CLINICAL COMPENDIUM

TRIFECTA™ VALVE
EIGHT-YEAR DATA

Abbott

TRIFECTA™ VALVE POST-MARKET PROSPECTIVE MULTICENTER STUDY

The Trifecta™ valve is a tri-leaflet stented pericardial valve designed for supra-annular placement in the aortic position. The valve is fabricated using a polyester-covered titanium stent. The stent, excluding the sewing cuff, is then covered with porcine pericardial tissue. This covering is designed to provide protection from mechanical wear by allowing only tissue-to-tissue contact during valve function. A silicone insert in the polyester sewing cuff is slightly contoured to conform to the shape of the native annulus. The valve leaflets are fabricated from bovine pericardium. The porcine and bovine pericardium are preserved and cross-linked in glutaraldehyde. Glutaraldehyde, formaldehyde, and ethanol are used in the valve sterilization process. Additionally, the Trifecta valve is processed with Linx™ anticalcification treatment, an anticalcification treatment that in animal studies has demonstrated resistance to calcification in four ways.*[1-6]

STUDY OBJECTIVE

The objective of the study is to further evaluate the long-term clinical safety and effectiveness of the Trifecta valve.

STUDY DESIGN

The clinical study is a multicenter, prospective, nonrandomized, follow-up study conducted in the United States and Canada.

Subjects (n = 710) enrolled in this study received the Trifecta valve during the investigational (IDE) study (2007–2009) conducted to obtain PMA approval.[7] Four hundred and forty-four (n = 444) of the subjects participated in an FDA mandated post-approval study (PAS), and the remaining subjects participated in a post-marketing long-term follow-up study (LTFU). Nine (9) investigational centers in the United States and two (2) investigational centers in Canada that enrolled subjects during the IDE are participating.

Subjects are followed on an annual basis with either an in-clinic visit or a telephone follow-up. Each in-clinic visit consists of a transthoracic echocardiogram (TTE) and assessments for NYHA classification, serious adverse events, and general clinical status. The seven-year follow-up consisted of an in-clinic visit, while the eight-year follow-up was a telephonic follow-up.

Table 1: Study Centers

STUDY CENTERS	LOCATION
Mayo Clinic	Rochester, MN
Hospital of the University of Pennsylvania	Philadelphia, PA
Abbott Northwestern Hospital	Minneapolis, MN
Mission Health and Hospitals	Asheville, NC
Vanderbilt University Medical Center	Nashville, TN
Intermountain Medical Center	Salt Lake City, UT
Cleveland Clinic Foundation	Cleveland, OH
Lankenau Hospital	Wynnewood, PA
University of Southern California	Los Angeles, CA
St. Paul's Hospital - University of British Columbia	Vancouver, BC
Institut de Cardiologie de Québec (Hôpital Laval)	Quebec City, Quebec

*There are no clinical data currently available that evaluates the long-term impact of anticalcification tissue treatment in humans.

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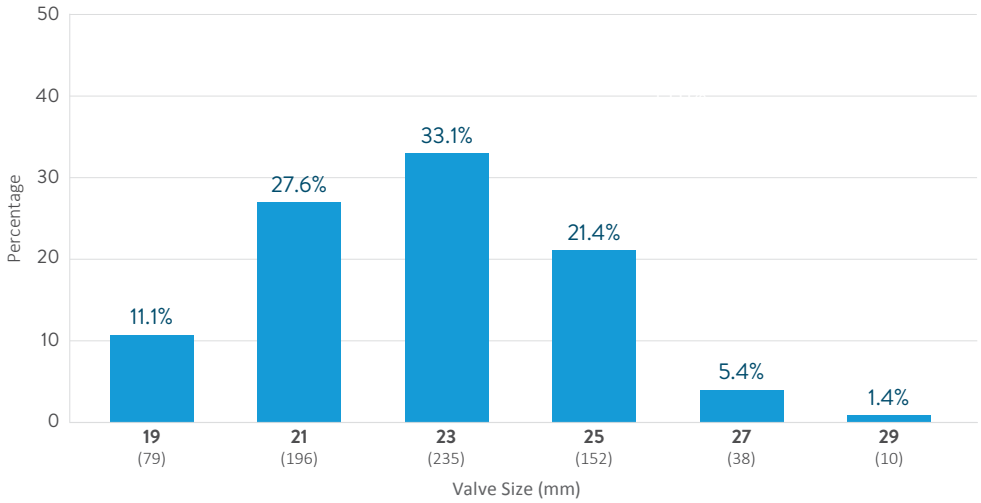
SUMMARY OF SUBJECT DEMOGRAPHICS[7]

The subject population in this study had the following characteristics:

- 471 subjects (66%) were male and 239 subjects (34%) were female
- Mean age was 72.4 years (± 9.3); age range was 33-95 years
- Prior to implantation, 5.4% were NYHA functional class I, 43.8% class II, 46.8% class III and 4.1% class IV

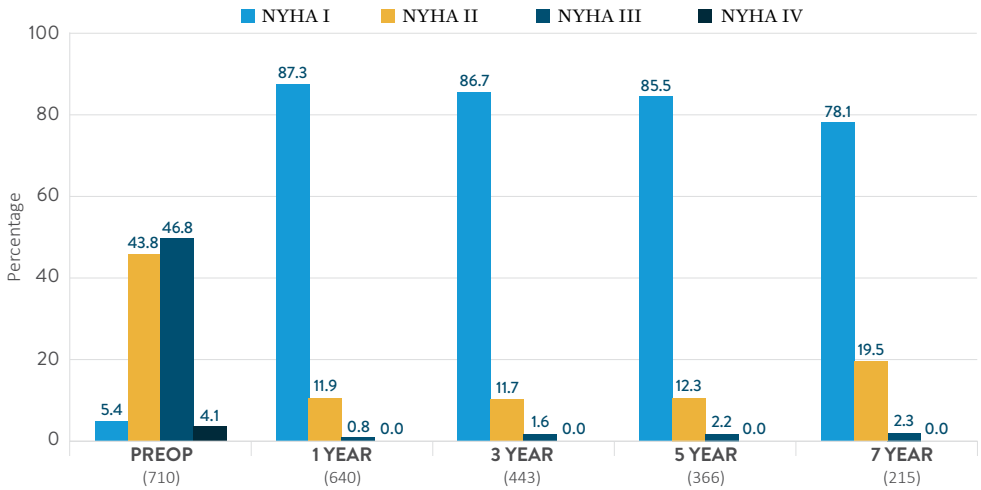
Figure 1: Distribution of Valve Sizes



- The most common size implanted was 23 mm (33.1%)

FOLLOW-UP DATA AND CLINICAL RESULTS

Figure 2: NYHA Over Time

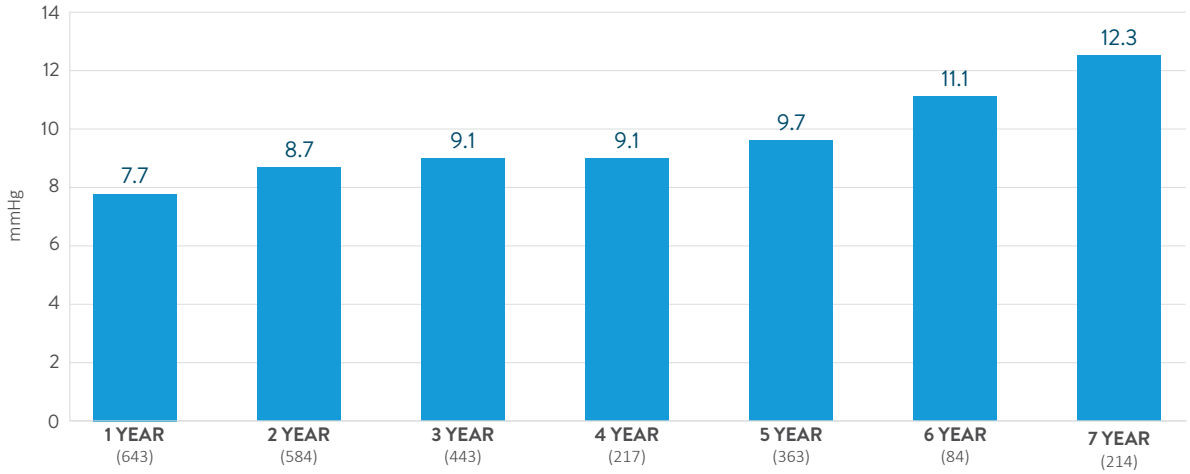


- Preoperatively 50.9% of subjects were in NYHA Class III or IV. At one-year postoperatively, 99.2% were NYHA Class I or II. At seven years postoperatively, 97.7% were NYHA Class I or II

HEMODYNAMIC DATA

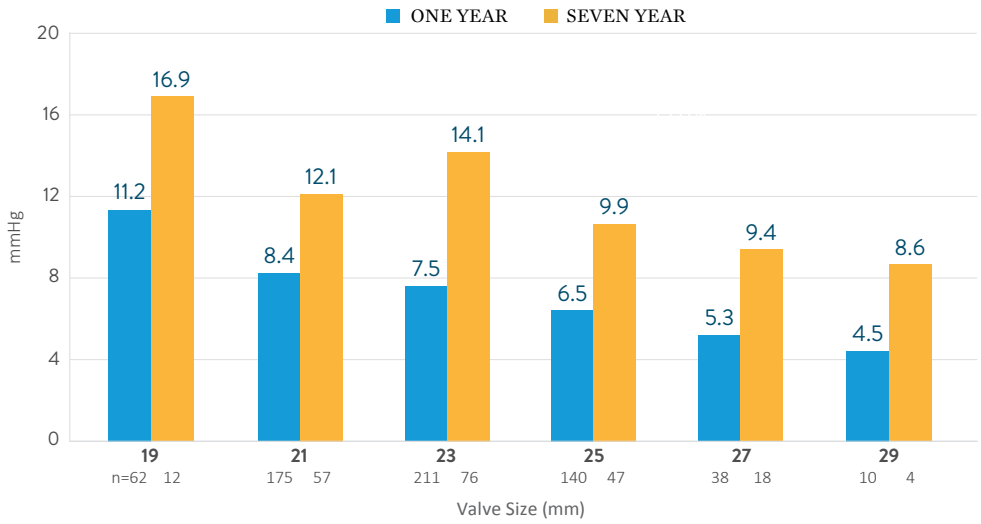
The following average hemodynamic parameters were evaluated by valve size: mean gradient, effective orifice area (EOA), effective orifice area indexed (EOAI) (see Figures 3-6). Average mean gradient and aortic regurgitation for all valve sizes over time are shown in Figures 3 and 7, respectively. All echocardiograms were evaluated at an independent core laboratory to minimize interobserver variability and ensure a standard of quality interpretation.

Figure 3: Average Mean Gradient Over Time



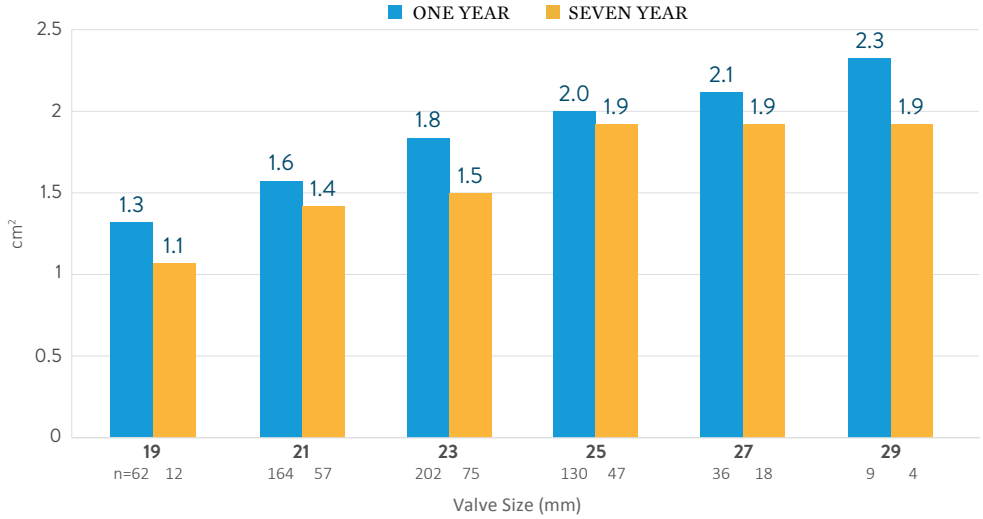
- Average mean gradients across all valve sizes was 12.3 mmHg at seven years postoperatively

Figure 4: Average Mean Gradient by Valve Size



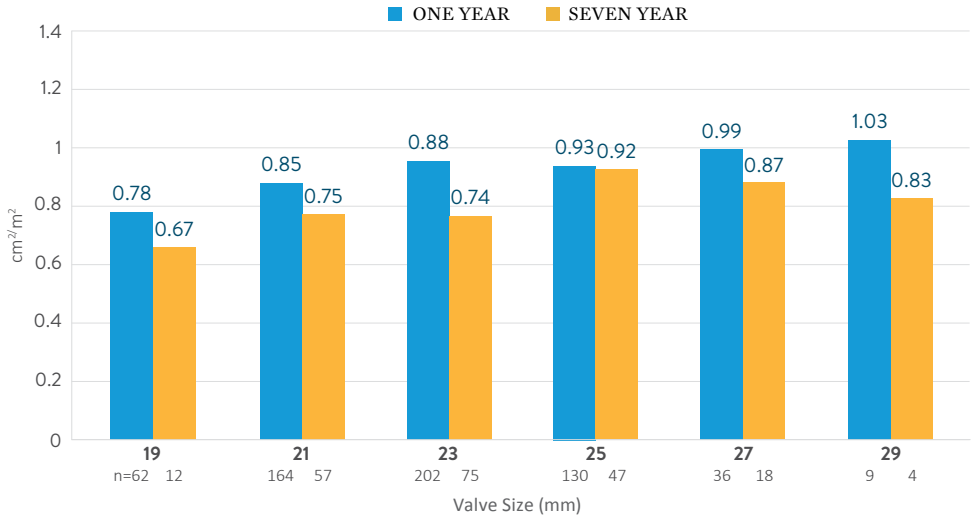
- Average mean gradient for 19 mm valve size was 16.9 mmHg at seven years postoperatively

Figure 5: Average Effective Orifice Area by Valve Size



- Large effective orifice areas across all valve sizes reduce the risk of prosthesis-patient mismatch

Figure 6: Average Effective Orifice Area Index by Valve Size

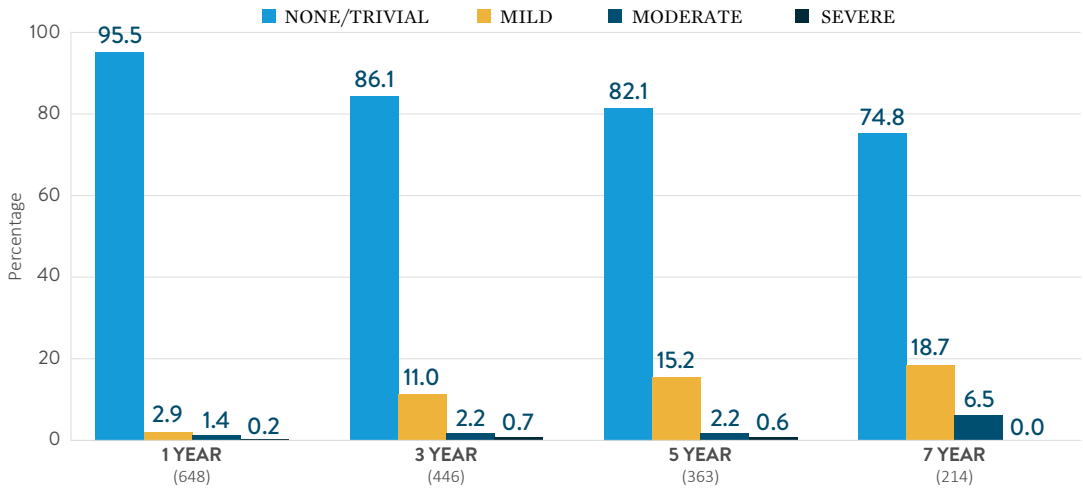


- Average EOAI across all valves sizes at one year = 0.88 cm^2/m^2 and at seven years = 0.79 cm^2/m^2

AORTIC REGURGITATION

The following chart presents the total aortic valve regurgitation over time for all valve sizes.

Figure 7: Aortic Regurgitation Over Time



- 93.5% of subjects were without moderate-to-severe valvular regurgitation at seven years

KAPLAN-MEIER ANALYSES

Figures 8-15 present the Kaplan-Meier analyses for structural valve deterioration, nonstructural valve dysfunction, paravalvular leak, reoperation and mortality. The 95% confidence interval is indicated by the dashed lines, and the number of subjects at risk for each interval is shown at the bottom. Cumulative percent freedom from the event at eight years is indicated on each graph.

Figure 8: Structural Valve Deterioration (Surgical Explant)

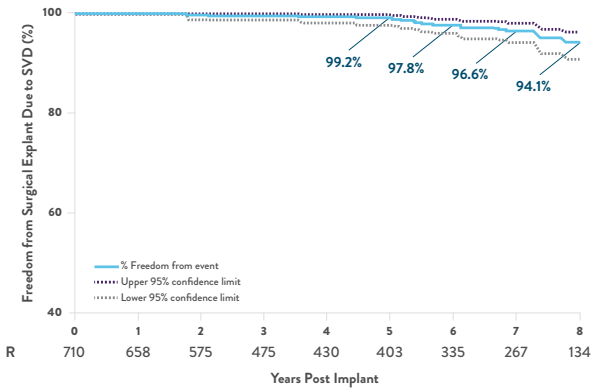


Figure 9: Structural Valve Deterioration (Transcatheter Valve-in-Valve Intervention)

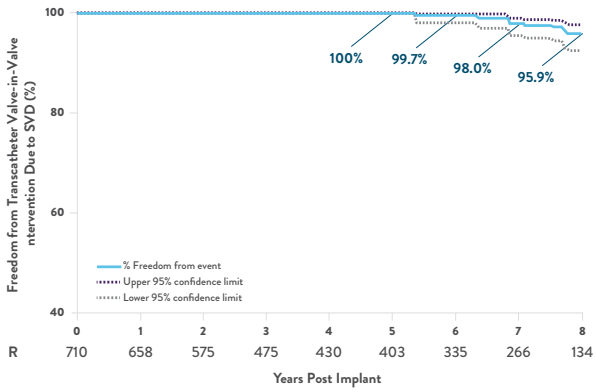


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Figure 10: Structural Valve Deterioration (Surgical Explant or Transcatheter Valve-in-Valve Intervention)

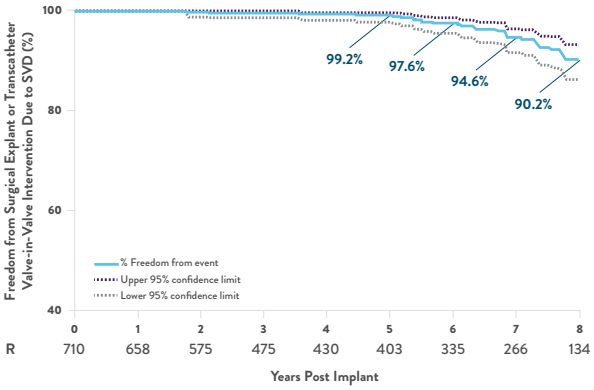


Figure 11: Nonstructural Valve Dysfunction

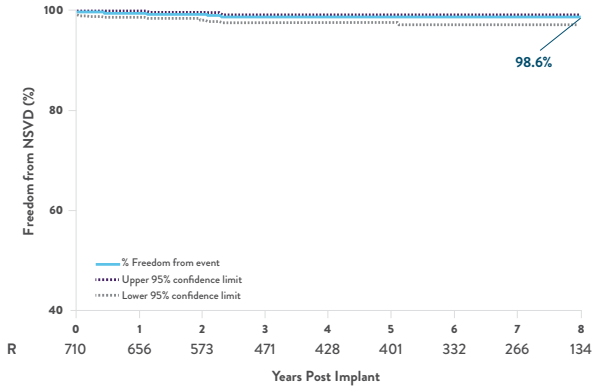


Figure 12: Paravalvular Leak

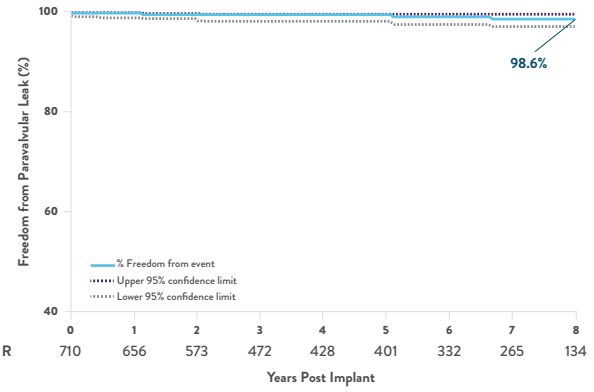


Figure 13: Reoperation (Surgical Explant or Transcatheter Valve-in-Valve Intervention)

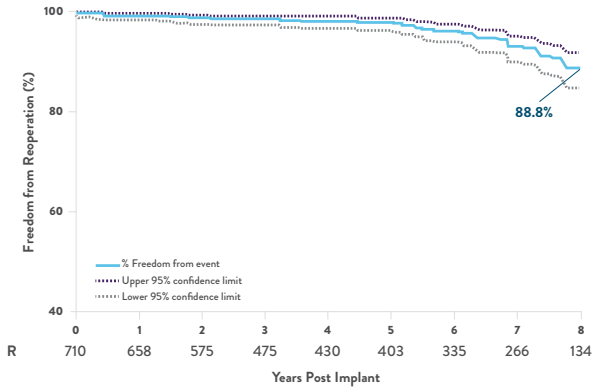


Figure 14: Valve-related Mortality

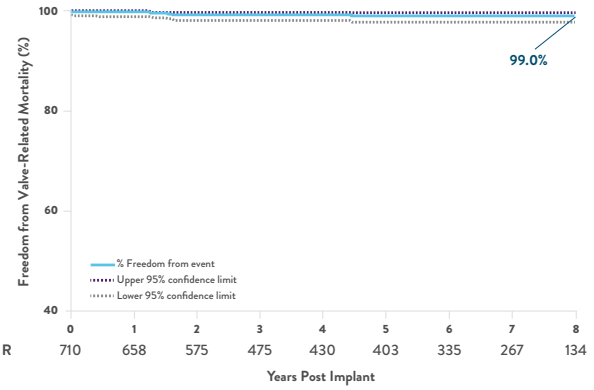
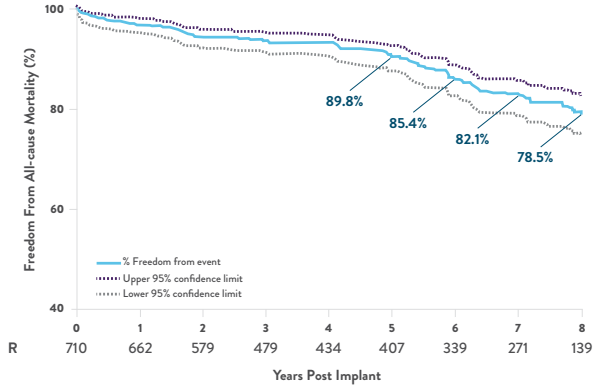


Figure 15: All-cause Mortality



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SUMMARY OF ADVERSE EVENTS

Early and late rates for serious adverse events are presented in Table 2. Early rates are presented as simple percentages, and rates for late events as percent per late patient-years of follow-up (%/Lt Pt-yr). No unanticipated device effects were reported.

Table 2: Early and Late Adverse Event Rates

	EARLY RATE (≤ 30 days)		LATE RATE (≥ 31 days) (%/Lt Pt-yrs = 3502.2)	
	EVENTS	%**	EVENTS	%/Lt Pt-yr
Embolism	20	2.8	31	0.89
Neurologic	18	2.5	28	0.80
TIA	2	0.3	15	0.43
RIND	10	1.4	3	0.09
Stroke	6	0.8	10	0.29
Systemic	2	0.3	1	0.03
Thrombosis	0	0.0	1	0.03
Major Bleed	52	7.3	57	1.63
Endocarditis	0	0.0	8	0.23
Structural Deterioration	0	0.0	36	1.03
Nonstructural Dysfunction	1	0.1	7	0.20
Paravalvular Leak	1	0.1	6	0.17
Reoperation	1	0.1	38	1.09
Explant due to SVD	0	0.0	19	0.54
ViV due to SVD	0	0.0	11	0.31
Mortality	11	1.5	91	2.60
Valve-related	1	0.1	5	0.14

**The early adverse rate (%) is calculated as the number of early events divided by the total number of subjects, times 100.

SUMMARY

Outcomes from the Trifecta™ valve post-market prospective, multicenter study (n=710) demonstrate that the Trifecta valve has excellent hemodynamic performance and remarkable survival:

- 99.0% freedom from valve-related mortality at 8-years post-implant
- 78.5% freedom from all-cause mortality at 8-years post-implant
- Average mean gradient across all valve sizes = 12.3 mmHg, and the average effective orifice area index across all sizes = 0.79 cm^2/m^2 at 7 years post-implant
- 93.5% of subjects were without moderate-to-severe valvular regurgitation at 7 years post implant
- 97.7% of subjects were NYHA Class I or II at 7 years post-implant

Subjects with SVD were managed with either a surgical explant, or a transcatheter valve-in-valve (ViV) intervention. The Trifecta valve has a low rate of SVD:

- 94.1%. freedom from surgical explant due to SVD at 8-years post-implant
- 90.2% freedom from surgical explant or transcatheter valve-in-valve intervention due to SVD at 8-years post-implant

REFERENCES

1. Frater, R. W. M., Seifter, E., & Liao, K. (1997). Anticalcification, Proendothelial, and Antiinflammatory Effects of Postaldehyde Polyol Treatment of Bioprosthetic Material. In S. Gabbay & D. Wheatley (Eds.), *Advances in Anticalcific and Antidegenerative Treatment of Heart Valve Bioprostheses*. (105-113 of Chapter 8). Austin, TX: Silent Partners, Inc. **2.** Kelly, S. J., Ogle, M. F., Carlyle, W. C., W. C., & Mirsch, M. W. (2000). *Biocompatibility and Calcification of Bioprosthetic Heart Valves*. Society for Biomaterials, Sixth World Biomaterials Congress Transaction, 1353. **3.** Vyavahare, N., Hirsch, D., Lerner, E., Baskin, J. Z., Schoen, F. J., Bianco, R., et al. Levy, R. J. (1997). Prevention of bioprosthetic heart valve calcification by ethanol preincubation. *Circulation*, 95(2):479-488. **4.** Vyavahare, N., Hirsch, D., Lerner, E., Baskin, J. Z., Zand, R., Schoen, F. J., & Levy, R. J. (1998). Prevention of calcification of glutaraldehyde-crosslinked porcine aortic cusps by ethanol preincubation. *Journal of Biomedical Materials Research*, 40(4):577-85. **5.** Shen, M., Kara-Mostefa, A., Chen, L., Daudon, M., Thevenin, M., Lacour, B., & Carpentier, A., (2001). Effect of ethanol and ether in the prevention of calcification of bioprostheses. *Annals of Thoracic Surgery*, 71(5 Suppl), S413-416. **6.** Vyavahare, N., Jones, P. L., Hirsch, D., Schoen, F. J., & Levy, R. J. (2000). Prevention of glutaraldehyde-fixed bioprosthetic heart valve calcification by alcohol pretreatment: further mechanistic studies. *Journal of Heart Valve Disease*, 9(4), 561-566. **7.** Goldman S, Cheung A, Bavaria JE, Petracek MR, Groh MA, Schaff HV. Midterm, multicenter clinical and hemodynamic results for the Trifecta aortic pericardial valve. *The Journal of Thoracic and Cardiovascular Surgery*. 2017 Mar;153(3):561-569.

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