Edwards

Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent

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 and the adaptive prestent 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. The Edwards Alterra adaptive prestent system is supplied sterilized with e-beam sterilization.

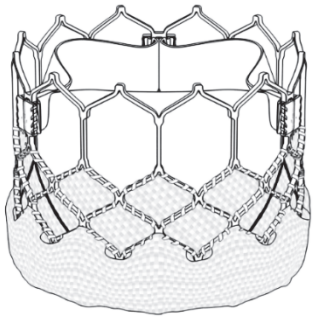
1.0 Device Description

Edwards SAPIEN 3 Transcatheter Pulmonary Valve (TPV) System with Alterra Adaptive Prestent

The Edwards SAPIEN 3 transcatheter pulmonary valve system with Alterra adaptive prestent consists of the Edwards 29-mm SAPIEN 3 transcatheter heart valve (THV), the Edwards Commander delivery system, the Edwards Alterra adaptive prestent system and accessories.

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

The Edwards SAPIEN 3 transcatheter heart valve 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.



9600TFX

Figure 1. Edwards SAPIEN 3 Transcatheter Heart Valve

Table 1

Valve Size	Valve Height
29 mm	22.5 mm

- **Edwards Commander Delivery System (Figures 2, 3, 4)**

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:

Table 2

Model	Nominal Balloon Diameter	Nominal Inflation Volume	Rated Burst Pressure (RBP)
9600LDS29	29 mm	33 mL	7 atm

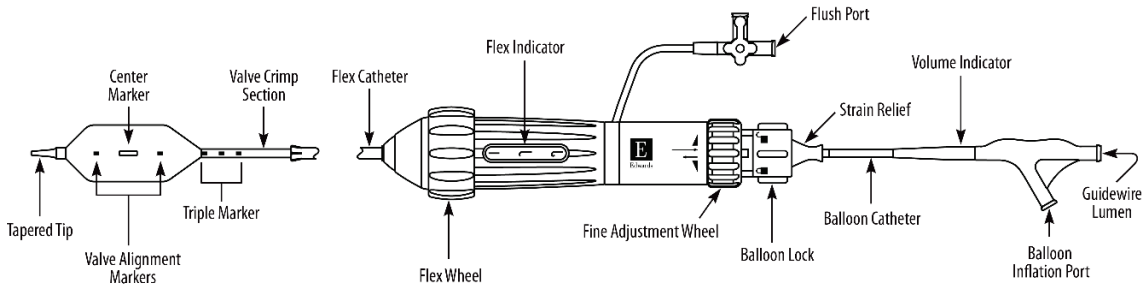


Figure 2. Edwards Commander Delivery System

- **Edwards Alterra Adaptive Prestent System**

Refer to the Edwards Alterra adaptive prestent system instructions for use.

Additional Accessories

Figure 3. Loader

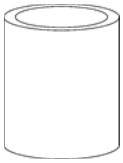


Figure 4. Qualcrimp Crimping Accessory

- **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 for device description.

- **Edwards Crimper**

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

2.0 Indications

The Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent is indicated for use in the management of pediatric and adult patients with severe pulmonary regurgitation as measured by echocardiography who have a native or surgically-repaired right ventricular outflow tract and are clinically indicated for pulmonary valve replacement.

3.0 Contraindications

The Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent 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.
- 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.
- 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.
- 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.
- Patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/or polymeric materials may have an allergic reaction to these materials.
- Accelerated deterioration of the valve may occur in patients with an altered calcium metabolism.
- Assessment for coronary compression risk prior to implantation is recommended.
- Patient venous anatomy should be evaluated to prevent the risk of access that would preclude the delivery and deployment of the device.
- 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.
- Fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. Patient radiation dose should be monitored during the procedure.
- 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.
- Patient should be heparinized to maintain the ACT at ≥ 250 sec prior to introduction of the delivery system in order to prevent thrombosis.
- To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon.
- 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 antiplatelet therapy.
- It is recommended that all prosthetic heart valve recipients be prophylactically treated for endocarditis to minimize the possibility of prosthetic valve infection.
- 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 patients of child-bearing potential

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
- Cardiac failure
- 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
- Deep vein thrombosis
- Arteriovenous (AV) fistula
- Systemic or peripheral nerve injury
- Systemic or peripheral ischemia
- Pulmonary edema
- Pneumothorax
- Pleural effusion
- Dyspnea
- Atelectasis
- Dislodgement of previously implanted devices (i.e., pacing lead)
- 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

Potential risks that may or may not require intervention 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
- Injury to tricuspid valve
- Device embolization
- Device acute migration or malposition
- Endocarditis
- Chest pain/discomfort
- Hemolysis / hemolytic anemia
- Device dysfunction (regurgitation and/or stenosis)
- Aortic root distortion

- Embolic event: device fragments
- Mechanical failure of delivery system, and/or accessories

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

7.0 Directions for Use

7.1 System Compatibility

Table 3

Product Name	Model
Edwards SAPIEN 3 Transcatheter Heart Valve (29 mm)	9600TFX29
Edwards Commander Delivery System	9600LDS29
Sheath provided by Edwards Lifesciences	
Inflation device, Qualcrimp crimping accessory, Crimp Stopper and Loader provided by Edwards Lifesciences	
Edwards Crimper	9600CR
Edwards Alterra Adaptive Prestent System[1]	29AP4045

[1] Includes an Alterra adaptive prestent that is fully loaded in an Alterra delivery system

Additional Equipment:

- Other compatible sheath:

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

- Balloon tip catheter
- Sizing balloons
- 20 cc syringe or larger (x2)
- 50 cc syringe or larger
- High-pressure 3-way stopcock
- Standard cardiac catheterization lab equipment
- Fluoroscopy (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 Edwards Alterra Adaptive Prestent System Procedure

See Edwards Alterra adaptive prestent system instructions for use for device preparation and implantation prior to transcatheter heart valve preparation and deployment.

Prior to valve implantation, assess Alterra prestent stability by evaluating apices engagement in surrounding tissue, wall apposition, and/or motion of prestent within the anatomy. If adequate stability is not noted, consider staging valve deployment after allowing sufficient time for prestent endothelialization.

CAUTION: Failure to identify prestent instability may lead to prestent migration/embolization when tracking interventional devices through the prestent.

7.3 Valve Handling and Preparation

Follow sterile technique during device preparation and implantation.

7.3.1 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.**

7.3.2 Prepare the System

Refer to the Edwards sheath, GORE DrySeal Flex Introducer Sheath, and Edwards Crimper 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. **CAUTION: Failure to replace the stylet in the guidewire lumen may result in damage to the lumen during the transcatheter heart valve 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 of diluted contrast medium relative to the indicated inflation volume. Lock 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.**

7.3.3 Mount and Crimp the Valve on the Delivery System

7.3.3.1 Procedure with the 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. **NOTE: Verify correct valve orientation with the inflow (outer sealing skirt) oriented towards the handle.**
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 for 5 seconds. **NOTE: Ensure that the Valve Crimp Section remains coaxial within the valve.**
11	Repeat the full crimp of the valve two more times (5 seconds each) 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.** **WARNING: The physician must verify correct orientation of the valve prior to its implantation.**

7.3.3.2 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**.** **NOTE: Verify correct valve orientation with the inflow (outer sealing skirt) oriented towards the handle.**
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 for 5 seconds. **NOTE: Ensure that the Valve Crimp Section remains coaxial within the valve.**
11	Repeat the full crimp of the valve two more times (5 seconds each) 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 for over 15 minutes.**
14	Close the stopcock to the delivery system. **CAUTION: Keep valve hydrated until ready for implantation.** **WARNING: The physician must verify correct orientation of the valve prior to its implantation.**
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.

Step	Procedure
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.

7.4 Valve Delivery

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.

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.

7.4.1 Procedure with the Edwards Provided Sheath

Step	Procedure
1	If necessary, gain access using standard catheterization techniques, prepare and insert the sheath per its instructions for use.
2	If not present, insert the guidewire into the vasculature. Advance the guidewire into the intended landing zone per standard technique.
3	Insert the loader assembly into the sheath until the loader stops.
4	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.**
5	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.**

Step	Procedure
6	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.** **CAUTION: Use caution when advancing devices/delivery systems into the implanted Alterra adaptive prestent to avoid engagement with the inflow apices.**
7	If additional working length is needed, remove the loader by unscrewing the loader cap and peeling the loader tubing from the delivery system.
8	Disengage the Balloon Lock and retract the tip of the Flex Catheter to the center of the Triple Marker. Engage the Balloon Lock.
9	Verify the correct position of the valve with respect to the landing zone.
10	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.
11	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.
12	Verify final position and 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, 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.

7.4.2 Procedure with GORE DrySeal Flex Introducer Sheath

Step	Procedure
1	If necessary, gain access using standard catheterization techniques, prepare and insert the sheath per its instructions for use.
2	If not present, insert the guidewire into the vasculature. Advance the guidewire into the intended landing zone per standard technique.
3	Insert the delivery system into the sheath.
4	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.**
5	Advance the catheter to the landing zone. **CAUTION: Use caution when advancing devices/delivery systems into the implanted Alterra adaptive prestent to avoid engagement with the inflow apices.**
6	Expose the valve by retracting the GORE DrySeal Flex Introducer Sheath tip beyond the Triple Marker.
7	Disengage the Balloon Lock and retract the tip of the Flex Catheter to the center of the Triple Marker. Engage the Balloon Lock.
8	Verify the correct position of the valve with respect to the landing zone.

Step	Procedure
9	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.
10	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.
11	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, 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.

7.5 System Removal

Step	Procedure
1	Once the balloon is fully deflated, 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. **NOTE: A sheath or other device may need to be inserted per standard of care.**
3	Close the access site.

8.0 How Supplied

STERILE: The valve is supplied sterilized with glutaraldehyde solution. The delivery system, sheath, and crimper are supplied sterilized with ethylene oxide gas. The Edwards Alterra adaptive prestent system is supplied pouched and sterilized by e-beam sterilization.

8.1 Storage

The transcatheter heart valve must be stored at 10 °C - 25 °C (50 °F - 77 °F). The delivery system and accessories should be stored in a cool, dry place. The prestent and delivery system must be stored in a cool, dry place.

9.0 MR Safety

MR Conditional

Non-clinical testing has demonstrated that the Edwards Alterra adaptive prestent, alone or with a deployed SAPIEN 3 transcatheter heart valve, is MR Conditional. A patient can be scanned safely immediately after placement of this implant in an MR system meeting the following conditions:

- Static magnetic fields of 1.5 Tesla and 3.0 Tesla
- Spatial magnetic gradient field of 3000 Gauss/cm (30 T/m) or less
- Maximum MR system-reported, whole body averaged specific absorption rate (SAR) of 2.0 W/kg (normal operating mode) scanning per sequence
- Gradient system is in normal operating mode

Under the scan conditions defined above, the Edwards Alterra adaptive prestent is expected to produce a maximum temperature rise of 4.0 °C or less after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends as far as 6.6 mm for gradient echo images when scanned using a 3.0 T MRI system. The artifact obscures the device lumen in spin and gradient echo images.

The delivery system has not been evaluated for MR compatibility and is considered MR unsafe.

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 and prestent. 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 lot number may be found on the prestent package. 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, Prestent 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. The explanted prestent should be placed into a suitable container 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

Patients were enrolled between August 2017 and September 2019 at 11 investigational sites in the U.S. An additional 25 patients were enrolled in a registry between January 2020 and August 2020 to evaluate use of the Pulmonic Delivery System at 13 investigational sites. The database for this PMA reflected data collected through June 2, 2021.

The Alterra Clinical 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

Enrollment in the Alterra Clinical Study was limited to patients who met the following inclusion criteria:

- The candidate/candidate's legal guardian has been informed of the nature of the study, agrees to its provisions and has provided written informed consent
- Weight is ≥ 20 kg (44 lbs)
- RVOT/pulmonary valve (PV) with moderate or greater PR by transthoracic echocardiogram (TTE)
- RVOT/PV proximal and distal landing zone diameter ≥ 27 mm and ≤ 38 mm, and minimum of 35 mm from contractile tissue to lowest pulmonary artery takeoff

Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

- Active infection requiring current antibiotic therapy (if temporary illness, patient may be a candidate 2 weeks after discontinuation of antibiotics)
- History of or active endocarditis (active treatment with antibiotics) within the past 180 days
- Leukopenia (white blood cell (WBC) < 2000 cells/μL), anemia (hemoglobin (Hgb) < 7 g/dL), thrombocytopenia (platelets < 50,000 cells/μL) or any known blood clotting disorder
- Inappropriate anatomy for introduction and delivery of Alterra or the SAPIEN 3
- Need for concomitant atrial septal defect or ventricular septal defect closure or other concomitant interventional procedures other than pulmonary artery or branch pulmonary artery stenting or angioplasty
- Interventional/surgical procedures within 30 days prior to the Alterra or valve implant procedure
- Any planned surgical, percutaneous coronary or peripheral procedure to be performed within the 30-day follow-up from the Alterra or valve implant procedure
- History of or current intravenous drug use
- Major or progressive non-cardiac disease resulting in a life expectancy of less than one year
- Known hypersensitivity to aspirin or heparin and cannot be treated with other antiplatelet and/or antithrombotic medications
- Known hypersensitivity to nitinol, cobalt-chromium, nickel or contrast media that cannot be adequately pre-medicated

- Currently participating in an investigational drug or another device study [Note: Trials requiring extended follow-up for products that were investigational, but have since become commercially available, are not considered investigational devices.]
- Positive urine or serum pregnancy test in female patients of child-bearing potential
- Renal insufficiency (creatinine > 3.0 mg/dL) and/or renal replacement therapy

Clinical Endpoints

The endpoints analyzed in this application included: valve performance based on echocardiographic data, RVOT reintervention, adjudicated adverse events (device embolization, major vascular complications, life-threatening or disabling bleeding, device-related endocarditis and death), successful delivery of the prestent and valve to the intended location, freedom from device explant, site reported adverse events, and New York Heart Association (NYHA) classification. The analyses in the application focused on the 30-day
and 6-month time points.

A. Accountability of the PMA Main Cohort

At the time of database lock, a total of 85 patients were enrolled in the study, including 60 in the main cohort and 25 in the PDS registry cohort.

There were 3 different analysis populations defined in the protocol: All Treated (AT), Attempted Implant (AI), and Valve Implant (VI), as summarized in Table 4.

Table 4: Analysis Populations

Analysis Population	Definition	Number of Patients	
		Main Cohort	PDS Registry
All Treated (AT)	All patients who signed informed consent, passed screening and for whom the procedure was begun (defined as the time of vascular access – incision or puncture).	60	25
Attempted Implant (AI)	All AT patients who had an attempted implant (the introducer sheath for vascular delivery of the Alterra adaptive prestent was inserted).	60	25
Valve Implant (VI)	All AI patients who received and retained a SAPIEN 3 THV upon leaving the catheterization laboratory/hybrid suite.	60	25

Study visit compliance is summarized in Table 5. One patient in the main cohort had not completed the 6-month at the time of the database lock.

Table 5: Study Visit Compliance

	Main Cohort (N=60)		PDS Registry (N=25)	
	30 Days	6 Months	30 Days	6 Months
Ineligible*	0	0	1	1
Eligible	60	60	24	24
Visit completed	60 (100.0%)	59 (98.3%)	24 (100%)	23 (95.8%)

*Ineligible patients included those who had died, withdrawn, lost to follow-up, or not reached the visit window.

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 6.

Table 6: Demographics and Baseline Characteristics (AT Population)

Demographics and Baseline Characteristics	Summary Statistics*	
	Main Cohort (N=60)	PDS Registry (N=25)
Age (years)	29.5 ± 2.14 (60)	29.1 ± 3.45 (25)
<12 years (child)	1.7% (1/60)	0.0% (0/25)
12-21 years (adolescent)	48.3% (29/60)	44.0% (11/25)
>21 years (adult)	50.0% (30/60)	56.0% (14/25)
Male Sex	56.7% (34/60)	56.0% (14/25)
Weight (kg)	73.1 ± 3.05 (60)	73.7 ± 4.44 (25)
New York Heart Association (NYHA) Class		
Class I	53.3% (32/60)	37.5% (9/24)
Class II	38.3% (23/60)	45.8% (11/24)
Class III	8.3% (5/60)	16.7% (4/24)
Class IV	0.0% (0/60)	0.0% (0/24)
NYHA Class Grouped		
Class I/II	91.7% (55/60)	83.3% (20/24)
Class III/IV	8.3% (5/60)	16.7% (4/24)
Primary diagnosis		
Pulmonary atresia	5.0% (3/60)	4.0% (1/25)
Pulmonary valve stenosis	23.3% (14/60)	20.0% (5/25)
Tetralogy of Fallot	70.0% (42/60)	68.0% (17/25)
Other	1.7% (1/59)	8.0% (2/25)
Secondary diagnosis		
Atrial septal defect	18.3% (11/60)	12.0% (3/25)
Coarctation of the aorta	3.3% (2/60)	4.0% (1/25)
Ventricular septal defect	30.0% (18/60)	12.0% (3/25)
Other	21.7% (13/60)	20.0% (5/25)
Most recent RVOT/PV intervention or surgery		
Pericardial/transannular patch	65.0% (39/60)	60.0% (15/25)
Valvuloplasty alone	25.0% (15/60)	20.0% (5/25)
Other†	10.0% (6/60)	20.0% (5/25)

*Continuous measures - mean ± SD (total no.); categorical measures - % (no./total no.)
†Tetralogy of Fallot repairs, unspecified RVOT/PV procedures, or none.

The breakdowns of prior cardiac interventions by patient age in the AT population are shown in Table 7 for the main cohort and Table 8 for the PDS registry cohort.

Table 7: Prior Cardiac Interventions by Age Group (AT Population) – Main Cohort

Most Recent RVOT/PV Intervention or Surgery	Summary Statistics*		
	<12 Years (N= 1)	12-21 Years (N= 29)	≥22 Years (N= 30)
Pericardial/transannular patch	100.0% (1/1)	82.8% (24/29)	46.7% (14/30)
Valvuloplasty alone	0.0% (0/1)	17.2% (5/29)	33.3% (10/30)
Other	0.0% (0/1)	0.0% (0/29)	20.0% (6/30)
Tetralogy of Fallot repairs	0.0% (0/0)	0.0% (0/29)	66.7% (4/6)
Unspecified RVOT/PV procedure	0.0% (0/0)	0.0% (0/29)	16.7% (1/6)
None	0.0% (0/0)	0.0% (0/29)	16.7% (1/6)

*Event rate (no./total no.)

Table 8: Prior Cardiac Interventions by Age Group (AT Population) – PDS Registry

Most Recent RVOT/PV Intervention or Surgery	Summary Statistics*	
	12-21 Years (N=11)	≥ 22 Years (N=14)
Pericardial/transannular patch	72.7% (8/11)	50.0% (7/14)
Valvuloplasty alone	18.2% (2/11)	21.4% (3/14)
Other	9.1% (1/11)	28.6% (4/14)
Tetralogy of Fallot repairs	100.0% (1/1)	25.0% (1/4)
Unspecified RVOT/PV procedure	0.0% (0/1)	50.0% (2/4)
None	0.0% (0/1)	25.0% (1/4)

*Event rate (no./total no.)

A. Safety and Effectiveness Results

(1) Primary Endpoint

The primary endpoint result for the main cohort is presented in Table 9. The rate of THV dysfunction at 6 months was 0% (two-sided confidence interval: 0.0% to 6.1%). Since the upper limit of the two-sided 95% confidence interval for the primary endpoint event rate was < 25%, the endpoint was met.

Table 9: Primary Endpoint Result – Main Cohort

Endpoint	Summary Statistics* (N=60)	95% Confidence Interval†	Less Than Prespecified Performance Goal (25%)?
Valve dysfunction‡	0.0% (0/59)	[0.0%, 6.1%]	Yes
RVOT/PV reintervention	0.0% (0/60)		
Moderate or greater pulmonary regurgitation	0.0% (0/59)		
Mean RVOT gradient ≥35 mmHg	0.0% (0/59)		

* Event rate (no./total no.)
†One patient did not have evaluable echocardiogram data.
‡Two-sided 95% confidence interval.

The primary endpoint result for the PDS registry cohort is presented in Table 10. Acute PDS success was achieved in 88.0% of the patients.

Table 10: Primary Endpoint Results - PDS Registry

Endpoint	Summary Statistics* (N=25)
Acute PDS success*	88.0% (22/25)
Single THV implanted in the desired location	100.0% (25/25)
RV-PA peak-to-peak gradient < 35 mmHg post implantation	100.0% (25/25)
Less than moderate PR by discharge TTE (or earliest evaluable TTE)	88.0% (22/25)
Free of explant at 24 hours post implantation	100.0% (25/25)

*Event rate (no./total no.)

(2) Additional Outcome Measures

Technical Success

Technical success at exit from the procedure room was achieved in 96.7% of the patients in the main cohort, as summarized in Table 11.

Table 11: Technical Success Result – Main Cohort

Endpoint	Summary Statistics* (N=60)
Technical Success	96.7% (58/60)
Alive	100.0% (60/60)
Successful access delivery and retrieval of the Alterra delivery system	100.0% (60/60)
Successful access delivery and retrieval of the SAPIEN 3 delivery system	100.0% (60/60)
Single Alterra deployed in the desired location	100.0% (60/60)
Single SAPIEN 3 valve deployed to the desired location	96.7% (58/60)
No need for unplanned or emergency surgery or intervention related to the device or access procedure	100.0% (60/60)

*Event rate (no./total no.)

Device Success

The device success rate in the main cohort was 88.3% at 30 days, and 76.3% at 6 months, as summarized in Table 12.

Table 12: Device Success Results – Main Cohort

Endpoint	Summary Statistics*	
	30 Days (N = 60)	6 Months (N = 59)
Device Success	88.3% (53/60)	76.3% (45/59)
Alive	100.0% (60/60)	100% (59/59)
No device explant	100.0% (60/60)	100% (59/59)
No additional surgical or interventional procedures related to access or the device since completion of the original procedure	100.0% (60/60)	100% (59/59)
Intended performance of the device†	88.3% (53/60)	76.3% (45/59)
Structural performance‡	90.0% (54/60)	76.3% (45/59)
Hemodynamic performance	100.0% (60/60)	100% (59/59)
Absence of para-device complications	98.3% (59/60)	100% (59/59)

*Event rate (no./total no.)

† Intended performance of the device is defined as a composite of: (1) structural performance - no migration, embolization, fracture, thrombosis (including reduce leaflet mobility if detected) or endocarditis; (2) hemodynamic performance - net pulmonary valve peak gradient ≤ 35 mmHg and transvalvular PR ≤ mild; and (3) absence of para-device complications – pulmonary valve regurgitation > mild, need for a permanent pacemaker, or new pulmonary embolism.

‡The structural performance events included 4 Alterra Prestent fracture events, 1 SAPIEN 3 THV thrombosis event, 1 Alterra Prestent thrombosis event, and 1 Alterra Prestent migration event at 30 days and an additional 8 Alterra Prestent fracture events at 6 months. Multiple events occurred on one patient are counted as one.

Procedural Success

Procedural success was met in 88.3% of patients in the main cohort at 30 days, as summarized in Table 13.

Table 13: Procedure Success Result – Main Cohort

Endpoint	Summary Statistics* (N=60)
Procedure Success	88.3% (53/60)
Device success	88.3% (53/60)
No device or procedure related SAEs†	100.0% (60/60)

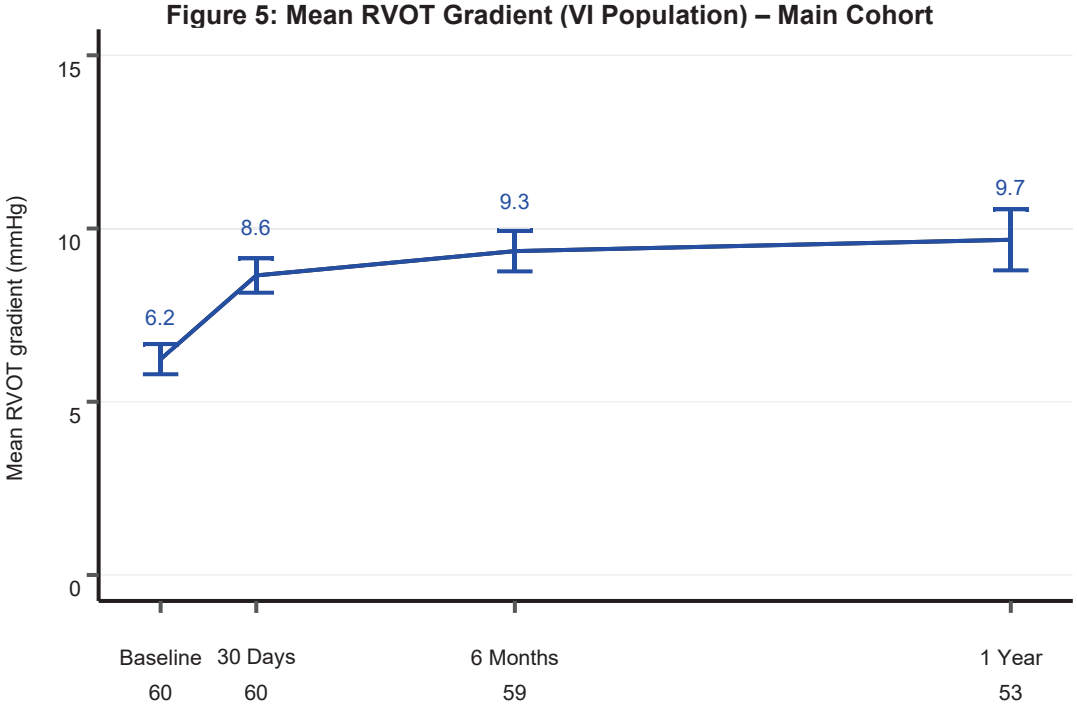
*Event rate (no./total no.)

† SAEs: life threatening bleed; major vascular or access site complications requiring unplanned reintervention or surgery; stage 2 or 3 acute kidney injury (including new dialysis); severe heart failure or hypotension requiring intravenous inotrope, ultrafiltration or mechanical circulatory support; prolonged intubation > 48 hours.

THV Hemodynamic Function

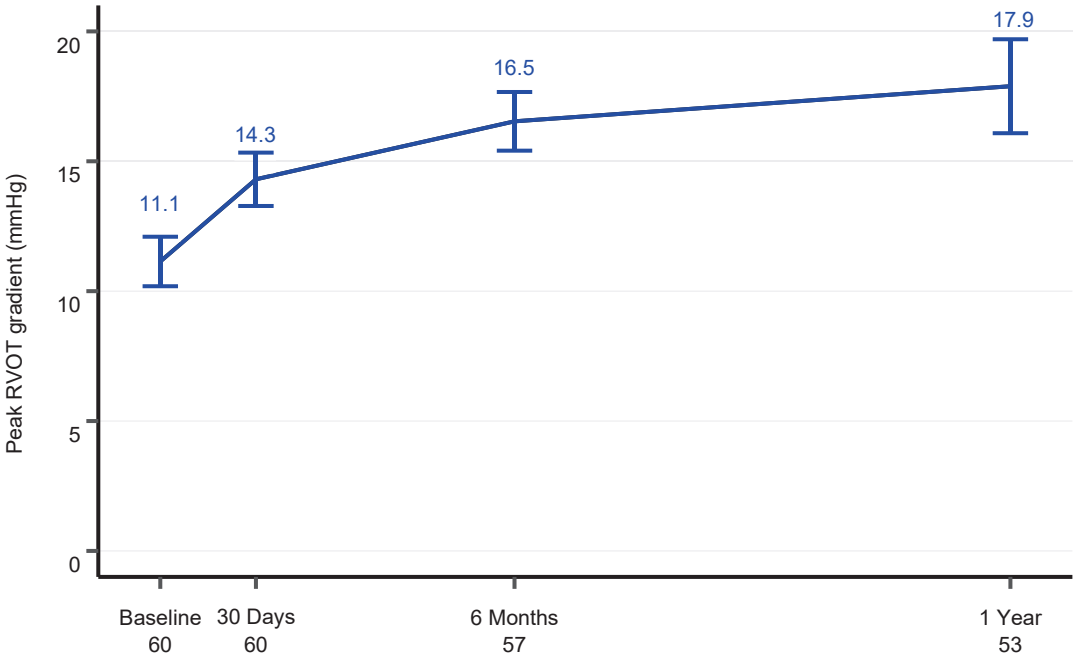
The mean RVOT gradient, peak RVOT gradient, total PR, and paravalvular regurgitation results through 1 year for the main cohort are shown in Figure 5 through Figure 8, respectively. The mean and peak RVOT gradients remained largely stable through 1 year post implant (9.7 mmHg and 17.9 mmHg, respectively, at 1 year). The proportion of patients with total PR ≥ moderate decreased from 100% to 9.6% at 1 year. The proportion of patients with paravalvular regurgitation ≥ moderate was 1.7% at 30 days, and 0% at both 6 months and 1 year.

Figure 5: Mean RVOT Gradient (VI Population) – Main Cohort



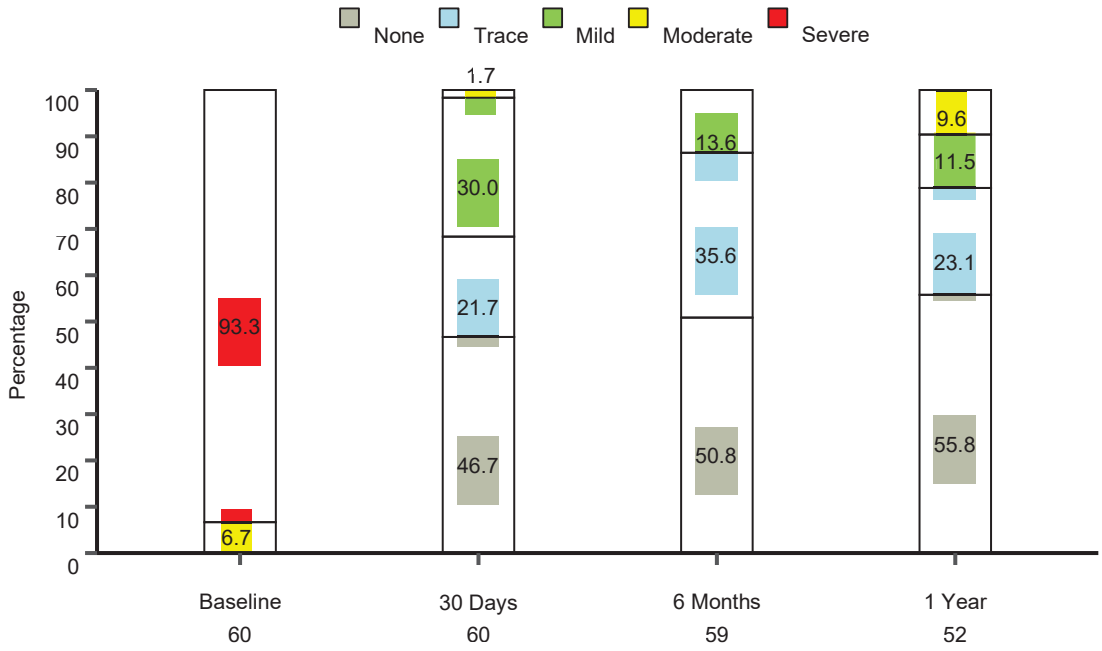
Note: Line plot with mean and standard error. The total number of patients at each visit time point only counted the patients with evaluable values.

Figure 6: Peak RVOT Gradient (VI Population) – Main Cohort



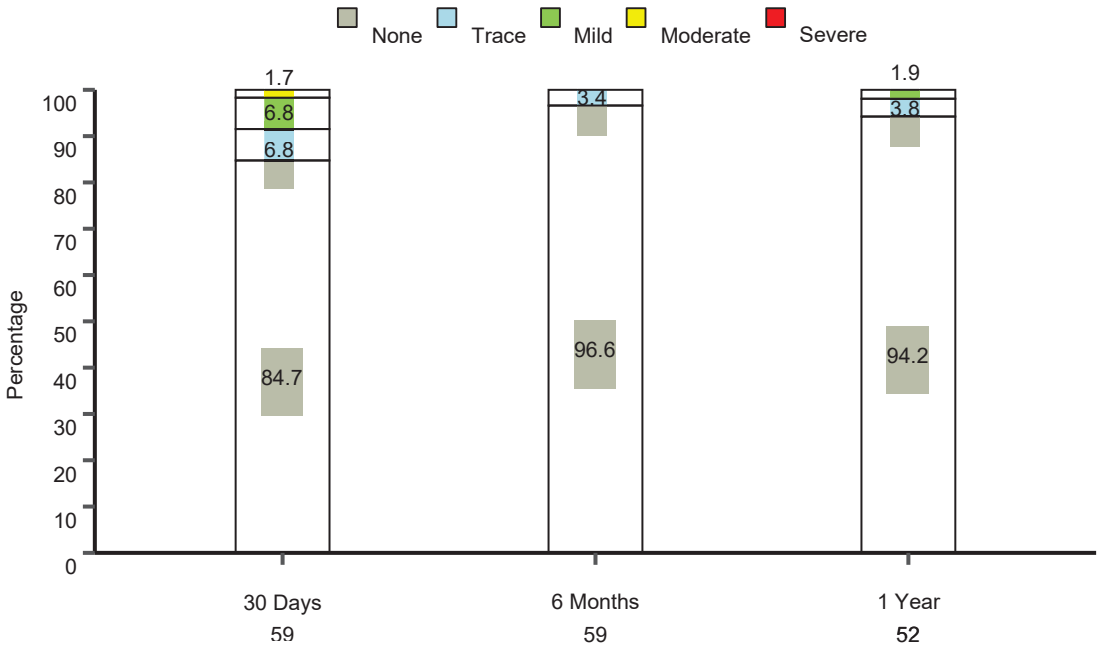
Note: Line plot with mean and standard error. The total number of patients at each visit time point only counted the patients with evaluable values.

Figure 7: Total Pulmonary Regurgitation (VI Population) – Main Cohort



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

Figure 8: Paravalvular Regurgitation (VI Population) – Main Cohort

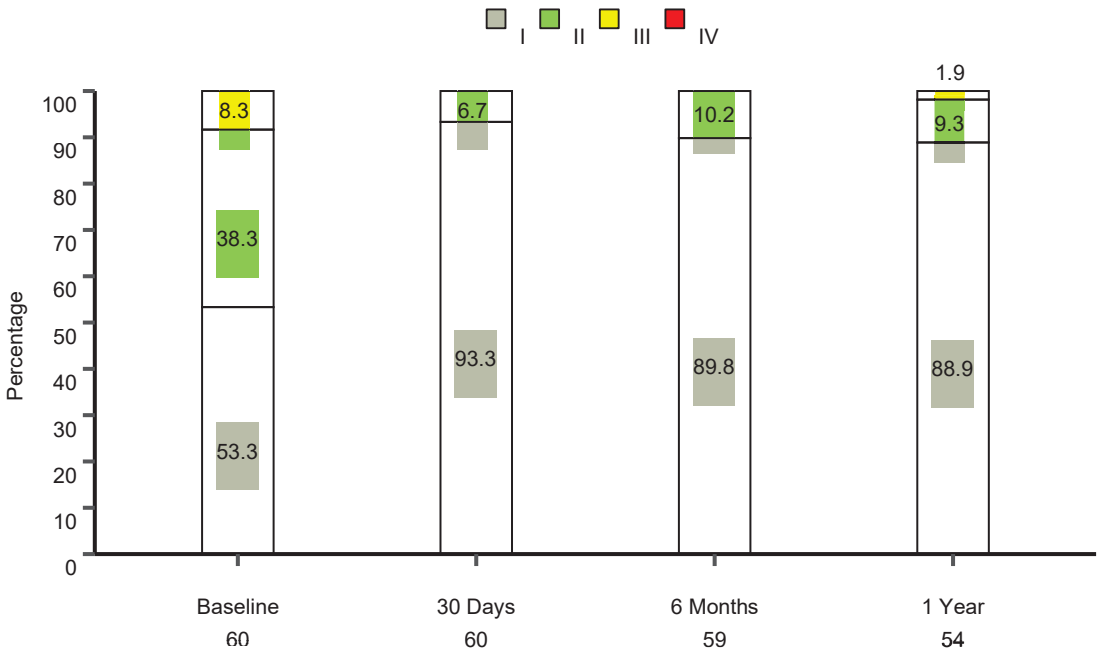


Note: The total number of patients at each visit time point only counted the patients with evaluable values.

NYHA Functional Class

The NYHA classifications by visit are presented for the main cohort in Figure 9. At baseline, 91.7% of patients in the main cohort were in NYHA Class I/II, which increased to 100% at 30 days and 6 months and 98.1% at 1 year.

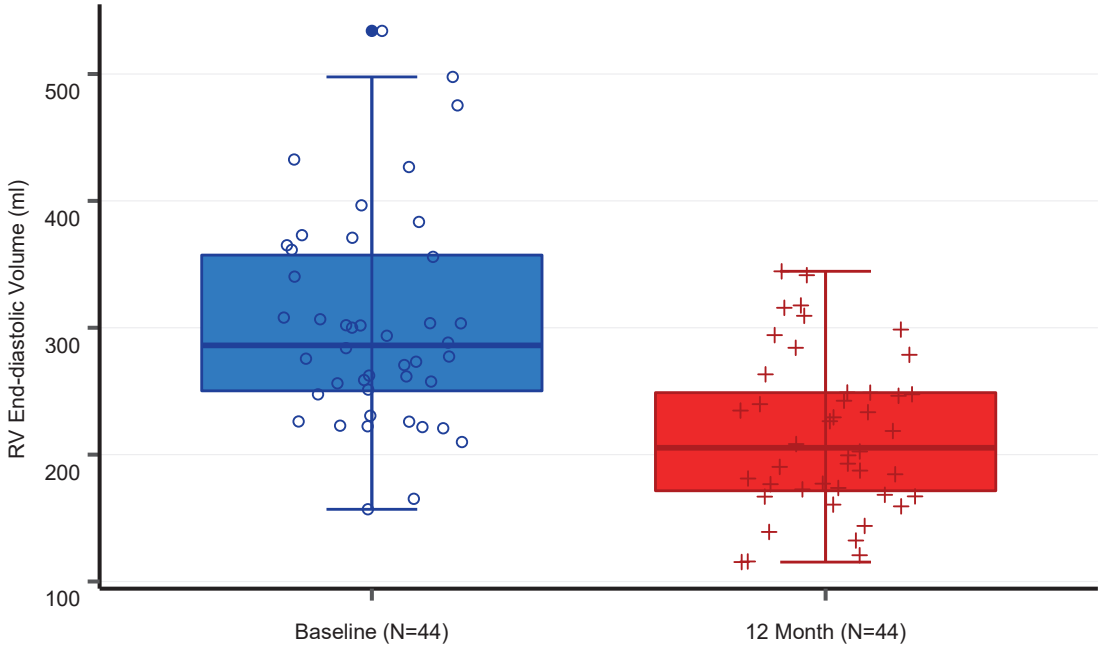
Figure 9: NYHA Class by Visit (VI Population) – Main Cohort



Characterization of Right Ventricular Remodeling

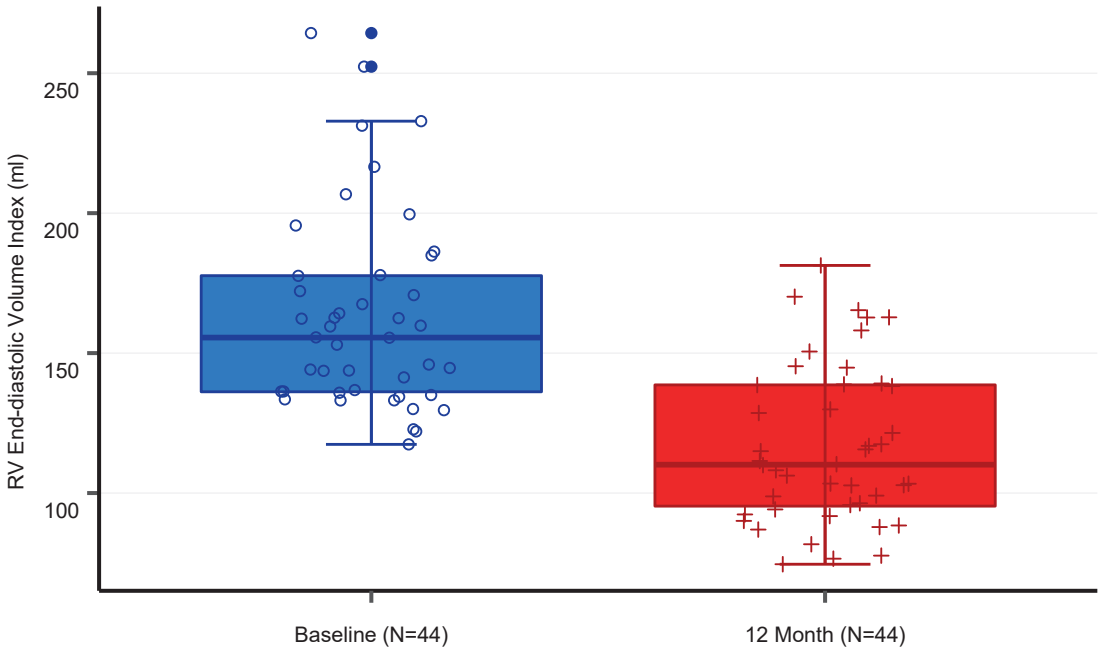
Right ventricular remodeling was characterized via magnetic resonance imaging (MRI) and computed tomography (CT) in the main cohort. Right ventricular end diastolic volume (RVEDV), RVEDV index, and main pulmonary artery regurgitant fraction at baseline and 1 year are presented in Figure 10 through Figure 12, respectively. The RVEDV decreased from 295.9 ml to 220.4 ml, with the corresponding RVEDV index decreasing from 162.7 ml/m^2 to 118.9 ml/m^2. The main pulmonary artery regurgitant fraction decreased from 47.4% to 4.1%.

Figure 10: Right Ventricular End Diastolic Volume (VI Population) – Main Cohort



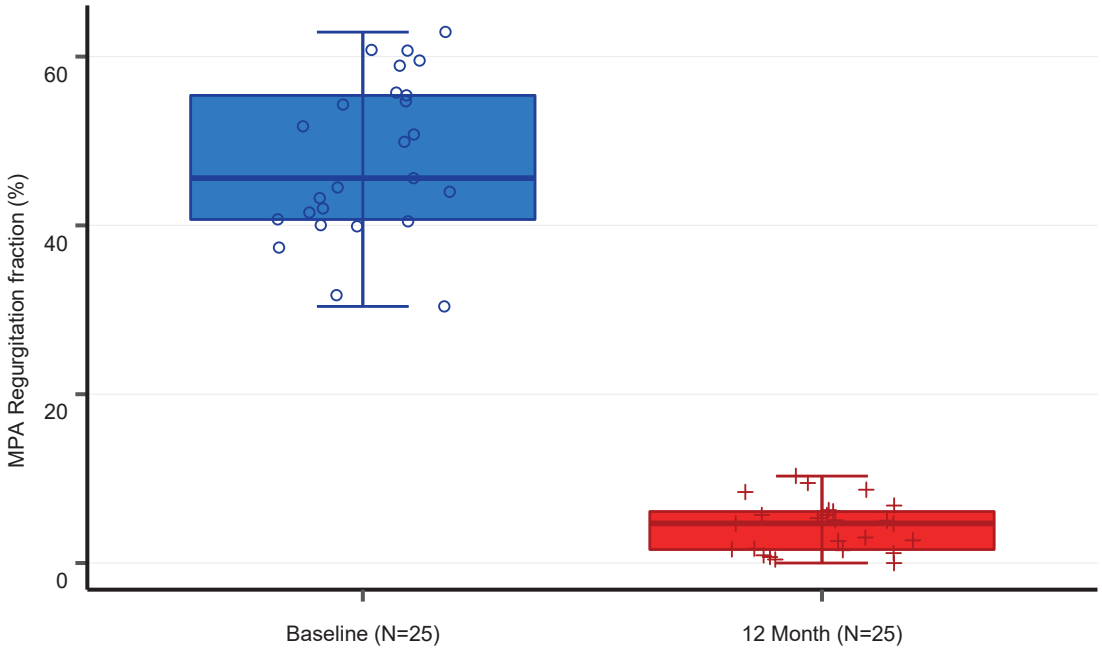
Note: The total number of patients at each visit time point only counted the patients with evaluable paired values.

Figure 11: Right Ventricular End Diastolic Volume Index (VI Population) – Main Cohort



Note: The total number of patients at each visit time point only counted the patients with evaluable paired values.

Figure 12: Main Pulmonary Artery Regurgitant Fraction (VI Population) – Main Cohort



Note: The total number of patients at each visit time point only counted the patients with evaluable paired values.

(3) Adverse Events

Kaplan-Meier estimates of the CEC-adjudicated adverse events through 1 year for the main cohort and through 6 months for the PDS registry cohort are presented in Table 14 and Table 15 respectively.

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

Event	Summary Statistics*		
	30 Days (N=60)	6 Months (N=59)	1 Year (N = 49)
All-cause death	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	33.3% (21, 20)	33.3% (21, 20)	33.3% (21, 20)
Permanent pacemaker	0.0% (0, 0)	0.0% (0, 0)	0.0% (0, 0)
Acute kidney injury	0.0% (0, 0)	0.0% (0, 0)	0.0% (0, 0)
Bleeding	18.3% (12, 11)	21.7% (14, 13)	23.5% (16, 14)
Life threatening or disabling	0.0% (0, 0)	1.7% (1, 1)	3.5% (2, 2)
Major	1.7% (1, 1)	1.7% (1, 1)	1.7% (1, 1)
Minor	16.7% (11, 10)	18.4% (12, 11)	20.1% (13, 12)
Coronary artery compression	0.0% (0, 0)	0.0% (0, 0)	0.0% (0, 0)
Endocarditis	0.0% (0, 0)	0.0% (0, 0)	0.0% (0, 0)
Myocardial infarction	0.0% (0, 0)	0.0% (0, 0)	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)
Transient ischemic attack	0.0% (0, 0)	0.0% (0, 0)	0.0% (0, 0)
Vascular injury or access site complication	5.0% (3, 3)	5.0% (3, 3)	6.8% (4, 4)
Major	0.0% (0, 0)	0.0% (0, 0)	1.8% (1,1)
Minor	5.0% (3, 3)	5.0% (3, 3)	5.0% (3, 3)

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

Table 15: CEC-Adjudicated Adverse Events Through 6 Months (AT Population) – PDS Registry

Event	Summary Statistics*	
	30 Days (N=24)	6 Months (N = 24)
All-cause death	4.0% (1, 1)	4.0% (1, 1)
Cardiovascular	0.0% (0, 0)	0.0% (0, 0)
Non-Cardiovascular	4.0% (1, 1)	4.0% (1, 1)
Reintervention	0.0% (0, 0)	0.0% (0, 0)
Arrhythmia	48.0% (15, 12)	48.0% (15, 12)
Permanent pacemaker	0.0% (0, 0)	0.0% (0, 0)
Acute kidney injury	0.0% (0, 0)	0.0% (0, 0)
Bleeding	20.0% (6, 5)	20.0% (6, 5)
Life threatening or disabling	0.0% (0, 0)	0.0% (0, 0)
Major	0.0% (0, 0)	0.0% (0, 0)
Minor	20.0% (6, 5)	20.0% (6, 5)
Coronary artery compression	0.0% (0, 0)	0.0% (0, 0)
Endocarditis	0.0% (0, 0)	0.0% (0, 0)
Myocardial infarction	0.0% (0, 0)	0.0% (0, 0)
Pulmonary embolism	0.0% (0, 0)	0.0% (0, 0)
Stroke	0.0% (0, 0)	0.0% (0, 0)
Transient ischemic attack	0.0% (0, 0)	0.0% (0, 0)
Vascular injury or access site complication	8.0% (4, 2)	8.0% (4, 2)
Major	0.0% (0, 0)	0.0% (0, 0)
Minor	8.0% (4, 2)	8.0% (4, 2)

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

(4) Other Study Observations

Procedural Information

Procedural data for the main cohort and PDS registry cohort are summarized in Table 16. Concomitant Alterra adaptive prestent and SAPIEN 3 THV procedures were performed on the majority of patients (98.3% for the main cohort & 100% for PDS registry cohort).

Table 16: Procedural Data (AT Population)

Variable	Summary Statistics*	
	Main Cohort (N=60)	**PDS Registry (N=25)**
Procedure type		
Staged procedure	1.7% (1/60)	0.0% (0/25)
Prestent procedure sheath time (min)	61.0	N/A
SAPIEN 3 procedure sheath time (min)	23.0	N/A
Concomitant Alterra adaptive prestent + SAPIEN 3 THV procedure	98.3% (59/60)	100.0% (25/25)
Procedure sheath time (min)	66.8 ± 4.73 (59)	58.2 ± 8.42 (25)
Alterra adaptive prestent procedure complications	3.3% (2/60)	0.0% (0/25)
SAPIEN 3 procedure complications	10.0% (6/60)	8.0% (2/25)
Total fluoroscopy time	37.2 ± 3.04 (60)	38.0 ± 4.88 (25)
Alterra adaptive prestent procedure post-dilatation performed	0.0% (0/60)	0.0% (0/25)
SAPIEN 3 procedure post-dilatation performed	11.7% (7/60)	0.0% (0/25)
Alterra adaptive prestent implanted in the intended location at the time the patient left the procedure room	100.0% (60/60)	100.0% (25/25)
SAPIEN 3 THV implanted in the intended location at the time the patient left the procedure room	100.0% (60/60)	100.0% (25/25)
Single SAPIEN 3 THV implanted	96.7% (58/60)	100.0% (25/25)

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

CT Core Laboratory Findings

The results of an imaging assessment by the CT Core Laboratory through 1 year for the main cohort and through 30 days for the PDS registry cohort are presented in Table 17 and Table 18, respectively. There were no device reinterventions associated with these findings.

Table 17: CT Core Laboratory Findings (VI Population) – Main Cohort

Finding	Summary Statistics*	
	30 Days (N = 60)	1 Year (N = 55)
Alterra Adaptive Prestent penetration†		
Minor penetration - into adjacent vasculature or cardiac structure without extravasation, pseudoaneurysm, or erosion	2.6% (1/39)	5.3% (1/19)
Major penetration - protrusion into surrounding tissue with blood pooling, or erosion, or pseudoaneurysm	0.0% (0/39)	0.0% (0/19)
Pedunculated mobile mass†	2.6% (1/39)	0.0% (0/19)
Alterra Adaptive Prestent fracture‡		
Fracture not requiring intervention	6.7% (4/60)	21.8% (12/55)
Fracture requiring intervention	0.0% (0/60)	0.0% (0/55)
SAPIEN 3 valve frame fracture‡	0.0% (0/60)	0.0% (0/55)

*Rate (no./total no.)
†Only included patients with evaluable images at visit time point.
‡Fracture was determined by either chest x-ray or fluoroscopy.

Table 18: CT Core Laboratory Findings (VI Population) – PDS Registry

Finding	Summary Statistics*
	30 Days (N = 25)
Alterra Adaptive Prestent penetration†	
Minor penetration - into adjacent vasculature or cardiac structure without extravasation, pseudoaneurysm, or erosion	8.7% (2/23)
Major penetration - protrusion into surrounding tissue with blood pooling, or erosion, or pseudoaneurysm	0.0% (0/23)
Pedunculated mobile mass†	4.3% (1/23)
Alterra Adaptive Prestent fracture‡	
Fracture not requiring intervention	20.0% (5/25)
Fracture requiring intervention	0.0% (0/25)
SAPIEN 3 valve frame fracture‡	0.0% (0/25)

*Rate (no./total no.)
†Only included patients with evaluable images at visit time point.
‡Fracture was determined by either chest x-ray or fluoroscopy.

These products are manufactured and sold under one or more of the following US patent(s): US Patent No. 7,530,253; 7,895,876; 8,690,936; 8,790,387; 9,301,840; 9,301,841; and 9,393,110; and corresponding foreign patents.

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	Drawing/Specification:	DOC-0001941	
	English Master/Revision:	N/A	
	eIFU Visual Representation/Revision:	N/A	
	Refer to supporting material for signatures.		

NOTE
1. ALL ART PRINTS 100% BLACK UNLESS OTHERWISE NOTED.

INKS
BLACK
GRAYSCALE 55% BLACK

Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent

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 and the adaptive prestent 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. The Edwards Alterra adaptive prestent system is supplied sterilized with e-beam sterilization.

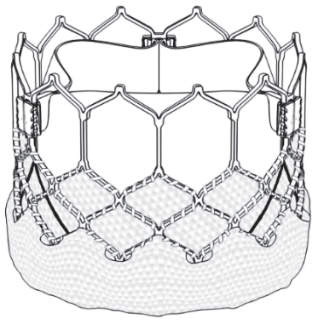
1.0 Device Description

Edwards SAPIEN 3 Transcatheter Pulmonary Valve (TPV) System with Alterra Adaptive Prestent

The Edwards SAPIEN 3 transcatheter pulmonary valve system with Alterra adaptive prestent consists of the Edwards 29-mm SAPIEN 3 transcatheter heart valve (THV), the Edwards SAPIEN 3 pulmonic delivery system (PDS), the Edwards Alterra adaptive prestent system and accessories.

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

The Edwards SAPIEN 3 transcatheter heart valve 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.



9600TFX

Figure 1. Edwards SAPIEN 3 Transcatheter Heart Valve

Table 1

Valve Size	Valve Height
29 mm	22.5 mm

- **Edwards SAPIEN 3 Pulmonic Delivery System (PDS) (Figures 2, 3, 4)**

The Edwards SAPIEN 3 PDS (Figure 2) facilitates the placement of the bioprosthesis. It consists of an inline sheath, balloon catheter for deployment of the Edwards SAPIEN 3 transcatheter heart valve, and an outer shaft and valve capsule to cover the transcatheter heart valve during insertion and tracking to the intended deployment location. The delivery system includes a tapered tip to facilitate crossing of right heart structures. The valve capsule and tapered tip are hydrophilic coated. A visual balloon shaft marker is provided to assist with balloon recapture. A stylet is included within the guidewire lumen of the delivery system. The 28F hydrophilic coated dilator (packaged with the delivery system) is used to predilate the vessel prior to insertion of the delivery system, if necessary (Figure 3). The inflation parameters for the valve deployment are shown in the table below:

Table 2

Model	Nominal Balloon Diameter	Nominal Inflation Volume	Rated Burst Pressure (RBP)
9630PL29	29 mm	33 mL	7 atm (709 kPa)

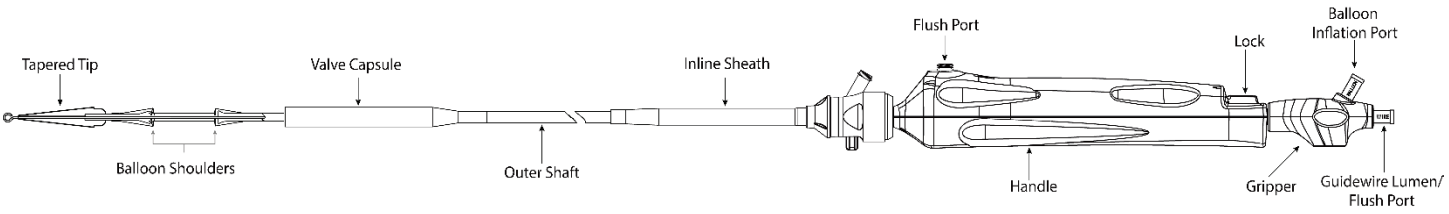


Figure 2. Edwards SAPIEN 3 Pulmonic Delivery System

- **Edwards Alterra Adaptive Prestent System**

Refer to the Edwards Alterra adaptive prestent system instructions for use.

Additional Accessories

Figure 3. Dilator

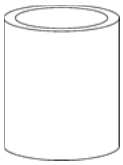


Figure 4. Qualcrimp Crimping Accessory

- **Dilator**

The dilator allows physicians to predilate the access site prior to valve delivery system insertion.

- **Edwards Sheath**

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

- **Edwards Crimper**

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

2.0 Indications

The Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent is indicated for use in the management of pediatric and adult patients with severe pulmonary regurgitation as measured by echocardiography who have a native or surgically-repaired right ventricular outflow tract and are clinically indicated for pulmonary valve replacement.

3.0 Contraindications

The Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent 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.
- 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.
- 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.
- 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.
- Patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/or polymeric materials may have an allergic reaction to these materials.
- Accelerated deterioration of the valve may occur in patients with an altered calcium metabolism.
- Assessment for coronary compression risk prior to implantation is recommended.
- Patient venous anatomy should be evaluated to prevent the risk of access that would preclude the delivery and deployment of the device.
- 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.
- Fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. Patient radiation dose should be monitored during the procedure.
- 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.
- Patient should be heparinized to maintain the ACT at ≥ 250 sec prior to introduction of the delivery system in order to prevent thrombosis.
- To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon.
- 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 antiplatelet therapy.
- It is recommended that all prosthetic heart valve recipients be prophylactically treated for endocarditis to minimize the possibility of prosthetic valve infection.
- 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 patients of child-bearing potential

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
- Cardiac failure
- 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
- Deep vein thrombosis
- Arteriovenous (AV) fistula
- Systemic or peripheral nerve injury
- Systemic or peripheral ischemia
- Pulmonary edema
- Pneumothorax
- Pleural effusion
- Dyspnea
- Atelectasis
- Dislodgement of previously implanted devices (i.e., pacing lead)
- 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

Potential risks that may or may not require intervention 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
- Injury to tricuspid valve
- Device embolization
- Device acute migration or malposition
- Endocarditis
- Chest pain/discomfort
- Hemolysis / hemolytic anemia
- Device dysfunction (regurgitation and/or stenosis)
- Aortic root distortion

- Embolic event: device fragments
- Mechanical failure of delivery system, and/or accessories

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

7.0 Directions for Use

7.1 System Compatibility

Table 3

Product Name	Model
Edwards SAPIEN 3 Transcatheter Heart Valve (29 mm)	9600TFX29
Edwards SAPIEN 3 Pulmonic Delivery System[1]	9630PL29
Sheath provided by Edwards Lifesciences	
Inflation device, Qualcrimp crimping accessory, Crimp Stopper provided by Edwards Lifesciences	
Edwards Crimper	9600CR
Edwards Alterra Adaptive Prestent System[2]	29AP4045

[1] Includes a 28F Dilator

[2] Includes an Alterra adaptive prestent that is fully loaded in an Alterra delivery system

Additional Equipment:

- Balloon tip catheter
- Sizing balloons
- 20 cc syringe or larger (x2)
- 50 cc syringe or larger
- High-pressure 3-way stopcock
- Standard cardiac catheterization lab equipment
- Fluoroscopy (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 Edwards Alterra Adaptive Prestent System Procedure

See Edwards Alterra adaptive prestent system instructions for use for device preparation and implantation prior to transcatheter heart valve preparation and deployment.

Prior to valve implantation, assess Alterra prestent stability by evaluating apices engagement in surrounding tissue, wall apposition, and/or motion of prestent within the anatomy. If adequate stability is not noted, consider staging valve deployment after allowing sufficient time for prestent endothelialization.

CAUTION: Failure to identify prestent instability may lead to prestent migration/embolization when tracking interventional devices through the prestent.

7.3 Valve Handling and Preparation

Follow sterile technique during device preparation and implantation.

7.3.1 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.**

7.3.2 Prepare the System

Refer to the Edwards sheath, Edwards Crimper instructions for use for device preparation.

Step	Procedure
1	Visually inspect all the components for damage. Ensure the handle is fully retracted to the gripper. **NOTE: The delivery system is packaged with a balloon cover placed over the balloon and should not be removed until instructed to do so.**
2	Remove the stylet from the distal end of the guidewire lumen and set aside.
3	Flush the guidewire lumen with heparinized saline. Insert the stylet back into the guidewire lumen. **CAUTION: Failure to replace the stylet in the guidewire lumen may result in damage to the lumen during the crimping process.**
4	Attach a 3-way stopcock to the balloon inflation port. Ensure stopcock is tightened securely. Fill a 50 cc or larger syringe with 15-20 mL of diluted contrast medium and attach to the 3-way stopcock.
5	Fill the inflation device provided by Edwards Lifesciences with excess volume of diluted contrast medium relative to the indicated inflation volume. Lock and attach to the 3-way stopcock.
6	Close stopcock to the inflation device. De-air the system using the 50 cc or larger syringe. Slowly release the plunger and return to neutral pressure. **NOTE: Do not remove the balloon cover during de-airing.** **NOTE: May take multiple negative pulls to de-air the balloon catheter.**
7	Close stopcock to the delivery system and de-air the inflation device. By rotating the knob of the inflation device, transfer the contrast medium into the syringe to achieve the appropriate volume required to deploy the valve per the inflation parameters.
8	Verify that the inflation volume in the inflation device is correct. Close the stopcock to the 50 cc or larger syringe. Lock the inflation device and remove the syringe. Verify stopcock is securely attached to the balloon inflation port. **CAUTION: Maintain the inflation device provided by Edwards Lifesciences in the locked position until valve deployment.**

7.3.3 Mount and Crimp the Valve 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 crimper from packaging. Rotate the crimper handle until the aperture is fully open. Attach the 2-piece crimp stopper to the base of the crimper and click into place.
4	Carefully remove the balloon cover from the delivery system. Visually inspect the balloon for damage. Ensure that the stylet is inserted into the guidewire lumen.
5	Remove the valve from the holder and remove the ID tag.
6	With the crimper in the open position, gently place the valve into the crimper aperture. Partially crimp the valve until it fits into the Qualcrimp crimping accessory.
7	Place the Qualcrimp crimping accessory over the valve making sure the edge of the Qualcrimp crimping accessory is parallel to the inflow of the valve.
8	Place the valve and Qualcrimp crimping accessory in crimper aperture. Insert the delivery system coaxially within the valve with the orientation of the valve on the delivery system with the inflow (outer sealing skirt) of the valve towards the handle. **NOTE: Verify correct valve orientation with the inflow (outer sealing skirt) oriented towards the handle.**
9	Crimp the valve between the internal shoulders until it reaches the Qualcrimp stop located on the 2-piece crimp stopper.
10	Gently remove the Qualcrimp crimping accessory from the valve. Remove the Qualcrimp stop from the crimp stopper, leaving the final stop in place.
11	Center the valve within the crimper aperture. Fully crimp the valve until it reaches the final stop and hold for 5 seconds. Repeat this crimp step three (3) more times for a total of 4 crimps. **NOTE: Ensure the valve is coaxial within the crimper aperture and remains between the two internal shoulders of the delivery system.** **WARNING: The physician must verify correct orientation of the valve prior to its implantation.**
12	Flush the outer shaft with heparinized saline through the flush port on the handle.
13	Cover the crimped valve with the valve capsule by retracting the balloon catheter into the outer shaft. Ensure that the distal edge of the valve capsule meets the tapered tip of the delivery system. **CAUTION: Keep valve hydrated until ready for implantation.**
14	Lock the delivery system.
15	Remove the stylet and flush the guidewire lumen of the delivery system.
16	Flush the inline sheath with heparinized saline. Immediately advance the inline sheath until the sheath tip is against the proximal end of the valve capsule. **NOTE: Do not force the inline sheath over the valve capsule.**
17	Hydrate the tapered tip and valve capsule of delivery system with heparinized saline.
18	Flush and hydrate the dilator.

7.4 Valve Delivery

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.

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.

Step	Procedure
1	If necessary, gain access using standard catheterization techniques.
2	Ensure tapered tip and valve capsule of delivery system are hydrated, and the delivery system is locked.
3	If not present, insert the guidewire into the vasculature. Advance the guidewire into the intended landing zone per standard technique.
4	If necessary, remove existing sheath.
5	Predilate the vessel with the provided dilator to prepare the vasculature for insertion and advancement of the delivery system and inline sheath.
6	Introduce the delivery system and inline sheath, until the inline sheath is fully inserted into the vasculature.
7	Continue to advance the delivery system while maintaining inline sheath position and advance to the intended landing zone. **CAUTION: Use caution when advancing devices/delivery systems into the implanted Alterra adaptive prestent to avoid engagement with the inflow apices.**
8	Position the valve within the waist of the Alterra adaptive prestent using the waist markers.
9	When at the intended landing zone, unlock the delivery system. Unsheathe the valve by retracting the outer shaft while maintaining balloon and inline sheath position. The valve is fully uncovered when the handle meets the gripper. Lock the delivery system. Verify the stopcock is securely attached to the balloon inflation port. **CAUTION: Maintain guidewire position in the pulmonary artery during valve unsheathing to prevent loss of guidewire position.**
10	Verify final position and begin valve deployment: • Unlock the inflation device provided by Edwards Lifesciences. • Using slow controlled inflation, deploy the valve with the entire volume in the inflation device, 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.

7.5 System Removal

Step	Procedure
1	Once the balloon is fully deflated, ensure the handle is in the locked position, and retract the delivery system into the vena cava.
2	Unlock the delivery system, retract the balloon into the valve capsule. **CAUTION: Completely cover the balloon prior to removal to minimize the risk of vascular injury.**
3	Lock the delivery system.
4	Remove all devices when the ACT level is appropriate. Continue to remove the delivery system until the valve capsule meets the inline sheath tip. Remove the inline sheath and the delivery system together. **NOTE: A sheath or other device may need to be inserted per standard of care.**
5	Remove all devices when the ACT level is appropriate. Close the access site.

8.0 How Supplied

STERILE: The valve is supplied sterilized with glutaraldehyde solution. The delivery system, sheath, and crimper are supplied sterilized with ethylene oxide gas. The Edwards Alterra adaptive prestent system is supplied pouched and sterilized by e-beam sterilization.

8.1 Storage

The transcatheter heart valve must be stored at 10 °C - 25 °C (50 °F - 77 °F). The delivery system and accessories should be stored in a cool, dry place. The prestent and delivery system must be stored in a cool, dry place.

9.0 MR Safety

MR Conditional

Non-clinical testing has demonstrated that the Edwards Alterra adaptive prestent, alone or with a deployed SAPIEN 3 transcatheter heart valve, is MR Conditional. A patient can be scanned safely immediately after placement of this implant in an MR system meeting the following conditions:

- Static magnetic fields of 1.5 Tesla and 3.0 Tesla
- Spatial magnetic gradient field of 3000 Gauss/cm (30 T/m) or less
- Maximum MR system-reported, whole body averaged specific absorption rate (SAR) of 2.0 W/kg (normal operating mode) scanning per sequence
- Gradient system is in normal operating mode

Under the scan conditions defined above, the Edwards Alterra adaptive prestent is expected to produce a maximum temperature rise of 4.0 °C or less after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends as far as 6.6 mm for gradient echo images when scanned using a 3.0 T MRI system. The artifact obscures the device lumen in spin and gradient echo images.

The delivery system has not been evaluated for MR compatibility and is considered MR unsafe.

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 and prestent. 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 lot number may be found on the prestent package. 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, Prestent 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. The explanted prestent should be placed into a suitable container 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

Patients were enrolled between August 2017 and September 2019 at 11 investigational sites in the U.S. An additional 25 patients were enrolled in a registry between January 2020 and August 2020 to evaluate use of the Pulmonic Delivery System at 13 investigational sites. The database for this PMA reflected data collected through June 2, 2021.

The Alterra Clinical 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

Enrollment in the Alterra Clinical Study was limited to patients who met the following inclusion criteria:

- The candidate/candidate's legal guardian has been informed of the nature of the study, agrees to its provisions and has provided written informed consent
- Weight is ≥ 20 kg (44 lbs)
- RVOT/pulmonary valve (PV) with moderate or greater PR by transthoracic echocardiogram (TTE)
- RVOT/PV proximal and distal landing zone diameter ≥ 27 mm and ≤ 38 mm, and minimum of 35 mm from contractile tissue to lowest pulmonary artery takeoff

Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

- Active infection requiring current antibiotic therapy (if temporary illness, patient may be a candidate 2 weeks after discontinuation of antibiotics)
- History of or active endocarditis (active treatment with antibiotics) within the past 180 days
- Leukopenia (white blood cell (WBC) < 2000 cells/μL), anemia (hemoglobin (Hgb) < 7 g/dL), thrombocytopenia (platelets < 50,000 cells/μL) or any known blood clotting disorder
- Inappropriate anatomy for introduction and delivery of Alterra or the SAPIEN 3
- Need for concomitant atrial septal defect or ventricular septal defect closure or other concomitant interventional procedures other than pulmonary artery or branch pulmonary artery stenting or angioplasty
- Interventional/surgical procedures within 30 days prior to the Alterra or valve implant procedure
- Any planned surgical, percutaneous coronary or peripheral procedure to be performed within the 30-day follow-up from the Alterra or valve implant procedure
- History of or current intravenous drug use
- Major or progressive non-cardiac disease resulting in a life expectancy of less than one year
- Known hypersensitivity to aspirin or heparin and cannot be treated with other antiplatelet and/or antithrombotic medications
- Known hypersensitivity to nitinol, cobalt-chromium, nickel or contrast media that cannot be adequately pre-medicated

- Currently participating in an investigational drug or another device study [Note: Trials requiring extended follow-up for products that were investigational, but have since become commercially available, are not considered investigational devices.]
- Positive urine or serum pregnancy test in female patients of child-bearing potential
- Renal insufficiency (creatinine > 3.0 mg/dL) and/or renal replacement therapy

Clinical Endpoints

The endpoints analyzed in this application included: valve performance based on echocardiographic data, RVOT reintervention, adjudicated adverse events (device embolization, major vascular complications, life-threatening or disabling bleeding, device-related endocarditis and death), successful delivery of the prestent and valve to the intended location, freedom from device explant, site reported adverse events, and New York Heart Association (NYHA) classification. The analyses in the application focused on the 30-day and 6-month time points.

A. Accountability of the PMA Main Cohort

At the time of database lock, a total of 85 patients were enrolled in the study, including 60 in the main cohort and 25 in the PDS registry cohort.

There were 3 different analysis populations defined in the protocol: All Treated (AT), Attempted Implant (AI), and Valve Implant (VI), as summarized in Table 4.

Table 4: Analysis Populations

Analysis Population	Definition	Number of Patients	
		Main Cohort	PDS Registry
All Treated (AT)	All patients who signed informed consent, passed screening and for whom the procedure was begun (defined as the time of vascular access – incision or puncture).	60	25
Attempted Implant (AI)	All AT patients who had an attempted implant (the introducer sheath for vascular delivery of the Alterra adaptive prestent was inserted).	60	25
Valve Implant (VI)	All AI patients who received and retained a SAPIEN 3 THV upon leaving the catheterization laboratory/hybrid suite.	60	25

Study visit compliance is summarized in Table 5. One patient in the main cohort had not completed the 6-month at the time of the database lock.

Table 5: Study Visit Compliance

	Main Cohort (N=60)		PDS Registry (N=25)	
	30 Days	6 Months	30 Days	6 Months
Ineligible*	0	0	1	1
Eligible	60	60	24	24
Visit completed	60 (100.0%)	59 (98.3%)	24 (100%)	23 (95.8%)

*Ineligible patients included those who had died, withdrawn, lost to follow-up, or not reached the visit window.

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 6.

Table 6: Demographics and Baseline Characteristics (AT Population)

Demographics and Baseline Characteristics	Summary Statistics*	
	Main Cohort (N=60)	PDS Registry (N=25)
Age (years)	29.5 ± 2.14 (60)	29.1 ± 3.45 (25)
<12 years (child)	1.7% (1/60)	0.0% (0/25)
12-21 years (adolescent)	48.3% (29/60)	44.0% (11/25)
>21 years (adult)	50.0% (30/60)	56.0% (14/25)
Male Sex	56.7% (34/60)	56.0% (14/25)
Weight (kg)	73.1 ± 3.05 (60)	73.7 ± 4.44 (25)
New York Heart Association (NYHA) Class		
Class I	53.3% (32/60)	37.5% (9/24)
Class II	38.3% (23/60)	45.8% (11/24)
Class III	8.3% (5/60)	16.7% (4/24)
Class IV	0.0% (0/60)	0.0% (0/24)
NYHA Class Grouped		
Class I/II	91.7% (55/60)	83.3% (20/24)
Class III/IV	8.3% (5/60)	16.7% (4/24)
Primary diagnosis		
Pulmonary atresia	5.0% (3/60)	4.0% (1/25)
Pulmonary valve stenosis	23.3% (14/60)	20.0% (5/25)
Tetralogy of Fallot	70.0% (42/60)	68.0% (17/25)
Other	1.7% (1/59)	8.0% (2/25)
Secondary diagnosis		
Atrial septal defect	18.3% (11/60)	12.0% (3/25)
Coarctation of the aorta	3.3% (2/60)	4.0% (1/25)
Ventricular septal defect	30.0% (18/60)	12.0% (3/25)
Other	21.7% (13/60)	20.0% (5/25)
Most recent RVOT/PV intervention or surgery		
Pericardial/transannular patch	65.0% (39/60)	60.0% (15/25)
Valvuloplasty alone	25.0% (15/60)	20.0% (5/25)
Other†	10.0% (6/60)	20.0% (5/25)

*Continuous measures - mean ± SD (total no.); categorical measures - % (no./total no.)

†Tetralogy of Fallot repairs, unspecified RVOT/PV procedures, or none.

The breakdowns of prior cardiac interventions by patient age in the AT population are shown in Table 7 for the main cohort and Table 8 for the PDS registry cohort.

Table 7: Prior Cardiac Interventions by Age Group (AT Population) – Main Cohort

Most Recent RVOT/PV Intervention or Surgery	Summary Statistics*		
	<12 Years (N= 1)	12-21 Years (N= 29)	≥22 Years (N= 30)
Pericardial/transannular patch	100.0% (1/1)	82.8% (24/29)	46.7% (14/30)
Valvuloplasty alone	0.0% (0/1)	17.2% (5/29)	33.3% (10/30)
Other	0.0% (0/1)	0.0% (0/29)	20.0% (6/30)
Tetralogy of Fallot repairs	0.0% (0/0)	0.0% (0/29)	66.7% (4/6)
Unspecified RVOT/PV procedure	0.0% (0/0)	0.0% (0/29)	16.7% (1/6)
None	0.0% (0/0)	0.0% (0/29)	16.7% (1/6)

*Event rate (no./total no.)

Table 8: Prior Cardiac Interventions by Age Group (AT Population) – PDS Registry

Most Recent RVOT/PV Intervention or Surgery	Summary Statistics*	
	12-21 Years (N=11)	≥ 22 Years (N=14)
Pericardial/transannular patch	72.7% (8/11)	50.0% (7/14)
Valvuloplasty alone	18.2% (2/11)	21.4% (3/14)
Other	9.1% (1/11)	28.6% (4/14)
Tetralogy of Fallot repairs	100.0% (1/1)	25.0% (1/4)
Unspecified RVOT/PV procedure	0.0% (0/1)	50.0% (2/4)
None	0.0% (0/1)	25.0% (1/4)

*Event rate (no./total no.)

A. Safety and Effectiveness Results

(1) Primary Endpoint

The primary endpoint result for the main cohort is presented in Table 9. The rate of THV dysfunction at 6 months was 0% (two-sided confidence interval: 0.0% to 6.1%). Since the upper limit of the two-sided 95% confidence interval for the primary endpoint event rate was < 25%, the endpoint was met.

Table 9: Primary Endpoint Result – Main Cohort

Endpoint	Summary Statistics* (N=60)	95% Confidence Interval†	Less Than Prespecified Performance Goal (25%)?
Valve dysfunction‡	0.0% (0/59)	[0.0%, 6.1%]	Yes
RVOT/PV reintervention	0.0% (0/60)		
Moderate or greater pulmonary regurgitation	0.0% (0/59)		
Mean RVOT gradient ≥35 mmHg	0.0% (0/59)		

*Event rate (no./total no.)
†One patient did not have evaluable echocardiogram data.
‡Two-sided 95% confidence interval.

The primary endpoint result for the PDS registry cohort is presented in Table 10. Acute PDS success was achieved in 88.0% of the patients.

Table 10: Primary Endpoint Results - PDS Registry

Endpoint	Summary Statistics* (N=25)
Acute PDS success*	88.0% (22/25)
Single THV implanted in the desired location	100.0% (25/25)
RV-PA peak-to-peak gradient < 35 mmHg post implantation	100.0% (25/25)
Less than moderate PR by discharge TTE (or earliest evaluable TTE)	88.0% (22/25)
Free of explant at 24 hours post implantation	100.0% (25/25)

*Event rate (no./total no.)

(2) Additional Outcome Measures

Technical Success

Technical success at exit from the procedure room was achieved in 96.7% of the patients in the main cohort, as summarized in Table 11.

Table 11: Technical Success Result – Main Cohort

Endpoint	Summary Statistics* (N=60)
Technical Success	96.7% (58/60)
Alive	100.0% (60/60)
Successful access delivery and retrieval of the Alterra delivery system	100.0% (60/60)
Successful access delivery and retrieval of the SAPIEN 3 delivery system	100.0% (60/60)
Single Alterra deployed in the desired location	100.0% (60/60)
Single SAPIEN 3 valve deployed to the desired location	96.7% (58/60)
No need for unplanned or emergency surgery or intervention related to the device or access procedure	100.0% (60/60)

*Event rate (no./total no.)

Device Success

The device success rate in the main cohort was 88.3% at 30 days, and 76.3% at 6 months, as summarized in Table 12.

Table 12: Device Success Results – Main Cohort

Endpoint	Summary Statistics*	
	30 Days (N = 60)	6 Months (N = 59)
Device Success	88.3% (53/60)	76.3% (45/59)
Alive	100.0% (60/60)	100% (59/59)
No device explant	100.0% (60/60)	100% (59/59)
No additional surgical or interventional procedures related to access or the device since completion of the original procedure	100.0% (60/60)	100% (59/59)
Intended performance of the device†	88.3% (53/60)	76.3% (45/59)
Structural performance‡	90.0% (54/60)	76.3% (45/59)
Hemodynamic performance	100.0% (60/60)	100% (59/59)
Absence of para-device complications	98.3% (59/60)	100% (59/59)

*Event rate (no./total no.)

† Intended performance of the device is defined as a composite of: (1) structural performance - no migration, embolization, fracture, thrombosis (including reduce leaflet mobility if detected) or endocarditis; (2) hemodynamic performance - net pulmonary valve peak gradient ≤ 35 mmHg and transvalvular PR ≤ mild; and (3) absence of para-device complications – pulmonary valve regurgitation > mild, need for a permanent pacemaker, or new pulmonary embolism.

‡The structural performance events included 4 Alterra Prestent fracture events, 1 SAPIEN 3 THV thrombosis event, 1 Alterra Prestent thrombosis event, and 1 Alterra Prestent migration event at 30 days and an additional 8 Alterra Prestent fracture events at 6 months. Multiple events occurred on one patient are counted as one.

Procedural Success

Procedural success was met in 88.3% of patients in the main cohort at 30 days, as summarized in Table 13.

Table 13: Procedure Success Result – Main Cohort

Endpoint	Summary Statistics* (N=60)
Procedure Success	88.3% (53/60)
Device success	88.3% (53/60)
No device or procedure related SAEs†	100.0% (60/60)

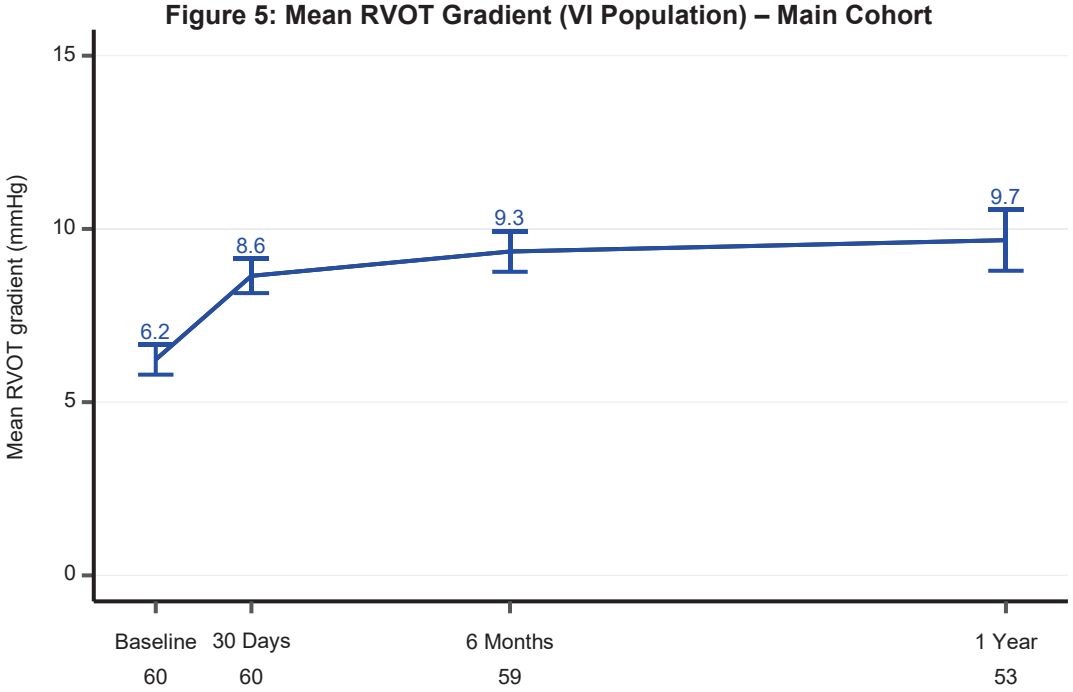
*Event rate (no./total no.)

† SAEs: life threatening bleed; major vascular or access site complications requiring unplanned reintervention or surgery; stage 2 or 3 acute kidney injury (including new dialysis); severe heart failure or hypotension requiring intravenous inotrope, ultrafiltration or mechanical circulatory support; prolonged intubation > 48 hours.

THV Hemodynamic Function

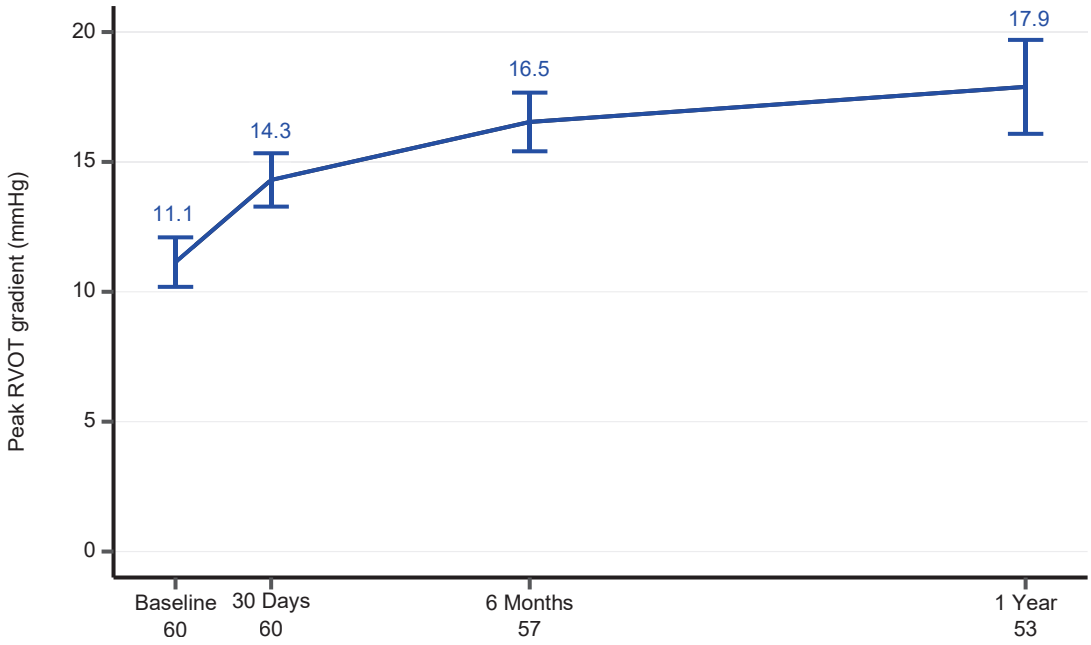
The mean RVOT gradient, peak RVOT gradient, total PR, and paravalvular regurgitation results through 1 year for the main cohort are shown in Figure 5 through Figure 8, respectively. The mean and peak RVOT gradients remained largely stable through 1 year post implant (9.7 mmHg and 17.9 mmHg, respectively, at 1 year). The proportion of patients with total PR ≥ moderate decreased from 100% to 9.6% at 1 year. The proportion of patients with paravalvular regurgitation ≥ moderate was 1.7% at 30 days, and 0% at both 6 months and 1 year.

Figure 5: Mean RVOT Gradient (VI Population) – Main Cohort



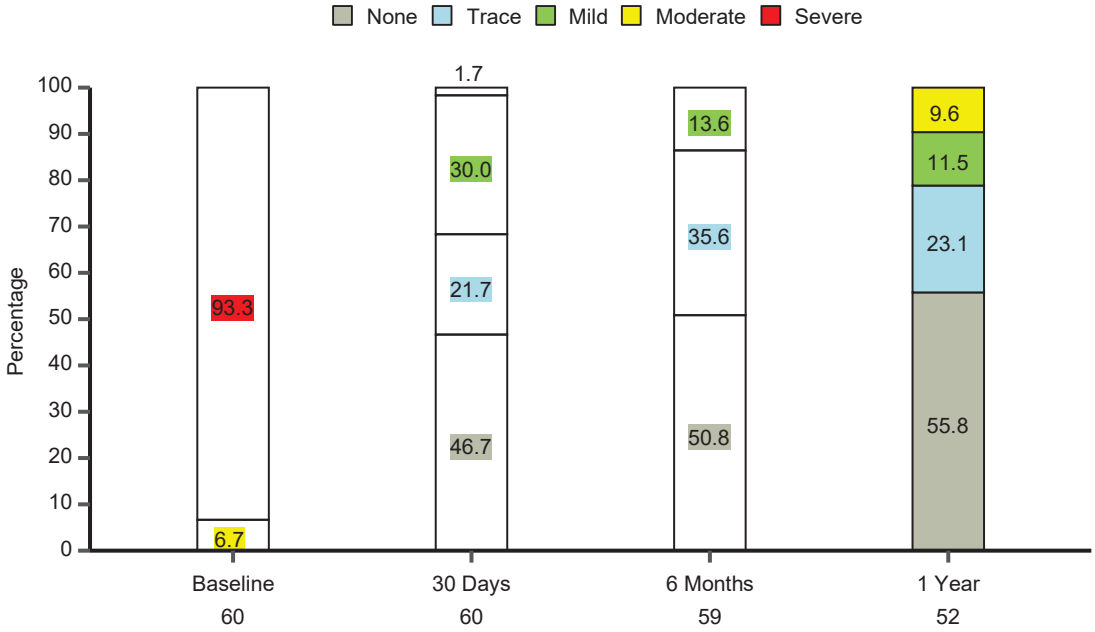
Note: Line plot with mean and standard error. The total number of patients at each visit time point only counted the patients with evaluable values.

Figure 6: Peak RVOT Gradient (VI Population) – Main Cohort



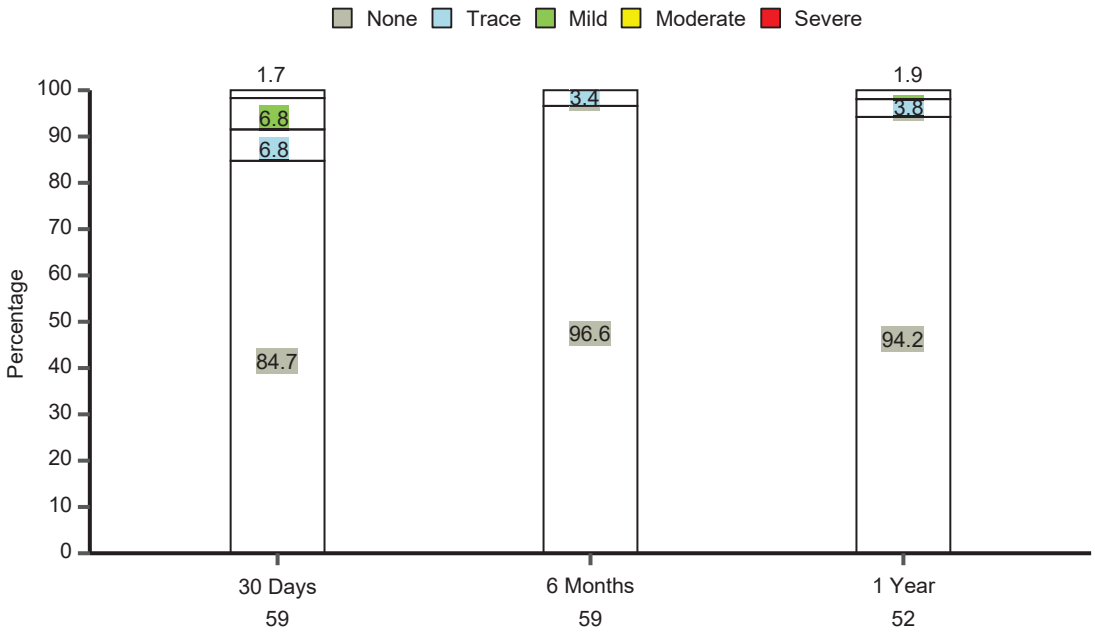
Note: Line plot with mean and standard error. The total number of patients at each visit time point only counted the patients with evaluable values.

Figure 7: Total Pulmonary Regurgitation (VI Population) – Main Cohort



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

Figure 8: Paravalvular Regurgitation (VI Population) – Main Cohort

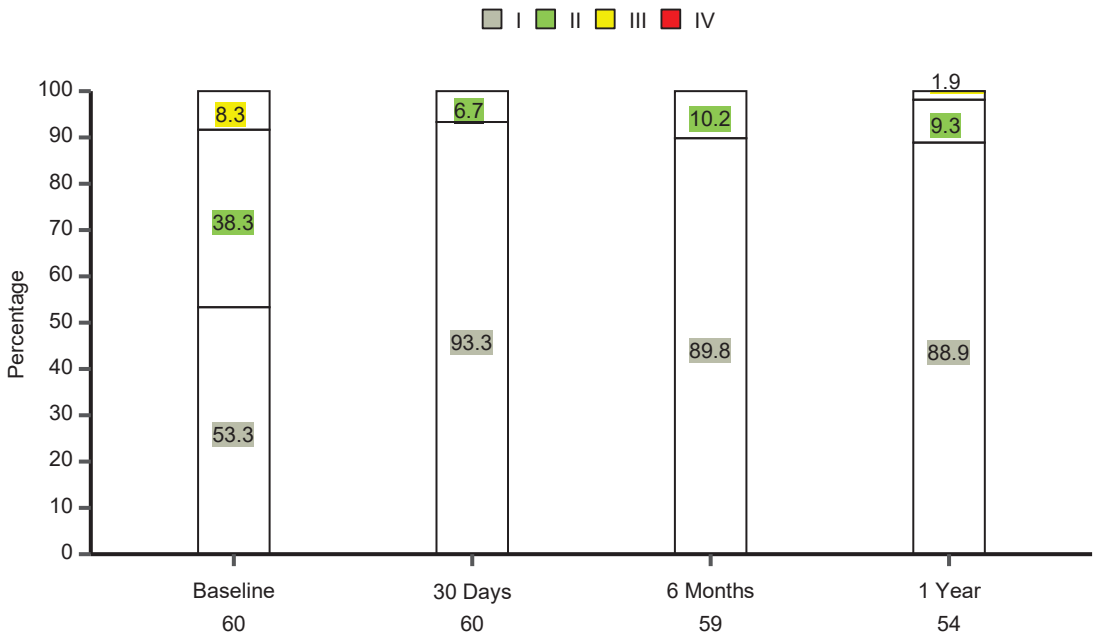


Note: The total number of patients at each visit time point only counted the patients with evaluable values.

NYHA Functional Class

The NYHA classifications by visit are presented for the main cohort in Figure 9. At baseline, 91.7% of patients in the main cohort were in NYHA Class I/II, which increased to 100% at 30 days and 6 months and 98.1% at 1 year.

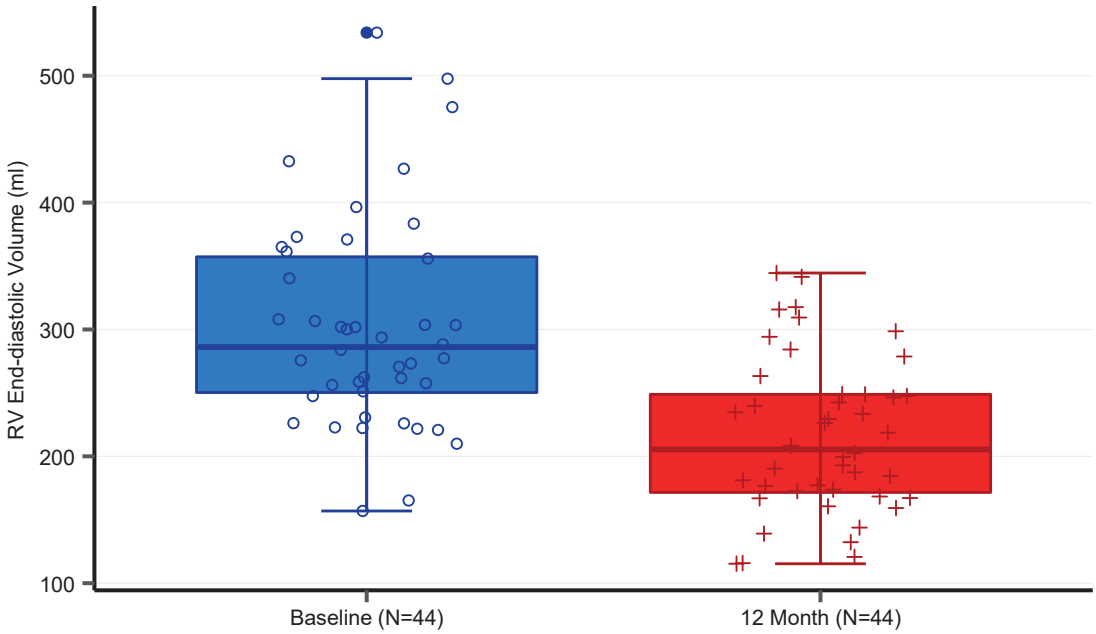
Figure 9: NYHA Class by Visit (VI Population) – Main Cohort



Characterization of Right Ventricular Remodeling

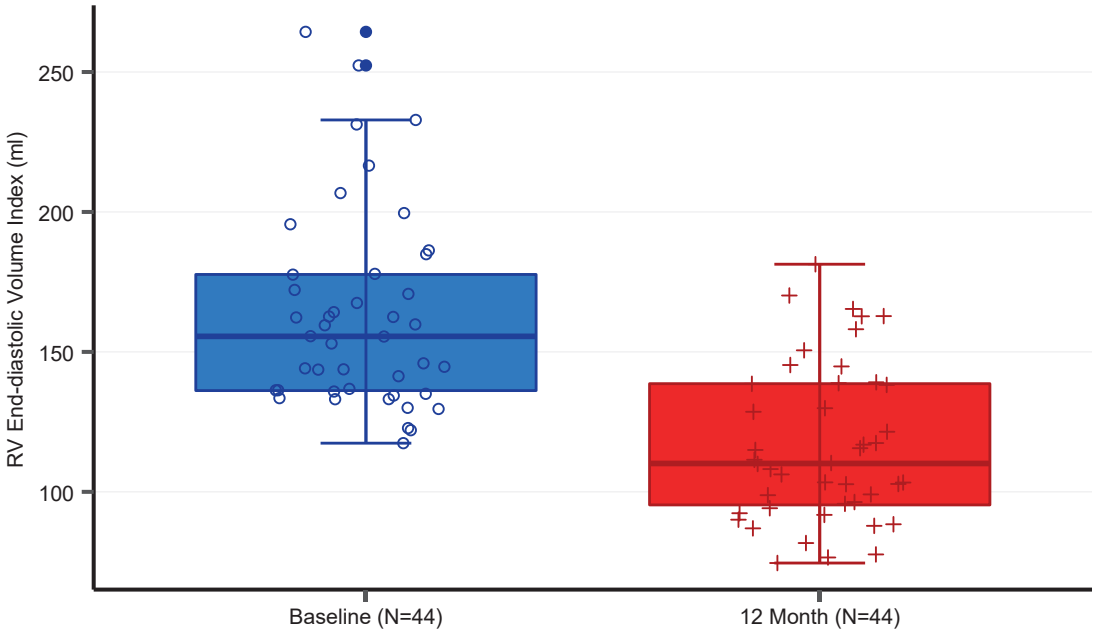
Right ventricular remodeling was characterized via magnetic resonance imaging (MRI) and computed tomography (CT) in the main cohort. Right ventricular end diastolic volume (RVEDV), RVEDV index, and main pulmonary artery regurgitant fraction at baseline and 1 year are presented in Figure 10 through Figure 12, respectively. The RVEDV decreased from 295.9 ml to 220.4 ml, with the corresponding RVEDV index decreasing from 162.7 ml/m^2 to 118.9 ml/m^2. The main pulmonary artery regurgitant fraction decreased from 47.4% to 4.1%.

Figure 10: Right Ventricular End Diastolic Volume (VI Population) – Main Cohort



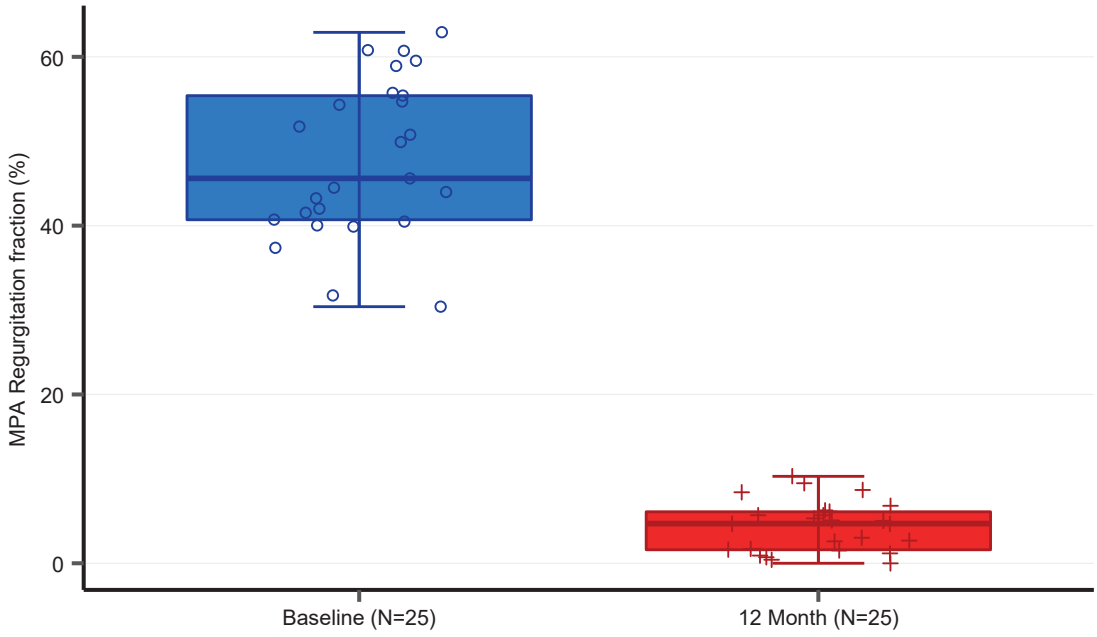
Note: The total number of patients at each visit time point only counted the patients with evaluable paired values.

Figure 11: Right Ventricular End Diastolic Volume Index (VI Population) – Main Cohort



Note: The total number of patients at each visit time point only counted the patients with evaluable paired values.

Figure 12: Main Pulmonary Artery Regurgitant Fraction (VI Population) – Main Cohort



Note: The total number of patients at each visit time point only counted the patients with evaluable paired values.

(3) Adverse Events

Kaplan-Meier estimates of the CEC-adjudicated adverse events through 1 year for the main cohort and through 6 months for the PDS registry cohort are presented in Table 14 and Table 15 respectively.

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

Event	Summary Statistics*		
	30 Days (N=60)	6 Months (N=59)	1 Year (N = 49)
All-cause death	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	33.3% (21, 20)	33.3% (21, 20)	33.3% (21, 20)
Permanent pacemaker	0.0% (0, 0)	0.0% (0, 0)	0.0% (0, 0)
Acute kidney injury	0.0% (0, 0)	0.0% (0, 0)	0.0% (0, 0)
Bleeding	18.3% (12, 11)	21.7% (14, 13)	23.5% (16, 14)
Life threatening or disabling	0.0% (0, 0)	1.7% (1, 1)	3.5% (2, 2)
Major	1.7% (1, 1)	1.7% (1, 1)	1.7% (1, 1)
Minor	16.7% (11, 10)	18.4% (12, 11)	20.1% (13, 12)
Coronary artery compression	0.0% (0, 0)	0.0% (0, 0)	0.0% (0, 0)
Endocarditis	0.0% (0, 0)	0.0% (0, 0)	0.0% (0, 0)
Myocardial infarction	0.0% (0, 0)	0.0% (0, 0)	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)
Transient ischemic attack	0.0% (0, 0)	0.0% (0, 0)	0.0% (0, 0)
Vascular injury or access site complication	5.0% (3, 3)	5.0% (3, 3)	6.8% (4, 4)
Major	0.0% (0, 0)	0.0% (0, 0)	1.8% (1,1)
Minor	5.0% (3, 3)	5.0% (3, 3)	5.0% (3, 3)

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

Table 15: CEC-Adjudicated Adverse Events Through 6 Months (AT Population) – PDS Registry

Event	Summary Statistics*	
	30 Days (N=24)	6 Months (N = 24)
All-cause death	4.0% (1, 1)	4.0% (1, 1)
Cardiovascular	0.0% (0, 0)	0.0% (0, 0)
Non-Cardiovascular	4.0% (1, 1)	4.0% (1, 1)
Reintervention	0.0% (0, 0)	0.0% (0, 0)
Arrhythmia	48.0% (15, 12)	48.0% (15, 12)
Permanent pacemaker	0.0% (0, 0)	0.0% (0, 0)
Acute kidney injury	0.0% (0, 0)	0.0% (0, 0)
Bleeding	20.0% (6, 5)	20.0% (6, 5)
Life threatening or disabling	0.0% (0, 0)	0.0% (0, 0)
Major	0.0% (0, 0)	0.0% (0, 0)
Minor	20.0% (6, 5)	20.0% (6, 5)
Coronary artery compression	0.0% (0, 0)	0.0% (0, 0)
Endocarditis	0.0% (0, 0)	0.0% (0, 0)
Myocardial infarction	0.0% (0, 0)	0.0% (0, 0)
Pulmonary embolism	0.0% (0, 0)	0.0% (0, 0)
Stroke	0.0% (0, 0)	0.0% (0, 0)
Transient ischemic attack	0.0% (0, 0)	0.0% (0, 0)
Vascular injury or access site complication	8.0% (4, 2)	8.0% (4, 2)
Major	0.0% (0, 0)	0.0% (0, 0)
Minor	8.0% (4, 2)	8.0% (4, 2)

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

(4) Other Study Observations

Procedural Information

Procedural data for the main cohort and PDS registry cohort are summarized in Table 16. Concomitant Alterra adaptive prestent and SAPIEN 3 THV procedures were performed on the majority of patients (98.3% for the main cohort & 100% for PDS registry cohort).

Table 16: Procedural Data (AT Population)

Variable	Summary Statistics*	
	Main Cohort (N=60)	**PDS Registry (N=25)**
Procedure type		
Staged procedure	1.7% (1/60)	0.0% (0/25)
Prestent procedure sheath time (min)	61.0	N/A
SAPIEN 3 procedure sheath time (min)	23.0	N/A
Concomitant Alterra adaptive prestent + SAPIEN 3 THV procedure	98.3% (59/60)	100.0% (25/25)
Procedure sheath time (min)	66.8 ± 4.73 (59)	58.2 ± 8.42 (25)
Alterra adaptive prestent procedure complications	3.3% (2/60)	0.0% (0/25)
SAPIEN 3 procedure complications	10.0% (6/60)	8.0% (2/25)
Total fluoroscopy time	37.2 ± 3.04 (60)	38.0 ± 4.88 (25)
Alterra adaptive prestent procedure post-dilatation performed	0.0% (0/60)	0.0% (0/25)
SAPIEN 3 procedure post-dilatation performed	11.7% (7/60)	0.0% (0/25)
Alterra adaptive prestent implanted in the intended location at the time the patient left the procedure room	100.0% (60/60)	100.0% (25/25)
SAPIEN 3 THV implanted in the intended location at the time the patient left the procedure room	100.0% (60/60)	100.0% (25/25)
Single SAPIEN 3 THV implanted	96.7% (58/60)	100.0% (25/25)

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

These products are manufactured and sold under one or more of the following US patent(s): US Patent No. 7,530,253; 7,895,876; 8,690,936; 8,790,387; 9,301,840; 9,301,841; and 9,393,110; and corresponding foreign patents.

CT Core Laboratory Findings

The results of an imaging assessment by the CT Core Laboratory through 1 year for the main cohort and through 30 days for the PDS registry cohort are presented in Table 17 and Table 18, respectively. There were no device reinterventions associated with these findings.

Table 17: CT Core Laboratory Findings (VI Population) – Main Cohort

Finding	Summary Statistics*	
	30 Days (N = 60)	1 Year (N = 55)
Alterra Adaptive Prestent penetration†		
Minor penetration - into adjacent vasculature or cardiac structure without extravasation, pseudoaneurysm, or erosion	2.6% (1/39)	5.3% (1/19)
Major penetration - protrusion into surrounding tissue with blood pooling, or erosion, or pseudoaneurysm	0.0% (0/39)	0.0% (0/19)
Pedunculated mobile mass†	2.6% (1/39)	0.0% (0/19)
Alterra Adaptive Prestent fracture‡		
Fracture not requiring intervention	6.7% (4/60)	21.8% (12/55)
Fracture requiring intervention	0.0% (0/60)	0.0% (0/55)
SAPIEN 3 valve frame fracture‡	0.0% (0/60)	0.0% (0/55)

*Rate (no./total no.)
†Only included patients with evaluable images at visit time point.
‡Fracture was determined by either chest x-ray or fluoroscopy.

Table 18: CT Core Laboratory Findings (VI Population) – PDS Registry

Finding	Summary Statistics*
	30 Days (N = 25)
Alterra Adaptive Prestent penetration†	
Minor penetration - into adjacent vasculature or cardiac structure without extravasation, pseudoaneurysm, or erosion	8.7% (2/23)
Major penetration - protrusion into surrounding tissue with blood pooling, or erosion, or pseudoaneurysm	0.0% (0/23)
Pedunculated mobile mass†	4.3% (1/23)
Alterra Adaptive Prestent fracture‡	
Fracture not requiring intervention	20.0% (5/25)
Fracture requiring intervention	0.0% (0/25)
SAPIEN 3 valve frame fracture‡	0.0% (0/25)

*Rate (no./total no.)
†Only included patients with evaluable images at visit time point.
‡Fracture was determined by either chest x-ray or fluoroscopy.

2021-12
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Edwards	Title: IFU, ALTERRA, S3 PULMONIC, US	Page: 27 of 27
	Label Item/Revision:	10043118001/A
	Visual Representation/Revision:	DOC-0158710/A
	Drawing/Specification:	DOC-0001941
	English Master/Revision:	N/A
	eIFU Visual Representation/Revision:	N/A
	Refer to supporting material for signatures.	

NOTE
1. ALL ART PRINTS 100% BLACK UNLESS OTHERWISE NOTED.

INKS
BLACK
GRAYSCALE 55% BLACK

Edwards

Edwards Alterra Adaptive Prestent System

Instructions for Use

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

Implantation of the Edwards Alterra adaptive prestent 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 Edwards Alterra adaptive prestent system is supplied sterilized with e-beam sterilization. The sheath is supplied sterilized with ethylene oxide gas.

1.0 Device Description

Edwards Alterra Adaptive Prestent System

The Edwards Alterra adaptive prestent system consists of an Alterra adaptive prestent that is fully loaded in an Alterra delivery system and supplied together in one package:

- **Edwards Alterra Adaptive Prestent (Figure 1)**

The Edwards Alterra adaptive prestent is used as a docking adaptor for the 29 mm Edwards SAPIEN 3 transcatheter heart valve (THV). It is comprised of a self-expanding, radiopaque, nitinol frame assembly and polyethylene terephthalate (PET) fabric covering. The prestent has designated inflow and outflow sides. The proximal inflow section is identifiable by the presence of two triangular tabs (prestent connector) that are attached to the catheter of the delivery system. The distal outflow section is distinguished by the open cells for blood flow. The PET fabric is attached by sutures to the inside surface of the frame to create sealing at the inflow section and opening for the outflow. Sutures are also used in the center to support the middle section when an Edwards SAPIEN 3 transcatheter heart valve is implanted. Three (3) radiopaque markers are positioned at the prestent waist.

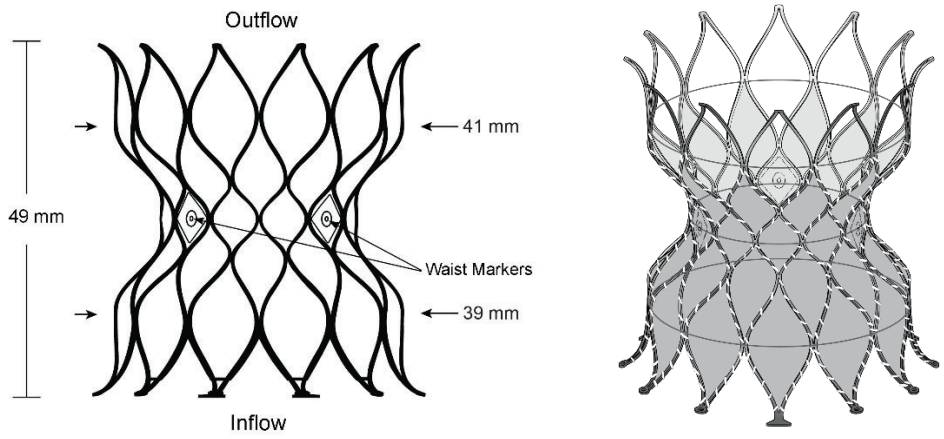

Figure 1. Edwards Alterra Adaptive Prestent

Table 1

Inflow Sealing OD	Outflow Sealing OD	Height
39 mm	41 mm	49 mm

Sizing recommendation for the prestent in the right ventricular outflow tract/pulmonary valve (RVOT/PV) landing zone are shown in the table below:

Table 2: Prestent Sizing in RVOT landing zone

Perimeter	Perimeter Derived Diameter[1]	Prestent Size Diameter[2] x Length	Valve Size
84.9 mm – 119.3 mm	27 mm – 38 mm	40 mm x 49 mm	29 mm

[1] Diameter range during systole

[2] Diameter is average of inflow and outflow diameters

NOTE: For Edwards SAPIEN 3 transcatheter heart valve implantation, refer to the Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent instructions for use.

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

The delivery system includes a handle which consists of a wheel that allows for deployment, two primary shafts with a flush port to flush the delivery system, and a long tapered tip at the distal end to facilitate tracking through the vasculature. A radiopaque delivery system marker band shows the location of the tip of the outer shaft. The prestent is fully loaded in the delivery system. A stylet is included within the guidewire lumen.

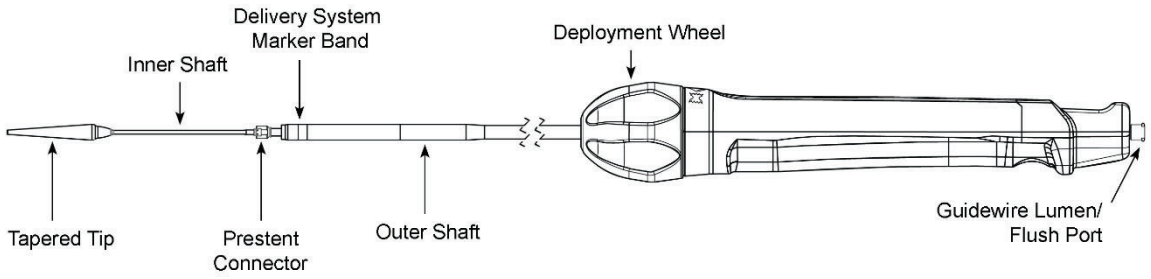

Figure 2. Edwards Alterra Delivery System

Additional Accessories

- **Edwards Sheath**

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

2.0 Indications

The Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent is indicated for use in the management of pediatric and adult patients with severe pulmonary regurgitation as measured by echocardiography who have a native or surgically-repaired right ventricular outflow tract and are clinically indicated for pulmonary valve replacement.

3.0 Contraindications

The Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent 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.

- Do not mishandle the delivery system or use if the packaging sterile barriers and any components have been opened or damaged, the expiration date has elapsed, or the delivery system cannot be flushed.

5.0 Precautions

- Correct sizing of the prestent into the RVOT is essential to minimize risks such as paravalvular leak, migration, embolization, and/or RVOT rupture.
- Long-term durability has not been established for the prestent. Medical follow-up is advised so that device related complications can be diagnosed and properly managed.
- Patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/or polymeric materials may have an allergic reaction to these materials.
- Assessment for coronary compression risk prior to implantation is recommended.
- Patient venous anatomy should be evaluated to prevent the risk of access that would preclude the delivery and deployment of the device.
- 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.
- Fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. Patient radiation dose should be monitored during the procedure.
- Patient should be heparinized to maintain the ACT at ≥ 250 sec prior to introduction of the delivery system in order to prevent thrombosis.
- Prestent 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 antiplatelet therapy.
- It is recommended that all prestent recipients be prophylactically treated for endocarditis to minimize the risk of infection.
- If a prestent fracture is detected with significant loss in valve functionality, reintervention should be considered.
- 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 patients of child-bearing potential

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
- Cardiac failure
- Embolic event: air, calcific material, thrombus
- Infection including incisional site infection, septicemia and endocarditis
- Myocardial infarction
- Renal insufficiency or renal failure
- Conduction system injury
- Arrhythmia
- Deep vein thrombosis
- Arteriovenous (AV) fistula
- Systemic or peripheral nerve injury

- Systemic or peripheral ischemia
- Pulmonary edema
- Pneumothorax
- Pleural effusion
- Dyspnea
- Atelectasis
- Dislodgement of previously implanted devices (i.e. pacing lead)
- 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

Potential risks that may or may not require intervention associated with the prestent, 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
- Injury to tricuspid valve
- Device fracture
- Device embolization
- Device migration or malposition
- Endocarditis
- Chest pain/discomfort
- Device penetration/perforation into surrounding vasculature
- Device dysfunction (regurgitation and/or stenosis)
- Aortic root distortion
- Embolic event: device fragments
- Mechanical failure of delivery system, and/or accessories

7.0 Directions for Use

7.1 System Compatibility

Table 3

Product Name	Model
Edwards Alterra Adaptive Prestent System[1]	29AP4045
Sheath provided by Edwards Lifesciences or equivalent	

[1] Includes an Alterra adaptive prestent that is fully loaded in an Alterra delivery system

Additional Equipment:

- Balloon tip catheter
- Sizing balloons
- 20 cc syringe or larger

- 50 cc syringe or larger
- Standard cardiac catheterization lab equipment
- Fluoroscopy (appropriate for use in percutaneous coronary interventions)
- Exchange length 0.035 inch (0.89 mm) stiff guidewire
- Physiological saline
- Sterile table for device preparation

Refer to the *Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent instructions for use* for additional materials required to prepare the *Edwards SAPIEN 3 Transcatheter Pulmonary Valve System.*

7.2 Device Handling and Preparation

Follow sterile technique during device preparation and implantation.

7.2.1 Prepare the System

Refer to the Edwards sheath instructions for use for device preparation.

Step	Procedure
1	Remove the delivery catheter with the preloaded prestent from packaging. Visually inspect all components for damage.
2	Ensure there is a small gap between the outer shaft and the tapered tip to facilitate flushing of the inner lumen. If needed retract the outer shaft using the deployment wheel. **NOTE: Do not allow the end of the prestent to begin to exit the delivery system.**
3	With the stylet still in place, flush the guidewire lumen with heparinized saline.
4	Using the deployment wheel, re-advance the outer shaft until it is even with the tapered tip. **NOTE: Do not overdrive the outer shaft onto the tapered tip.**
5	Remove the stylet and repeat flushing the guidewire lumen.

7.3 Prestent Delivery

Prestent 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.

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.

Step	Procedure
1	Gain access using standard catheterization techniques.
2	If necessary, predilate the vessel.
3	Introduce the sheath per its instructions for use.
4	Insert and advance the delivery system to the RVOT landing zone. **NOTE: Advance the delivery system from the shaft. Do not push the delivery system in by using the handle. Do not rotate the deployment wheel during advancement of the delivery system.**
5	Position the delivery system marker band distal to the intended landing zone.

Step	Procedure
6	Begin deployment by rotating the deployment wheel to retract the outer shaft. **NOTE: The delivery system marker band is located slightly proximal to the distal edge of the outer shaft.** **NOTE: Waist markers on the prestent indicate the middle of the prestent.** **NOTE: The prestent can be recaptured into the outer shaft and repositioned if deployed no more than 50%.** **CAUTION: Once deployment has begun, do not reposition the device more distally. Advancement of the device with the prestent exposed may increase the risk for vascular damage.**
7	Once the device is deployed to 50%, assess the device position within the landing zone. At 50% deployment, the delivery system marker band will be at the inflow edge of the Alterra waist markers.
8	If needed, recapture and reposition the prestent by rotating the deployment wheel in the reverse direction from deployment until the outer shaft fully covers the prestent as shown by the delivery system marker band. **NOTE: The prestent can be recaptured and redeployed one time. If a second recapture of the partially deployed prestent is performed, remove and replace the device.** **NOTE: Several rotations of the deployment wheel may be necessary before the Alterra begins to be recaptured.** **CAUTION: Do not overdrive the outer shaft onto the tapered tip when recapturing the prestent. This may cause the delivery system to cinch down on the guidewire preventing independent movement of the delivery system and guidewire.** **CAUTION: Recapturing and redeploying a prestent more than one time may impact implant integrity**. **CAUTION: Recapturing a prestent that has been deployed more than 50% may cause system damage.**
9	After achieving an acceptable position, completely deploy the prestent by continuing to rotate the deployment wheel until the delivery system marker band is beyond the prestent connector.
10	Confirm release of prestent. **CAUTION: Failure to identify release of the prestent connector tabs from the prestent connector may lead to prestent embolization during removal of the Alterra delivery system.**

7.4 System Removal

Step	Procedure
1	Slowly retract the system through the prestent. Remove the delivery system. **CAUTION: Ensure that the tapered tip and delivery system do not interfere with the prestent upon removal to prevent movement of the prestent.**
2	Assess Alterra prestent stability by evaluating apices engagement in surrounding tissue, wall apposition, and/or motion of prestent within the anatomy. If adequate stability is not noted, consider staging valve deployment after allowing sufficient time for prestent endothelialization. **CAUTION: Failure to identify prestent instability may lead to prestent migration/embolization when tracking interventional devices through the prestent.**

8.0 How Supplied

The Edwards Alterra adaptive prestent system is supplied pouched and sterilized by e-beam sterilization.

8.1 Storage

The prestent and delivery system must be stored in a cool, dry place.

9.0 MR Safety

MR Conditional

Non-clinical testing has demonstrated that the Edwards Alterra adaptive prestent, alone or with a deployed SAPIEN 3 transcatheter heart valve, is MR Conditional. A patient can be scanned safely immediately after placement of this implant in an MR system meeting the following conditions:

- Static magnetic fields of 1.5 Tesla and 3.0 Tesla
- Spatial magnetic gradient field of 3000 Gauss/cm (30 T/m) or less
- Maximum MR system-reported, whole body averaged specific absorption rate (SAR) of 2.0 W/kg (normal operating mode) scanning per sequence
- Gradient system is in normal operating mode

Under the scan conditions defined above, the Edwards Alterra adaptive prestent is expected to produce a maximum temperature rise of 4.0 °C or less after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends as far as 6.6 mm for gradient echo images when scanned using a 3.0 T MRI system. The artifact obscures the device lumen in spin and gradient echo images.

The delivery system has not been evaluated for MR compatibility and is considered MR unsafe.

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 prestent. After implantation, all requested information should be completed on this form. The lot number may be found on the package. 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 Prestent and Device Disposal

The explanted prestent should be placed into a suitable container 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

For clinical studies and results related to the use of the Edwards Alterra Adaptive Prestent System, refer to the Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent instructions for use.

These products are manufactured and sold under one or more of the following US patent(s): US Patent No. 7,530,253; 7,895,876; 8,690,936; 8,790,387; 9,301,840; 9,301,841; 9,393,110; and corresponding foreign patents.

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Edwards	Title: IFU, ALTERRA RECAPTURE, US	Page: 10 of 10
	Label Item/Revision:	10043119001/A
	Visual Representation/Revision:	DOC-0158711/A
	Drawing/Specification:	DOC-0001941
	English Master/Revision:	N/A
	eIFU Visual Representation/Revision:	N/A
	Refer to supporting material for signatures.	

NOTE
1. ALL ART PRINTS 100% BLACK UNLESS OTHERWISE NOTED.

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