Heterotopic Cross-Caval TTVR in Patients with Severe TR – Initial Results of the Trillium Early Feasibility Study

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On behalf of TRILLIUM EFS Investigators

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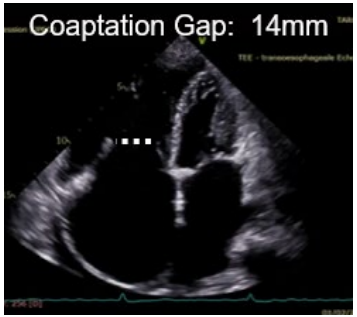
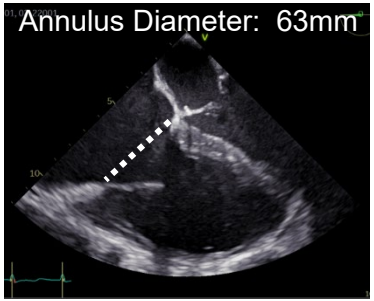
Heterotopic Approach – Patient Population

The following tricuspid regurgitation patient populations have no current surgical or transcatheter treatment option:

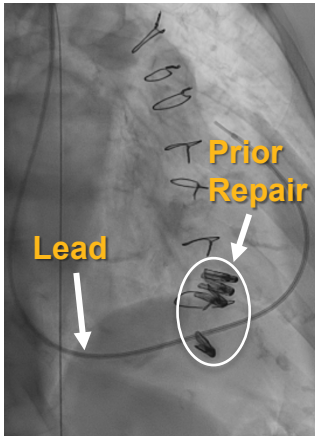
Anatomical and Physiological Constraints

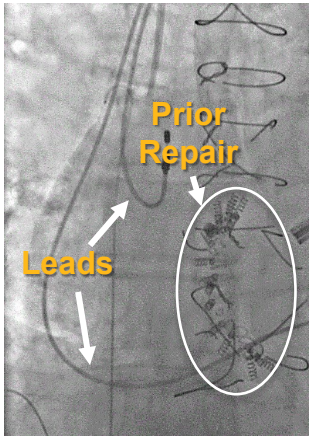


- Large Annulus
- Large coaptation gap
- Reduced RV function



Failed Prior Repair/ PM Lead Impingement

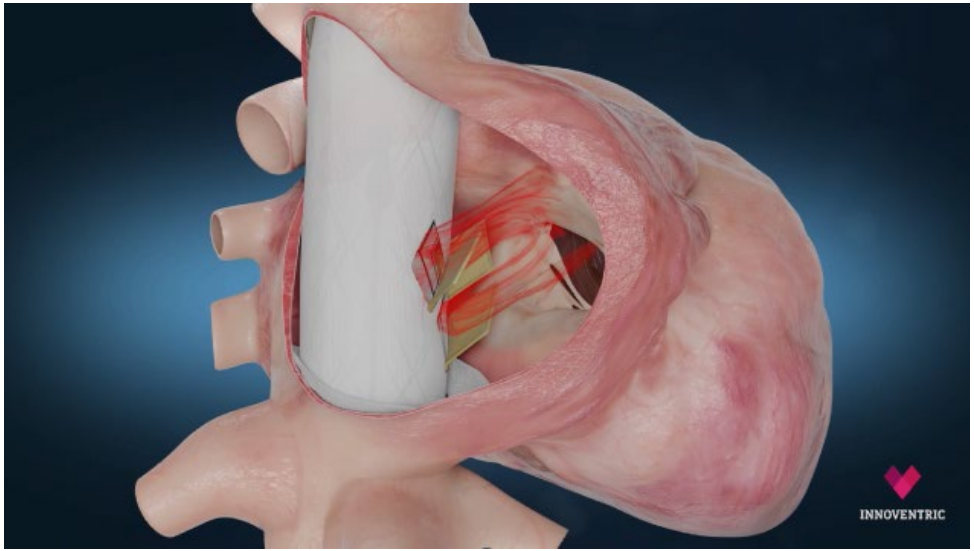




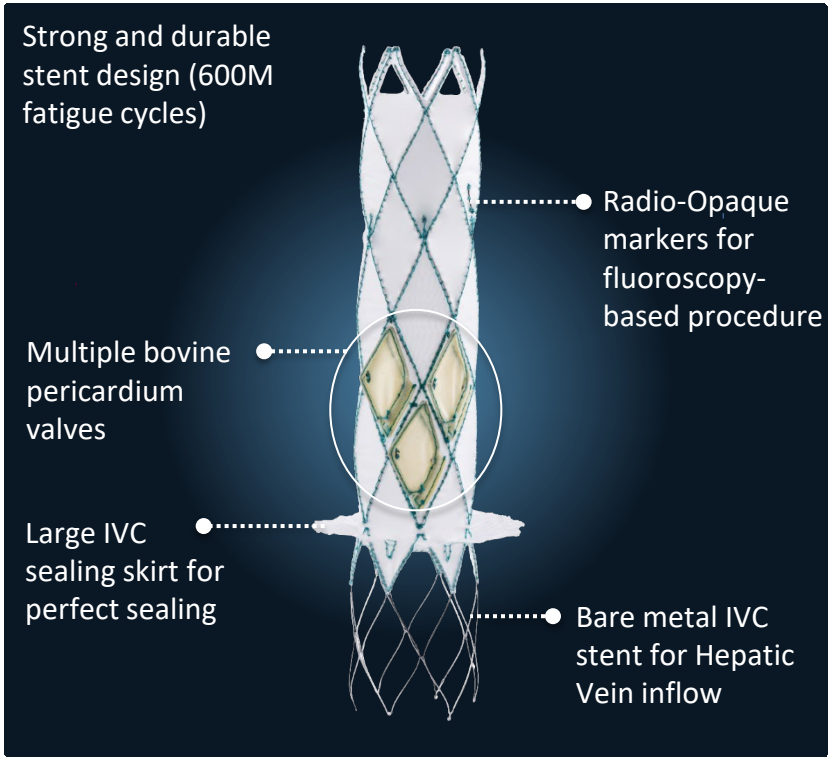
- Lead-induced TR
- Failed prior tricuspid repair
- Prohibitive TEE risk
- Prohibitive General Anesthesia risk
- Poor TV echo Imaging

Heterotopic tricuspid valve replacement can treat this otherwise “still forgotten” patient populations

The Trillium



- Simplest tricuspid regurgitation approach
- <10-minute device implantation time
- Dual vena cava anchoring for full migration resistance
- TEE is optional→ Conscious Sedation



Study Design and Primary Endpoints

A prospective, single-arm, multi-center early feasibility study (EFS) to evaluate the safety and performance of Trillium. Fifteen (15) patients at 8 US sites were enrolled.

Safety	Technical Performance
Rate of device or procedure-related MAEs, AND Rate of unplanned surgery or re-intervention due to a life-threatening device or procedure failure. [at the end of the procedure, discharge, and 30 days]	Successful access, delivery, and retrieval of the Trillium delivery system, the device is anchored both in SVC and IVC [at the end of the procedure] AND No need for re-intervention due to device valve regurgitation or para-stent leak. [at discharge, and 30 days]

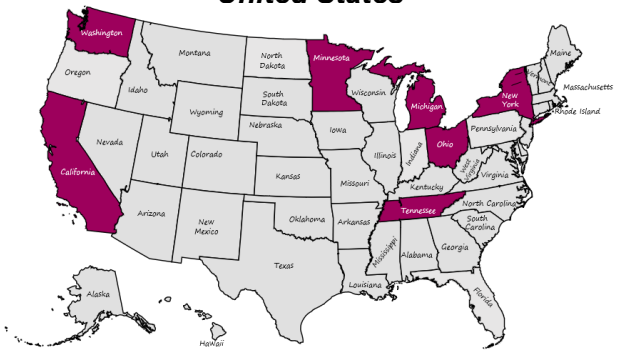
Key Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria

• Severe or greater TR (Symptomatic despite optimal medical therapy)
• Peak CVP of ≥ 15mmHg
• NYHA functional classification of III or IV
• Patient is not eligible for standard-of-care surgical or interventional therapy
	• Echocardiographic parameters:
	  • LVEF < 35%
	  • TAPSE < 14.0 mm
	  • RVFAC < 30%
	• Systolic PAP > 65mmHg
	• PVR >3 WU
	• Life expectancy < 12 months
	• Moderate or greater mitral or tricuspid valve stenosis
	• Greater than moderate mitral valve regurgitation or aortic valve stenosis/regurgitation
	• eGFR < 35 ml/min/1.73 m^2
	• 6MWD <120m

8 Enrolling Sites

United States



Germany

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TR Tricuspid regurgitation; **CVP** Central venous pressure; **LVEF** Left ventricular ejection fraction; **TAPSE** Tricuspid annular plane Systolic excursion; **RVFAC** Right ventricle fractional area change; **PAP** Pulmonary artery pressure; **PVR** Pulmonary vascular resistance; **eGFR** Estimated glomerular filtration rate; **6MWD** – 6-minute walking distance

Baseline Parameters (N=15)

Age [yrs.]	77.7 ± 5.4
Female	5 (33%)
Weight [Kg]	75.6 ± 19.9
Body mass index	25.8 ± 7.4
Atrial fibrillation	**12 (80%)**
Previous cerebral vascular accident/ TIA	3 (20%)
Hypertension	10 (67%)
Diabetes Mellitus	3 (20%)
Renal and urinary disorders	**6 (40%)**
COPD	1 (6.7%)
Ascites	**9 (64%)**
Coronary artery disease	7 (47%)
Previous Cardiac Surgery	8 (53%)
Previous Tricuspid Valve Interventions **TriClip (implanted or attempted)** **Tricuspid Annuloplasty**	**4 (27%)** 3 (20%) 1 (6.7%)
Previous Mitral Valve Interventions	7 (47%)
Previous Aortic Valve Interventions	3 (20%)
Transvalvular CIED lead	**7 (47%)**

Baseline Parameters (N=15)

Tricuspid Regurgitation Impact on Outcome Score (TRIO-Score)		5.2 ± 1.1
6-Minute Walking Distance [m]		**265.2 ± 107.6**
New York Heart Association	III	14 (93.3%)
	IV	1 (6.7%)
KCCQ [Overall score]		45.5 ± 26.0
Cardiac Index [L]		2.2 ± 0.6
CVP Mean [mmHg] V-wave [mmHg]		**14.1 ± 3.0** **20.8 ± 4.6**
Diuretic Treatment - Furosemide* [mg] * Torsemide was converted to Furosemide (conversion factor of 4)		153.3 ± 111.6
Anticoagulation	Coumadin	8 (53%)
	Direct Oral Anticoagulant	6 (40%)
eGFR [ml/min/1.73 m^2]		59.2± 16.6
Creatinine [mg/dl]		1.2 ± 0.3
NT-Pro BNP [pg/ml]		2095.1± 2181.6

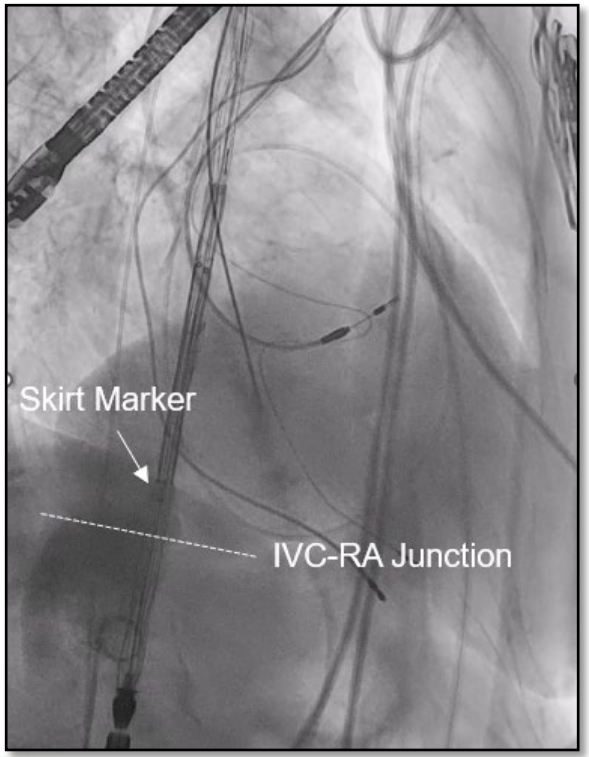
Echocardiographic parameters (evaluated by Echo core-lab):

TR Severity	**Torrential**	**9 (60%)**
	Massive	**4 (26.7%)**
	Severe	**2 (13.3%)**
Left Ventricular Ejection Fraction [%]		51.7 ± 11.5
Right ventricle fractional area change [%]		39.8 ±6.5
Tricuspid Annular Plane Systolic Excursion [mm]		17.1 ± 3.2
RA area [cm^2]		46.5 ± 14.0

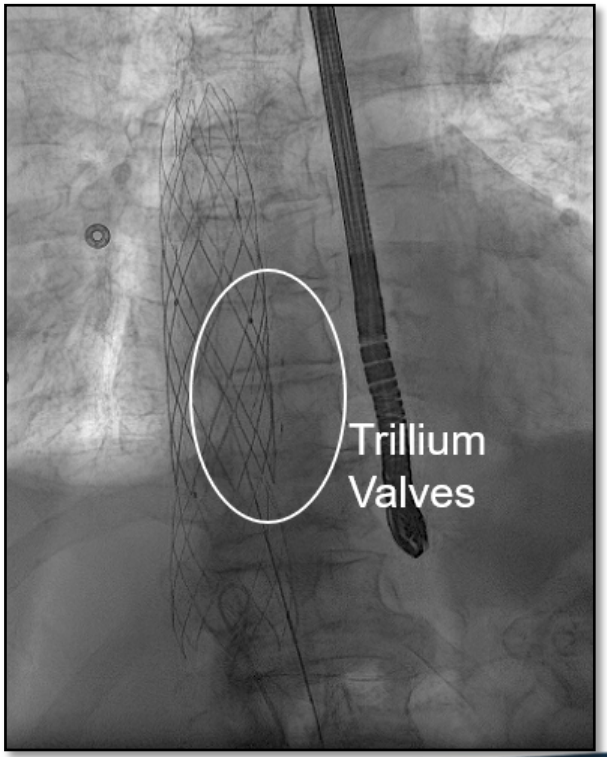
>80% with Massive or Torrential TR

The Trillium Procedure

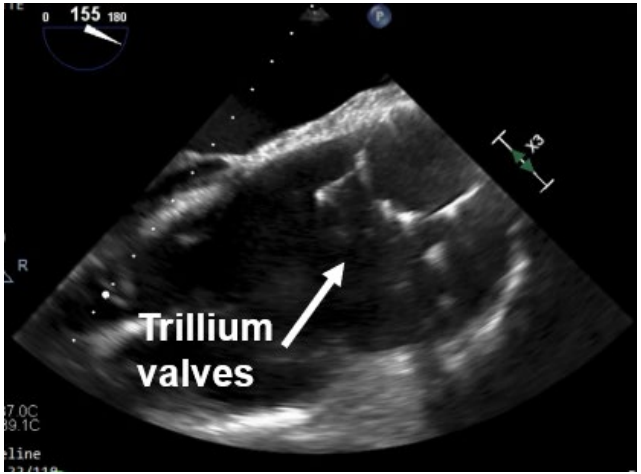
Fluoroscopic roadmap for Trillium positioning

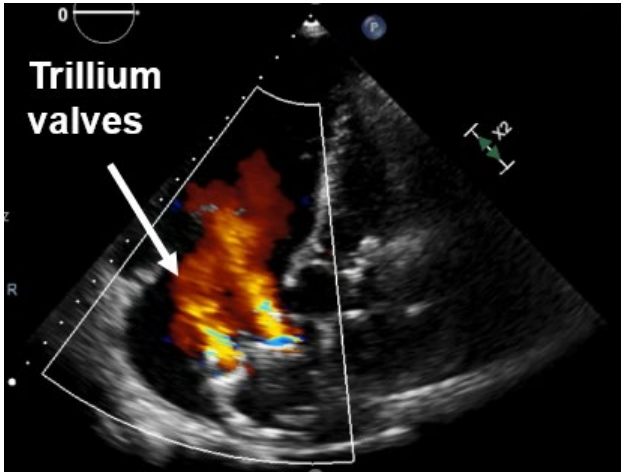


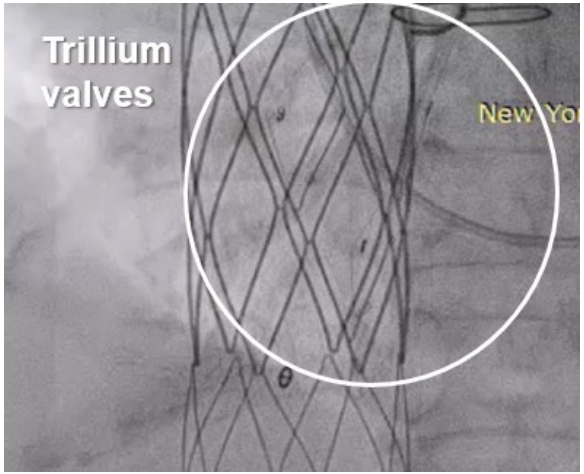
Deployed Trillium device



Trillium Post- Procedure







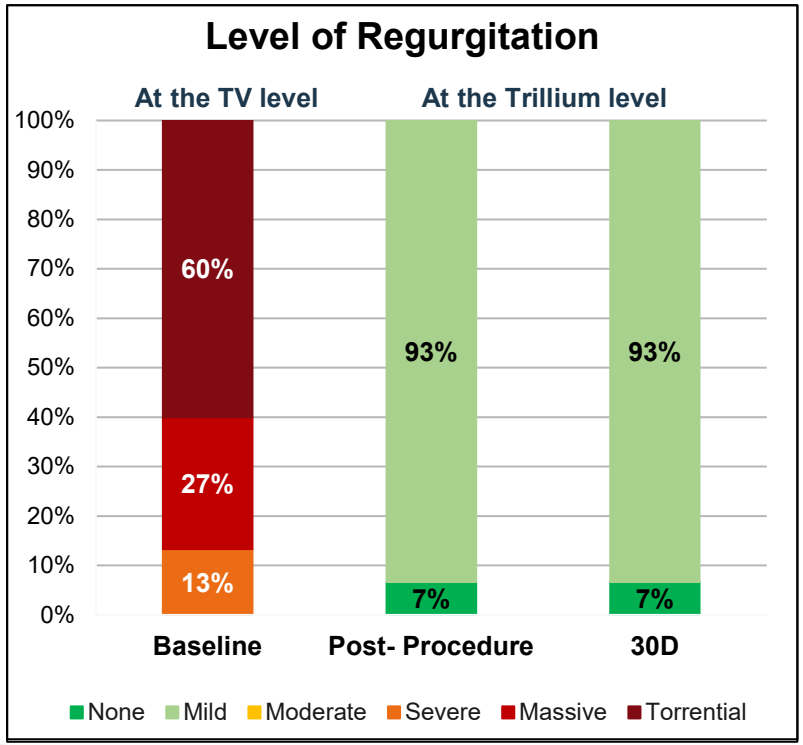
Full inflow and abolition of the venous backflow

Parameter	N=15
Technical Success	**100%**
Device Implantation Time	**5.9 ± 3.4** minutes
Skin to Skin Time	**16.7 ± 7.4** minutes

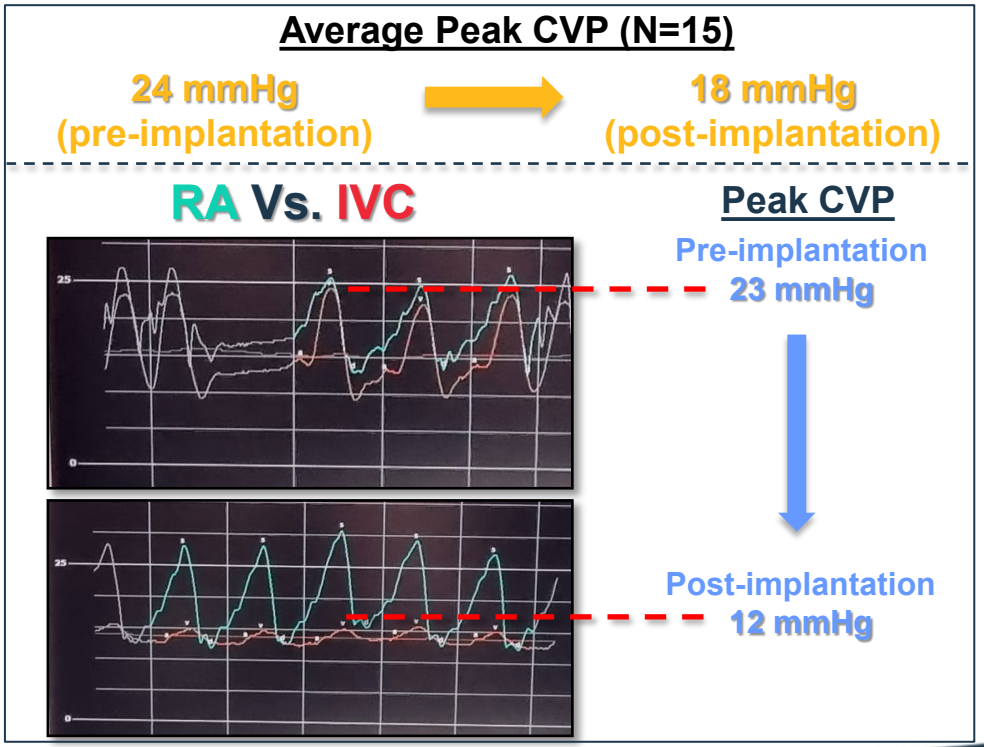
Technical Performance Primary Endpoint is successfully met

Procedure Acute Outcomes

100% TR grade **reduction** to mild or none



Peak central venous pressure was reduced **immediately** post-implantation



30-Day Safety Data

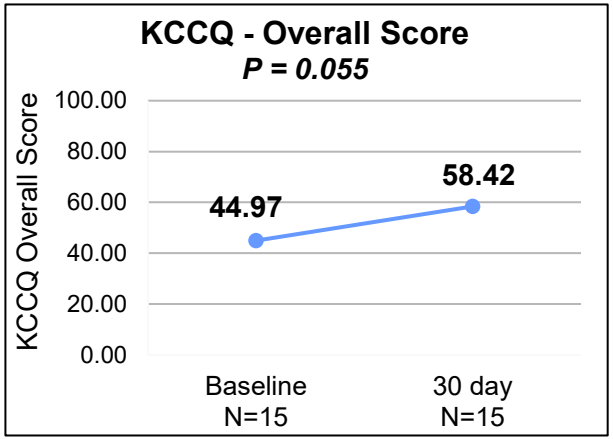
The following table summarizes the technical and safety results at 30-day (N=15):

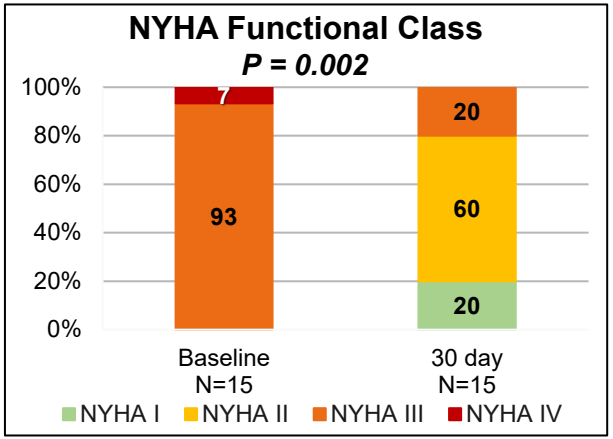
Parameter at 30-day	N (%)	Comments
All-Cause Mortality	0 (0)	
Cardiovascular Mortality	0 (0)	
Tricuspid Valve Re-Intervention or Re-Operation or Conversion to Surgery	0 (0)	
New Need for Pacemaker	0 (0)	
Thrombosis	0 (0)	
New Onset of Dialysis	0 (0)	
Pulmonary Embolism	0 (0)	
Bleeding GI Bleeding Access Site Bleeding	 1 (6.7) 2 (13.3)	 Based on TVARC type 3a type 2
Migration (as long as the device is still anchored)*	0 (0)*	
Device Embolization	0 (0)	
Device Fractures	0 (0)	
Device/Procedure related Major Adverse Events	0 (0)	

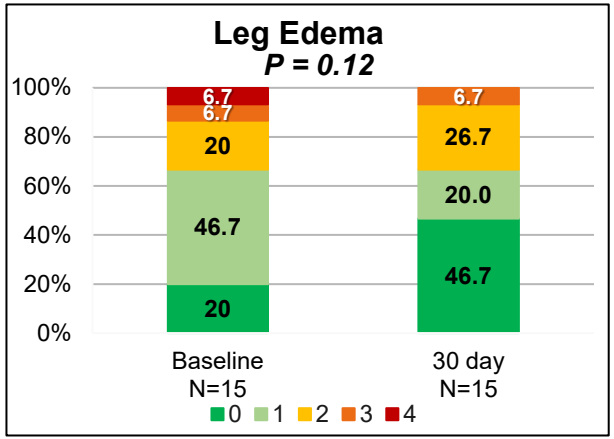
Safety Primary Endpoint is Successfully met

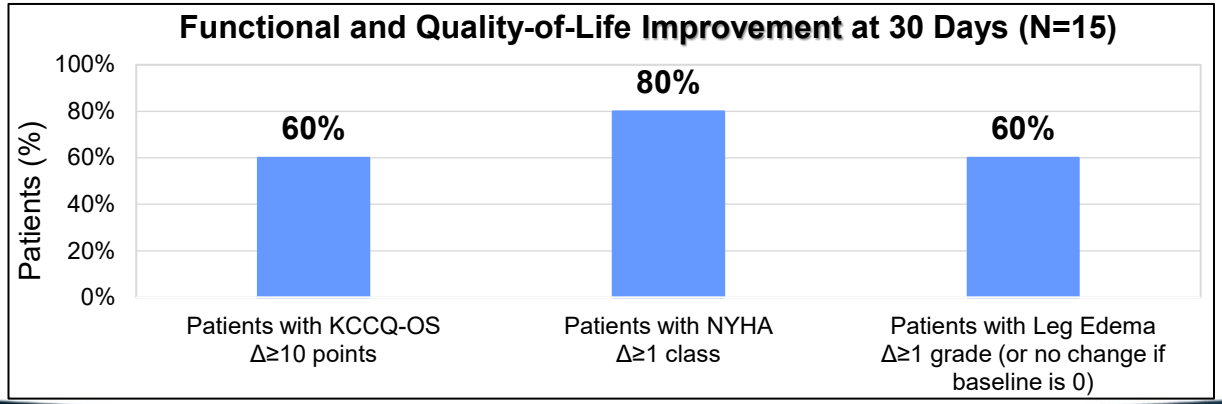
**At 6M follow-up visit 1 patient presented with ~1.5cm migration of the device deeper into the IVC, while the device is still anchored. The timing of the event is unclear and was first identified at 6M.*

30 Days Clinical Outcomes









Leg edema grade: **0** - No pitting edema; 1 - Mild pitting edema. 2mm depression that disappears rapidly; **2** - Moderate pitting edema. 4mm depression that disappears in 10-15 seconds; **3** - Moderately severe pitting edema. 6mm depression that may last more than 1 minute; **4** – Severe pitting edema. 8mm depression that can last more than 2 minutes.

Conclusions

Heterotopic TTVR with Trillium:

- Suitable treatment option for patients deemed ineligible for orthotopic replacement/repair
- Feasible and safe
- Offers a straightforward procedure requiring <10 minutes procedure time, optional echo guidance and conscious sedation
- Reduces venous backflow and central venous pressure
- Reduces symptomatic burden with improvement in NYHA FC

Results of EFS will Inform Pivotal Trial