18	Under fluoroscopy, utilize the Fine Adjustment Wheel to position the valve between the Valve Alignment Markers. **CAUTION: Do not turn the Fine Adjustment Wheel if the Balloon Lock is not engaged.** **WARNING: Do not position the valve past the distal Valve Alignment Marker. This will prevent proper valve deployment.**
19	Remove the stylet and flush the guidewire lumen of the delivery system.

7.3 Landing Zone Predilation and Valve Delivery

Landing zone predilation prior to implantation is optional as deemed appropriate by physician.

Landing zone predilation and valve delivery should be performed under local and/or general anesthesia with hemodynamic monitoring in a catheterization lab/hybrid operating room with fluoroscopic imaging 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.

7.3.1 Landing Zone Predilation (at physician's discretion)

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

CAUTION: To minimize the risk of conduit rupture, use caution when using a balloon with a diameter greater than the nominal diameter (original implant size) of the conduit for predilation of the intended deployment site.

7.3.2 Valve Delivery

7.3.2.1 Procedure with Edwards Provided Sheath

Step	Procedure
1	Gain access using standard catheterization techniques.
2	Prepare the Edwards sheath. Refer to the Edwards sheath IFU for information on device preparation and handling.
3	If necessary, predilate the vessel.
4	Introduce the sheath per its instructions for use.
5	Insert the loader assembly into the sheath until the loader stops.

Step	Procedure
6	Advance the delivery system, with the Edwards logo in the proper orientation (the delivery system articulates in a direction opposite from the flush port), through the sheath until the valve exits the sheath. Retract the loader to the proximal end of the delivery system. **NOTE: The delivery system articulates in a direction opposite from the flush port.** **CAUTION: The valve should not be advanced through the sheath if the sheath tip is not past the IVC bifurcation to minimize the risk of damage to the iliac vessel(s).** **CAUTION: To prevent possible leaflet damage, the valve should not remain in the sheath for over 5 minutes.**
7	In the vena cava, initiate valve alignment by disengaging the Balloon Lock and pulling the balloon catheter straight back until part of the Warning Marker is visible. Do not pull past the Warning Marker. **WARNING: To prevent possible damage to the balloon shaft, ensure that the proximal end of the balloon shaft is not subjected to bending.** Engage the Balloon Lock. Utilize the Fine Adjustment Wheel to position the valve between the Valve Alignment Markers. **CAUTION: Do not turn the Fine Adjustment Wheel if the Balloon Lock is not engaged.** **WARNING: Do not position the valve past the distal Valve Alignment Marker. This will prevent proper valve deployment.** **CAUTION: Maintain guidewire position during valve alignment.** **WARNING: If valve alignment is not performed in a straight section, there may be difficulties performing this step which may lead to delivery system damage and inability to inflate the balloon. Utilizing alternate fluoroscopic views may help with assessing curvature of the anatomy. If excessive tension is experienced during valve alignment, repositioning the delivery system to a different straight section of the vena cava and relieving compression (or tension) in the system will be necessary.**
8	Advance the catheter and use the Flex Wheel, if needed, and cross the landing zone. **NOTE: Verify the orientation of the Edwards logo to ensure proper articulation. The delivery system articulates in a direction opposite from the flush port.**
9	If additional working length is needed, remove the loader by unscrewing the loader cap and peeling the loader tubing from the delivery system.
10	Disengage the Balloon Lock and retract the tip of the Flex Catheter to the center of the Triple Marker. Engage the Balloon Lock.
11	Verify the correct position of the valve with respect to the landing zone.
12	As necessary, utilize the Flex Wheel to adjust the coaxial orientation of the valve and the Fine Adjustment Wheel to adjust the position of the valve.
13	Before deployment, ensure that the valve is correctly positioned between the Valve Alignment Markers and the Flex Catheter tip is locked over the Triple Marker.
14	Begin valve deployment: • Unlock the inflation device provided by Edwards Lifesciences. • Using slow controlled inflation, deploy the valve by inflating the balloon with the entire volume in the inflation device provided by Edwards Lifesciences, hold for 3 seconds and confirm that the barrel of the inflation device is empty to ensure complete inflation of the balloon. • Deflate the balloon.

7.3.2.2 Procedure with GORE DrySeal Flex Introducer Sheath

Step	Procedure
1	Gain access using standard catheterization techniques.
2	Prepare the GORE DrySeal Flex Introducer Sheath. Refer to the GORE DrySeal Flex Introducer Sheath IFU for information on device preparation and handling.
3	If necessary, predilate the vessel.
4	Introduce the sheath per its instructions for use.
5	Insert the delivery system into the sheath.
6	Advance the delivery system, with the Edwards logo in the proper orientation (the delivery system articulates in a direction opposite from the flush port), through the sheath. **NOTE: The delivery system articulates in a direction opposite from the flush port.** **CAUTION: The valve should not be advanced through the sheath if the sheath tip is not past the IVC bifurcation to minimize the risk of damage to the iliac vessel(s).** **CAUTION: To prevent possible leaflet damage, the valve should not remain in the sheath for over 5 minutes.**
7	Advance the catheter to the landing zone.
8	Expose the valve by retracting the GORE DrySeal Flex Introducer Sheath tip beyond the Triple Marker.
9	Disengage the Balloon Lock and retract the tip of the Flex Catheter to the center of the Triple Marker. Engage the Balloon Lock.
10	Verify the correct position of the valve with respect to the landing zone.
11	As necessary, utilize the Flex Wheel to adjust the coaxial orientation of the valve and the Fine Adjustment Wheel to adjust the position of the valve.
12	Before deployment, ensure that the valve is correctly positioned between the Valve Alignment Markers and the Flex Catheter tip is locked over the Triple Marker.
13	Begin valve deployment: • Unlock the inflation device provided by Edwards Lifesciences. • Using slow controlled inflation, deploy the valve by inflating the balloon with the entire volume in the inflation device provided by Edwards Lifesciences, hold for 3 seconds and confirm that the barrel of the inflation device is empty to ensure complete inflation of the balloon. • Deflate the balloon.

7.3.3 System Removal

Step	Procedure
1	Unflex the delivery system. Verify that the Flex Catheter tip is locked over the Triple Marker. If using the Edwards provided sheath, remove the delivery system from the sheath. If using the GORE DrySeal Flex Introducer Sheath, retract the sheath and delivery system into the vena cava, then remove the delivery system 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 sheath or the GORE DrySeal Flex Introducer Sheath instructions for use for device removal.
3	Close the access site.

8.0 How Supplied

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

8.1 Storage

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

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

9.0 MR Safety

MR Conditional

Non-clinical testing has demonstrated that the Edwards SAPIEN 3 transcatheter heart valve is MR Conditional. A patient with this device can be scanned safely, immediately after placement of this device under the following conditions:

- Static magnetic field of 1.5 T or 3.0 T
- 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 Edwards SAPIEN 3 transcatheter heart valve is expected to produce a maximum temperature rise of 3.0 °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 artifact obscures the device lumen in gradient echo images.

The implant has not been evaluated in MR systems other than 1.5 T or 3.0 T.

For valve-in-valve implantation or in the presence of other implants, please refer to the MRI safety information for the surgical valve or other devices prior to MR imaging.

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

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

11.0 Recovered valve and Device Disposal

The explanted valve 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 devices may be handled and disposed of in the same manner as hospital waste and biohazardous materials. There are no special risks related to the disposal of these devices.

12.0 Clinical Studies

SUMMARY OF CLINICAL STUDY

The COMPASSION S3 Trial Overview, SAPIEN 3 Valve

Patients were enrolled between July 2016 and July 2018. The database for this PMA reflected data collected through November 4, 2019.

The COMPASSION S3 study used an independent Data Safety Monitoring Board (DSMB) that was instructed to notify the applicant of any safety or compliance issues and a Clinical Events Committee (CEC) that was responsible for adjudicating endpoint-related events reported during the study. An independent echocardiographic core laboratory was used for standardized assessment of echocardiograms.

Clinical Inclusion and Exclusion Criteria

Patients receiving an Edwards SAPIEN 3 transcatheter heart valve in the clinical study included those with a dysfunctional RVOT conduit or previously implanted valve in the pulmonic position with a clinical indication for intervention.

Clinical Endpoints

The endpoints analyzed in this application included: valve performance based on echocardiographic data, RVOT reintervention, adjudicated adverse events (coronary artery compression requiring intervention, major vascular complications, life-threatening or disabling bleeding, device-related endocarditis and death), THV frame fracture, site reported adverse events, and New York Heart Association (NYHA) classification. The analyses in the application focused on the 30-day and one-year time points.

A. Accountability of the PMA Main Cohort

At the time of database lock, a total of 58 subjects were enrolled in the study, including 38 with a dysfunctional RVOT and 20 with a dysfunctional bioprosthetic valve in the pulmonic position.

There were three different analysis populations defined in the protocol: All Treated (AT), Attempted Implant (AI), and Valve Implant (VI), as summarized in Table 6.

Table 6: Analysis Populations

Analysis Population	Definition	Number of Patients
All Treated	All subjects who signed informed consent, passed screening and for whom the procedure was begun (defined as the time of vascular access – incision or puncture)	58
Attempted Implant	All AT subjects who had an attempted implant of the study valve (introducer sheath for vascular delivery of the Edwards SAPIEN 3 THV was inserted into the subject).	56

Valve Implant	All AI patients who received and retained the intended valve upon leaving the catheterization laboratory/hybrid suite.	56

Study visit compliance is summarized in Table 7. Three subjects have exited the study.

Table 7: Study Visit Compliance

	AT Population (N=58)		
	30 Days	**6 Months**	**1 Year**
Ineligible*	2	2	2
Eligible	56	56	56
Visit performed	55 (98.2%)	54 (96.4%)	52 (92.9%)

*Ineligible subjects included those who exited the study prior to the visit

B. Study Population Demographics and Baseline Characteristics

The demographics and baseline characteristics of the study population are typical for a transcatheter pulmonary valve study performed in the U.S., as shown in Table 8.

Table 8: Demographics and Baseline Characteristics (AT Population)

Variable	Summary Statistics* (N=58)
Age (years)	31.8 ± 13.2 (58)
<12 years (child)	8.6% (5/58)
12-21 years (adolescent)	13.8% (8/58)
≥22 years (adult)	77.6% (45/58)
Gender	
Male	69.0% (40/58)
Weight (kg)	74.1 ± 21.2 (58)
NYHA class	
Class I	15.8% (9/57)
Class II	73.7% (42/57)
Class III	10.5% (6/57)
Class IV	0.0% (0/57)
NYHA class grouped	
Class I/II	89.5% (51/57)
Class III/IV	10.5% (6/57)
Primary indication	
Pulmonary stenosis only	12.3% (7/57)
Pulmonary regurgitation only	19.3% (11/57)
Both	68.4% (39/57)
Original CHD diagnosis	

Variable	Summary Statistics* (N=58)
Aortic valve disease resulting in Ross procedure	21.1% (12/57)
Atrial septal defect	17.2% (10/58)
Coarctation of the aorta	1.7% (1/58)
Double outlet right ventricle	5.2% (3/58)
Pulmonary atresia	17.2% (10/58)
Pulmonary valve stenosis	50.0% (29/58)
Tetralogy of Fallot	55.2% (32/58)
Transposition of the great arteries	6.9% (4/58)
Truncus arteriosus	5.2% (3/58)
Ventricular septal defect	34.5% (20/58)
Other	32.8% (19/58)
Most recent RVOT/PV repair/replacement	
Homograft	50.0% (29/58)
Biological valved conduit	13.8% (8/58)
Synthetic valved conduit	1.7% (1/58)
Surgical heart valve	34.5% (20/58)

*Continuous measures - Mean ± SD (Total no.); categorical measures - % (no./Total no.)

The distribution of prior cardiac interventions in the AT population stratified by patient age is shown in Table 9. The minimum and maximum diameters of the landing zone stratified by prior cardiac intervention and patient age are provided in Table 10.

Table 9: Prior Cardiac Interventions by Age Group (AT Population)

Endpoint	Summary Statistics*		
	<12 Years (N= 5)	12-21 Years (N= 8)	≥22 Years (N= 45)
Most recent RVOT/PV repair/replacement			
Homograft	60.0% (3/5)	37.5% (3/8)	51.1% (23/45)
Biological valved conduit	20.0% (1/5)	50.0% (4/8)	6.7% (3/45)
Synthetic valved conduit	0.0% (0/5)	0.0% (0/8)	2.2% (1/45)
Surgical heart valve	20.0% (1/5)	12.5% (1/8)	40.0% (18/45)

*Categorical measures - No. / Total no. (%).

Table 10 Landing Zone Diameters by Prior Cardiac Interventions and Patient Age (AT Population)

Most Recent RVOT Repair / Replacement	Summary Statistics*					
	<12 Years (N=5)		12-21 Years (N=8)		≥22 Years (N=45)	
	Landing Zone Minimum Diameter (mm)	Landing Zone Maximum Diameter (mm)	Landing Zone Minimum Diameter (mm)	Landing Zone Maximum Diameter (mm)	Landing Zone Minimum Diameter (mm)	Landing Zone Maximum Diameter (mm)
All Subjects	17.8±1.8 (5/5)	19.3±0.8 (5/5)	21.9±4.7 (6/8)	24.3±0.9 (6/8)	20.4±3.1 (40/45)	23.0±4.3 (41/45)
Homograft	17.4±2.4 (3/5)	19.2±1.0 (3/5)	18.4±7.9 (2/8)	24.2±0.2 (3/8)	20.1±3.5 (22/45)	23.0±5.4 (23/45)
Biological valved conduit	19.0±NA (1/5)	20.0±NA (1/5)	22.8±1.8 (3/8)	23.5±0.2 (2/8)	18.0±2.6 (3/45)	21.0±1.0 (3/45)
Synthetic valved conduit	NA	NA	NA	NA	18.7±NA (1/45)	19.7±NA (1/45)
Surgical heart valve	18.0±NA (1/5)	19.0±NA (1/5)	25.9±NA (1/8)	25.9±NA (1/8)	21.6±2.0 (14/45)	23.7±2.3 (14/45)

*Continuous measures - Mean ± SD (No./Total no.)

C. Safety and Effectiveness Results

(1) Primary Endpoint

The primary endpoint results are presented in Table 11. THV dysfunction at 1 year was 4.3% (CI: 0.5% to 14.5%). Since the upper limit of the 95% confidence interval for the primary endpoint event rate was < 25%, the endpoint was met.

Table 11: Primary Endpoint: THV Dysfunction at 1 Year (VI Population)

Variable	Summary Statistics* (N=56)	95% Confidence Interval	Less than the pre-specified performance goal (25%)?
THV dysfunction	4.3% (2/47)	(0.5%, 14.5%)	Yes
RVOT reintervention†	0.0% (0/56)	(0.0%, 6.4%)	
Moderate or greater PR	2.1% (1/47)	(0.1%, 11.3%)	
Mean RVOT gradient > 40 mmHg	2.1% (1/48)	(0.1%, 11.1%)	

*Summary statistics: Categorical measures - % (no./Total no.)
†Includes reintervention for both RVOT conduit and THV

(2) Secondary Safety Endpoints

The results of the secondary safety endpoints as adjudicated by the CEC are summarized in Table 12.

Table 12. Summary of Secondary Safety Endpoint Results (AT Population)

Freedom from Adverse Events	Summary Statistics*
30-day endpoints (at risk† =57)	
Coronary artery compression requiring intervention post-implantation	100.0% (0, 0)
Major vascular complications	100.0% (0, 0)
Life threatening or disabling bleeding	100.0% (0, 0)
6-month endpoint (at risk =55)	
THV frame fracture (site-reported)	100.0% (0, 0)
1-year endpoints (at risk =51)	
All-cause death	100.0% (0, 0)
Procedure- or device-related death	100.0% (0, 0)
Device related endocarditis	100.0% (0, 0)

*Kaplan-Meier estimate (No. events, No. patients with event)

†At risk numbers reflect the number of subjects on study at the end of the interval.

(3) Secondary Effectiveness Endpoints

Device Success

Device success was achieved in 98.1% of the subjects, as shown in Table 13.

Table 13: Device Success (AI Population)

Endpoint	Summary Statistics* (N=56)
Device success	98.1% (53/54)
Single THV implanted in the desired location	98.2% (55/56)
RV-PA peak-to-peak gradient < 35 mmHg post implantation	100.0% (56/56)
Less than moderate PR by discharge TTE (or earliest evaluable TTE)	100.0% (54/54)
Free of explant at 24 hours post implantation	100.0% (56/56)

*Categorical measures - % (no./Total no.)

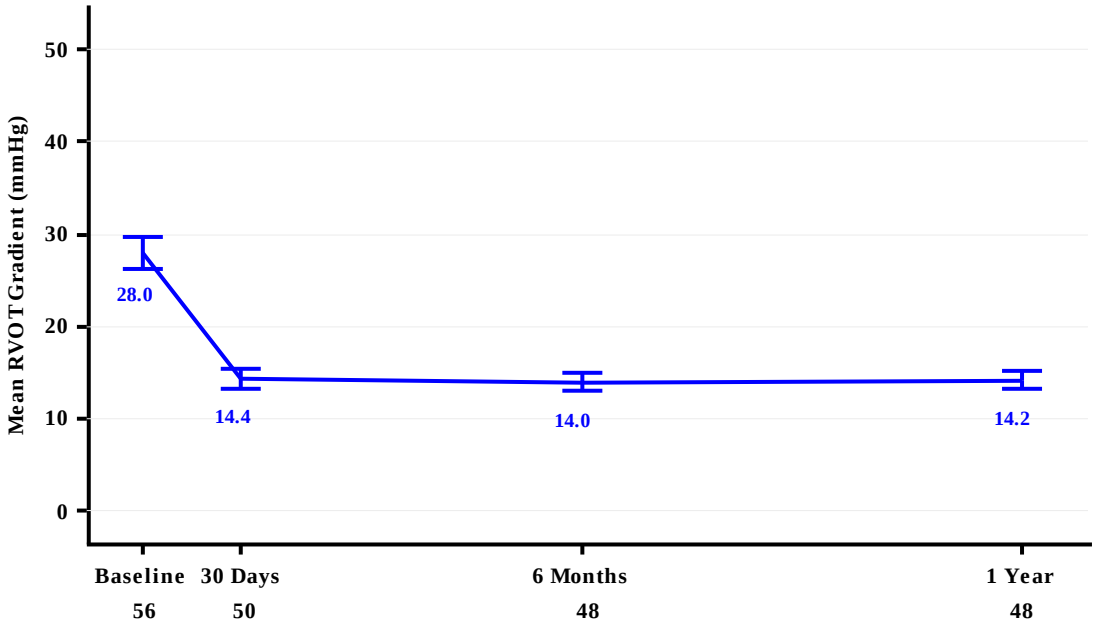
RVOT Reintervention

No subject had RVOT intervention within 1 year of the valve implant procedure.

THV Hemodynamic Function

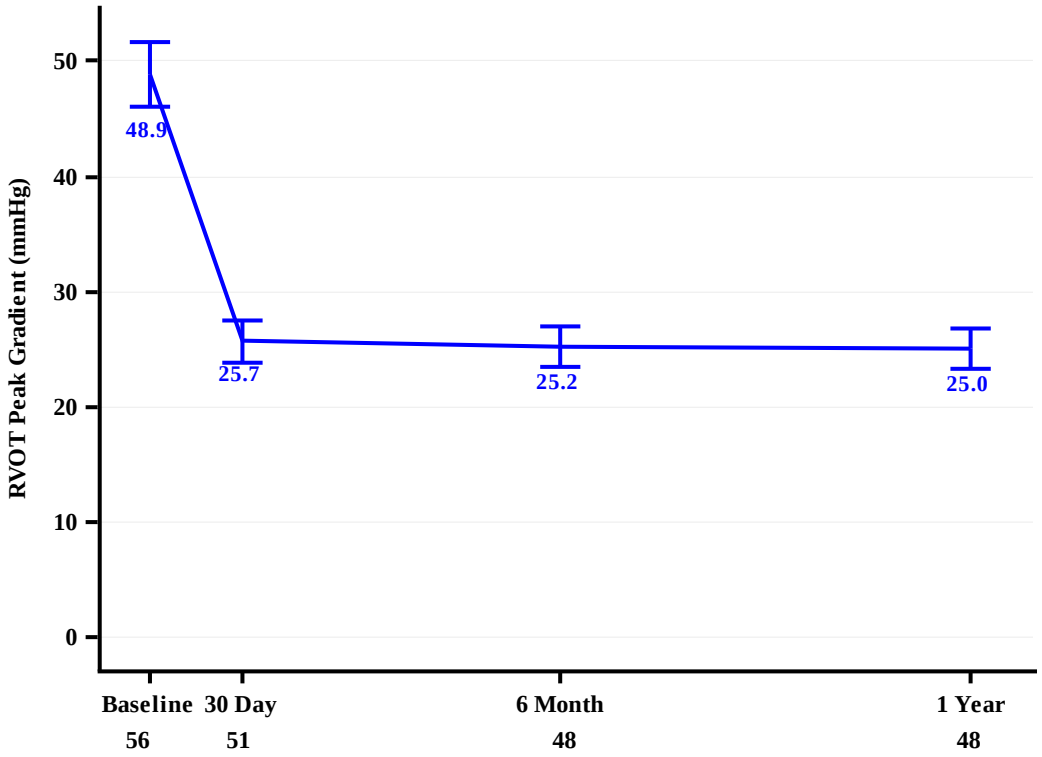
The mean RVOT gradient, peak RVOT gradient, peak RVOT gradient stratified by landing zone type, total PR and paravalvular regurgitation results at 1 year are shown in Figure 5 through Figure 9, respectively. The decrease in gradient was sustained through 1 year. The proportion of patients with total PR ≥ moderate was 0.0% at 30 days and 2.1% at 1 year. The proportion of patients with paravalvular regurgitation ≥ moderate was 0.0% at 30 days and 1 year.

Figure 5: Mean RVOT Gradient (VI Population)



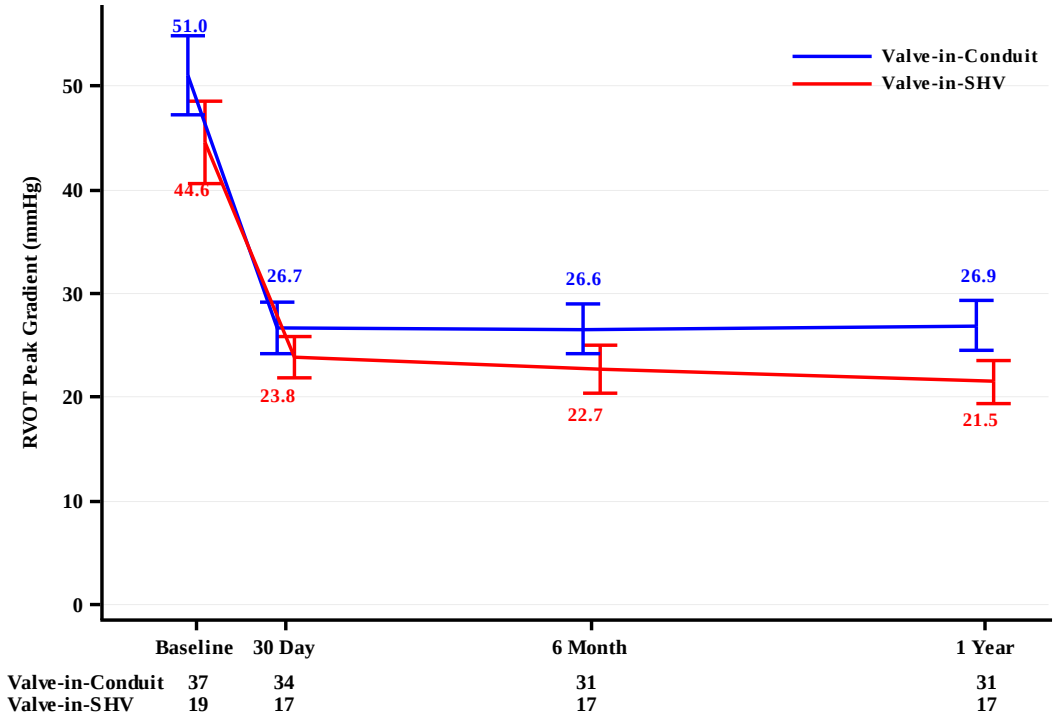
Note: Line plot with mean and standard error. The total number of subjects at each visit time point only counted the subjects with valid values.

Figure 6: Peak RVOT Gradient (VI Population)



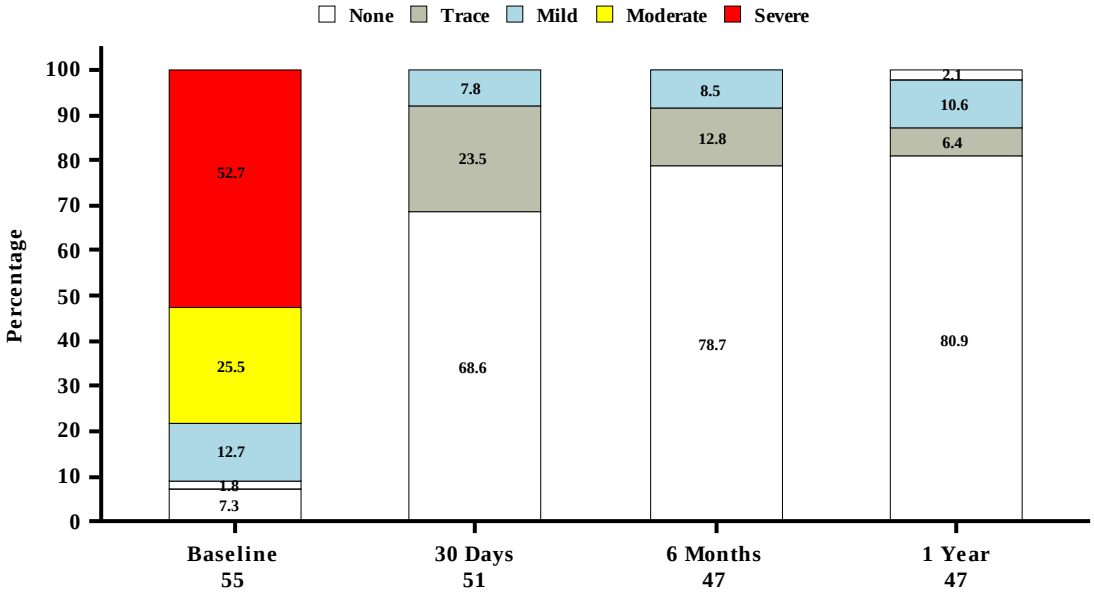
Note: Line plot with mean and standard error. The total number of subjects at each visit time point only counted the subjects with valid values.

Figure 7: RVOT Peak Gradient by Landing Zone Type (VI Population)



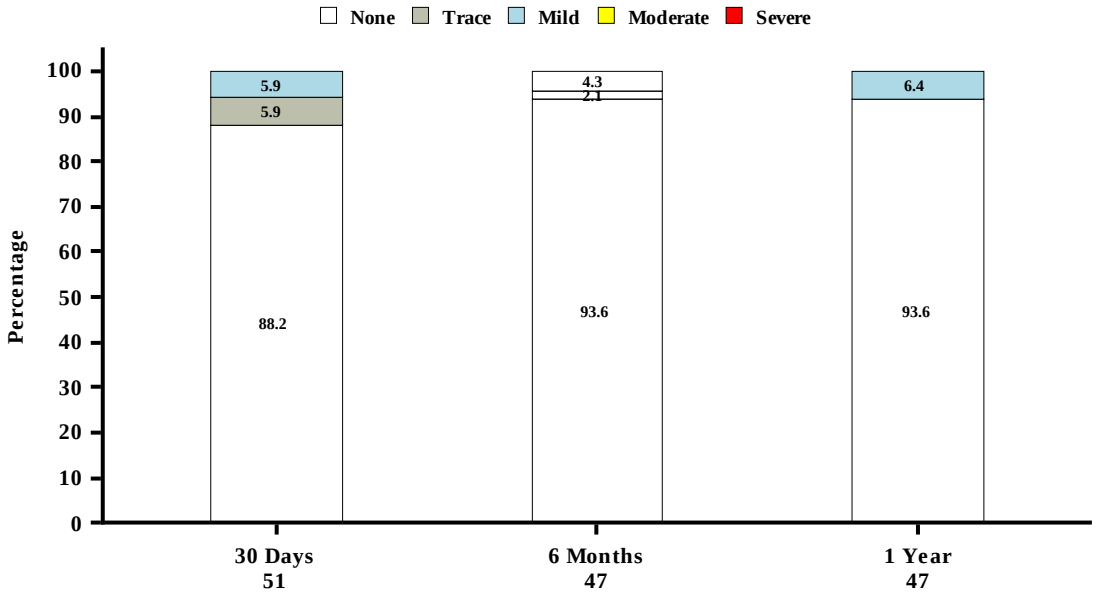
Note: Line plot with mean and standard error. The total number of subjects at each visit time point only counted the subjects with valid values.

Figure 8: Total Pulmonary Regurgitation (VI Population)



Note: The total number of subjects at each visit time point only counted the subjects with valid values.

Figure 9: Paravalvular Regurgitation (VI Population)

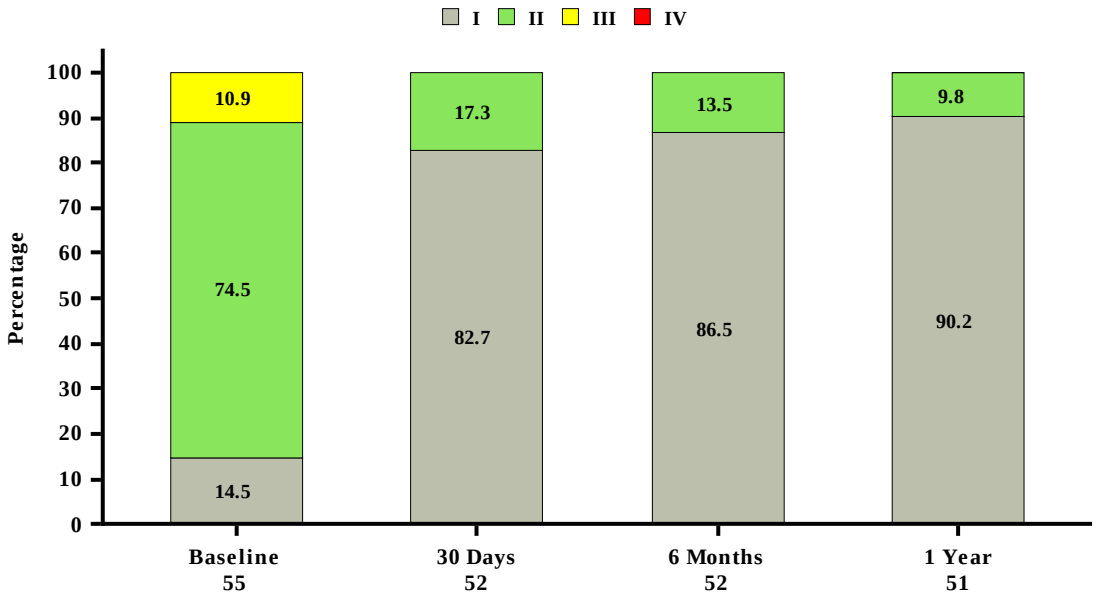


Note: The total number of subjects at each visit time point only counted the subjects with valid values.

NYHA Functional Class

NYHA classifications by visit are presented in Figure 10. At baseline, 89.1% of subjects were in NYHA Class I/II. At 1 year, all subjects were in NYHA Class I/II.

Figure 10: NYHA Class by Visit (VI Population)



(4) Adverse Events

The Kaplan-Meier estimates of the CEC-adjudicated adverse events through 1 year are presented in Table 14.

Table 14: CEC-Adjudicated Adverse Events Through 1 Year (AT Population)

Event	Summary Statistics*		
	30 Days (N=57)	6 Months (N=55)	1 Year (N=51)
Death	0.0% (0,0)	0.0% (0,0)	0.0% (0,0)
Cardiovascular	0.0% (0,0)	0.0% (0,0)	0.0% (0,0)
Non-Cardiovascular	0.0% (0,0)	0.0% (0,0)	0.0% (0,0)
Reintervention†	0.0% (0,0)	0.0% (0,0)	0.0% (0,0)
Arrhythmia	3.4% (2,2)	7.1% (5,4)	7.1% (5,4)
Permanent Pacemaker	0.0% (0,0)	1.8% (1,1)	1.8% (1,1)
Acute Kidney Injury	0.0% (0,0)	--	--
Bleeding	10.3% (6,6)	--	--
Life Threatening or Disabling	0.0% (0,0)	--	--
Major	0.0% (0,0)	--	--
Minor	10.3% (6,6)	--	--
Coronary Artery Compression	0.0% (0,0)	--	--
Endocarditis	0.0% (0,0)	0.0% (0,0)	0.0% (0,0)
Myocardial Infarction	0.0% (0,0)	--	--
Pulmonary Embolism	0.0% (0,0)	0.0% (0,0)	0.0% (0,0)
Stroke	0.0% (0,0)	0.0% (0,0)	0.0% (0,0)
TIA	0.0% (0,0)	0.0% (0,0)	0.0% (0,0)
Vascular Injury or Access Site Complication	12.1% (7,7)	--	--
Major	0.0% (0,0)	--	--
Minor	12.1% (7,7)	--	--

*Kaplan-Meier estimate (No. events, No. patients with event).

†Includes reintervention for both RVOT conduit and THV

(5) Other Study Observations

Procedural Information

Procedural data are summarized in Table 15. General anesthesia was used in the majority of subjects (91.4%). Pre-stenting occurred in 53.4% of the procedures. The most frequent procedural complication was RVOT conduit tear, which occurred in 8.6% of patients. The interventions associated with these procedural complications are summarized in Table 16.

Table 15: Procedural Data (AT Population)

Variable	Summary Statistics* (N=58)
Catheterization laboratory time (min)	238.2 ± 92.5 (58)
Procedure time (min)	120.4 ± 97.8 (57)
Anesthesia time (min)	227.7 ± 93.3 (55)
Type of anesthesia used	
General	91.4% (53/58)
Conscious sedation	8.6% (5/58)
Planned concomitant procedures	6.9% (4/58)
Procedural complications	12.1% (7/58)
RVOT conduit tear	8.6% (5/58)
Difficulty removing delivery system	1.7% (1/58)
Difficulty advancing the delivery system	1.7% (1/58)
Pre-dilatation performed	79.3% (46/58)
Pre-stenting performed	53.4% (31/58)
Any stent placed	53.4% (31/58)
Stent placed during procedure	53.4% (31/58)
Edwards SAPIEN 3 THV implanted	96.6% (56/58)
20 mm	19.6% (11/56)
23 mm	37.5% (21/56)
26 mm	37.5% (21/56)
29 mm	5.4% (3/56)
Post-dilatation performed	26.8% (15/56)
Valve not fully expanded	86.7% (13/15)
Other	13.3% (2/15)
Second SAPIEN 3 THV implanted	1.8% (1/57)

*Continuous measures - Mean ± SE (Total no.); categorical measures - % (no./Total no.)

Table 16: Procedural Complication Interventions

Variable	Summary Statistics* (N=58)
Action taken to resolve complication	
Transcatheter implant of commercial valve	1.7% (1/58)
Placement of covered stent	6.9% (4/58)
Other	3.4% (2/58)
Venotomy to remove ruptured balloon	1.7% (1/58)
Prolonged intubation	1.7% (1/58)

*Categorical measures - % (no./Total no.)

Subgroup Analyses

The pre-specified subgroup analyses by age, gender, valve size, and pre-stenting are summarized in Table 17.

Table 17: THV Dysfunction at 1 Year: Subgroup Analysis (VI Population)

Subgroup	Endpoint	Summary Statistics* (N=56)
By Age Group		
≤ 21 (N=12)	THV Dysfunction	0.0% (0/11)
	RVOT reintervention	0.0% (0/12)
	Moderate or greater PR	0.0% (0/11)
	Mean RVOT gradient >40 mmHg	0.0% (0/11)
≥ 22 (N=44)	THV Dysfunction	5.6% (2/36)
	RVOT reintervention	0.0% (0/44)
	Moderate or greater PR	2.8% (1/36)
	Mean RVOT gradient >40 mmHg	2.7% (1/37)
By Gender		
Female (N=18)	THV Dysfunction	0.0% (0/17)
	RVOT reintervention	0.0% (0/18)
	Moderate or greater PR	0.0% (0/17)
	Mean RVOT gradient >40 mmHg	0.0% (0/17)
Male (N=38)	THV Dysfunction	6.7% (2/30)
	RVOT reintervention	0.0% (0/38)
	Moderate or greater PR	3.3% (1/30)
	Mean RVOT gradient >40 mmHg	3.2% (1/31)
By Valve Size		
20mm (N=11)	THV Dysfunction	22.2% (2/9)
	RVOT reintervention	0.0% (0/11)
	Moderate or greater PR	11.1% (1/9)
	Mean RVOT gradient >40 mmHg	11.1% (1/9)
23mm (N=21)	THV Dysfunction	0.0% (0/17)
	RVOT reintervention	0.0% (0/21)
	Moderate or greater PR	0.0% (0/17)
	Mean RVOT gradient >40 mmHg	0.0% (0/17)
26mm (N=21)	THV Dysfunction	0.0% (0/18)
	RVOT reintervention	0.0% (0/21)
	Moderate or greater PR	0.0% (0/18)
	Mean RVOT gradient >40 mmHg	0.0% (0/19)
29mm (N=3)	THV Dysfunction	0.0% (0/3)
	RVOT reintervention	0.0% (0/3)
	Moderate or greater PR	0.0% (0/3)
	Mean RVOT gradient >40 mmHg	0.0% (0/3)
By Pre-stenting		
Pre-stented (N=31)	THV Dysfunction	8.0% (2/25)
	RVOT reintervention	0.0% (0/31)
	Moderate or greater PR	4.0% (1/25)
	Mean RVOT gradient >40 mmHg	4.0% (1/25)
No pre-stent (N=25)	THV Dysfunction *	0.0% (0/22)

Subgroup	Endpoint	Summary Statistics* (N=56)
	RVOT reintervention	0.0% (0/25)
	Moderate or greater PR	0.0% (0/22)
	Mean RVOT gradient >40 mmHg	0.0% (0/23)

*Categorical measures - % (no./Total no.)

13.0 References

[1] Bapat V, Attia R, Thomas M. Effect of Valve Design on the Stent Internal Diameter of a Bioprosthetic Valve: A Concept of True Internal Diameter and Its Implications for the Valve-in-Valve Procedure. JACC: Cardiovascular Interventions. Vol. 7, No. 2 2014: 115-127.

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