Edwards Lifesciences

Edwards SAPIEN XT
Transcatheter Heart Valve with the Ascendra+ Delivery System

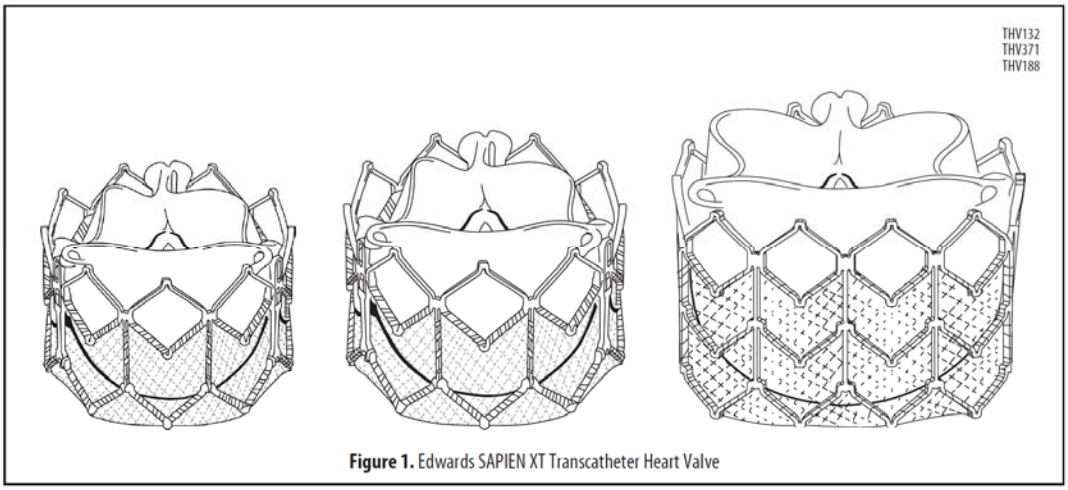


Figure 1. Edwards SAPIEN XT Transcatheter Heart Valve

Instructions for Use

Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.

Implantation of the transcatheter heart valve should be performed only by physicians who have received Edwards Lifesciences training. The implanting physician should be experienced in balloon aortic valvuloplasty.

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

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

1.0 Device Description

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

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

Table 1

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

Table 2

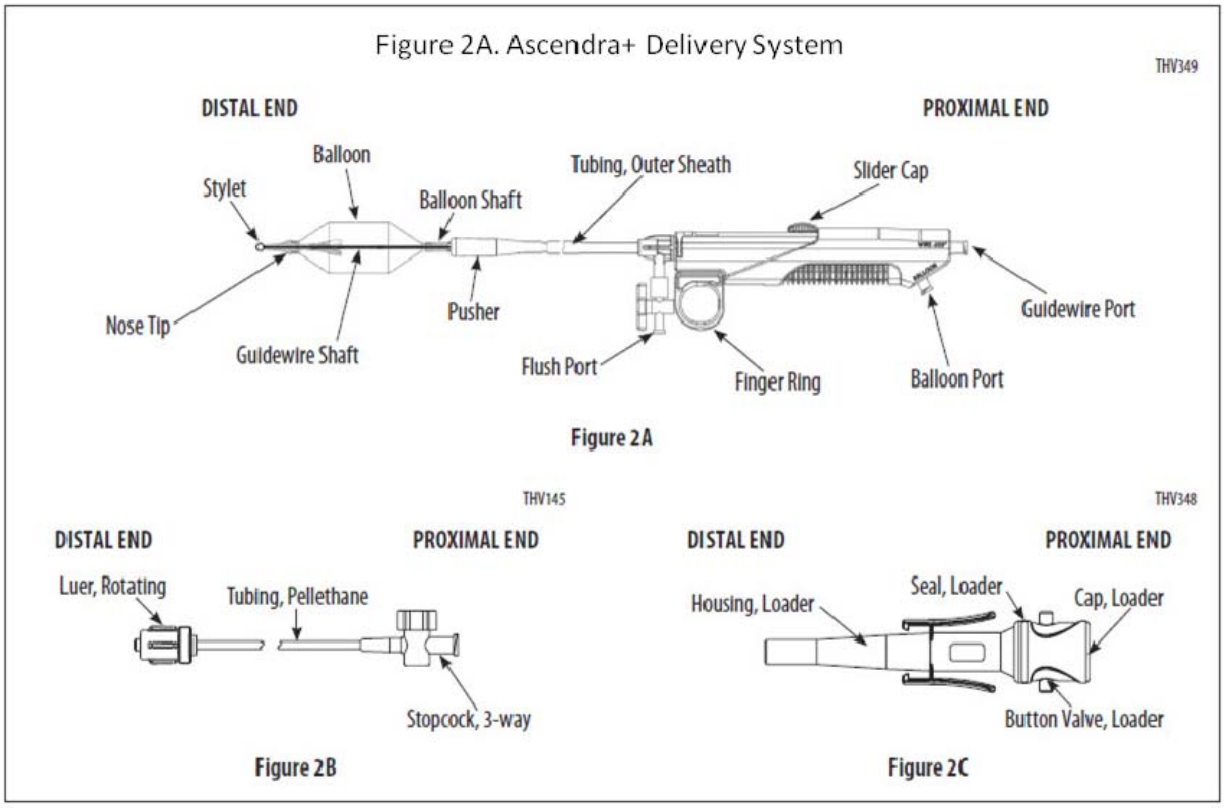
Native Valve Annulus Size (TEE)	Native Valve Annulus Size (CT)		THV Size
	Area	Area Derived Diameter	
18-22 mm	314 – 415 mm^2	20-23 mm	23 mm
21-25 mm	415 – 530 mm^2	23-26 mm	26 mm
24-27 mm	530 – 660 mm^2	26-29 mm	29 mm
THV size recommendations are based on native valve annulus size, as measured by transesophageal echocardiography (TEE) or computed tomography (CT). Patient anatomical factors and multiple imaging modalities should be considered during THV size selection. Note: Risks associated with undersizing and oversizing should be considered.			

- **Ascendra+ Delivery System (Figures 2a, 2b, 2c)**

The Ascendra+ delivery system (useable length 55 cm) is used for delivery of the Edwards SAPIEN XT transcatheter heart valve. The delivery system has radiopaque markers for visualization under fluoroscopy and a balloon for deployment of the THV. A balloon inflation hub, a guidewire hub, and a pusher retraction feature are housed in the handle assembly. The handle is labeled “BALLOON” at the balloon inflation hub and “WIRE 0.035"” at the guidewire hub. The system also comes with a loader that is used to cover the THV during delivery. An extension tube is supplied for use with the delivery system during inflation.

Table 3

Model	Nominal Balloon Diameter	Nominal Inflation Volume	Rated Burst Pressure (RBP)
9355AS23	23 mm	16 mL	7 atm
9355AS26	26 mm	20 mL	7 atm
9355AS29	29 mm	30 mL	7 atm



2.0 Indications

The Edwards SAPIEN XT Transcatheter Heart Valve, model 9300TFX, systems are indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis (aortic valve area ≤ 1.0 cm^2 or aortic valve area index ≤ 0.6 cm^2/m^2, a mean aortic valve gradient of ≥ 40 mmHg, or a peak aortic-jet velocity of ≥ 4.0 m/s), and with native anatomy appropriate for the 23, 26, or 29 mm valve system, who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (i.e., Society of Thoracic Surgeons operative risk score ≥ 8% or at a ≥ 15% risk of mortality at 30 days).

3.0 Contraindications

The THV and delivery system are contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections.

4.0 Warnings

- Observation of the pacing lead throughout the procedure is essential to avoid the potential risk of pacing lead perforation.
- There is an increased risk of stroke in transcatheter aortic valve replacement procedures, as compared to balloon aortic valvuloplasty or other standard treatments.
- 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.
- Incorrect sizing of the THV may lead to paravalvular leak, migration, embolization and/or annular rupture.
- Accelerated deterioration of the THV may occur in patients with an altered calcium metabolism.
- Prior to delivery, the THV must remain hydrated at all times and cannot be exposed to solutions other than its shipping storage solution and sterile physiologic rinsing solution. THV leaflets mishandled or damaged during any part of the procedure will require replacement of the THV.
- Caution should be exercised in implanting a THV in patients with clinically significant coronary artery disease.
- Patients with pre-existing mitral valve devices should be carefully assessed prior to implantation of the THV to ensure proper THV positioning and deployment.

- Patients presenting with combination AV low flow, low gradient should undergo additional evaluation to establish the degree of aortic stenosis.
- Do not use the THV if the tamper evident seal is broken, the storage solution does not completely cover the THV, the temperature indicator has been activated, the THV is damaged, or the expiration date has elapsed.
- Do not mishandle the Ascendra+ 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.
- Care should be exercised in patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/or polymeric materials.
- The procedure should be conducted under fluoroscopic guidance. Some fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. These injuries may be painful, disfiguring, and long-lasting.
- THV recipients should be maintained on anticoagulant/antiplatelet therapy, except when contraindicated, as determined by their physician. This device has not been tested for use without anticoagulation.
- Do not add or apply antibiotics to the storage solution, rinse solutions, or to the THV.

5.0 Precautions

- Long-term durability has not been established for the THV. Regular medical follow-up is advised to evaluate THV performance.
- Glutaraldehyde may cause irritation of the skin, eyes, nose and throat. Avoid prolonged or repeated exposure to, or breathing of, the solution. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water; in the event of contact with eyes, seek immediate medical attention. For more information about glutaraldehyde exposure, refer to the Material Safety Data Sheet available from Edwards Lifesciences.
- To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon.
- Appropriate antibiotic prophylaxis is recommended post-procedure in patients at risk for prosthetic valve infection and endocarditis.
- Safety, effectiveness, and durability have not been established for valve-in-valve procedures.
- Safety and effectiveness have not been established for patients with the following characteristics/comorbidities:
    - Non-calcified aortic annulus
    - Severe ventricular dysfunction with ejection fraction < 20%
    - Congenital unicuspid or congenital bicuspid aortic valve
    - Mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation > 3+)
    - Pre-existing prosthetic heart valve or prosthetic ring in any position
    - Severe mitral annular calcification (MAC), severe (> 3+) mitral insufficiency, or Gorlin syndrome
    - Blood dyscrasias defined as: leukopenia (WBC < 3000 cells/mL), acute anemia (Hb < 9 g/dL), thrombocytopenia (platelet count < 50,000 cells/mL), or history of bleeding diathesis or coagulopathy
    - Hypertrophic cardiomyopathy with or without obstruction (HOCM)
    - Echocardiographic evidence of intracardiac mass, thrombus, or vegetation
    - A known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid™), or clopidogrel (Plavix™), or sensitivity to contrast media, which cannot be adequately premedicated
    - Excessive calcification of vessel at access site
    - Bulky calcified aortic valve leaflets in close proximity to coronary ostia

6.0 Potential Adverse Events

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

- Death
- Stroke/transient ischemic attack, clusters or neurological deficit
- Paralysis
- Permanent disability
- Respiratory insufficiency or respiratory failure
- Hemorrhage requiring transfusion or intervention
- Cardiovascular injury including perforation or dissection of vessels, ventricle, myocardium or valvular structures that may require intervention
- Pericardial effusion or cardiac tamponade
- Embolization including air, calcific valve material or thrombus
- Infection including septicemia and endocarditis
- Heart failure
- Myocardial infarction
- Renal insufficiency or renal failure
- Conduction system defect which may require a permanent pacemaker
- Arrhythmia
- Retroperitoneal bleed
- AV fistula or pseudoaneurysm
- Reoperation
- Ischemia or nerve injury
- Restenosis
- Pulmonary edema
- Pleural effusion
- Bleeding
- Anemia
- Abnormal lab values (including electrolyte imbalance)
- Hypertension or hypotension
- Allergic reaction to anesthesia, contrast media, or device materials
- Hematoma
- Syncope
- Pain or changes at the access site
- Exercise intolerance or weakness
- Inflammation
- Angina

- Heart murmur
- Fever

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

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

7.0 Directions for Use

7.1 Required Equipment

Table 4

Product Name	**23 mm System (9355ASP23A)**	**26 mm System (9355ASP26A)**	**29 mm System (9355ASP29A)**
	Model		
Edwards SAPIEN XT Transcatheter Heart Valve	9300TFX (23 mm)	9300TFX (26 mm)	9300TFX (29 mm)
Ascendra+ Delivery System*	9355AS23	9355AS26	9355AS29
Ascendra+ Introducer Sheath Set	9350IS23	9350IS26	9350IS29
Ascendra Balloon Aortic Valvuloplasty Catheter	9100BAVC		
Inflation devices provided by Edwards Lifesciences			
Edwards Crimper	9350CR		
* Includes the Crimp Stopper			

Additional Equipment:

- 20 cc syringe or larger (x2)
- 50 cc syringe or larger
- Standard cardiac catheterization lab equipment
- Fluoroscopy (fixed, mobile or semi-mobile fluoroscopy systems appropriate for use in percutaneous coronary interventions)
- Transesophageal or transthoracic echocardiography capabilities
- Exchange length 0.035 inch (0.89 mm) extra-stiff guidewire
- Temporary pacemaker (PM) and pacing lead
- Sterile rinsing basins, physiological saline, heparinized saline, 15% diluted radiopaque contrast medium
- Sterile table for THV and device preparation

7.2 THV Handling and Preparation

Follow sterile technique during device preparation and implantation.

7.2.1 THV Rinsing Procedure

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

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

Step	Procedure
1	Set up two (2) sterile bowls with at least 500 mL of sterile physiological saline to thoroughly rinse the glutaraldehyde sterilant from the THV.
2	Carefully remove the THV/holder assembly from the jar without touching the tissue. Verify the THV serial identification number with the number on the jar lid and record in the patient information documents. Inspect the THV for any signs of damage to the frame or tissue.
3	Rinse the THV as follows: Place the THV in the first bowl of sterile, physiological saline. Be sure the saline solution completely covers the THV and holder. With the THV and holder submerged, slowly agitate (to gently swirl the THV and holder) back and forth for a minimum of 1 minute. Transfer the THV and holder to the second rinsing bowl of physiological saline and gently agitate for at least one more minute. Ensure the rinse solution in the first bowl is not used. The THV should be left in the final rinse solution until needed to prevent the tissue from drying. **CAUTION: Do not allow the THV to come into contact with the bottom or sides of the rinse bowl during agitation or swirling in the rinse solution. Direct contact between the identification tag and THV is also to be avoided during the rinse procedure. No other objects should be placed in the rinse bowls. The THV should be kept hydrated to prevent the tissue from drying.**

7.2.2 Prepare the Components

Step	Procedure
1	Visually inspect all components for damage.
2	Refer to Ascendra+ Introducer Sheath Set and Crimper instructions for use on device preparation and handling.
3	Ensure the delivery system pusher is in the distal locked position using the slider cap. Flush delivery system at the flush port with heparinized saline and close stopcock to delivery system.
4	Carefully remove distal balloon cover.
5	Flush loader through the distal end with heparinized saline and insert the delivery system (with proximal balloon cover on) into loader until loader is completely proximal.

<table>
<tr><th>Step</th><th>Procedure</th></tr>
<tr><td>6</td><td>Fully retract slider cap and rotate into proximal slot.</td></tr>
<tr><td>7</td><td>Slide the proximal balloon cover onto the balloon shaft and carefully peel off the proximal balloon cover from the delivery system.</td></tr>
<tr><td>8</td><td>Flush and attach balloon extension tube to the balloon inflation hub.</td></tr>
<tr><td>9</td><td>Prepare a 50 cc or larger luer-lock syringe with diluted contrast solution (15:85 contrast to heparinized saline) and attach to the extension tubing.</td></tr>
<tr><td>10</td><td>Completely fill the inflation device provided by Edwards with diluted contrast and attach to the extension tubing stopcock. Ensure there are no air bubbles in the balloon. If an air bubble is detected, eliminate it while deflating the balloon. Close the stopcock to the delivery system.</td></tr>
<tr><td>11</td><td>Remove excess contrast medium from the inflation device provided by Edwards into the syringe to achieve the appropriate volume required to deploy the THV per the following. Then lock the inflation device:
<table>
<tr><th>Delivery System</th><th>THV</th><th>Inflation Volume</th></tr>
<tr><td>Model 9355AS23</td><td>23 mm</td><td>16 mL</td></tr>
<tr><td>Model 9355AS26</td><td>26 mm</td><td>20 mL</td></tr>
<tr><td>Model 9355AS29</td><td>29 mm</td><td>30 mL</td></tr>
</table>
Note: Correct balloon sizing is critical to successful valve deployment and valve function.</td></tr>
<tr><td>12</td><td>Close the stopcock to the 50 cc or larger syringe and remove the syringe.

CAUTION: Maintain the inflation device provided by Edwards in the locked position until THV deployment.</td></tr>
</table>

7.2.3 Mount and Crimp the THV onto the Delivery System

Step	Procedure
1	Rotate the crimper until the aperture is fully opened.
2	Remove the THV from the holder and remove ID tag using sterile scissors.
3	Place THV into crimper aperture and partially crimp so that it fits loosely over the prepared balloon.
4	Remove the THV from the crimper and place it on the delivery system with the inflow (fabric cuff end) of the THV proximally towards the pusher if accessing antegrade. If accessing retrograde, place the THV on the delivery system with the inflow (fabric cuff end) of the THV towards the distal end away from the pusher. Ensure that the THV is aligned between the radiopaque markers.
5	Place the THV/balloon assembly in crimper aperture and gradually crimp. Periodically open crimper to verify correct placement of THV during crimping. Completely crimp until the handle contacts the crimp stopper. **CAUTION: The implanting physician must verify correct mounting/orientation of the THV prior to its implantation.**
6	Advance the slider cap distally to allow the tip of the pusher to align with the proximal end of the crimped THV.
7	Advance the loader onto crimped THV until it reaches the balloon shoulder and the THV is fully covered.

Step	Procedure
8	While holding the loader in place, fully retract the slider cap and rotate into locked position. Flush through the flush port to fill the loader and hydrate the THV. Once the THV is hydrated, advance the slider cap and rotate into distal locked position. Be sure to maintain position of the crimped THV between the radiopaque markers during hydration. Close the flush port stopcock to the delivery system. **Note: To facilitate flushing, keep the delivery system straight.** **CAUTION: To prevent possible leaflet damage, the THV should not remain in the loader over 30 minutes.**
9	Ensure the slider cap is locked in the distal position and that the THV is still centered between radiopaque markers and fully inside the loader. **Note: Keep THV hydrated until ready for implantation.**
10	Remove the stylet and flush the guidewire lumen of the delivery system. **CAUTION: The implanting physician must verify correct orientation of the THV prior to its implantation.**

7.3 Valvuloplasty and THV Delivery

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

The following table shows the minimum required distances from the native valve annulus to the distal tip of the Ascendra+ sheath to allow the Ascendra+ delivery system balloon to inflate properly during THV deployment. These distances should be considered during the transaortic approach when selecting the access site on the ascending aorta and determining the insertion depth of the Ascendra+ sheath into the aorta.

Delivery System	THV	Minimum Required Distance From Annulus to Sheath Tip
Model 9355AS23	23 mm	5.0 cm
Model 9355AS26	26 mm	5.5 cm
Model 9355AS29	29 mm	6.0 cm

Administer heparin to maintain the ACT at ≥ 250 sec.

CAUTION: Contrast media use should be monitored to reduce the risk of renal injury.

7.3.1 Baseline Parameters

Step	Procedure
1	Perform a supra-aortic angiogram with the projection of the native aortic valve perpendicular to the view.
2	Evaluate the height between the inferior aspect of the annulus and the inferior aspects of the lowest coronary ostium for subsequent prosthetic aortic valve implantation.
3	Introduce a pacemaker (PM) lead until its distal end is positioned in the right ventricle.
4	Set the stimulation parameters, and test pacing.

7.3.2 Valvuloplasty

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

Note: Rapid ventricular pacing should be performed when using the Ascendra Balloon Aortic Valvuloplasty Catheter for valvuloplasty prior to transcatheter valve implantation.

After placement of the balloon at the intended site, begin rapid ventricular pacing. Once the blood pressure has decreased to 50 mmHg or below, balloon inflation can commence.

CAUTION: THV implantation should not be carried out if the balloon cannot be fully inflated during valvuloplasty.

7.3.3 THV Delivery

Step	Procedure
1	Insert the introducer sheath. Refer to the Ascendra+ Introducer Sheath Set IFU for additional information on device preparation and handling.
2	Advance delivery system over guidewire. Engage loader into introducer sheath housing while maintaining a firm grip. Tap lightly on the introducer sheath housing to release air to the proximal end of the loader. Lightly depress button valves on loader to aspirate the loader.
3	Cross the native aortic valve and position the THV within the valve.
4	Retract pusher by rotating slider cap out of distal locked position and moving it proximally to ensure that the tip of the pusher is retracted completely on to the balloon shaft. **CAUTION: The pusher must be pulled back completely on the balloon shaft for proper balloon inflation and THV deployment.**
5	Position the mid-point of the THV at the plane of the hinge points of the native valve leaflets.
6	Verify the correct location of the THV with respect to the native aortic valve.
7	Begin THV deployment: • Unlock the inflation device. • Begin rapid pacing; once arterial blood pressure has decreased to 50 mmHg or below, balloon inflation can commence. • Deploy the THV by inflating the balloon with the entire volume in the Inflation device provided by Edwards Lifesciences, hold for 3 seconds and confirm that the barrel of the inflation device is empty to ensure complete inflation of the balloon. When the balloon catheter has been completely deflated, turn off the pacemaker. • Retract the delivery system into the introducer sheath.
8	Disengage loader from sheath and remove delivery system and loader.
9	Remove sheath when the ACT level is appropriate (e.g. reaches < 150 sec). Close access site.

8.0 How Supplied

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

8.1 Storage

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

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

9.0 MR Safety

MR Conditional

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

- Static magnetic field of 1.5 tesla (T) or 3.0 T.
- Maximum spatial gradient field of 2500 gauss/cm (25 T/m) or less.
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2 W/kg (Normal Operating Mode).

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

In non-clinical testing, the image artifact caused by the device extends as far as 10 mm from the implant for spin echo images and 30 mm for gradient echo images when scanned in a 3.0 T MRI system.

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

10.0 Patient Information

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

11.0 Recovered THV and Device Disposal

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

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

12.0 Clinical Studies

The PARTNER II Cohort B Registries

Cohort B of The Placement of Aortic Transcatheter Valves II (PARTNER II) Trial included registries for the transapical and transaortic delivery of the SAPIEN XT THV. These registries include the following:

- NR1 is an Inoperable Transapical Registry for transapical delivery of the 23 mm or 26 mm SAPIEN XT THV in patients deemed eligible for Cohort B but do not have eligible transfemoral access. A maximum of 100 patients were to be enrolled in this arm. Primary endpoint of this registry was freedom from mortality at one year. Non-powered secondary endpoints for safety and effectiveness were consistent with additional secondary endpoint analyses for both Cohorts A and B. Patients previously enrolled as a Cohort A control could not be enrolled in this registry.
- NR4 is an Inoperable Transaortic Registry for transaortic delivery of the 23 mm or 26 mm SAPIEN XT THV in patients deemed eligible for Cohort B but do not have eligible transfemoral access. A maximum of 100 patients were to be enrolled in this arm. Primary endpoint of this registry was freedom from mortality at one year. Non-powered secondary endpoints for safety and effectiveness were consistent with additional secondary endpoint analyses for both Cohorts A and B. Patients previously enrolled as a Cohort A control could not be enrolled in this registry.
- NR6 is an Inoperable Transapical Registry for the delivery of 29 mm SAPIEN XT THV for Cohort B patients that do not have eligible transfemoral access. A maximum of 50 patients were to be enrolled in this arm. Primary endpoint of this registry was freedom from mortality at one year. Non-powered secondary endpoints for safety and effectiveness were consistent with additional secondary endpoint analyses for both Cohorts A and B. Patients previously enrolled as a Cohort A control could not be enrolled in this registry.

SOURCE Registry XT:

SOURCE Registry XT is an international multi-center prospective, consecutively enrolled, observational registry. Consecutive patient data have been collected at discharge, 30 days, and 12 months post-implant, and will be collected annually thereafter up to 5 years post-implant.

Results of PARTNER II Cohort B Registries (NR1, NR4 and NR6)

A total of 265 patients were enrolled in PARTNER II Cohort B Nested Registries 1, 4, and 6. The primary safety and effectiveness endpoint was freedom from all-cause mortality at 1 year. The KM estimate at 30 days involving freedom from all-cause mortality was 92.0 ± 1.7%.

There were 1.9% major strokes, no incidence of endocarditis, 1.5% myocardial infarction, 5.7% major vascular complications, 11.3% disabling bleeding events, 3.0% cardiac intervention, and 4.5% new pacemaker at 30 days.

NYHA went from 3.2 ± 0.61 at baseline to 1.9 ± 0.88 at 30 days. The mean change was -1.3 ± 1.10. Device success was observed in 69.6% of patients (165/237). The mean hospitalization stay was 11.1 ± 8.96 days which included 4.5 ± 7.12 days in the ICU. The mean EOA was 0.7 ± 0.19 cm^2 at baseline and 1.6 ± 0.43 cm^2 at 30 days, and the average mean gradient decreased from 41.2 ± 12.17 mmHg at baseline to 8.6 ± 3.59 mmHg at 30 days. The mean peak gradient decreased from 73.2 ± 21.51 mmHg at baseline to 17.7 ± 7.30 mmHg at 30 days.

Results of SOURCE XT

A total of 2688 patients were enrolled. The vast majority of patients (96%) were treated with either the transapical (TA) or transfemoral (TF) approach. Only a small proportion of patients were treated with transaortic (TAo) or subclavian approaches. The implant approach was 62.7% for TF, 33.3% for TA, 3.76% for TAo and 0.3% for subclavian. The results only include the TF, TA and TAo approaches (n = 2680).

Using K-M event rates at 30 days post implant for the TF, TA/TAo population, 6.2% of patients had died, 3% due to a cardiac death, 3.6% of patients had suffered a stroke, and 6.6% had a major vascular complication. Major/life threatening bleeding had occurred in 14.9% of patients, major bleeding in 10.2%, and renal failure or AKI in 17.8%. Permanent pacemakers were implanted in 9.5% of patients. Using K-M event rates at 1 year post implant for the TF, TA/TAo population, 19.5% of patients had died, 9.5% of these from cardiac death, and 6.3% of patients had suffered a stroke. Major/life-threatening bleeding had occurred in 17.3% of patients, major bleeding in 12%, major vascular complications in 7.2%, renal failure or AKI in 20.5% and 11% of patients had a new pacemaker implanted.

PARTNER II Cohort B Registries Clinical Data

Clinical Table 1: Cohort B (Inoperable) Baseline Characteristics and Echocardiographic Findings for NR1, NR4 and NR6 (AT Population)*	
	SAPIEN XT (TA/TAo)
Characteristic	(N = 265)
Age - yr	82.0 ± 7.79
Male sex — no. (%)	141/265 (53.2%)
STS score†	10.3 ± 5.51
Logistic EuroSCORE‡	13.2 ± 11.96
NYHA class — no. (%):	
I/II	24/264 (9.1%)
III/IV	240/264 (90.9%)
Coronary artery disease — no./total no. (%)	194/265 (73.2%)
Previous myocardial infarction — no./total no. (%)	56/265 (21.1%)
Previous intervention — no./total no. (%)	
CABG	118/265 (44.5%)
PCI	107/265 (40.4%)
Balloon aortic valvuloplasty	72/265 (27.2%)
Peripheral vascular disease — no./total no. (%)	150/265 (56.6%)
COPD — no./total no. (%):	
Any	101/265 (38.1%)
Oxygen-dependent	41/265 (15.5%)
Creatinine > 2 mg/dL (177 µmol/liter) — no./total no. (%)	28/265 (10.6%)
Atrial fibrillation — no./total no. (%)	95/265 (35.8%)
Permanent pacemaker — no./total no. (%)	43/265 (16.2%)
Pulmonary hypertension — no./total no. (%)	34/254 (13.4%)
Frailty§ — no./total no. (%)	97/254 (38.2%)
Extensively calcified aorta — no./total no. (%)	42/254 (16.5%)
Chest-wall deformity — no./total no. (%)	6/254 (2.4%)
Liver disease — no./total no. (%)	9/265 (3.4%)
Echocardiographic findings	
Aortic-valve area — cm^2	0.7 ± 0.19
Mean aortic-valve gradient — mmHg	41.2 ± 12.17
Mean LVEF — %	52.5 ± 13.37
Moderate or severe mitral regurgitation** — no./total no. (%)	70/232 (30.2%)

* Plus–minus values are mean ± SD. To convert the value for creatinine to micromoles per liter, multiply by 88.4. AT denotes As Treated population, CABG denotes coronary-artery bypass grafting, COPD chronic obstructive pulmonary disease, LVEF left ventricular ejection fraction, NYHA New York Heart Association, PCI percutaneous coronary intervention, and TAVR transcatheter aortic-valve implantation.
† The Society of Thoracic Surgeons (STS) score measures patient risk at the time of cardiovascular surgery on a scale that ranges from 0% to 100%, with higher numbers indicating greater risk. An STS score higher than 10% indicates very high surgical risk.
‡ The logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE), which measures patient risk at the time of cardiovascular surgery, is calculated with the use of a logistic-regression equation. Scores range from 0% to 100%, with higher scores indicating greater risk. A logistic EuroSCORE higher than 20% indicates very high surgical risk.
§ Frailty was determined by the surgeons according to prespecified criteria.
** Moderate or severe mitral regurgitation was defined as regurgitation of grade 3+ or higher.

Clinical Table 2: Cohort B (Inoperable) Clinical Outcomes at 30 days for NR1, NR4 and NR6 (AT Population)*	
Outcome[a]	**SAPIEN XT (N = 265)**
Death from any cause	21/265 (7.9%)
Major Stroke	5/265 (1.9%)
Repeat hospitalization[b]	8/265 (3.0%)
Death from any cause or major stroke or repeat hospitalization	31/265 (11.7%)
Myocardial Infarction	4/265 (1.5%)
Major Vascular Complications	15/265 (5.7%)
Renal Failure[c]	7/265 (2.6%)
Disabling Bleeding Event[d]	30/265 (11.3%)
Cardiac Reintervention[e]	8/265 (3.0%)
Endocarditis	0/265 (0.0%)
New Atrial Fibrillation[f]	9/167 (5.4%)
New pacemaker	12/265 (4.5%)

* AT = As Treated, NA = not applicable, TAVR = transcatheter aortic valve replacement. Data presented as n (%) of patients.
a. CEC adjudicated
b. Repeat hospitalizations were included if they were due to aortic stenosis or complications of the valve procedure (e.g., TAVR).
c. Renal failure is defined as stage III acute kidney injury: Increase in serum creatinine to ≥ 300% (3 x increase compared with baseline) or serum creatinine of ≥ 4 mg/d (≥ 354 µmol/L) with an acute increase of at least 0.5 mg/dl (44 µmol/L)
d. Disabling bleeding: Fatal bleeding OR bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, or pericardial necessitating pericardiocentesis, or intramuscular with compartment syndrome OR bleeding causing hypovolemic shock or severe hypotension requiring vasopressors or surgery OR overt source of bleeding with drop in hemoglobin of ≥ 5 g/dL or whole blood of packed red blood cells (RBC) transfusion ≥ 4 units
e. Cardiac reintervention includes any intervention that repairs, alters or replaces a previously operated valve OR balloon aortic valvuloplasty OR Surgical aortic valve replacement OR valve in valve
f. Based on 167 patients at 30 days

Clinical Table 3: Conduction Disturbance Requiring Pacemaker to 30 Days for NR1, NR4 and NR6 (CEC Adjudicated) – AT Population		
	SAPIEN XT (TA/TAo)(N = 265)	
Event	**Events**	**Patients with Event**
New Permanent Pacemaker- All Patients[1]		
0-30 Days	12	12/265 (4.5%)
New Permanent Pacemaker – Patients without pre-procedural pacemaker[2]		
0-30 Days	12	12/222 (5.4%)

[1] Subjects with pacemaker or ICD at baseline are included (all patients included in denominator).
[2] Subjects with pacemaker or ICD at baseline are excluded (patients with baseline pacemaker/ICD subtracted from denominator).

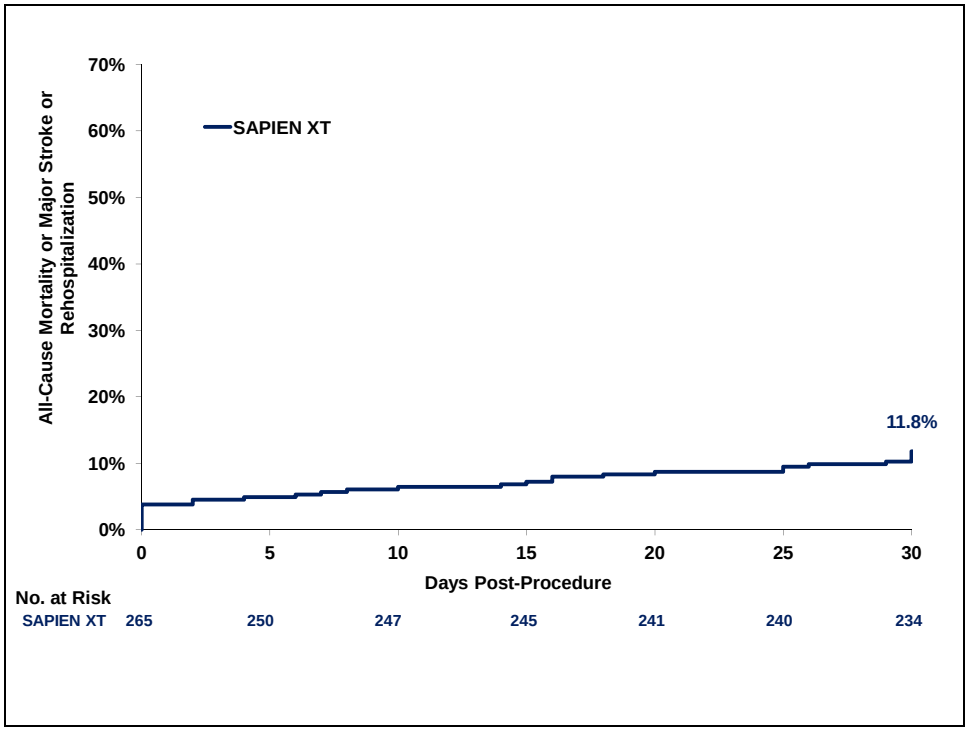


Figure 3: All-Cause Mortality, Major Stroke or Re-Hospitalization to 30 Days, NR1, NR4, and NR6 – TA/TAo (AT Population)

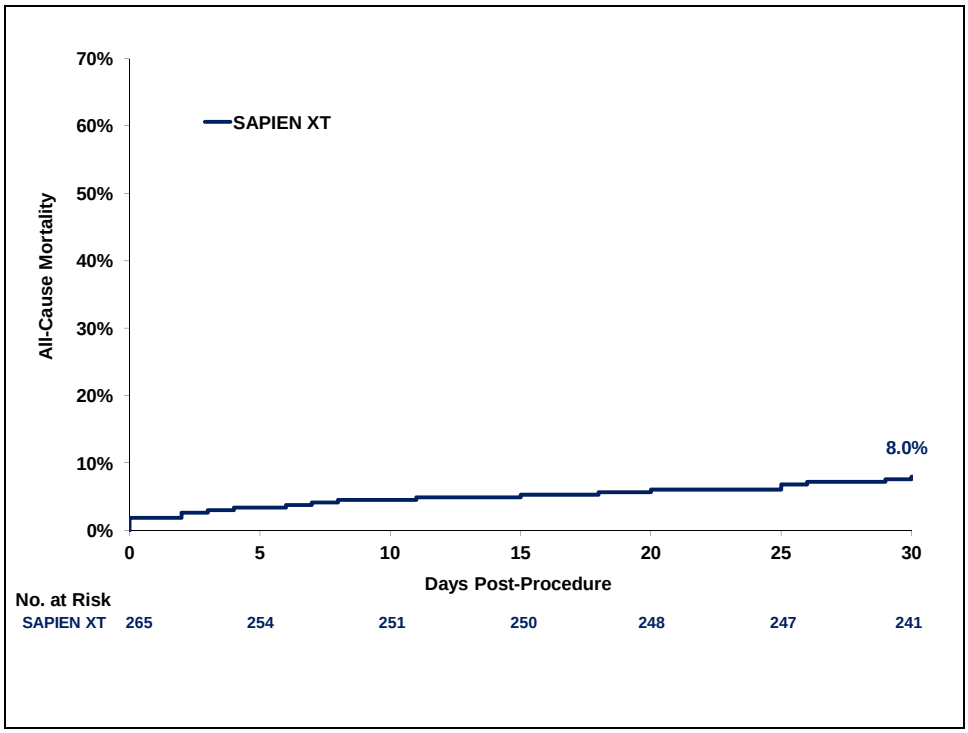


Figure 4: All-Cause Mortality to 30 Days, NR1, NR4, and NR6 – TA/TAo (AT Population)

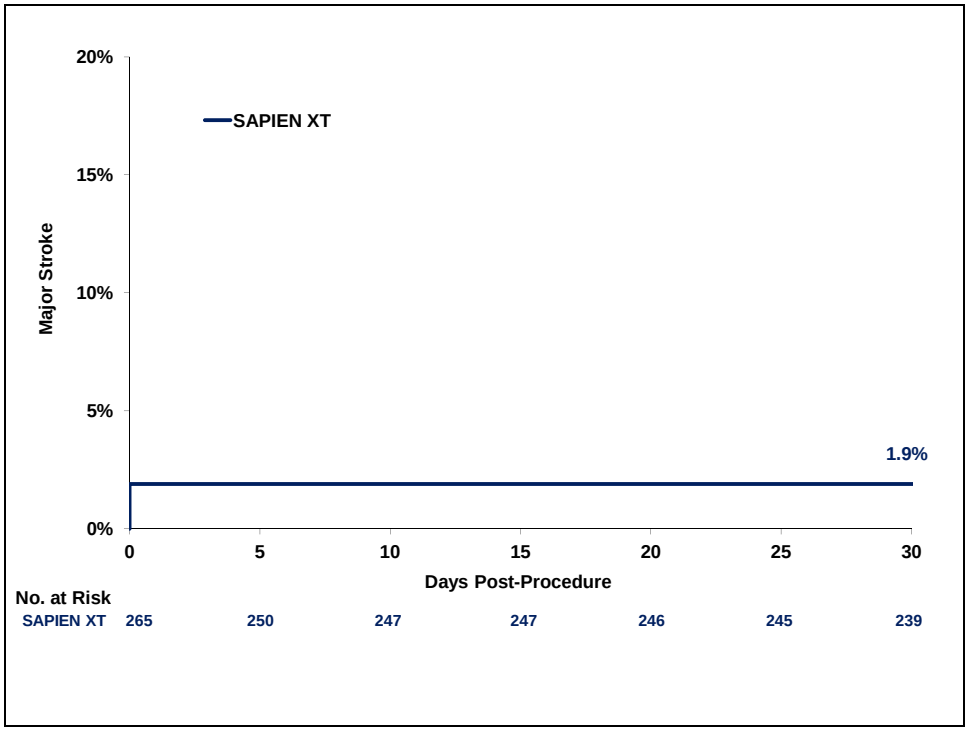


Figure 5: Major Stroke at 30 Days, NR1, NR4, and NR6 – TA/TAo (AT Population)

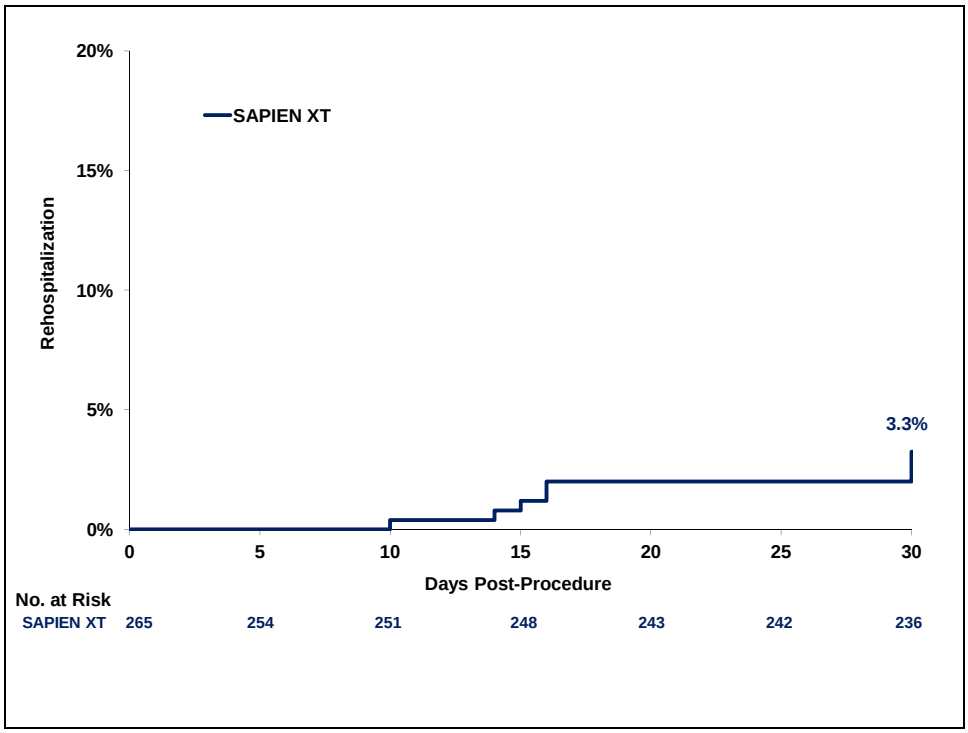


Figure 6: Re-Hospitalization at 30 Days, NR1, NR4, and NR6 – TA/TAo (AT Population)

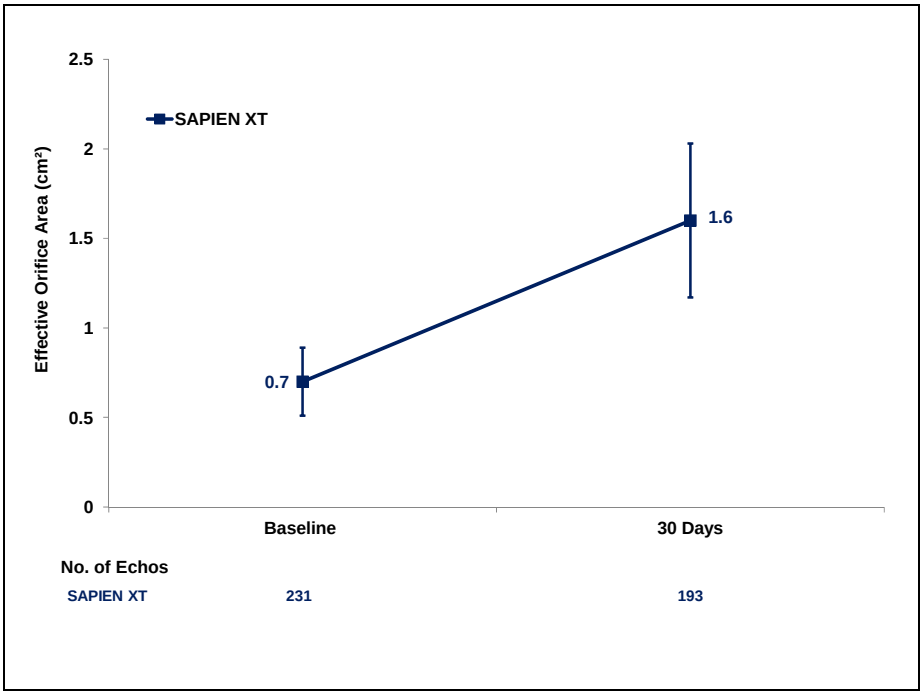


Figure 7: Effective Orifice Area, NR1, NR4, and NR6 – TA/TAo (Valve Implant Population)

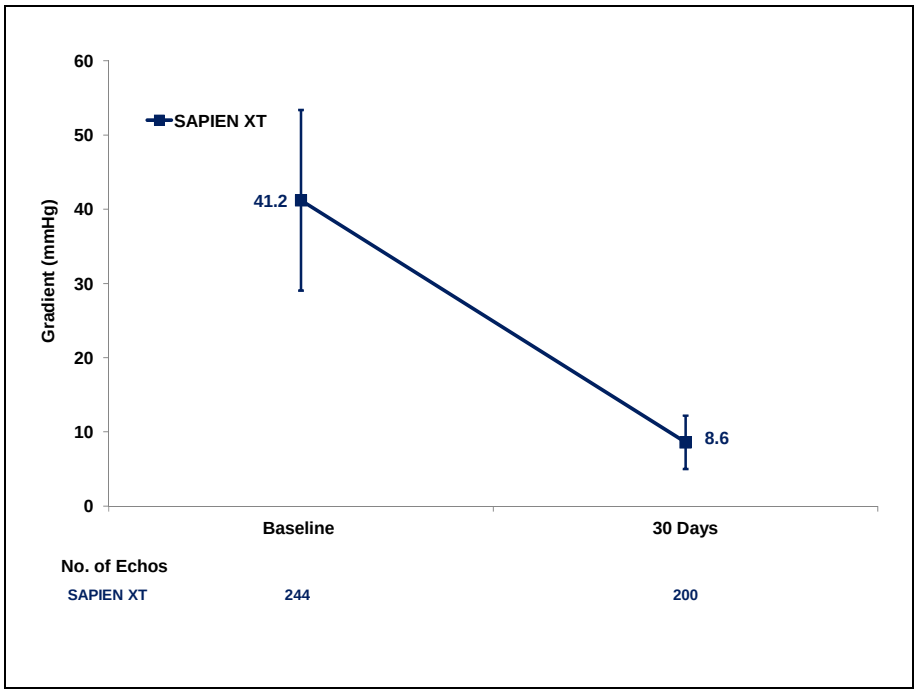


Figure 8: Mean Gradient, NR1, NR4, and NR6 – TA/TAo (Valve Implant Population)

Clinical Table 4: NYHA Functional Class By Visit for NR1, NR4 and NR6 (AT Population)

	SAPIEN XT (N = 265)				
Visit	I	II	III	IV	Total
Baseline	1	23	158	82	264
30 Days	84	88	45	12	229

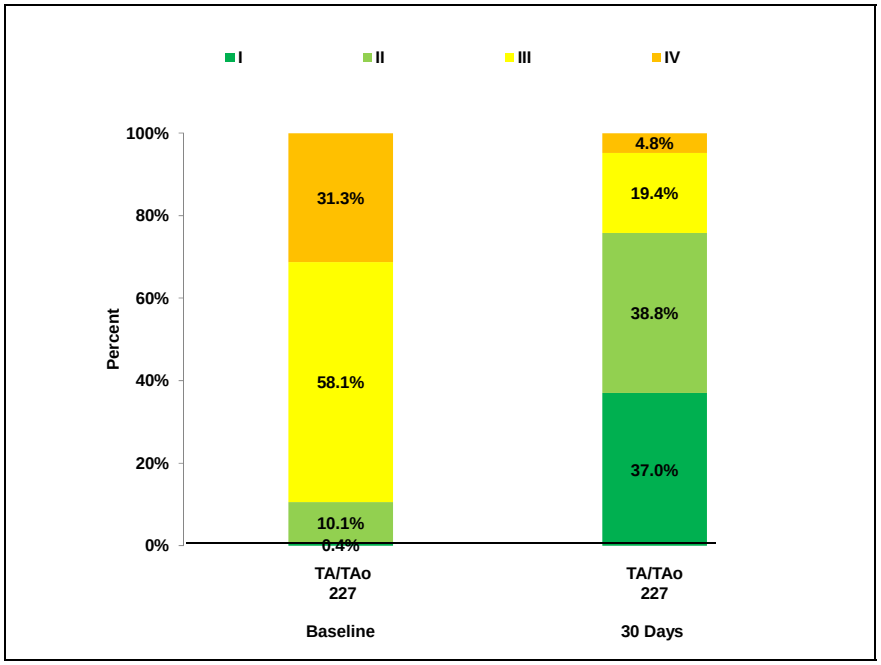


Figure 9: NYHA Class by Visit, NR1, NR4, and NR6 – TA/TAo (Intent-to-Treat Population)

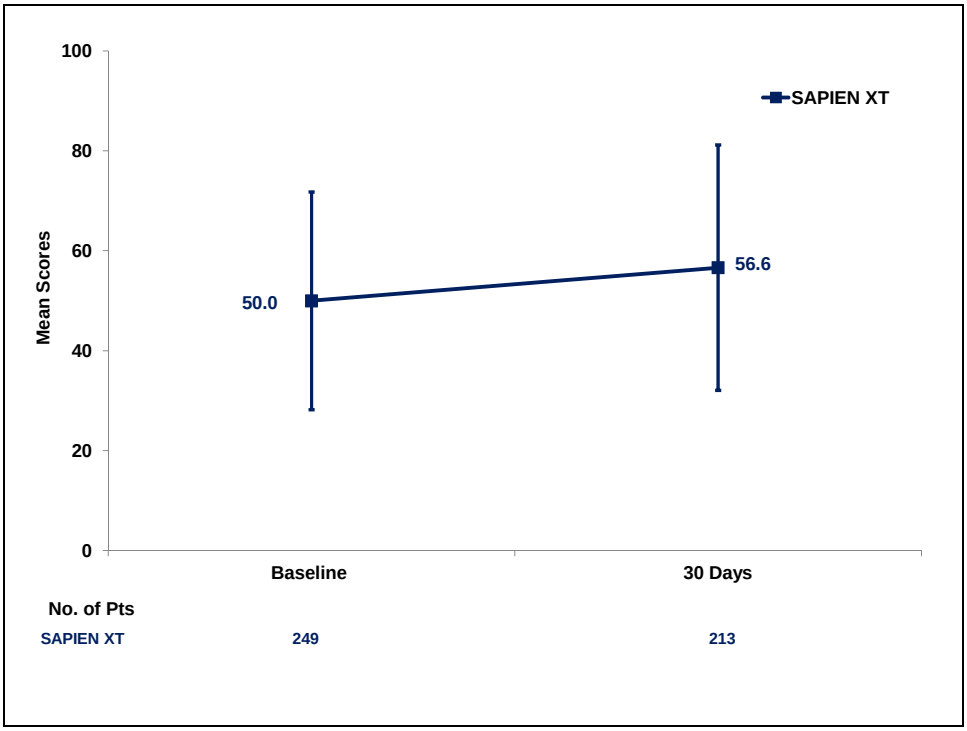


Figure 10: KCCQ Clinical Summary Score, NR1, NR4, and NR6 – TA/TAo (AT Population)

SOURCE XT Clinical Data

Clinical Table 5: SOURCE XT (High Risk) Baseline Characteristics of the Patients and Echocardiographic Findings (AT Population)*		
	Transfemoral	**TA/TAo Pooled**
Characteristic	(N = 1685)	(N = 995)
Age - yr	82.0 ± 6.5	80.3 ± 6.5
Male sex — no. (%)	600 / 1685 (35.6%)	536 / 995 (53.9%)
STS score†	8.0 ± 6.8	7.9 ± 6.2
Logistic EuroSCORE‡	19.8 ± 11.6	21.6 ± 13.7
NYHA class		
I/II — no./total no. (%)	377 / 1676 (22.5%)	242 / 992 (24.4%)
III/IV — no./total no. (%)	1299 / 1676 (77.5%)	750 / 992 (75.6%)
Coronary artery disease — no./total no. (%)	667 / 1685 (39.6%)	518 / 995 (52.1%)
Previous myocardial infarction — no./total no. (%)	205 / 1685 (12.2%)	197 / 995 (19.8%)
Previous intervention		
CABG — no./total no. (%)	204 / 1685 (12.1%)	226 / 995 (22.7%)
PCI — no./total no. (%)	460 / 1685 (27.3%)	355 / 995 (35.7%)
Balloon aortic valvuloplasty — no./total no. (%)	128 / 1685 (7.6%)	66 / 995 (6.6%)
Cerebral vascular disease — no./total no. (%)	191 / 1685 (11.3%)	143 / 995 (14.4%)
Peripheral vascular disease — no./total no. (%)	248 / 1684 (14.7%)	320 / 995 (32.2%)
COPD		
Pulmonary Artery Disease COPD — no./total no. (%)	327 / 1684 (19.4%)	218 / 995 (21.9%)
Pulmonary Artery Disease Oxygen Dependent — no./total no. (%)	31 / 1684 (1.8%)	11 / 995 (1.1%)
Creatinine > 2 mg/dL (177 µmol/liter) — no./total no. (%)	104 / 1681 (6.2%)	114 / 994 (11.5%)
Atrial fibrillation — no./total no.	395 / 1678 (23.5%)	289 / 990 (29.2%)
Permanent pacemaker — no./total no. (%)	170 / 1685 (10.1%)	134 / 995 (13.5%)
Pulmonary hypertension — no./total no. (%)	440 / 1684 (26.1%)	204 / 995 (20.5%)
Frailty§ — no./total no. (%)	896 / 932 (96.1%)	548 / 579 (94.6%)
Extensively calcified aorta — no./total no. (%)	71 / 1684 (4.2%)	103 / 995 (10.4%)
Chest-wall deformity — no./total no. (%)	52 / 1685 (3.1%)	27 / 995 (2.7%)
Liver disease — no./total no. (%)	18 / 1684 (1.1%)	6 / 995 (0.6%)
Echocardiographic findings		
Aortic-valve area — cm^2	0.7 ± 0.21	0.7 ± 0.21
Mean aortic-valve gradient — mmHg	49.2 ± 16.54	45.0 ± 15.43
Mean LVEF — %	55.1 ± 12.48	53.2 ± 12.50
Moderate or severe mitral regurgitation** — no./total no. (%)	345 / 1633 (21.1%)	174 / 976 (17.8%)

* Plus–minus values are means ± SD. To convert the value for creatinine to micromoles per liter, multiply by 88.4. AT denotes as treated population, CABG denotes coronary-artery bypass grafting, COPD chronic obstructive pulmonary disease, LVEF left ventricular ejection fraction, NYHA New York Heart Association, PCI percutaneous coronary intervention, and TAVR transcatheter aortic-valve implantation.

† The Society of Thoracic Surgeons (STS) score measures patient risk at the time of cardiovascular surgery on a scale that ranges from 0% to 100%, with higher numbers indicating greater risk. An STS score higher than 10% indicates very high surgical risk.

‡ The logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE), which measures patient risk at the time of cardiovascular surgery, is calculated with the use of a logistic-regression equation. Scores range from 0% to 100%, with higher scores indicating greater risk. A logistic EuroSCORE higher than 20% indicates very high surgical risk.

§ Frailty was determined by the surgeons according to prespecified criteria.

** Moderate or severe mitral regurgitation was defined as regurgitation of grade 3+ or higher.

Clinical Table 6: SOURCE XT (High Risk) Clinical Outcomes[a] at 30 days and 1 year (AT Population)*				
	30 Days		1-Year	
	Transfemoral	TA/TAo	Transfemoral	TA/TAo
Outcome	**(N = 1685)**	**(N = 995)**	**(N = 1685)**	**(N = 995)**
All Cause Death	71 (4.2%)	96 (9.7%)	248 (15.0%)	266 (27.0%)
Cardiac Death	28 (1.7%)	51 (5.2%)	106 (6.7%)	132 (14.4%)
Stroke				
All Stroke	56 (3.4%)	39 (4.1%)	90 (5.6%)	66 (7.6%)
Major Stroke	34 (2.0%)	27 (2.8%)	55 (3.5%)	44 (5.0%)
Repeat hospitalization[b]	80 (4.9%)	83 (9.0%)	396 (25.5%)	314 (36.7%)
Myocardial Infarction	7 (0.4%)	9 (0.9%)	23 (1.5%)	21 (2.5%)
Major Vascular Complications	132 (7.9%)	43 (4.4%)	139 (8.3%)	52 (5.5%)
Renal Failure[d]/AKI	197 (11.9%)	270 (28.0%)	240 (14.7%)	292 (30.6%)
Life-threatening bleeding[c]	63 (3.8%)	84 (8.6%)	74 (4.5%)	101 (10.6%)
Endocarditis	2 (0.1%)	2 (0.2%)	15 (1.0%)	10 (1.2%)
New Atrial Fibrillation	54 (3.3%)	83 (8.8%)	89 (5.6%)	109 (12.0%)
New pacemaker	145 (8.7%)	105 (10.8%)	165 (10.0%)	120 (12.7%)

* AT = As Treated, TAVR = transcatheter aortic valve replacement. Data presented as n (%) of patients where % is the Kaplan-Meier event rate at 30-days and 1-year respectively.
a. CEC adjudicated
b. Repeat hospitalizations were included if they were due to aortic stenosis or complications of the valve procedure (e.g., TAVR).
c. Disabling bleeding: Fatal bleeding OR bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, or pericardial necessitating pericardiocentesis, or intramuscular with compartment syndrome OR bleeding causing hypovolemic shock or severe hypotension requiring vasopressors or surgery OR overt source of bleeding with drop in hemoglobin of ≥ 5 g/dL or whole blood of packed red blood cells (RBC) transfusion ≥ 4 units
d. Renal failure is defined as stage III acute kidney injury: Increase in serum creatinine to ≥ 300% (3 x increase compared with baseline) or serum creatinine of ≥ 4 mg/d (≥ 354 µmol/L) with an acute increase of at least 0.5 mg/dl (44 µmol/L)

These products are manufactured and sold under one or more of the following US patent(s): US Patent No. 5,411,552; 6,214,054; 6,547,827; 6,561,970; 6,908,481; 7,214,344; 7,510,575; 7,530,253; and 7,993,394 and corresponding foreign patents. Additional patents are pending.

The FDA has requested Edwards to increase product surveillance with the SAPIEN XT THV in order to ensure a high-quality product experience. If you have any quality questions or concerns, please immediately call 1-949-250-3612, option 4.

Edwards

05/2014

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Edwards Lifesciences

Edwards SAPIEN XT
Transcatheter Heart Valve with the NovaFlex+ Delivery System

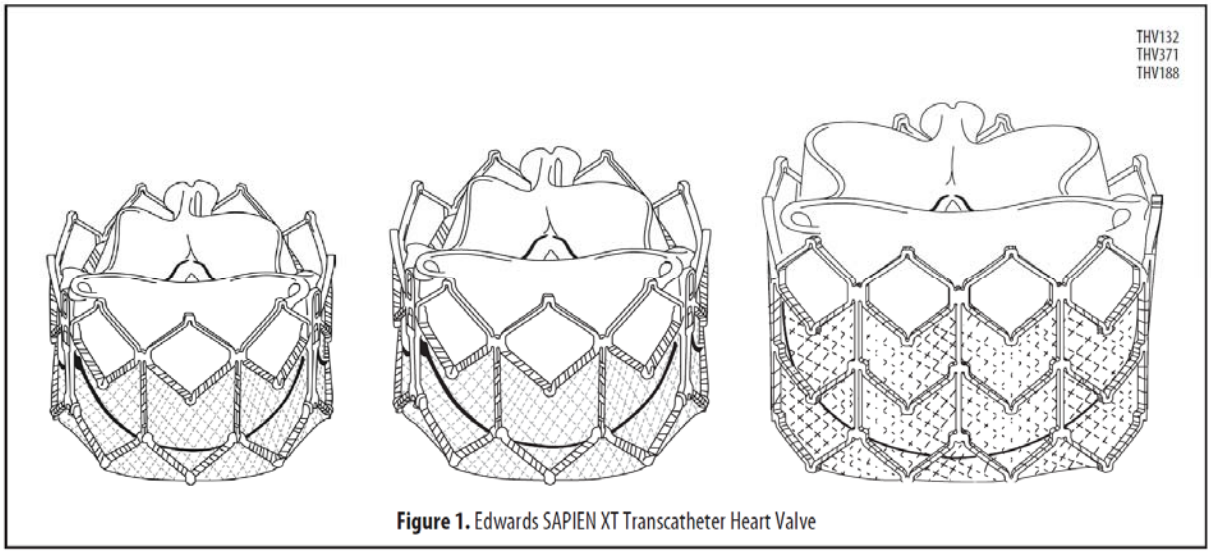


Figure 1. Edwards SAPIEN XT Transcatheter Heart Valve

Instructions for Use

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

Implantation of the transcatheter heart valve should be performed only by physicians who have received Edwards Lifesciences training. The implanting physician should be experienced in balloon aortic valvuloplasty.

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

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

1.0 Device Description

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

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

Table 1

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

Table 2

Native Valve Annulus Size (TEE)	Native Valve Annulus Size (CT)		THV Size
	Area	Area Derived Diameter	
18-22 mm	314 – 415 mm^2	20-23 mm	23 mm
21-25 mm	415 – 530 mm^2	23-26 mm	26 mm
24-27 mm	530 – 660 mm^2	26-29 mm	29 mm
THV size recommendations are based on native valve annulus size, as measured by transesophageal echocardiography (TEE) or computed tomography (CT). Patient anatomical factors and multiple imaging modalities should be considered during THV size selection. Note: Risks associated with undersizing and oversizing should be considered.			

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

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

Table 3

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

Figure 2a. NovaFlex+ Delivery System

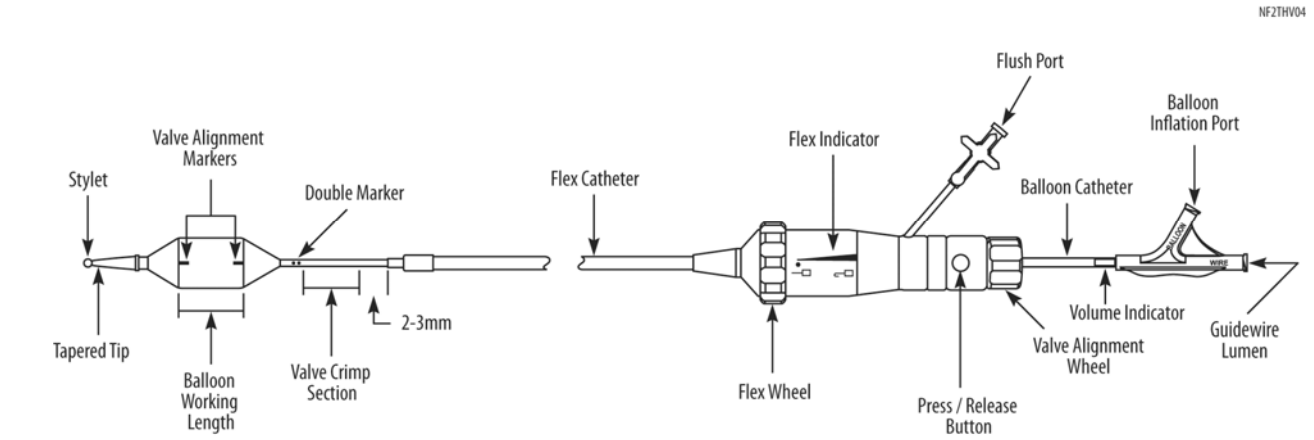
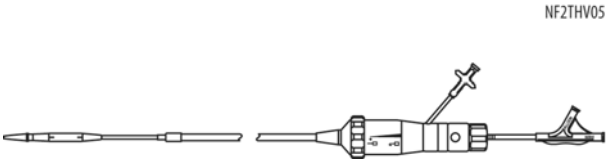
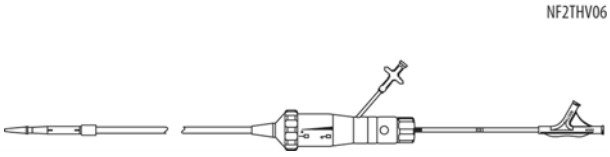


Figure 2b. Default Position

Figure 2c. Valve Alignment Position

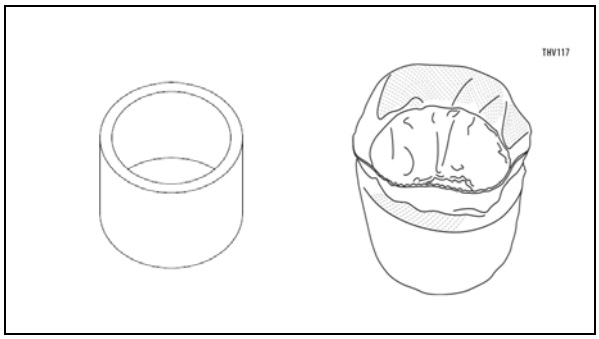




- **Qualcrimp Crimping Accessory (Figure 3)**

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

Figure 3



Laminated Qualcrimp **Cloth Qualcrimp**

2.0 Indications

The Edwards SAPIEN XT Transcatheter Heart Valve, model 9300TFX, systems are indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis (aortic valve area ≤ 1.0 cm^2 or aortic valve area index ≤ 0.6 cm^2/m^2, a mean aortic valve gradient of ≥ 40 mmHg, or a peak aortic-jet velocity of ≥ 4.0 m/s), and with native anatomy appropriate for the 23, 26, or 29 mm valve system, who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (i.e., Society of Thoracic Surgeons operative risk score ≥ 8% or at a ≥ 15% risk of mortality at 30 days).

3.0 Contraindications

The THV and delivery systems are contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections.

4.0 Warnings

- Observation of the pacing lead throughout the procedure is essential to avoid the potential risk of pacing lead perforation.
- There is an increased risk of stroke in transcatheter aortic valve replacement procedures, as compared to balloon aortic valvuloplasty or other standard treatments.
- 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.
- Incorrect sizing of the THV may lead to paravalvular leak, migration, embolization and/or annular rupture.
- Accelerated deterioration of the THV may occur in patients with an altered calcium metabolism.
- Prior to delivery, the THV must remain hydrated at all times and cannot be exposed to solutions other than its shipping storage solution and sterile physiologic rinsing solution. THV leaflets mishandled or damaged during any part of the procedure will require replacement of the THV.
- Caution should be exercised in implanting a THV in patients with clinically significant coronary artery disease.
- Patients with pre-existing mitral valve devices should be carefully assessed prior to implantation of the THV to ensure proper THV positioning and deployment.
- Do not use the THV if the tamper evident seal is broken, the storage solution does not completely cover the THV, the temperature indicator has been activated, the THV is damaged, or the expiration date has elapsed.
- Do not mishandle the NovaFlex+ delivery system or use it if the packaging or any components are not sterile, have been opened or are damaged (e.g. kinked or stretched), or the expiration date has elapsed.
- Use of excessive contrast media may lead to renal failure. Measure the patient's creatinine level prior to the procedure. Contrast media usage should be monitored.
- Patient injury could occur if the delivery system is not un-flexed prior to removal.
- Care should be exercised in patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/or polymeric materials.
- The procedure should be conducted under fluoroscopic guidance. Some fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. These injuries may be painful, disfiguring, and long-lasting.
- THV recipients should be maintained on anticoagulant/antiplatelet therapy, except when contraindicated, as determined by their physician. This device has not been tested for use without anticoagulation.
- Do not add or apply antibiotics to the storage solution, rinse solutions, or to the THV.

5.0 Precautions

- Long-term durability has not been established for the THV. Regular medical follow-up is advised to evaluate THV performance.
- Glutaraldehyde may cause irritation of the skin, eyes, nose and throat. Avoid prolonged or repeated exposure to, or breathing of, the solution. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water; in the event of contact with eyes, seek immediate medical attention. For more information about glutaraldehyde exposure, refer to the Material Safety Data Sheet available from Edwards Lifesciences.
- To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon.
- Appropriate antibiotic prophylaxis is recommended post-procedure in patients at risk for prosthetic valve infection and endocarditis.

- Safety, effectiveness, and durability have not been established for valve-in-valve procedures.
- Safety and effectiveness have not been established for patients with the following characteristics/comorbidities:
  - Non-calcified aortic annulus
  - Severe ventricular dysfunction with ejection fraction < 20%
  - Congenital unicuspid or congenital bicuspid aortic valve
  - Mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation > 3+)
  - Pre-existing prosthetic heart valve or prosthetic ring in any position
  - Severe mitral annular calcification (MAC), severe (> 3+) mitral insufficiency, or Gorlin syndrome
  - Blood dyscrasias defined as: leukopenia (WBC < 3000 cells/mL), acute anemia (Hb < 9 g/dL), thrombocytopenia (platelet count < 50,000 cells/mL), or history of bleeding diathesis or coagulopathy
  - Hypertrophic cardiomyopathy with or without obstruction (HOCM)
  - Echocardiographic evidence of intracardiac mass, thrombus, or vegetation
  - A known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid™), or clopidogrel (Plavix™), or sensitivity to contrast media, which cannot be adequately premedicated
  - Significant aortic disease, including abdominal aortic or thoracic aneurysm defined as maximal luminal diameter 5 cm or greater; marked tortuosity (hyperacute bend), aortic arch atheroma (especially if thick [> 5 mm], protruding, or ulcerated) or narrowing (especially with calcification and surface irregularities) of the abdominal or thoracic aorta, severe “unfolding” and tortuosity of the thoracic aorta
  - Access characteristics that would preclude safe placement of 16F, 18F, or 20F Edwards Expandable Introducer Sheath Set, such as severe obstructive calcification, severe tortuosity or diameter less than 6 mm, 6.5 mm, or 7 mm, respectively
  - Bulky calcified aortic valve leaflets in close proximity to coronary ostia

6.0 Potential Adverse Events

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

- Death
- Stroke/transient ischemic attack, clusters or neurological deficit
- Paralysis
- Permanent disability
- Respiratory insufficiency or respiratory failure
- Hemorrhage requiring transfusion or intervention
- Cardiovascular injury including perforation or dissection of vessels, ventricle, myocardium or valvular structures that may require intervention
- Pericardial effusion or cardiac tamponade
- Embolization including air, calcific valve material or thrombus
- Infection including septicemia and endocarditis
- Heart failure
- Myocardial infarction
- Renal insufficiency or renal failure
- Conduction system defect which may require a permanent pacemaker

- Arrhythmia
- Retroperitoneal bleed
- AV fistula or pseudoaneurysm
- Reoperation
- Ischemia or nerve injury
- Restenosis
- Pulmonary edema
- Pleural effusion
- Bleeding
- Anemia
- Abnormal lab values (including electrolyte imbalance)
- Hypertension or hypotension
- Allergic reaction to anesthesia, contrast media, or device materials
- Hematoma
- Syncope
- Pain or changes at the access site
- Exercise intolerance or weakness
- Inflammation
- Angina
- Heart murmur
- Fever

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

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

- Hemolysis
- Device explants
- Nonstructural dysfunction
- Mechanical failure of delivery system, and/or accessories
- Non-emergent reoperation

7.0 Directions for Use

7.1 Required Equipment

Table 4

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

* Includes the Qualcrimp Crimping Accessory and 2-piece Crimp Stopper
** Or other compatible sheath provided by Edwards Lifesciences

Additional Equipment:

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

7.2 THV Handling and Preparation

Follow sterile technique during device preparation and implantation.

7.2.1 THV Rinsing Procedure

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

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

Step	Procedure
1	Set up two (2) sterile bowls with at least 500 mL of sterile physiological saline to thoroughly rinse the glutaraldehyde sterilant from the THV.
2	Carefully remove the THV/holder assembly from the jar without touching the tissue. Verify the THV serial identification number with the number on the jar lid and record in the patient information documents. Inspect the THV for any signs of damage to the frame or tissue.
3	Rinse the THV as follows: Place the THV in the first bowl of sterile, physiological saline. Be sure the saline solution completely covers the THV and holder. With the THV and holder submerged, slowly agitate (to gently swirl the THV and holder) back and forth for a minimum of 1 minute. Transfer the THV and holder to the second rinsing bowl of physiological saline and gently agitate for at least one more minute. Ensure the rinse solution in the first bowl is not used. The THV should be left in the final rinse solution until needed to prevent the tissue from drying. **CAUTION: Do not allow the THV to come into contact with the bottom or sides of the rinse bowl during agitation or swirling in the rinse solution. Direct contact between the identification tag and THV is also to be avoided during the rinse procedure. No other objects should be placed in the rinse bowls. The THV should be kept hydrated to prevent the tissue from drying.**

7.2.2 Prepare the Components

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

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

<table>
<tr><th>Step</th><th>Procedure</th></tr>
<tr><td>10</td><td>Close the stopcock to the delivery system. By rotating the knob of the inflation device provided by Edwards Lifesciences, transfer the contrast medium into the syringe to achieve the appropriate volume required to deploy the THV, per the following:
<table>
<tr><th>Delivery System</th><th>THV Size</th><th>Inflation Volume</th></tr>
<tr><td>Model 9355FS23</td><td>23 mm</td><td>17 mL</td></tr>
<tr><td>Model 9355FS26</td><td>26 mm</td><td>22 mL</td></tr>
<tr><td>Model 9355FS29</td><td>29 mm</td><td>33 mL</td></tr>
</table></td></tr>
<tr><td>11</td><td>Close the stopcock to the 50 cc or larger syringe. Remove the syringe. Verify that the inflation volume is correct and lock the Inflation device provided by Edwards Lifesciences.
CAUTION: Maintain the Inflation device provided by Edwards Lifesciences in the locked position until THV deployment.</td></tr>
</table>

7.2.3 Mount and Crimp the THV on the Delivery System

Step	Procedure
1	Set up two (2) additional sterile bowls with at least 100 mL of sterile physiological saline to thoroughly rinse the Qualcrimp crimping accessory.
2	Completely submerge the Qualcrimp crimping accessory in the first bowl and gently compress it to ensure complete saline absorption. Slowly swirl the Qualcrimp crimping accessory for a minimum of 1 minute. Repeat this process in the second bowl.
3	Remove the THV from the holder and remove the ID tag.
4	Attach the 2-piece crimp stopper to the base of the crimper and click into place.
5	With the crimper in the open position, gently place the THV into the crimper aperture. Gradually crimp the THV until it fits into the Qualcrimp crimping accessory.
6	Place the Qualcrimp crimping accessory over the THV making sure the THV is parallel to the edge of the Qualcrimp.
7	Place the THV and Qualcrimp crimping accessory in crimper aperture. Insert the delivery system coaxially within the THV on the Valve Crimp Section (2-3 mm distal to the balloon shaft) with the inflow (fabric cuff end) of the THV towards the distal end of the delivery system.
8	Crimp the THV until it reaches the Qualcrimp Stop located on the 2-piece Crimp Stopper.
9	Gently remove the Qualcrimp crimping accessory from the THV. Remove the Qualcrimp Stop from the Final Stop, leaving the Final Stop in place.
10	Fully crimp the THV until it reaches the Final Stop. **NOTE: Ensure that the Valve Crimp Section remains coaxial within the THV.**
11	Repeat the full crimp of the THV for a total of two full crimps.
12	Pull the balloon shaft until it is locked in the default position.
13	Flush the loader with heparinized saline. Immediately advance the THV into the loader until the tapered tip of the delivery system is exposed. **CAUTION: To prevent possible leaflet damage, the THV should not remain fully crimped and/or in the loader for over 15 minutes.**
14	Attach the loader cap to the loader, re-flush the delivery system through the flush port and close the stopcock to the delivery system. Remove the stylet and flush the guidewire lumen of the delivery system. **CAUTION: Keep the THV hydrated until ready for implantation.** **CAUTION: The physician must verify correct orientation of the THV prior to its implantation; its inflow (fabric cuff end) should be oriented distally towards the tapered tip.**

7.3 Valvuloplasty and THV Delivery

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

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

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

CAUTION: Procedure may require an arterial cut-down with surgical closure of the puncture site due to the size of the arteriotomy.

7.3.1 Baseline Parameters

Step	Procedure
1	Perform a supra-aortic angiogram with fluoroscopic view perpendicular to the aortic valve.
2	Evaluate the distance of the left and right coronary ostia from the aortic annulus in relation to the THV frame height.
3	Introduce a pacemaker (PM) lead until its distal end is positioned in the right ventricle.
4	Set the stimulation parameters to obtain 1:1 capture, and test pacing.

7.3.2 Valvuloplasty

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

Note: Rapid ventricular pacing should be performed when using the Edwards Balloon Catheter for valvuloplasty prior to aortic transcatheter valve implantation.

After placement of the balloon at the intended site, begin rapid ventricular pacing. Once the systolic blood pressure has decreased to 50 mmHg or below, balloon inflation can commence.

CAUTION: THV implantation should not be carried out if the balloon cannot be fully inflated during valvuloplasty.

7.3.3 THV Delivery

Step	Procedure
1	Dilate the access site using the Edwards Dilator Kit, if needed. Refer to the Edwards Dilator Kit IFU for information on device preparation and handling.
2	Prepare and insert the Edwards Expandable Introducer Sheath Set. Refer to the Edwards Expandable Introducer Sheath Set IFU for information on device preparation and handling.
3	Insert the loader into the sheath until the loader stops.
4	Advance the NovaFlex+ delivery system, with the Edwards logo facing up, through the sheath until the THV exits the sheath. Retract the loader to the proximal end of the delivery system. **NOTE: Maintain the proper orientation of the flex catheter (with the Edwards logo facing up) throughout the procedure.** **CAUTION: If accessing femorally or via the iliac, the THV should not be advanced through the sheath if the sheath tip is not past the aortic bifurcation.** **CAUTION: To prevent possible leaflet damage, the THV should not remain in the sheath for over 2 minutes.**

Step	Procedure
5	In a straight section of the aorta, initiate valve alignment by pressing the button, begin pull back of the balloon catheter, and release the button. Continue pulling back the balloon catheter until the delivery system locks into the valve alignment position (Refer to **Figure 2c**). Use the Valve Alignment Wheel to position the THV between the valve alignment markers. **CAUTION: Do not turn the Valve Alignment Wheel if the delivery system is not locked in the Valve Alignment Position.** **WARNING: Do not position the THV past the distal Valve Alignment Marker. This will prevent proper valve deployment.** **CAUTION: Maintain guidewire position in the left ventricle during valve alignment.**
6	Advance the catheter and use the flex wheel, if needed, and cross the aortic valve. **NOTE: Verify the Edwards logo is facing up. The delivery system articulates in a direction opposite from the flush port.**
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	Press the button and retract the Flex Catheter to the Double Marker and position the THV within the aortic annulus.
9	Verify the correct position of the THV with respect to the aortic annulus.
10	Begin THV deployment: • Unlock the Inflation device provided by Edwards Lifesciences. • Begin rapid pacing; once systolic blood pressure has decreased to 50 mmHg or below, balloon inflation can commence. • Deploy the THV by inflating the balloon with the entire volume in the Inflation device provided by Edwards Lifesciences, hold for 3 seconds and confirm that the barrel of the inflation device is empty to ensure complete inflation of the balloon. • Deflate the balloon. When the balloon catheter has been completely deflated, turn off the pacemaker.

7.3.4 System Removal

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

8.0 How Supplied

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

8.1 Storage

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

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

9.0 MR Safety

MR Conditional

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

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

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

In non-clinical testing, the image artifact caused by the device extends as far as 10 mm from the implant for spin echo images and 30 mm for gradient echo images when scanned in a 3.0 T MRI system.

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

10.0 Patient Information

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

11.0 Recovered THV and Device Disposal

The explanted THV should be placed into a suitable histological fixative such as 10% formalin or 2% glutaraldehyde and returned to the company. Refrigeration is not necessary under these circumstances. Contact Edwards Lifesciences to request an Explant Kit.
Used delivery system may be disposed of in the same manner that hospital waste and biohazardous materials are handled. There are no special risks related to the disposal of these devices.

12.0 Clinical Studies

The PARTNER II Trial Overview

Cohort B of The Placement of Aortic Transcatheter Valves II (PARTNER II) Trial was a 1:1 randomized, controlled study independently powered to compare THV therapy with the first generation (SAPIEN THV) system to THV therapy with the second generation (Edwards SAPIEN XT THV) system in patients who cannot undergo surgery (inoperable). Patients in the control arm of Cohort B received an Edwards SAPIEN THV with the RetroFlex 3 delivery system (transfemoral approach). Patients in the treatment arm of Cohort B received an Edwards SAPIEN XT THV with the NovaFlex+ delivery system (transfemoral). The randomized sample size was set to 500 patients. Enrollment is complete and patients have reached at least 1 year of follow-up.

Cohort B (29 mm / Transfemoral / Inoperable) is an Inoperable Transfemoral Registry for the delivery of 29 mm SAPIEN XT THV in ≥ 7 mm femoral arteries. A maximum of 50 patients were to be enrolled in this arm. Primary endpoint of this registry was freedom from mortality at one year. Non-powered secondary endpoints for safety and effectiveness were consistent with additional secondary endpoint analyses for both Cohorts A and B and as described below. Patients previously enrolled as a Cohort A control could not be enrolled in this registry.

SOURCE Registry XT

The SOURCE Registry XT is an international multi-center prospective, consecutively enrolled, observational registry. Consecutive patient data have been collected at discharge, 30 days, and 12 months post-implant, and will be collected annually thereafter up to 5 years post-implant.

Results of Cohort B

The primary endpoint of Cohort B of the PARTNER II Trial was met. At 1 year the non-hierarchical composite of all-cause mortality, disabling strokes, and re-hospitalizations was similar (p non-inferiority = 0.0037). At 30 days, all-cause mortality and major strokes were similar (mortality: SAPIEN THV 5.1% vs. SAPIEN XT THV 3.5%; major strokes: SAPIEN THV 3.0% vs. SAPIEN XT THV 3.2%, p>0.9999).

The Edwards SAPIEN XT THV treatment arm was associated with a reduction in anesthesia time (p=0.0196), cath lab time (p=0.0094), multiple valve implants (p=0.1534), aborted procedures (p=0.0585), and the need for hemodynamic support (p=0.0637).

The trial showed that there was a reduction in the Edwards SAPIEN XT THV arm as compared to Edwards SAPIEN THV arm for the following complications: major vascular complications involving dissection (from 9.2% to 4.3%, p=0.0195), perforation (from 4.8% to 0.7%, p=0.0031), and infection (from 5.5% to 1.8%, p=0.0163).

Secondary endpoints for the study included days alive and out of the hospital (DAOH), NYHA, 6MWT, valve area (EOA), and total aortic regurgitation at one year as well as 6MWT improvement from baseline to 1 year and device success.

Mean adjusted days alive and out of the hospital (DAOH) at 1 year: In the ITT population, the mean adjusted days alive and out of the hospital (DAOH) was 299.2 ± 111.4 days for the SAPIEN group and 302.7 ± 108.7 days for the SAPIEN XT group at 1 year. The difference between groups was 3.5 days (two sided 95% CI 1.8, 5.2), p< 0.0001.

NYHA at 1 year: In the SAPIEN group, mean NYHA was 3.5 ± 0.6 at baseline and 1.8 ± 0.8 at 1 year which constituted a reduction of 1.7 ± 0.9. In the SAPIEN XT group, mean NYHA was 3.4 ± 0.6 at baseline and 1.7 ± 0.7 at 1 year which was a mean decrease of 1.8 ± 0.9. The difference between groups was -0.13, (two sided 95% CI -0.32, 0.06), p< 0.0001. Figure 14 illustrates the NYHA classification by visit for the ITT population.

6MWT at 1 year: Hypothesis testing was based on a difference of 70 meters which is considered clinically relevant. The mean 6 minute walk distance (6MWD) at 1 year was 132.3 ± 136.3 meters in the SAPIEN group, and 159.0 ± 138.5 meters in the SAPIEN XT group. The difference between groups was 26.7 meters (95% CI 24.2, 29.2), p<0.0001.

EOA at 1 year (hypothesis testing was based on a difference of 0.2 cm^2): In the SAPIEN group, mean EOA was 0.6 ± 0.17 cm^2 at baseline and 1.5 ± 0.40 cm^2 at 1 year, which was an improvement of 0.9 ± 0.38 cm^2. In the SAPIEN XT group, mean EOA was 0.6 ± 0.18 cm^2 at baseline and 1.5 ± 0.43 cm^2 at 1 year, a mean increase of 0.9 ± 0.41 cm^2. The difference between groups in change from baseline to 1 year was -0.01 (95% CI -0.15, 0.13), p=0.0038.

Device success: Device success was defined as successful vascular access, delivery and deployment and retrieval of delivery system; correct positioning, intended performance (aortic valve area > 1.2 cm^2 and mean aortic valve gradient < 20 mmHg or peak velocity < 3 m/s, without moderate or severe prosthetic valve AR), and only one valve implanted. The proportion of device success was 45.3% in the SAPIEN group and 58.5% in the SAPIEN XT group. The relative risk ratio of SAPIEN XT vs. SAPIEN was 0.759 (95% CI 0.582, 0.990), p<0.0001.

6MWT improvement in the SAPIEN XT arm from baseline to 1 year was assessed as a superiority comparison. The improvement for each subject was computed, and the superiority comparison was evaluated by a two-sided paired sample t-test. In the SAPIEN XT arm, the mean improvement in 6MWD from baseline to 1 year was 52.7 ± 111.5 meters, which was statistically significant (p<0.0001).

Total regurgitation at 1 year was analyzed in the valve implant population. Total aortic regurgitation was assessed by the core lab as 0 = None, 1+ = Trace, 2+ = Mild, 3+ = Moderate, and 4+ = Severe. The change in mean total aortic regurgitation from baseline to 1 year was 0.1 ± 1.23 in the SAPIEN group, and 0.2 ± 1.38 in the SAPIEN XT group. The difference between group in change from baseline to 1 year was 0.09 (95% CI -0.16, 0.34), p=0.1027.

In conclusion, there were significant improvements from baseline in NYHA class, echo valve performance (EOA and gradients), and Quality of Life (QOL) for patients in both the Edwards SAPIEN THV and Edwards SAPIEN XT THV arms.

In the inoperable cohort of the PARTNER II trial, the new lower profile Edwards SAPIEN XT THV system was associated with improved procedural outcomes, similar low 30-day mortality and strokes, reduced vascular complications, and similar 1-year major clinical events and valve performance.

The Edwards SAPIEN XT THV has demonstrated objective evidence of safety, efficacy and clinical utility for patients in whom transcatheter heart valve therapy is indicated and represents an advance with incremental clinical value.

Results of Cohort B (29 mm / Transfemoral / Inoperable)

A total of 61 patients were enrolled. The primary safety and effectiveness endpoint was freedom from all-cause mortality at 1 year. The KM estimate at 30 days involving freedom from all-cause mortality was 94.9 ± 2.8%.

There were no reported major strokes or incidence of renal failure, cardiac intervention or endocarditis, 1.6% myocardial infarction, 8.2% major vascular complications, 11.5% disabling bleeding events, 2.7% new atrial fibrillation and 4.9% new pacemaker.

The mean change (negative value = improvement) in NYHA from baseline at 30 days was -1.6 ± 0.9. Device success was observed in 82.5%. The mean hospitalization stay was 6.1 ± 6.3 days which included 2.4 ± 3.4 days in the ICU.

The mean EOA was 0.8 ± 0.16 cm^2 at baseline and 2.2 ± 0.53 cm^2 at 30 days, and the average mean gradient decreased from 40.3 ± 11.8 mmHg at baseline to 7.7 ± 2.8 mmHg at 30 days. The mean peak gradient decreased from 71.7 ± 20.8 mmHg at baseline to 15.5 ± 5.7 mmHg at 30 days.

Results of SOURCE XT

A total of 2688 patients were enrolled. The vast majority of patients (96%) were treated with either the transapical (TA) or transfemoral (TF) approach. Only a small proportion of patients were treated with transaortic (TAo) or subclavian approaches. The implant approach was 62.7% for TF, 33.3% for TA, 3.76% for TAo and 0.3% for subclavian. The results only include the TF, TA and TAo approaches (n=2680).

Using K-M event rates at 30 days post implant for the TF, TA/TAo population, 6.2% of patients had died, 3% due to a cardiac death, 3.6% of patients had suffered a stroke, and 6.6% had a major vascular complication. Major/life threatening bleeding had occurred in 14.9% of patients, major bleeding in 10.2%, and renal failure or AKI in 17.8%. Permanent pacemakers were implanted in 9.5% of patients. Using K-M event rates at 1 year post implant for the TF, TA/TAo population, 19.5% of patients had died, 9.5% of these from cardiac death, and 6.3% of patients had suffered a stroke. Major/life-threatening bleeding had occurred in 17.3% of patients, major bleeding in 12%, major vascular complications in 7.2%, renal failure or AKI in 20.5% and 11% of patients had a new pacemaker implanted.

PARTNER II Cohort B Clinical Data

Clinical Table 1: Cohort B (Inoperable) Baseline Characteristics of the Patients and Echocardiographic Findings (AT Population)*		
	SAPIEN XT	SAPIEN
Characteristic	(N = 282)	(N = 271)
Age - yr	84.0 ± 8.68	84.5 ± 8.65
Male sex — no./total no. (%)	140/282 (49.6%)	138/271 (50.9%)
STS score†	10.3 ± 5.40	11.0 ± 5.72
Logistic EuroSCORE‡	18.8 ± 14.66	21.0 ± 16.78
NYHA class		
I/II — no./total no. (%):	9/282 (3.2%)	11/271 (4.1%)
III/IV — no./total no. (%):	273/282 (96.8%)	260/271 (95.9%)
Coronary artery disease — no./total no. (%)	184/282 (65.2%)	183/271 (67.5%)
Previous myocardial infarction — no./total no. (%)	55/282 (19.5%)	57/271 (21.0%)
Previous intervention		
CABG — no./total no. (%):	76/282 (27.0%)	72/271 (26.6%)
PCI — no./total no. (%):	89/282 (31.6%)	98/271 (36.2%)
Balloon aortic valvuloplasty — no./total no. (%):	51/282 (18.1%)	53/271 (19.6%)
Cerebral vascular disease — no./total no. (%)	31/282 (11.0%)	35/271 (12.9%)
Peripheral vascular disease — no./total no. (%)	88/282 (31.2%)	73/271 (26.9%)
COPD		
Any — no./total no. (%):	83/282 (29.4%)	71/271 (26.2%)
Oxygen-dependent — no./total no. (%):	38/282 (13.5%)	43/271 (15.9%)
Creatinine > 2 mg/dL (177 µmol/liter) — no./total no. (%)	31/282 (11.0%)	30/271 (11.1%)
Atrial fibrillation — no./total no. (%)	102/282 (36.2%)	108/271 (39.9%)
Permanent pacemaker — no./total no. (%)	57/282 (20.2%)	47/271 (17.3%)
Pulmonary hypertension — no./total no. (%)	72/282 (25.5%)	56/271 (20.7%)
Frailty§ — no./total no. (%)	168/282 (59.6%)	162/271 (59.8%)
Extensively calcified aorta — no./total no. (%)	19/282 (6.7%)	11/271 (4.1%)
Chest-wall deformity — no./total no. (%)	10/282 (3.5%)	10/271 (3.7%)
Liver disease — no./total no. (%)	12/282 (4.3%)	13/271 (4.8%)
Echocardiographic findings		
Aortic-valve area — cm^2	0.6 ± 0.18	0.6 ± 0.17
Mean aortic-valve gradient — mmHg	45.1 ± 13.67	45.2 ± 14.36
Mean LVEF — %	52.5 ± 13.39	52.9 ± 13.61
Moderate or severe mitral regurgitation** — no./total no. (%)	71/264 (26.9%)	77/251 (30.7%)

* Plus–minus values are means ± SD. To convert the value for creatinine to micromoles per liter, multiply by 88.4. AT denotes as treated population, CABG denotes coronary-artery bypass grafting, COPD chronic obstructive pulmonary disease, LVEF left ventricular ejection fraction, NYHA New York Heart Association, PCI percutaneous coronary intervention, and TAVR transcatheter aortic-valve implantation.
† The Society of Thoracic Surgeons (STS) score measures patient risk at the time of cardiovascular surgery on a scale that ranges from 0% to 100%, with higher numbers indicating greater risk. An STS score higher than 10% indicates very high surgical risk.
‡ The logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE), which measures patient risk at the time of cardiovascular surgery, is calculated with the use of a logistic-regression equation. Scores range from 0% to 100%, with higher scores indicating greater risk. A logistic EuroSCORE higher than 20% indicates very high surgical risk.
§ Frailty was determined by the surgeons according to prespecified criteria.
** Moderate or severe mitral regurgitation was defined as regurgitation of grade 3+ or higher.

Clinical Table 2: Cohort B (Inoperable) Clinical Outcomes at 30 days and 1 year (AT Population)*				
Outcome [a]	**30 Days**		**1 Year**	
	SAPIEN XT	**SAPIEN**	**SAPIEN XT**	**SAPIEN**
	(N = 282)	**(N = 271)**	**(N = 282)**	**(N = 271)**
Death[b]				
From any cause	10/282 (3.5%)	12/271 (4.42%)	63/282 (22.34%)	61/271 (22.50%)
From cardiovascular cause	9/282 (3.2%)	10/271 (3.69%)	46/282 (16.31%)	46/271 (16.97%)
Major Stroke	9/282 (3.2%)	8/271 (2.95%)	13/282 (4.61%)	14/271 (5.17%)
Repeat hospitalization[c]	32/282 (11.3%)	28/271 (10.33%)	61/282 (21.63%)	61/271 (22.51%)
Death from any cause or major stroke or repeat hospitalization	48/282 (17.0%)	43/271 (15.87%)	105/282 (37.23%)	100/271 (36.90%)
Myocardial Infarction				
All	5/282 (1.8%)	2/271 (0.74%)	19/282 (6.74%)	8/271 (2.95%)
Peri-procedural	4/282 (1.4%)	1/271 (0.37%)	NA	NA
Major Vascular Complications	32/282 (11.3%)	43/271 (15.87%)	35/282 (12.41%)	47/271 (17.34%)
Renal Failure[d]	10/282 (3.5%)	5/271 (1.85%)	16/282 (5.67%)	10/271 (3.69%)
Disabling Bleeding Event[e]	22/282 (7.8%)	34/271 (12.55%)	38/282 (13.48%)	52/271 (19.19%)
Cardiac Reintervention[f]	9/282 (3.2%)	13/271 (4.80%)	10/282 (3.55%)	13/271 (4.80%)
Endocarditis	0/282 (0.00%)	0/271 (0.00%)	1/282 (0.35%)	2/271 (0.74%)
New Atrial Fibrillation	6/186 (3.2%)	7/190 (3.68%)	10/154 (6.49%)	9/144 (6.25%)
New pacemaker[g]	19/282 (6.7%)	16/271 (5.90%)	22/282 (7.80%)	21/271 (7.75%)

* AT= As Treated, NA= not applicable, TAVR = transcatheter aortic valve replacement. Data presented as n (%) of patients.

a. CEC adjudicated

b. Deaths from unknown causes were assumed to be deaths from cardiovascular causes.

c. Repeat hospitalizations were included if they were due to aortic stenosis or complications of the valve procedure (e.g. TAVR).

d. Renal failure is defined as stage III acute kidney injury: Increase in serum creatinine to ≥ 300% (3 x increase compared with baseline) or serum creatinine of ≥ 4 mg/d (≥ 354 µmol/L) with an acute increase of at least 0.5 mg/dl (44 µmol/L)

e. Disabling bleeding: Fatal bleeding OR bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, or pericardial necessitating pericardiocentesis, or intramuscular with compartment syndrome OR bleeding causing hypovolemic shock or severe hypotension requiring vasopressors or surgery OR overt source of bleeding with drop in hemoglobin of ≥ 5 g/dL or whole blood of packed red blood cells (RBC) transfusion ≥ 4 units

f. Cardiac reintervention includes any intervention that repairs, alters or replaces a previously operated valve OR balloon aortic valvuloplasty OR Surgical aortic valve replacement OR valve in valve

g. Refer to Clinical Table 3 for breakdown of subjects with and without pacemaker or ICD at baseline.

Clinical Table 3 Conduction Disturbance Requiring Pacemaker (CEC Adjudicated) – Pooled AT Population)

	SAPIEN (N = 271)		**SAPIEN XT (N = 282)**	
Event	**Events**	**Patients with Event**	**Events**	**Patients with Event**
New Permanent Pacemaker- All Patients[1]				
0-30 Days	16	16/271 (5.9%)	19	19/282 (6.7%)
0-12 Months	21	21/271 (7.7%)	22	22/282 (7.8%)
New Permanent Pacemaker – Patients without pre-procedural pacemaker[2]				
0-30 Days	16	16/224 (7.1%)	19	19/225 (8.4%)
0-12 Months	21	21/224 (9.4%)	22	22/225 (9.8%)

[1] Subjects with pacemaker or ICD at baseline are included (all patients included in denominator).

[2] Subjects with pacemaker or ICD at baseline are excluded (patients with baseline pacemaker/ICD subtracted from denominator).

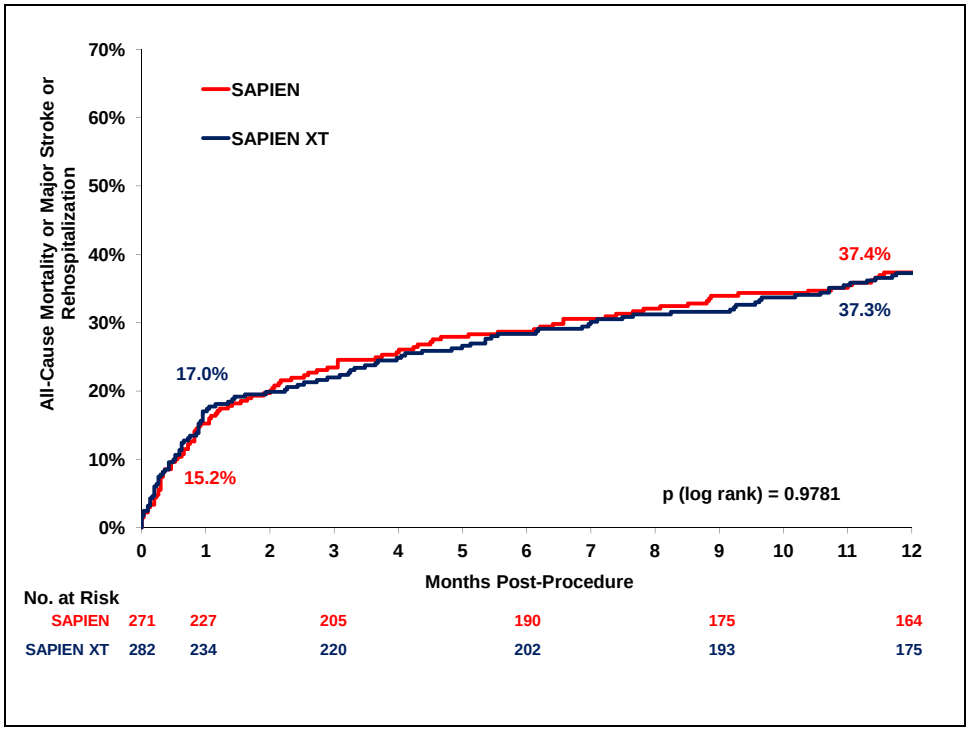


Figure 4: All-Cause Mortality or Major Stroke or Re-Hospitalization at One Year (AT Population)

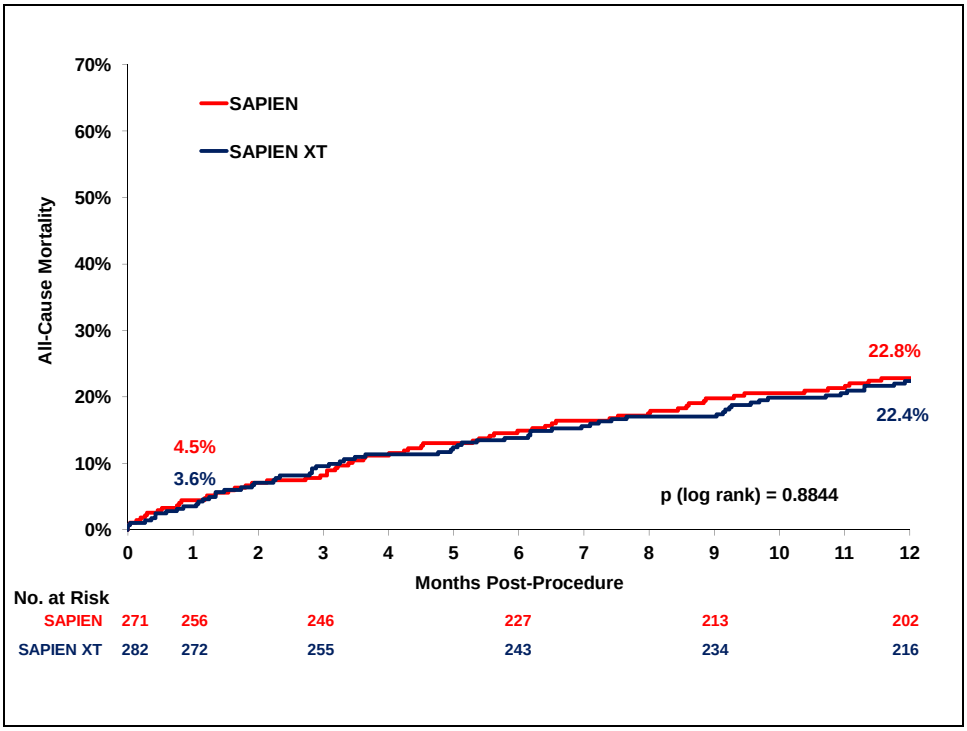


Figure 5: All-Cause Mortality at One Year (AT Population)

K-M curves for all-cause mortality by STS scores up to 1-Year for the pooled valve implant populations for SAPIEN and SAPIEN XT are presented in Figures 6 and 7 respectively. The p-value for each log-rank test for the SAPIEN arm shows a statistically significant difference among the 3 STS score groups (p-value=0.0336).

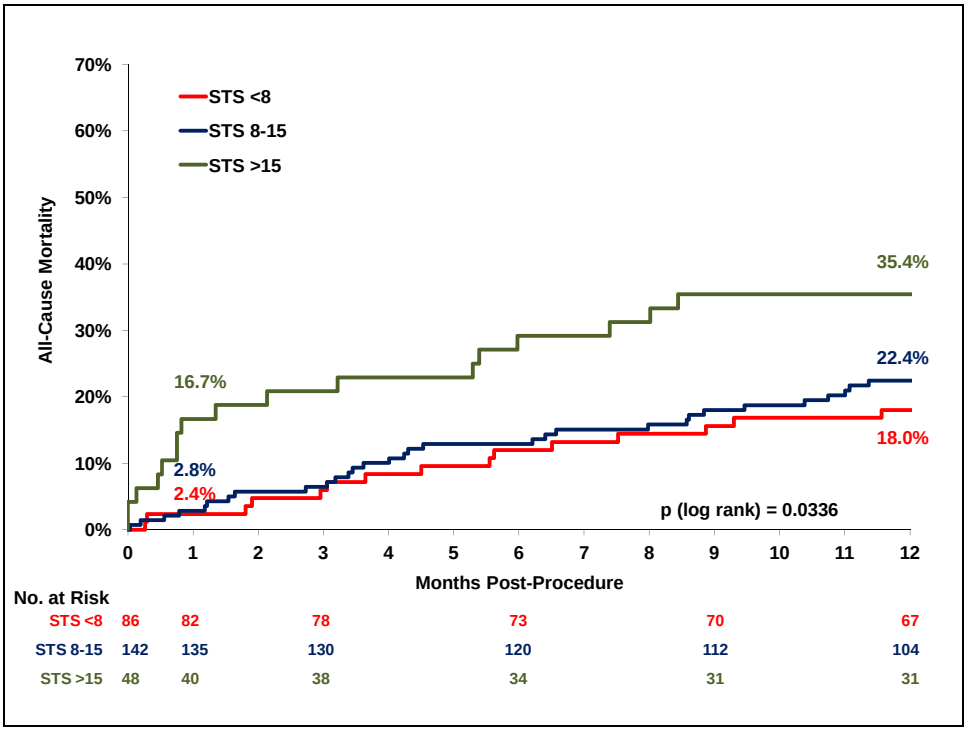


Figure 6: All-Cause Mortality by STS Score to One Year - SAPIEN (Intent-to-Treat Population)

This difference between STS risk groups was not present in the SAPIEN XT arm (p-value=0.0647).

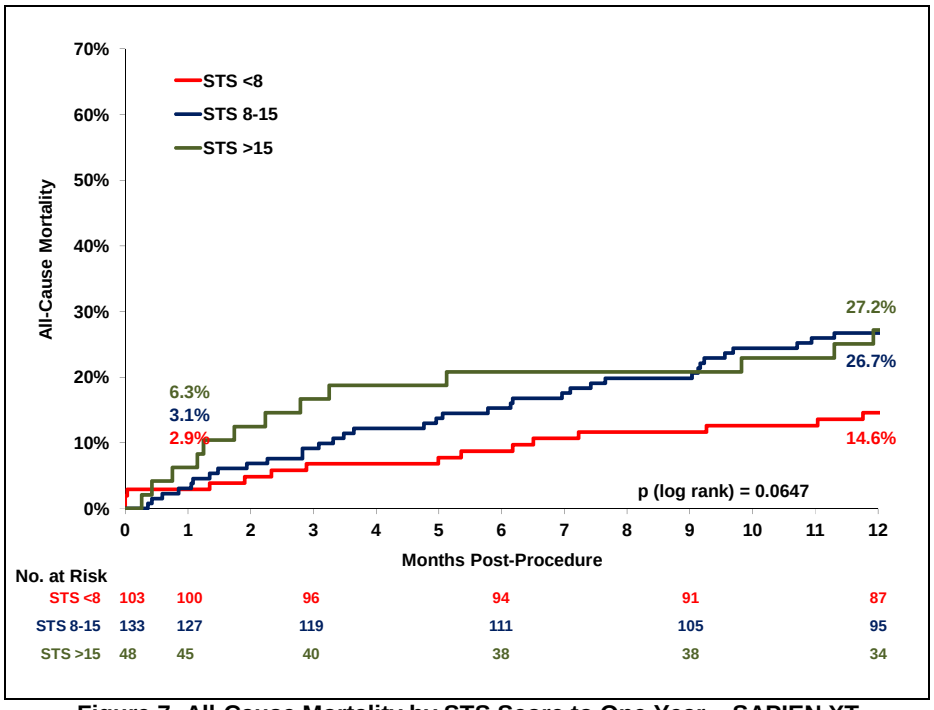


Figure 7: All-Cause Mortality by STS Score to One Year – SAPIEN XT (Intent-to-Treat Population)

Figures 8 and 9 show the results of a landmark analysis of all-cause mortality by STS scores for SAPIEN and SAPIEN XT respectively. In this analysis the overall mortality at day 30 was reset to 0 for patients still at risk at day 30 and day 30 was relabeled as day 0. The Kaplan-Meier plots were produced based on the re-zeroed data, and all-cause mortality was analyzed to one year from the new day 0. Any events that occurred before day 30 were not included in this analysis. There were no statistically significant differences in overall mortality among the STS score groups in either arm.

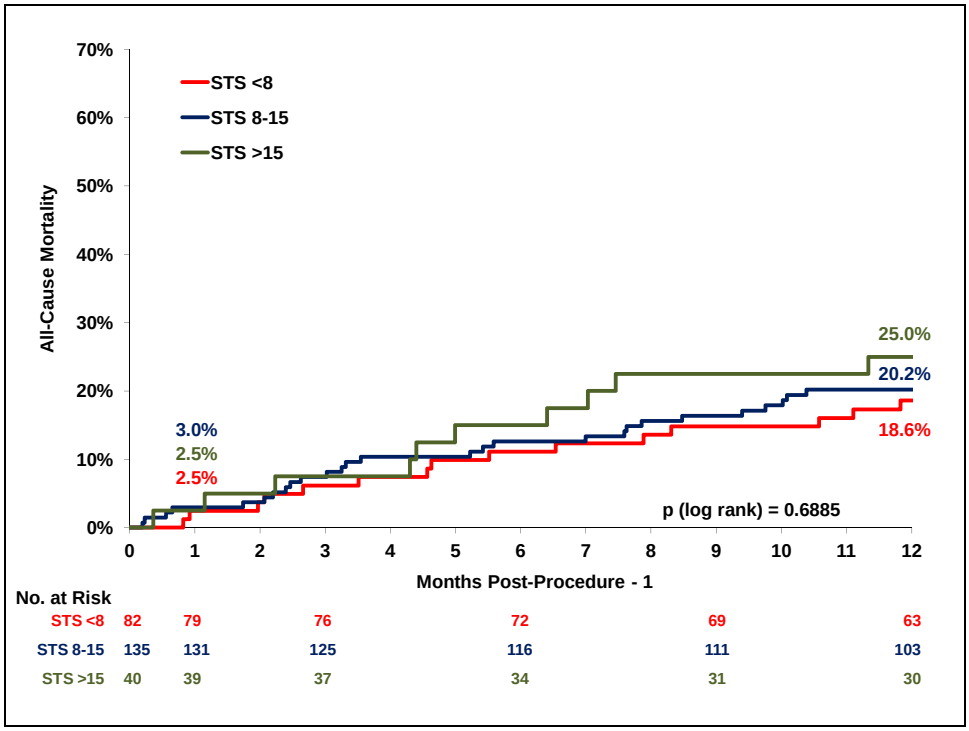


Figure 8: All-Cause Mortality by STS Score Rezeroing at 30-Days – SAPIEN (Intent-to-Treat Population)

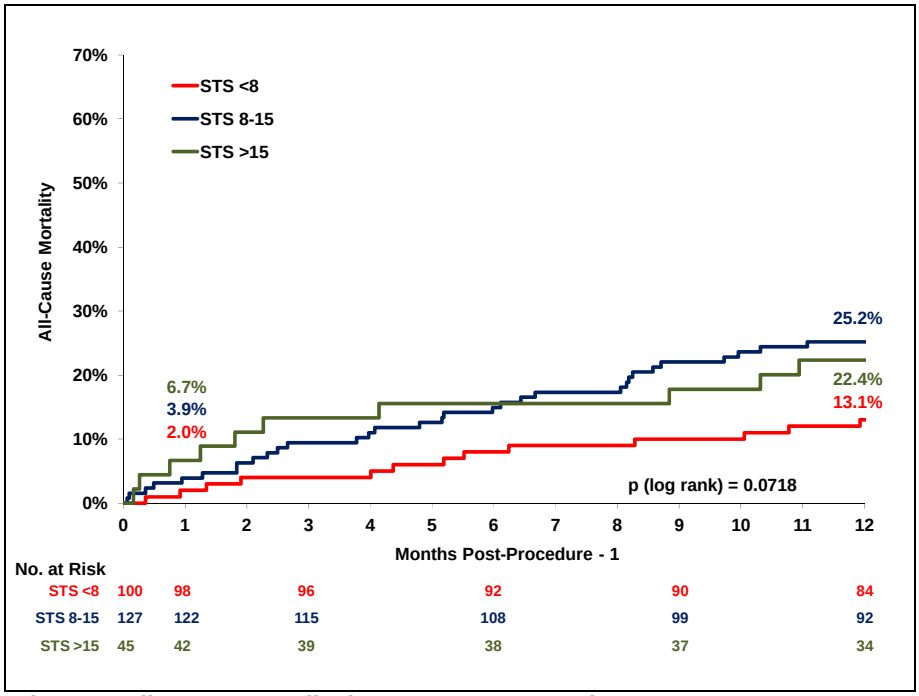


Figure 9: All-Cause Mortality by STS Score Rezeroing at 30-Days – SAPIEN XT (Intent to Treat Population)

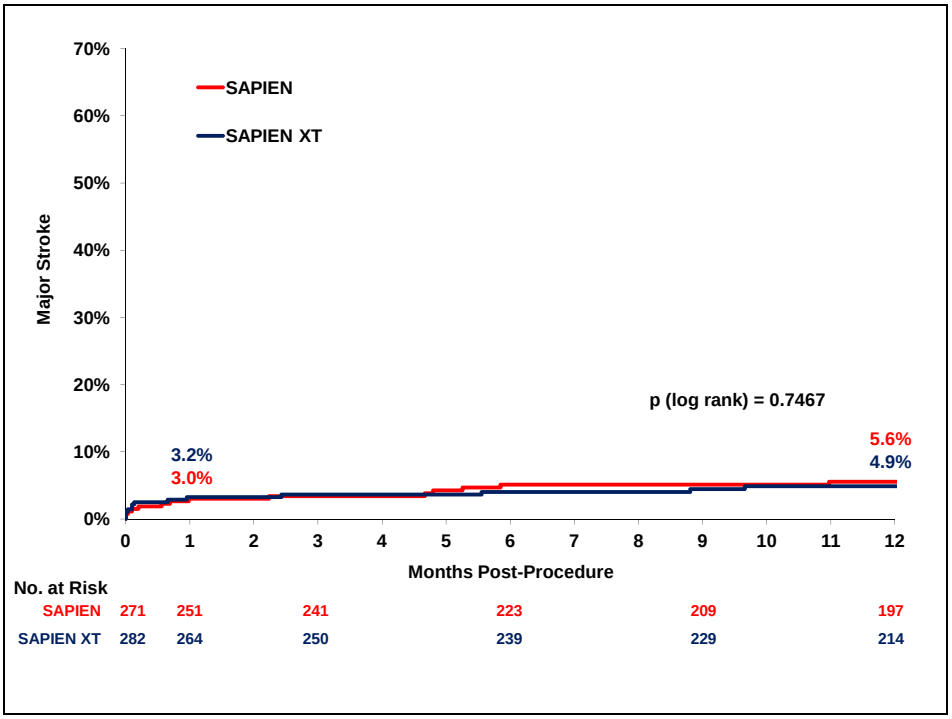


Figure 10: Major Stroke to One Year (AT Population)

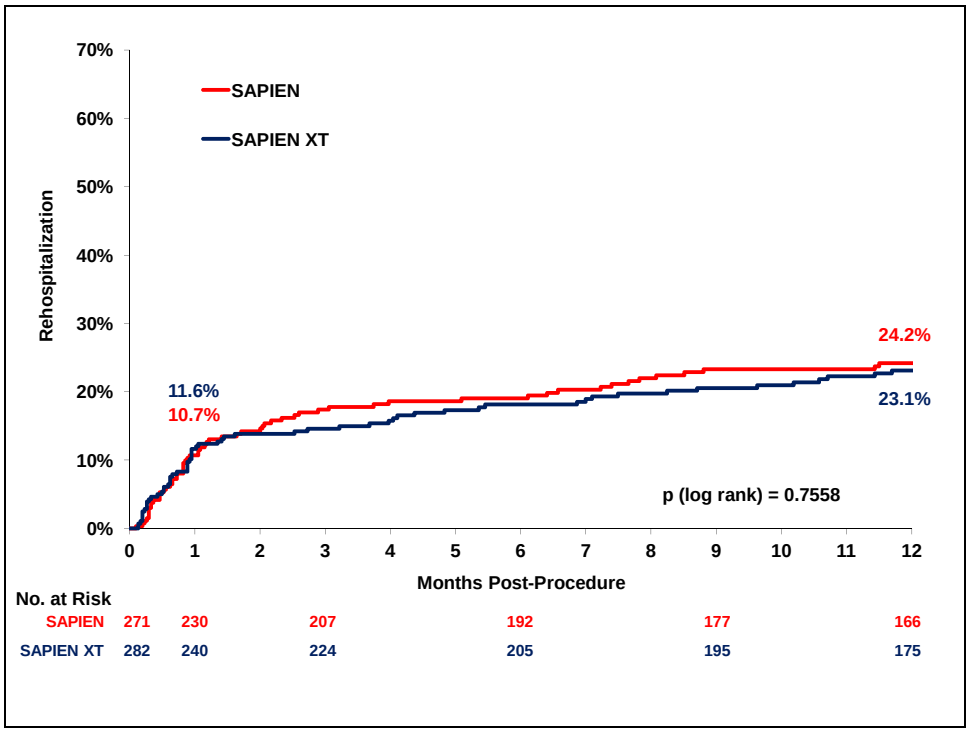


Figure 11: Rehospitalization to One Year (AT Population)

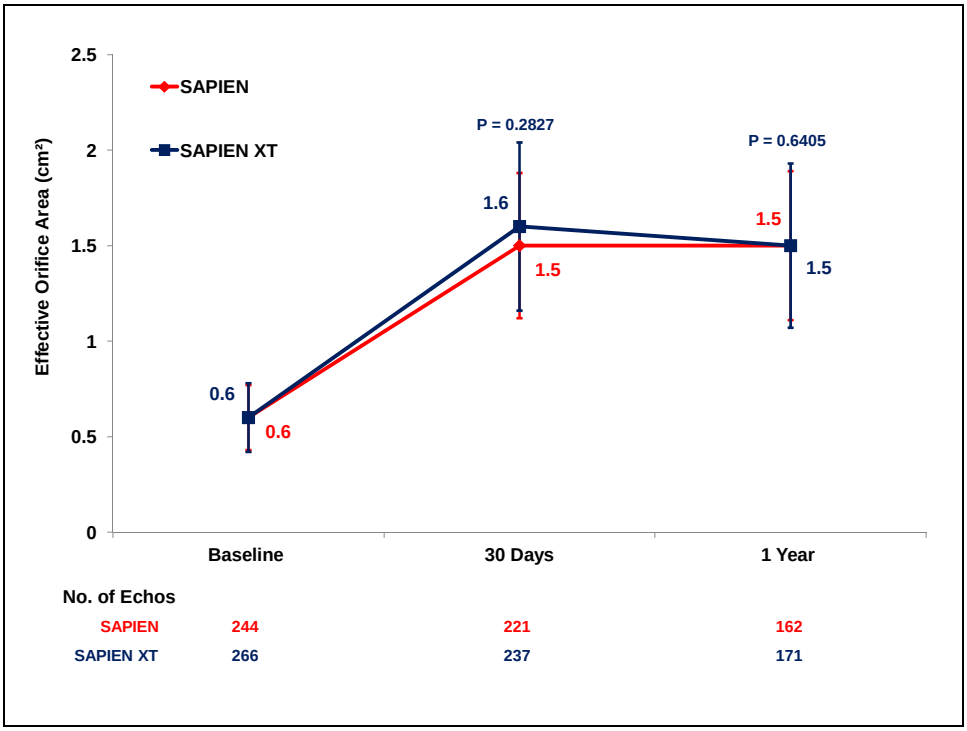


Figure 12: Effective Orifice Area (Valve Implant Population)

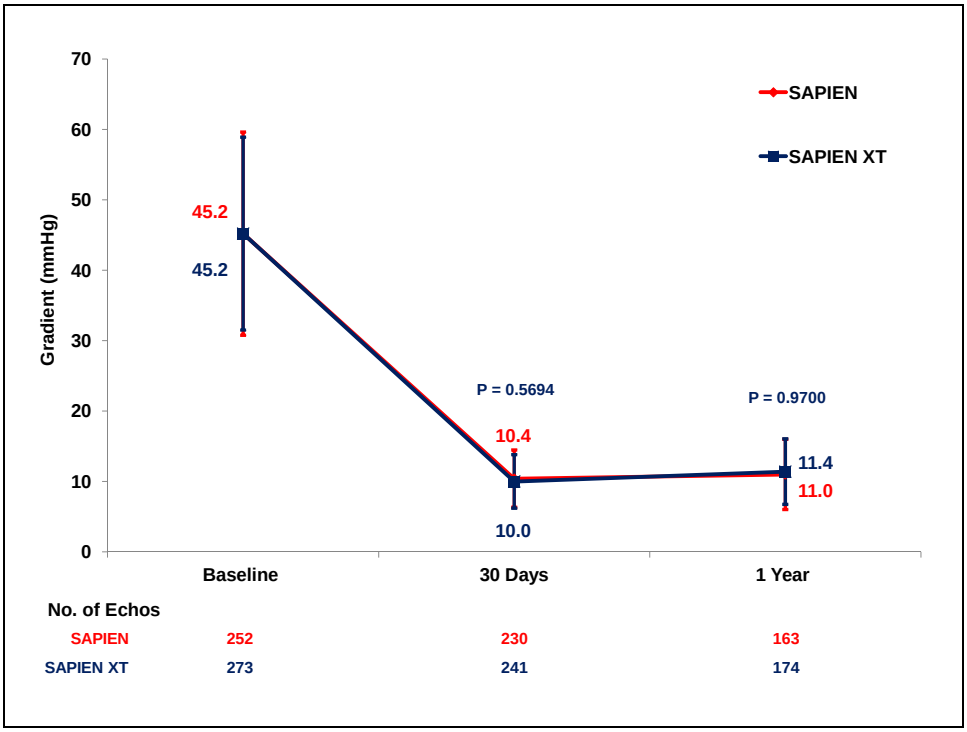


Figure 13: Mean Gradient (Valve Implant Population)

Clinical Table 4
NYHA Functional Class by Visit
AT Population

	SAPIEN (N=271)					SAPIEN XT (N=282)				
Visit	I	II	III	IV	Total	I	II	III	IV	Total
Baseline	0	11	129	131	271	0	9	137	136	282
30 Days	90	99	55	5	249	97	107	51	8	263
6 Months	90	86	27	4	207	111	80	21	5	217
1 Year	80	82	26	4	192	99	81	20	4	204

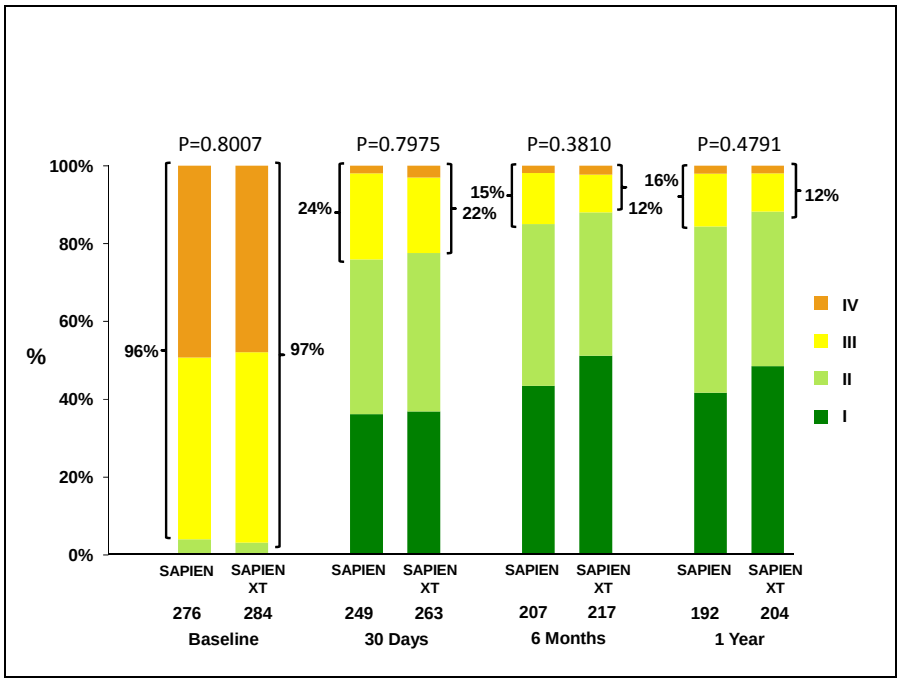


Figure 14: NYHA Class by Visit (Intent-to-Treat Population)

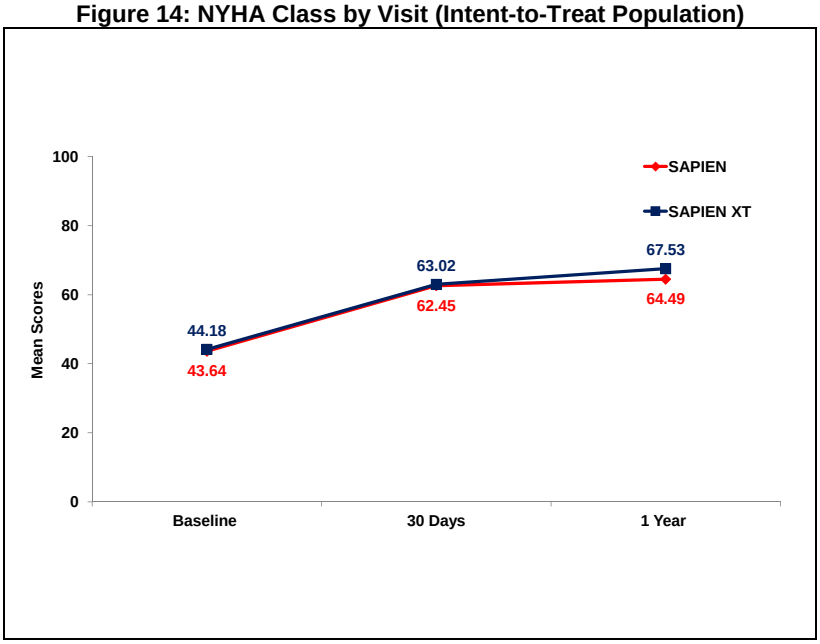


Figure 15: KCCQ Clinical Summary Score (AT Population)

Clinical Table 5: Cohort B (29 mm / Transfemoral / Inoperable)
Baseline Characteristics of the Patients and Echocardiographic Findings (Intent to Treat Population)

	SAPIEN XT
Characteristic	(N= 61)
Age - yr	83.3 ± 7.89
Male sex — no. (%)	61 (100.0%)
STS score†	8.3 ± 4.39
Logistic EuroSCORE‡	11.3 ± 13.75
NYHA class — no. (%):	
I/II	6 (9.8%)
III/IV	55 (90.2%)
Coronary artery disease — no. (%)	48 (78.7%)
Previous myocardial infarction — no./total no. (%)	14/61 (23.0%)
Previous intervention — no./total no. (%)	
CABG	34/61 (55.7%)
PCI	19/61 (31.1%)
Balloon aortic valvuloplasty	20/61 (32.8%)
Cerebral vascular disease — no./total no. (%)	10/61 (16.4%)
Peripheral vascular disease — no./total no. (%)	16/61 (26.2%)
COPD — no. (%):	
Any	19 (31.1%)
Oxygen-dependent	6 (9.8%)
Creatinine > 2 mg/dL (177 µmol/liter) — no./total no. (%)	8/61 (13.1%)
Atrial fibrillation — no./total no. (%)	30/61 (49.2%)
Permanent pacemaker — no./total no. (%)	18/61 (29.5%)
Pulmonary hypertension — no./total no. (%)	13/61 (21.3%)
Frailty§ — no./total no. (%)	30/61 (49.2%)
Extensively calcified aorta — no. (%)	3 (4.9%)
Chest-wall deformity — no. (%)	5 (8.2%)
Liver disease — no./total no. (%)	2/61 (3.3%)
Echocardiographic findings	
Aortic-valve area — cm^2	0.8 ± 0.16
Mean aortic-valve gradient — mmHg	40.3 ± 11.67
Mean LVEF — %	46.1 ± 14.52
Moderate or severe mitral regurgitation** — no./total no. (%)	15/56 (26.8%)

Note: Plus–minus values are means ± SD. To convert the value for creatinine to micromoles per liter, multiply by 88.4. ITT denotes intent to treat population, CABG denotes coronary-artery bypass grafting, COPD chronic obstructive pulmonary disease, LVEF left ventricular ejection fraction, NYHA New York Heart Association, PCI percutaneous coronary intervention, and TAVR transcatheter aortic-valve implantation.

† The Society of Thoracic Surgeons (STS) score measures patient risk at the time of cardiovascular surgery on a scale that ranges from 0% to 100%, with higher numbers indicating greater risk. An STS score higher than 10% indicates very high surgical risk.

‡ The logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE), which measures patient risk at the time of cardiovascular surgery, is calculated with the use of a logistic-regression equation. Scores range from 0% to 100%, with higher scores indicating greater risk. A logistic EuroSCORE higher than 20% indicates very high surgical risk.

§ Frailty was determined by the surgeons according to prespecified criteria.

** Moderate or severe mitral regurgitation was defined as regurgitation of grade 3+ or higher.

Clinical Table 6: Cohort B (29 mm / Transfemoral / Inoperable) – CEC Adjudicated Adverse Events at 30 days (AT Population)*

Outcome [a]	SAPIEN XT N=61
Death[b]	
From any cause	3/61 (4.9%)
From cardiovascular cause	3/61 (4.9%)
Major Stroke	0/61 (0.0%)
Myocardial Infarction	1/61 (1.6%)
Major Vascular Complications	5/61 (8.2%)
Renal Failure[c]	0/61 (0.0%)
Disabling Bleeding Event[d]	7/61 (11.5%)
Cardiac Reintervention[e]	0/61 (0.0%)
Endocarditis	0/61 (0.0%)
New Atrial Fibrillation	1/37 (2.7%)
New pacemaker	3/61 (4.9%)

* AT= As Treated, NA= not applicable, TAVR = transcatheter aortic valve replacement. Data presented as n (%) of patients.

a. CEC adjudicated

b. Deaths from unknown causes were assumed to be deaths from cardiovascular causes.

c. Renal failure is defined as stage III acute kidney injury: Increase in serum creatinine to ≥300% (3 x increase compared with baseline) or serum creatinine of ≥ 4 mg/d (≥354 µmol/L) with an acute increase of at least 0.5 mg/dl (44 µmol/L)

d. Disabling bleeding: Fatal bleeding OR bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, or pericardial necessitating pericardiocentesis, or intramuscular with compartment syndrome OR bleeding causing hypovolemic shock or severe hypotension requiring vasopressors or surgery OR overt source of bleeding with drop in hemoglobin of ≥5 g/dL or whole blood of packed red blood cells (RBC) transfusion ≥4 units

e. Cardiac reintervention includes any intervention that repairs, alters or replaces a previously operated valve OR balloon aortic valvuloplasty OR Surgical aortic valve replacement OR valve in valve

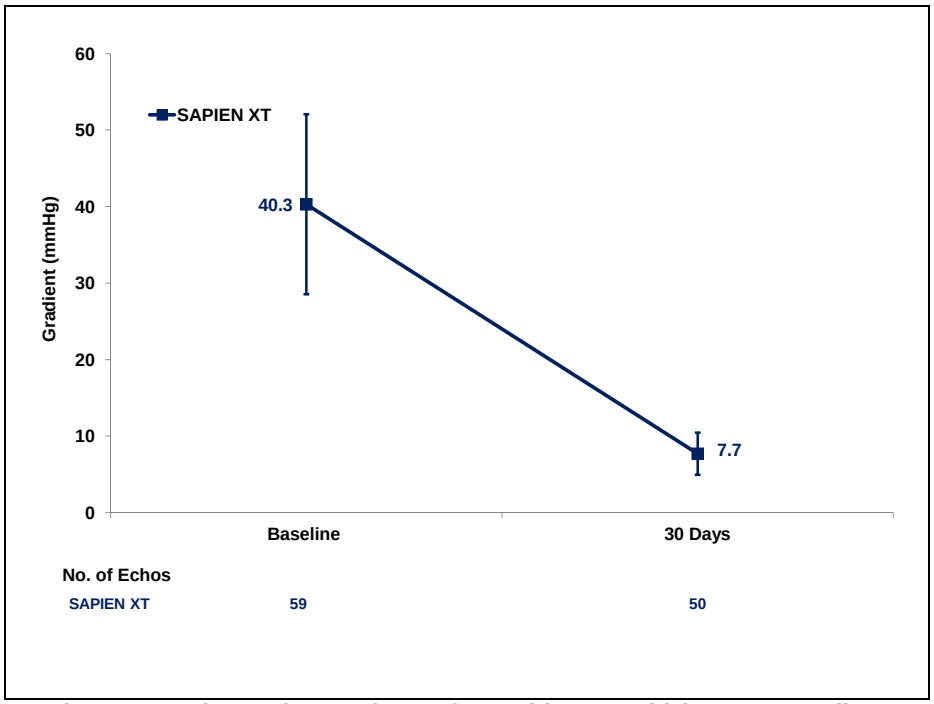


Figure 16: Cohort B (29 mm / Transfemoral / Inoperable) – Mean Gradient (Valve Implant Population)

Gradient data for this figure only contains data from 29 mm valve sizes and does not include 23 or 26 mm.

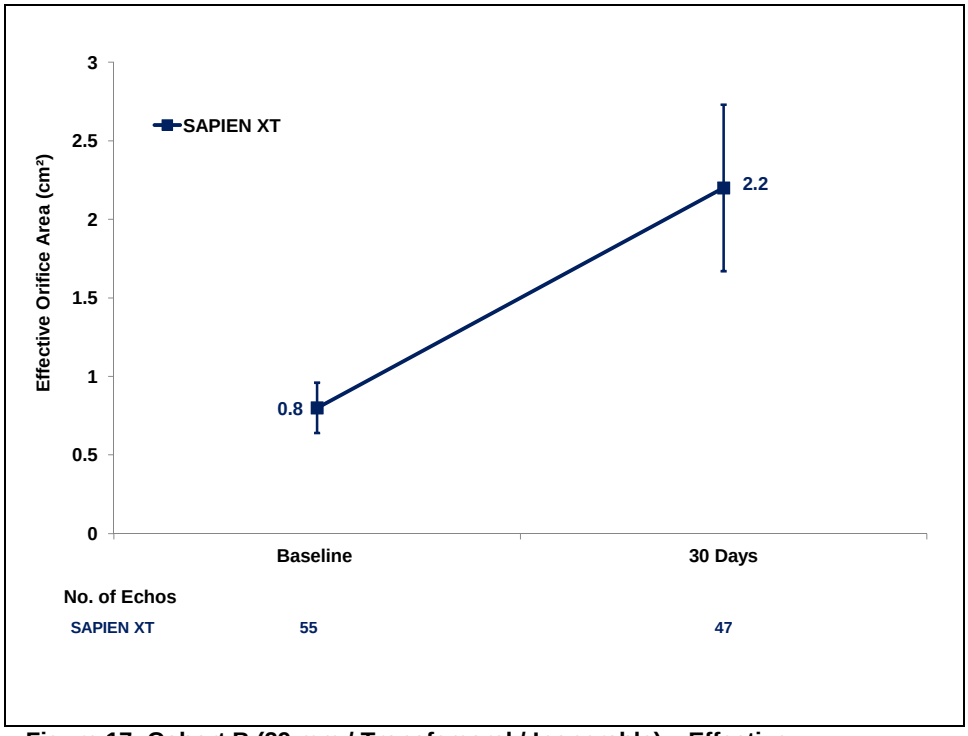


Figure 17: Cohort B (29 mm / Transfemoral / Inoperable) – Effective Orifice Area (Valve Implant Population)

Effective orifice area data for this figure only contains data from 29 mm valve sizes and does not include 23 or 26 mm.

SOURCE XT Clinical Data

Clinical Table 7: SOURCE XT (High Risk)
Baseline Characteristics of the Patients and Echocardiographic Findings
(AT Population)

	Transfemoral	TA/TAo Pooled
Characteristic	(N = 1685)	(N = 995)
Age - yr	82.0 ± 6.5	80.3 ± 6.5
Male sex — no./total no. (%):	600 / 1685 (35.6%)	536 / 995 (53.9%)
STS score†	8.0 ± 6.8	7.9 ± 6.2
Logistic EuroSCORE‡	19.8 ± 11.6	21.6 ± 13.7
NYHA class — no./total no. (%):		
I/II	377 / 1676 (22.5%)	242 / 992 (24.4%)
III/IV	1299 / 1676 (77.5%)	750 / 992 (75.6%)
Coronary artery disease — no./total no. (%):	667 / 1685 (39.6%)	518 / 995 (52.1%)
Previous myocardial infarction — no./total no. (%)	205 / 1685 (12.2%)	197 / 995 (19.8%)
Previous intervention — no./total no. (%)		
CABG	204 / 1685 (12.1%)	226 / 995 (22.7%)
PCI	460 / 1685 (27.3%)	355 / 995 (35.7%)
Balloon aortic valvuloplasty	128 / 1685 (7.6%)	66 / 995 (6.6%)
Cerebral vascular disease — no./total no. (%)	191 / 1685 (11.3%)	143 / 995 (14.4%)
Peripheral vascular disease — no./total no. (%)	248 / 1684 (14.7%)	320 / 995 (32.2%)
COPD — no./total no. (%):		
Any — no./total no. (%)	327 / 1684 (19.4%)	218 / 995 (21.9%)
Oxygen-Dependent — no./total no. (%)	31 / 1684 (1.8%)	11 / 995 (1.1%)
Creatinine > 2 mg/dL (177 µmol/liter) — no./total no. (%)	104 / 1681 (6.2%)	114 / 994 (11.5%)
Atrial fibrillation — no./total no. (%)	395 / 1678 (23.5%)	289 / 990 (29.2%)
Permanent pacemaker — no./total no. (%)	170 / 1685 (10.1%)	134 / 995 (13.5%)
Pulmonary hypertension — no./total no. (%)	440 / 1684 (26.1%)	204 / 995 (20.5%)
Frailty§ — no./total no. (%)	896 / 932 (96.1%)	548 / 579 (94.6%)
Extensively calcified aorta — no./total no. (%):	71 / 1684 (4.2%)	103 / 995 (10.4%)
Chest-wall deformity — no./total no. (%):	52 / 1685 (3.1%)	27 / 995 (2.7%)
Liver disease — no./total no. (%)	18 / 1684 (1.1%)	6 / 995 (0.6%)
Echocardiographic findings		
Aortic-valve area — cm^2	0.7 ± 0.21	0.7 ± 0.21
Mean aortic-valve gradient — mmHg	49.2 ± 16.54	45.0 ± 15.43
Mean LVEF — %	55.1 ± 12.48	53.2 ± 12.50
Moderate or severe mitral regurgitation** — no./total no. (%)	345 / 1633 (21.1%)	174 / 976 (17.8%)

Note: Plus–minus values are means ± SD. To convert the value for creatinine to micromoles per liter, multiply by 88.4. AT denotes as treated population, CABG denotes coronary-artery bypass grafting, COPD chronic obstructive pulmonary disease, LVEF left ventricular ejection fraction, NYHA New York Heart Association, PCI percutaneous coronary intervention, and TAVR transcatheter aortic-valve implantation.

† The Society of Thoracic Surgeons (STS) score measures patient risk at the time of cardiovascular surgery on a scale that ranges from 0% to 100%, with higher numbers indicating greater risk. An STS score higher than 10% indicates very high surgical risk.

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§ Frailty was determined by the surgeons according to prespecified criteria.

** Moderate or severe mitral regurgitation was defined as regurgitation of grade 3+ or higher.

Clinical Table 8: SOURCE XT (High Risk) Clinical Outcomes[a] at 30 days and 1 year (AT Population)*				
	30 Days		1-Year	
	Transfemoral	TA/TAo	Transfemoral	TA/TAo
Outcome	**(N = 1685)**	**(N = 995)**	**(N = 1685)**	**(N = 995)**
All Cause Death	71 (4.2%)	96 (9.7%)	248 (15.0%)	266 (27.0%)
Cardiac Death	28 (1.7%)	51 (5.2%)	106 (6.7%)	132 (14.4%)
Stroke				
All Stroke	56 (3.4%)	39 (4.1%)	90 (5.6%)	66 (7.6%)
Major Stroke	34 (2.0%)	27 (2.8%)	55 (3.5%)	44 (5.0%)
Repeat hospitalization[b]	80 (4.9%)	83 (9.0%)	396 (25.5%)	314 (36.7%)
Myocardial Infarction	7 (0.4%)	9 (0.9%)	23 (1.5%)	21 (2.5%)
Major Vascular Complications	132 (7.9%)	43 (4.4%)	139 (8.3%)	52 (5.5%)
Renal Failure[d]/AKI	197 (11.9%)	270 (28.0%)	240 (14.7%)	292 (30.6%)
Life-threatening bleeding[c]	63 (3.8%)	84 (8.6%)	74 (4.5%)	101 (10.6%)
Endocarditis	2 (0.1%)	2 (0.2%)	15 (1.0%)	10 (1.2%)
New Atrial Fibrillation	54 (3.3%)	83 (8.8%)	89 (5.6%)	109 (12.0%)
New pacemaker	145 (8.7%)	105 (10.8%)	165 (10.0%)	120 (12.7%)

* AT= As Treated, TAVR = transcatheter aortic valve replacement. Data presented as n (%) of patients where % is the Kaplan-Meier event rate at 30-days and 1-year respectively.
a. CEC adjudicated
b. Repeat hospitalizations were included if they were due to aortic stenosis or complications of the valve procedure (e.g. TAVR).
c. Disabling bleeding: Fatal bleeding OR bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, or pericardial necessitating pericardiocentesis, or intramuscular with compartment syndrome OR bleeding causing hypovolemic shock or severe hypotension requiring vasopressors or surgery OR overt source of bleeding with drop in hemoglobin of ≥ 5 g/dL or whole blood of packed red blood cells (RBC) transfusion ≥ 4 units
d. Renal failure is defined as stage III acute kidney injury: Increase in serum creatinine to ≥ 300% (3 x increase compared with baseline) or serum creatinine of ≥ 4 mg/d (≥ 354 µmol/L) with an acute increase of at least 0.5 mg/dl (44 µmol/L)

These products are manufactured and sold under one or more of the following US patent(s): US Patent No. 5,411,552; 6,214,054; 6,547,827; 6,561,970; 6,908,481; 7,214,344; 7,510,575; 7,530,253; 7,585,321; 7,780,723; 7,846,203; 7,993,394; 8,057,540; 8,382,826; and 8,591,575 and corresponding foreign patents. Additional patents are pending.

The FDA has requested Edwards to increase product surveillance with the SAPIEN XT THV in order to ensure a high-quality product experience. If you have any quality questions or concerns, please immediately call 1-949-250-3612, option 4.

Edwards

05/2014

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