Alterra Adaptive Prestent and SAPIEN 3 THV for Congenital Pulmonic Valve Dysfunction: 5-year Outcomes of the ALTERRA Early Feasibility Study

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PICS | San Diego | September 4th, 2024

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Disclosure Information

Evan Zahn, MD

As a faculty member for this program, I disclose the following relationships with industry:

- Paid Consultant, Investigator and Proctor: Edwards Lifesciences

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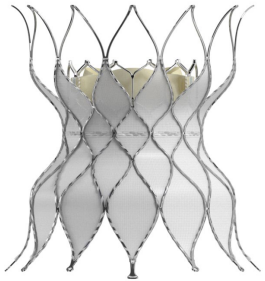
The ALTERRA Trials

IDE

EFS → Pivotal Main Cohort → PDS Registry → CAP

PAS

2017	2019	2020	2021	2022	2024
Initiate **EFS Trial**	Complete Enrollment **EFS Trial** Initiate Pivotal Trial	PDS Registry Initiated Initiate CAP	★ US approval	PAS Initiated	★ CE mark



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Patient Population

Key Inclusion Criteria

- Weight ≥20 kg
- ≥ Moderate PR
- Suitable Anatomy
  - **≥ 27 mm landing zone diameter ≤ 38 mm**
  - **≥ 35 mm landing zone length**

Key Exclusion Criteria

- Inappropriate anatomy for introduction or delivery of Alterra/SAPIEN 3
- Need for concomitant procedures*
- Any intervention or surgical procedure within 30 days pre- or post-implantation (Alterra/SAPIEN 3)
- Renal insufficiency (creatinine > 3.0 mg/dL) and/or renal replacement therapy

Exceptions: pulmonary artery or branch pulmonary artery stenting or angioplasty

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Procedural Information

Variable, % (n/N) or mean ± SD (N)	All Treated Population N=21
Single SAPIEN 3 THV implanted	100.0% (21/21)
Both devices implanted in a single procedure	100.0% (21/21)
Alterra implanted in the intended location	100.0% (21/21)
SAPIEN 3 implanted in the intended location	100.0% (21/21)
Total fluoroscopy time, min	33.0 (27.0, 42.0)
Free of explant at 24 hours post implantation	100.0% (21/21)

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6-month Outcomes from the EFS*

Primary Endpoint – Device success

Composite of:

- 1 Alterra prestent deployed in the desired location
- 1 S3 THV deployed in the desired location
- < Moderate total PR (TTE) at discharge
- Mean RVOT/PV gradient < 35mmHg (TTE) post-implant
- No explant within 24 hours of procedure

Alterra Adaptive Prestent and SAPIEN 3 THV for Congenital Pulmonic Valve Dysfunction

An Early Feasibility Study

Shabana Shahanavaz, MBBS,[a] David Balzer, MD,[a] Vasilis Babaliaros, MD,[b] Dennis Kim, MD, PhD,[c] Vivian Dimas, MD,[d] Suredranath R. Veeram Reddy, MD,[d] Jonathan Leipsic, MD,[e] Philipp Blanke, MD,[e] Girish Shirali, MD, MBBS,[f] Anitha Parthiban, MD,[f] Jeremy Gorelick, PhD,[g] Evan M. Zahn, MD[h]

100%

Secondary Endpoint – Freedom from THV dysfunction at 6 months

- RVOT/PV reintervention
- ≥ Moderate total PR (TTE)
- Mean RVOT/PV gradient ≥ 35mmHg (TTE)

100%

This presentation is the 5-year follow-up data

*Shahanavaz *et al., JACC Cardiov Interv* 2020 13(21):2510-2524.

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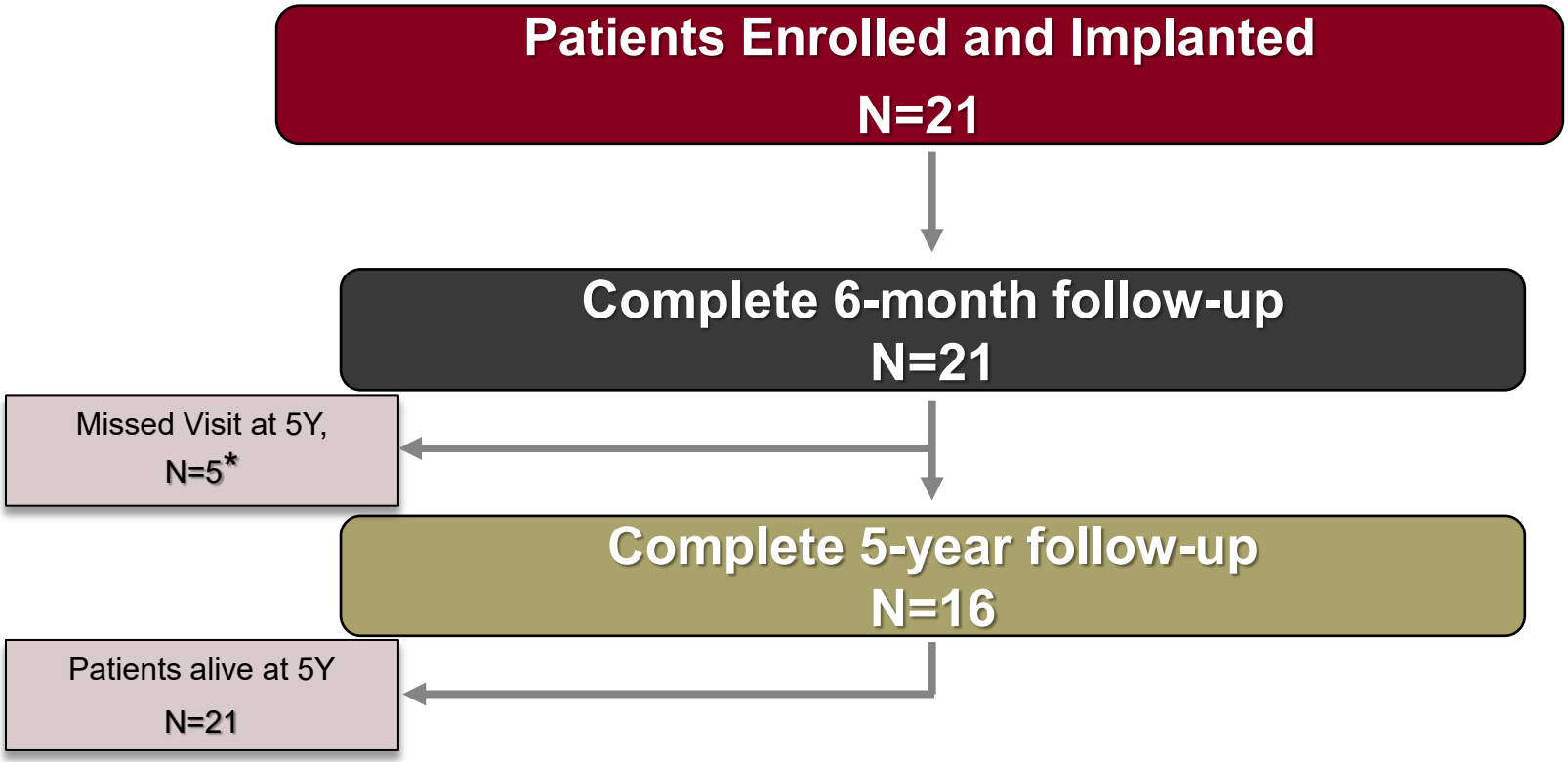
ALTERRA EFS Patient Flow



*4 yr visit completed = 2
3 yr visit completed = 1
2 yr visit completed = 2

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Baseline Characteristics

Characteristic, mean ± SD (N) or % (n/N)	Enrolled Population N=21
Age, years	26.7 ± 14.4 (21)
< 12 years	52.4% (11/21)
Weight, kg	76.9 ± 25.3 (21)
Primary CHD Diagnosis	
Tetralogy of Fallot	61.9% (13/21)
Pulmonary valve stenosis	33.3% (7/21)
Pulmonary atresia	4.8% (1/21)

Additional Outcomes

Incidence, n events N=21	0 - 5 Years
All-cause mortality	0
RVOT reintervention	1
Transient pericardial effusion*	1
Coronary artery compression	0
Perforation/erosion	0
Endocarditis	0
Prestent thrombus**	1
SAPIEN 3 valve thrombus#	1

*Self resolved without drainage, believed to be reactive effusion

**Resolved with oral medications

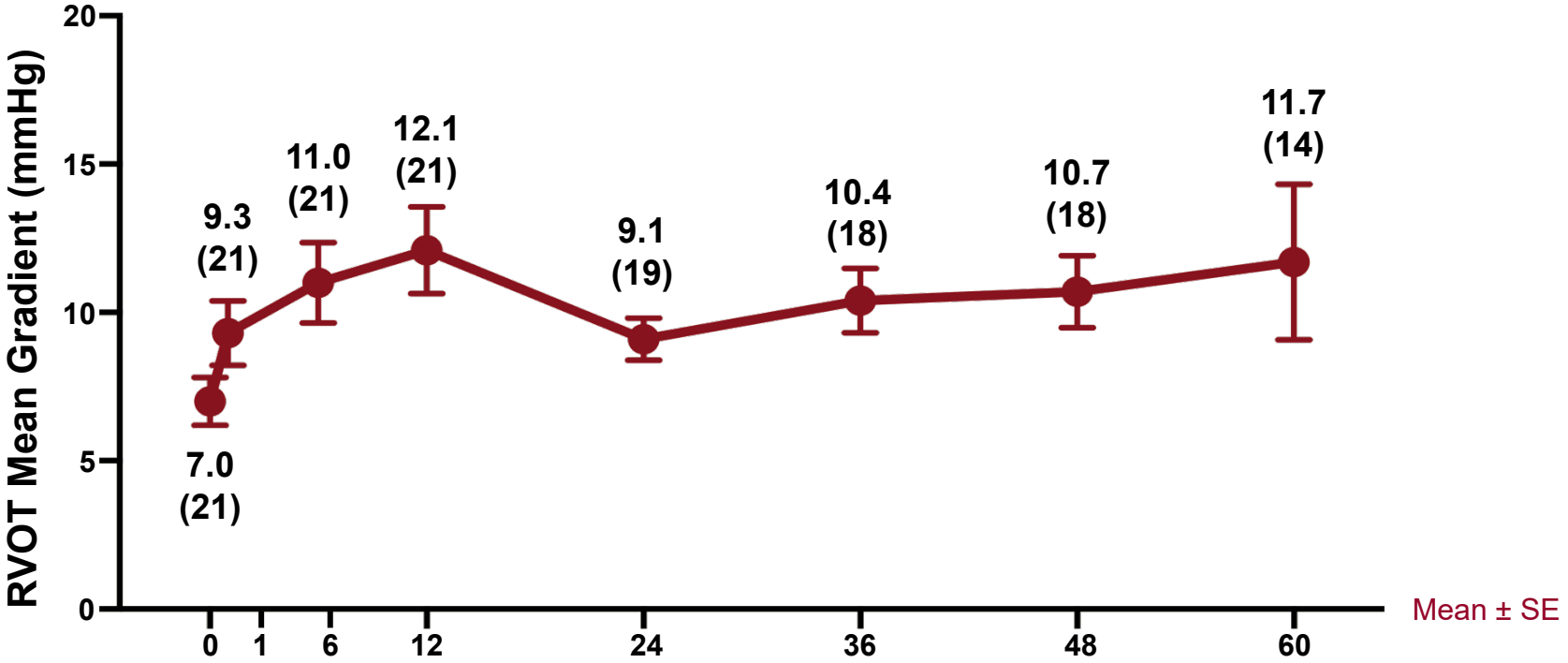
#Small PV thrombus detected by TTE. No hospitalization, progression or other clinical or hemodynamic sequelae out to 6Y

CEC Adjudicated Arrhythmias

Incidence Rate % (n) or n/N	0 - 30 Days	31 Days – 6 Months	6 Months – 5 Years
Arrhythmias*	**23.8% (5)**	**0%**	**0%**
Non-sustained ventricular tachycardia	3/5	0	0
Atrial fibrillation/flutter	1/5	0	0
PVCs	1/5	0	0
New beta blocker medication	4/5	0	0

*4/5 resolved within 30 days.

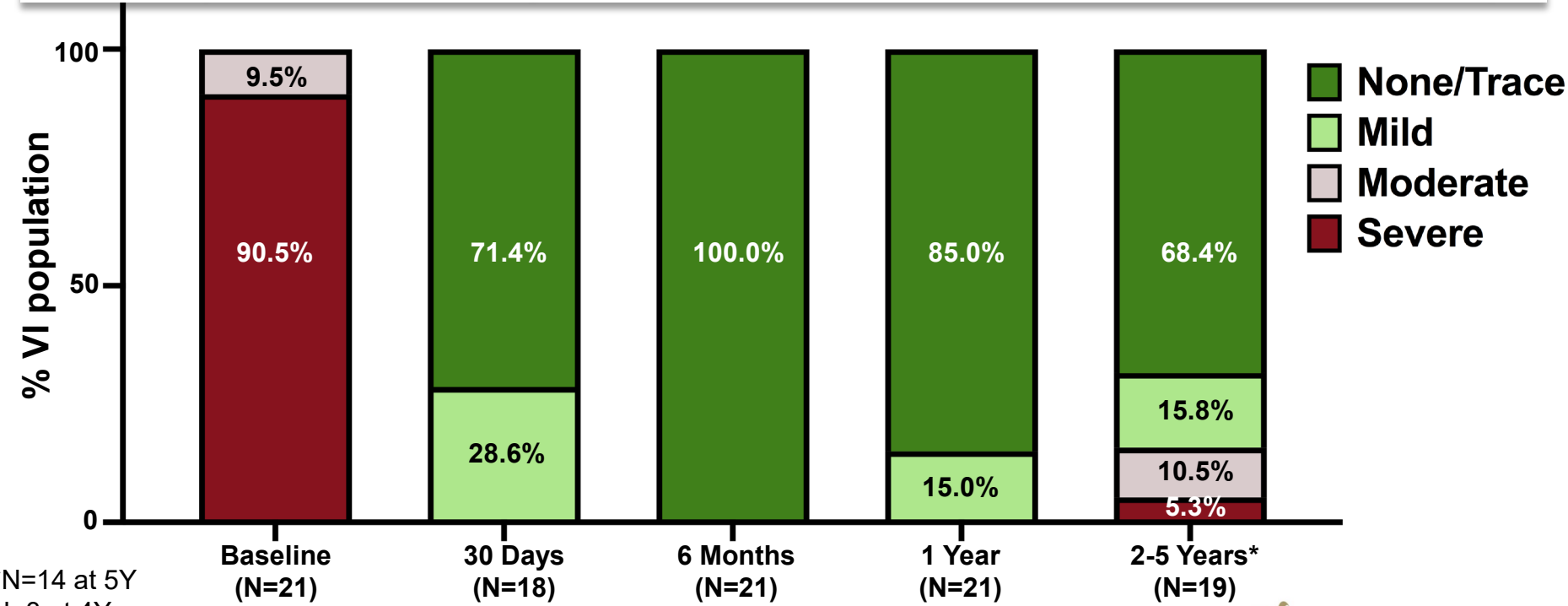
Mean RVOT Gradient – out to 5 years



Core Lab TTE

Total PR – out to 5 years

94.7% patients had **improved total PR** from baseline at last follow-up



*N=14 at 5Y
N=3 at 4Y
N=1 at 3Y
N=1 at 2Y

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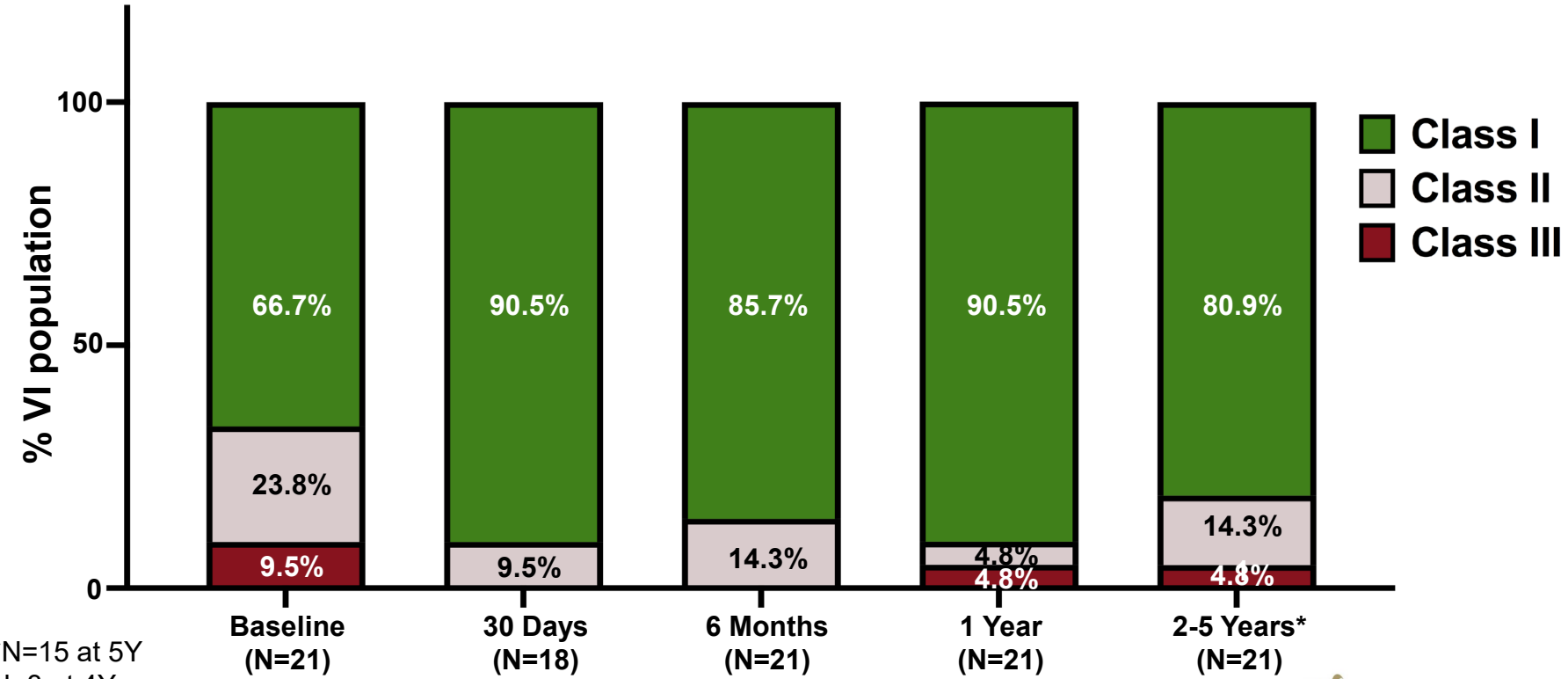
NYHA Class



*N=15 at 5Y
N=3 at 4Y
N=1 at 3Y
N=2 at 2Y

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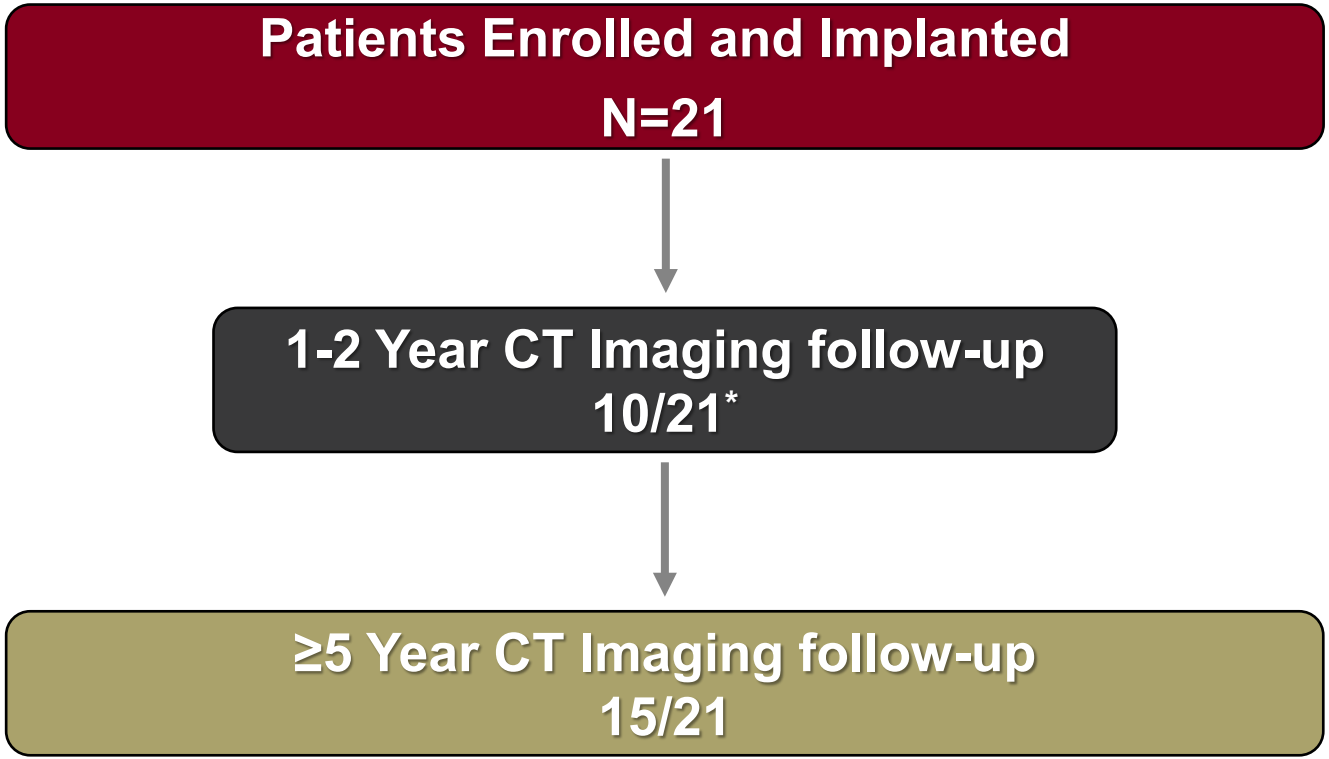
5-year CT Follow-up



* CT imaging at 1-2Y was not required per the protocol
10 of the 15 patients who had a 5Y CT, also had CT at 1-2 years.

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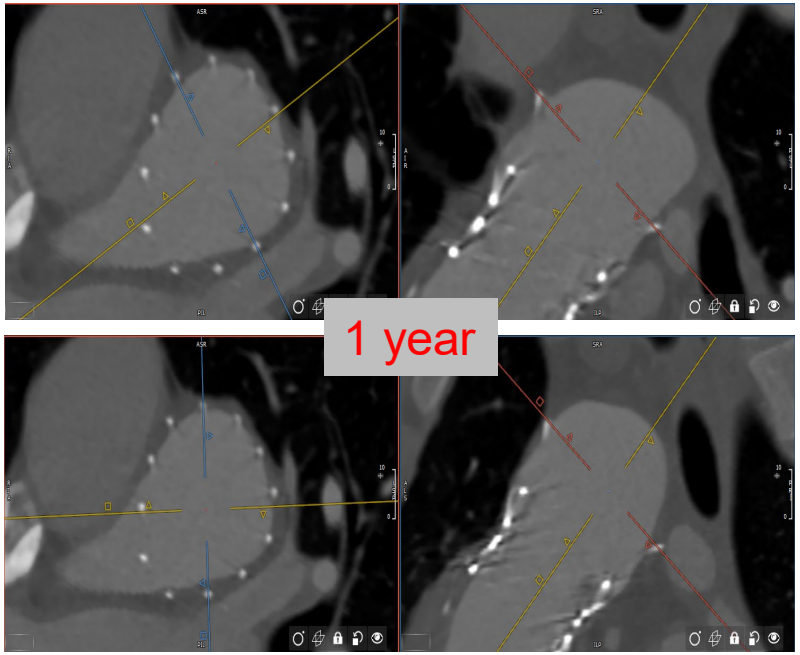
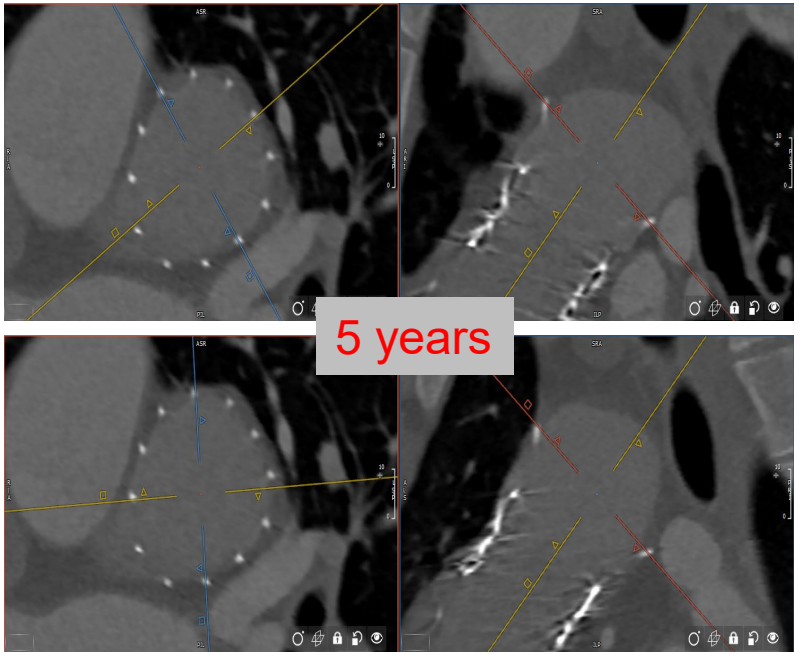
Mid-term CT Follow-up: Case Example #1





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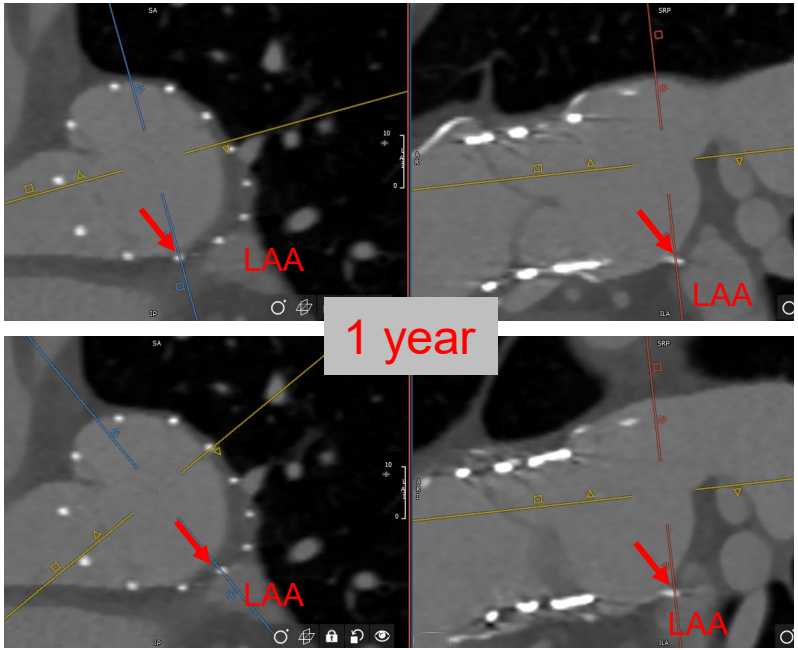
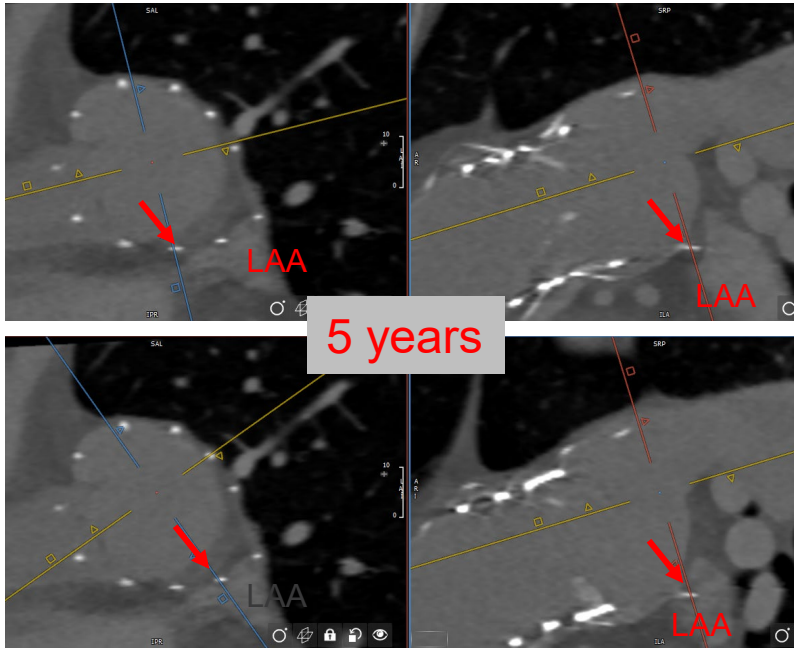
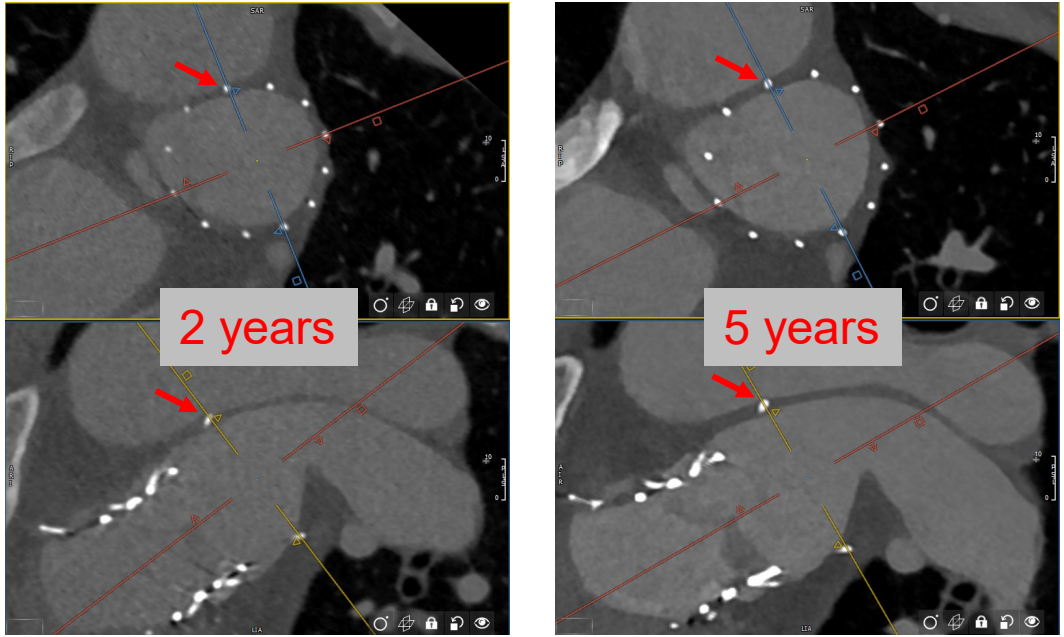
Mid-term CT Follow-up: Case Example #2

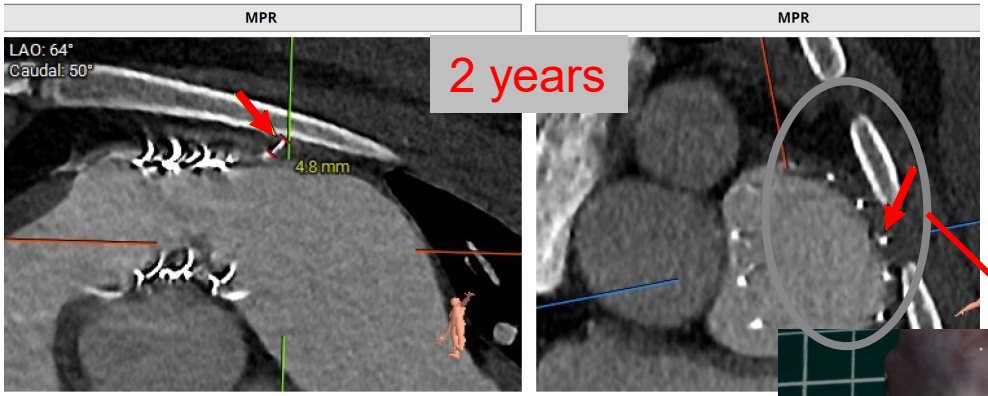




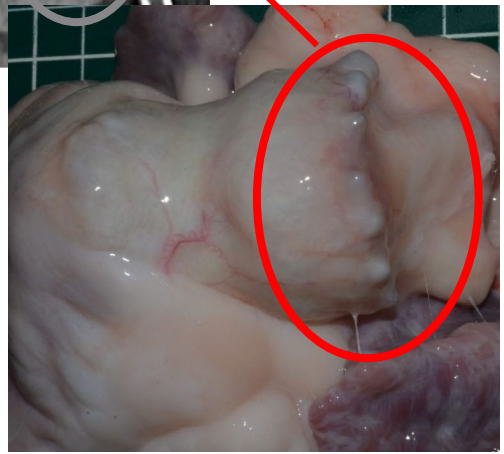
Mid-term CT Follow-up: Case Example #3

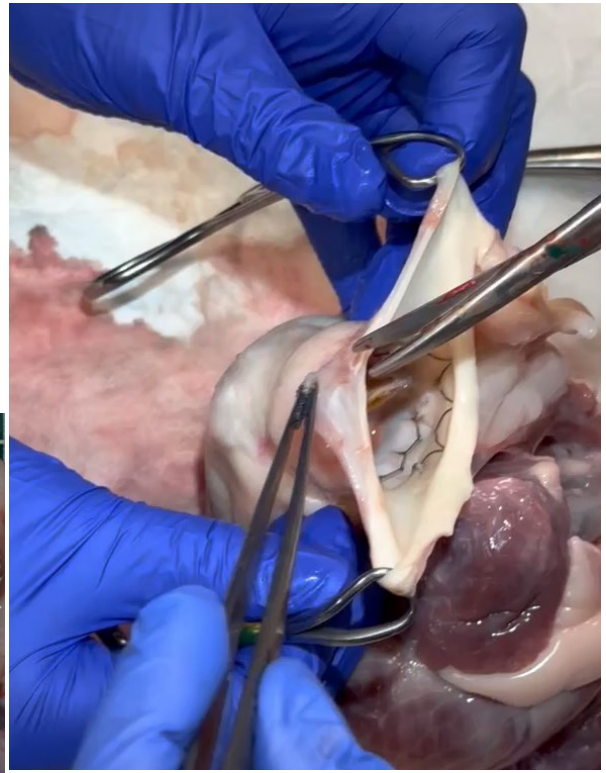


Chronic Animal Explant Study



CT suggests externalization apices





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Conclusions

5-year results from the ALTERRA EFS cohort reveal:

- **100% survival**
- **Excellent valve function through 5 years**
  - 94.7% improved PR from baseline
  - 0 patients requiring surgical intervention
- **Low rate of reintervention at 5 years**
  - 1/21 patients
- **Resolution of ventricular arrhythmias**

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Conclusions

- **No endocarditis**
- **No perforation or erosion**
- Concerning extravascular appearance of frame apices on CT
  - Did NOT result in clinical sequelae at 5 years
  - Appear stable at 5 years without progression
  - Warrant further observation and follow-up

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Thank You and Recognition

Participating Sites

St. Louis Children's Hospital, MO
Shabana Shahanavaz*, David Balzer

Cedars-Sinai Medical Center, CA
Evan Zahn

Children's Health Dallas, TX
Vivian Dimas†

Emory University, GA
Vasilis Babaliaros, Dennis Kim

Data & Safety Monitoring Board

Cardiovascular Research Foundation, New York, NY

Clinical Events Committee

Cardiovascular Research Foundation, New York, NY

CT Core Laboratory

St. Paul's Hospital, Vancouver, Canada
Directors: Jonathon Leipsic, Philipp Blanke

Echocardiographic Core Laboratory

Children's Mercy, Kansas City, MO
Directors: Girish Shirali, Anitha Parthiban‡

Sponsor

Edwards Lifesciences, Irvine, CA

*Dr. Shahanavaz is now with Cincinnati Children's Hospital, OH
†Dr. Dimas is now with Medical City Children's Hospital Heart Center, TX
‡Dr. Parthiban is now with Texas Children's Hospital, Baylor College of Medicine, TX

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Important Safety Information

Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent

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

Contraindications: The Edwards SAPIEN 3 Transcatheter Pulmonary Valve System with Alterra Adaptive Prestent is contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections.

Warnings: The devices are designed, intended, and distributed for single use only. **Do not resterilize or reuse the devices.** There are no data to support the sterility, nonpyrogenicity, and functionality of the devices after reprocessing. The physician must verify correct orientation of the valve prior to its implantation; the inflow (outer skirt end) of the valve should be oriented towards the proximal end (handle) of the delivery system to prevent the risk of severe patient harm. Prior to delivery, the valve must remain hydrated at all times and cannot be exposed to solutions other than its shipping storage solution and sterile physiologic rinsing solution. Valve leaflets mishandled or damaged during any part of the procedure will require replacement of the valve. Do not use the valve if the tamper evident seal is broken, the storage solution does not completely cover the valve, the temperature indicator has been activated, the valve is damaged, or the expiration date has elapsed. Do not mishandle the delivery system or use it if the packaging or any components are not sterile, have been opened or are damaged (e.g., kinked or stretched), or the expiration date has elapsed. Do not add or apply antibiotics to the storage solution, rinse solutions or to the valve.

Precautions: Long-term durability has not been established for the device. Regular medical follow-up is advised to evaluate device performance. Patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/or polymeric materials may have an allergic reaction to these materials. Accelerated deterioration of the valve may occur in patients with an altered calcium metabolism. Assessment for coronary compression risk prior to implantation is recommended. Patient venous anatomy should be evaluated to prevent the risk of access that would preclude the delivery and deployment of the device. Use of excessive contrast media may lead to renal failure. Measure the patient's creatinine level prior to the procedure. Contrast media usage should be monitored. Fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. Patient radiation dose should be monitored during the procedure. Glutaraldehyde may cause irritation of the skin, eyes, nose and throat. Avoid prolonged or repeated exposure to, or breathing of, the solution. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water; in the event of contact with eyes, seek immediate medical attention. For more information about glutaraldehyde exposure, refer to the Material Safety Data Sheet available from Edwards Lifesciences. Patient should be heparinized to maintain the ACT at ≥ 250 sec prior to introduction of the delivery system in order to prevent thrombosis. To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon. Device recipients should be maintained on anticoagulant/antiplatelet therapy, except when contraindicated, as determined by their physician. This device has not been tested for use without antiplatelet therapy. It is recommended that all device recipients be prophylactically treated for endocarditis to minimize the possibility of prosthetic valve infection. Correct sizing of the prestent into the RVOT is essential to minimize risks such as paravalvular leak, migration, embolization, and/or RVOT rupture. If a prestent fracture is detected with significant loss in valve functionality, reintervention should be considered. Safety and effectiveness have not been established for patients with the following characteristics/comorbidities: blood dyscrasias defined as: leukopenia, acute anemia, thrombocytopenia, or history of bleeding diathesis or coagulopathy; a known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid™), or clopidogrel (Plavix™), or sensitivity to contrast media, which cannot be adequately premedicated; positive urine or serum pregnancy test in female patients of child- bearing potential.

Potential Adverse Events: Potential risks associated with the anesthesia, interventional procedure, and imaging include but are not limited to death; stroke/transient ischemic attack; respiratory insufficiency or respiratory failure; cardiovascular or vascular injury, such as perforation or damage (dissection) of vessels, myocardium, or valvular structures, including rupture of the RVOT that may require intervention; pericardial effusion/cardiac tamponade; cardiac failure; embolic event: air, calcific material, thrombus, device fragments; infection, including incisional site infection, septicemia, and endocarditis; myocardial infarction; renal insufficiency or renal failure; conduction system injury; arrhythmia; deep vein thrombosis; arteriovenous (AV) fistula; systemic or peripheral nerve injury; systemic or peripheral ischemia; pulmonary edema; pneumothorax; pleural effusion; dyspnea; atelectasis; dislodgement of previously implanted devices (i.e. pacing lead); blood loss requiring transfusion; anemia; radiation injury; electrolyte imbalance; hypertension or hypotension; allergic reaction to anesthesia, contrast media, antithrombotic therapy, device materials; hematoma or ecchymosis; syncope; pain; exercise intolerance or weakness; inflammation; angina; fever. Potential risks, that may or may not require intervention, associated with the valve, prestent, delivery system, and/or accessories include, but may not be limited to, the following: cardiac arrest; cardiogenic shock; coronary flow obstruction/transvalvular flow disturbance; device thrombosis; injury to tricuspid valve; device fracture; device embolization; device acute migration or malposition; endocarditis; chest pain/discomfort; hemolysis/hemolytic anemia; device penetration/perforation into surrounding vasculature; device dysfunction (regurgitation and/or stenosis); aortic root distortion; embolic events: device fragments; mechanical failure of delivery system, and/or accessories.

Important Safety Information (continued)

Edwards Crimper

Indications: The Edwards crimper is indicated for use in preparing the Edwards SAPIEN 3 Ultra transcatheter heart valve and the Edwards SAPIEN 3 transcatheter heart valve, for implantation.

Contraindications: There are no known contraindications.

Warnings: The device is designed, intended, and distributed for single use only. **Do not resterilize or reuse the device.** There are no data to support the sterility, nonpyrogenicity, and functionality of the device after reprocessing. Do not mishandle the device. Do not use the device if the packaging or any components are not sterile, have been opened or damaged, or the expiration date has elapsed.

Precautions: For special considerations associated with the use of the Edwards crimper prior to THV implantation, refer to the THV Instructions for Use.

Potential Adverse Events: There are no known potential adverse events associated with the Edwards crimper.

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

PP--US-10289 v1.0