Important Information Regarding SVD in Trifecta Family of Valves

Trifecta™ Valve and Trifecta™ Valve with Glide Technology

Model: TF-19A, TF-21A, TF23A, TF25A, TF-27A, TF-29A, TFGT-19A, TFGT-21A, TFGT-23A, TFGT-25A, TFGT-27A, and TFGT-29A

February 27, 2023

Attention: Heart Team

Dear Valued Customer,

Abbott is providing information regarding Structural Valve Deterioration (SVD)[1] related to its Trifecta™ family of bioprosthetic heart valves. This communication is intended to raise awareness regarding the potential for early SVD[2] and provide patient management considerations.

The Trifecta™ Valve and Trifecta™ Valve with Glide™ Technology (GT) constitute the Trifecta family and are tri-leaflet stented bovine pericardial valves designed for supra-annular placement in the aortic position. The valves are fabricated using a covered titanium stent with leaflets mounted externally to maximize valve opening and improve hemodynamic performance.[3-4] The valves are intended as a replacement for a diseased, damaged, or malfunctioning native or prosthetic aortic heart valve.

Incidence and Clinical Outcome:
Abbott monitors product performance through clinical trial data, literature reviews, and complaint reporting. This section addresses all three sources of data and raises awareness of recent literature around SVD.

Clinical Trial Data: As background, Abbott has assessed Trifecta valve performance and durability in two prospective clinical trials (ClinicalTrials.gov Identifier: NCT01593917 and NCT01256710) for the 1st generation Trifecta valve and a third prospective clinical trial (NCT03016169) for the Trifecta GT valve. Hemodynamic performance assessed by an echocardiography core lab demonstrated the absence of a rapid rise in transvalvular gradients through 10 years post-implant in patients implanted with the 1st generation Trifecta valve.[5] The clinical trial data for the 1st generation Trifecta valve showed that most cases of SVD occurred after 5 years of implant with a peak occurrence at 8 years. **Table 1** provides measures of valve durability for the 1st generation Trifecta valve and Trifecta GT valve relative to a comparator bovine pericardial valve.[6] At 8 years post-implant, the 1st generation Trifecta valve has a slightly reduced durability relative to the comparator valve.

Table 1

Prospective Clinical Trials	Freedom from SVD			Freedom from reintervention due to SVD		
Implant Duration	**5 years***	**8 years**	**10 years**	**5 years***	**8 years**	**10 years**
Trifecta LTFU Study (NCT01593917) **N=710**	98.2% N=401	87.6% N=229	67.7% N=96	99.2% N=404	89.8% N=233	75.4% N=105
Trifecta Durability Study (NCT01256710) **N=1151**	96.7% N=884	87.4% N=594	76.0% N=130	97.5% N=889	91.3% N=609	85.0% N=137
Trifecta GT PMCF Study (NCT03016169) **N=362**	98.0%* N=152	N/A	N/A	99.2%* N=154	N/A	N/A
Comparator Valve Study (NCT01171625) **N=258**	99.1% N=202	90.1% N=62	N/A	99.1% N=202	93.6% N=64	N/A

* Data for the Trifecta GT valve are reported at 4 years post-implant; study is still ongoing. All other data shown for the 1st generation Trifecta valve and comparator valve are reported at 5 years post-implant. LTFU = Long-Term Follow-Up; PMCF = Post-Market Clinical Follow-up; N/A = not available.

Recent Literature: An Abbott review of literature published since 2020 identified 21 articles (Appendix A) assessing retrospectively the early (≤ 5 years) and midterm (6 to 10 years) durability of the Trifecta valve. Twelve of these articles compared the durability of the Trifecta valve to other commercially available bovine pericardial valves and four (4) of these articles used propensity matching. **Figure 1** provides measures of valve durability for the Trifecta valve versus comparator valves from the literature review, where each data point (marked with “o” or “x”) represents the results from one publication. Based on the literature review, there appears to be a higher early and midterm cumulative incidence of SVD, and a lower freedom from early and midterm reintervention due to SVD for the Trifecta valve. The

reported rates of SVD for the Trifecta valve do not consistently align with the prospective clinical trial data and demonstrate greater variation across medical centers relative to the comparator valves.

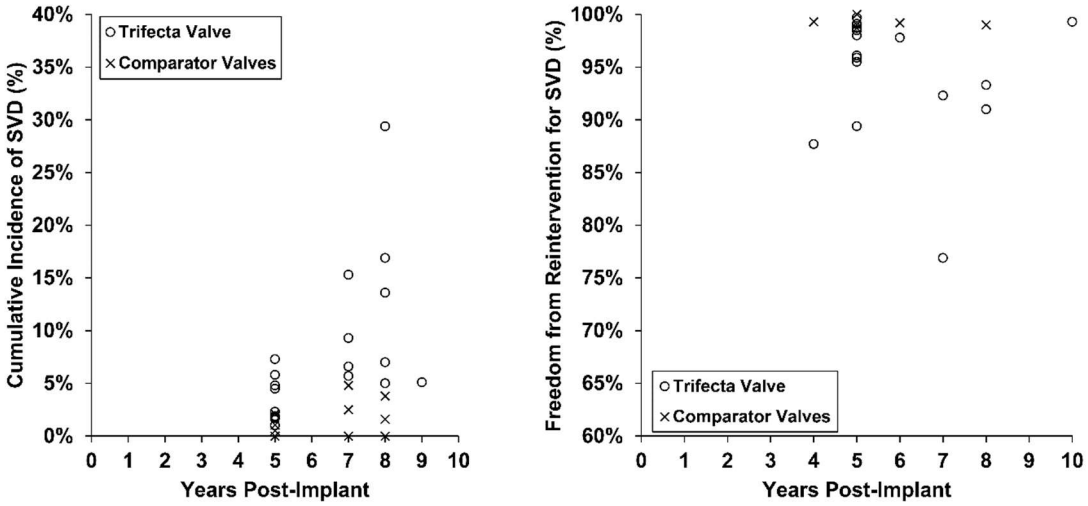

Figure 1: Scatter Diagram of SVD Rates from Literature Review

Complaint Data: Abbott's complaint analysis has shown that most cases of early SVD which occur within 5 years post-implant are characterized as a non-calcific leaflet tear, while most cases of late SVD which occur beyond 5 years post-implant are characterized as a fibrous-calcific SVD. **Figure 2** shows a histogram of the time to SVD based on all reported complaint data with known implant duration stratified by the various clinical outcomes. While the clinical trial data show a peak time to SVD of 8 years, the complaint data shows a shorter peak time to SVD of 3 to 4 years. There are generally limitations associated with interpreting data collected via passive surveillance through complaint reporting which likely result in under-estimating events due to under-reporting.

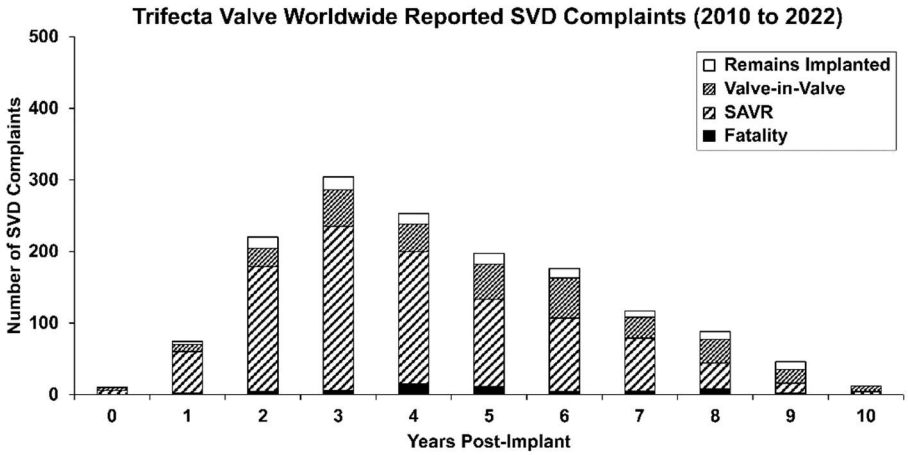

Figure 2: Histogram of Time to SVD based on Worldwide Reported Complaints

SAVR = Surgical Aortic Valve Replacement; Valve-in-Valve = Transcatheter valve-in-valve intervention

In summary, a recent literature review of the Trifecta valve indicates a higher early and midterm cumulative incidence of SVD relative to comparator bovine pericardial valves. While the data primarily reflects the 1st generation Trifecta valve, the 4-year clinical trial data for the Trifecta GT valve suggests that its performance and durability is comparable to the 1st generation Trifecta valve, such that the following patient management considerations apply to the entire Trifecta family of valves.

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Patient Management Considerations

Clinically significant early SVD will compromise the hemodynamic performance of the valve; therefore, in choosing a Trifecta valve, the potential for early SVD should be balanced against its hemodynamic benefits[3-5,7-8] and discussed with the patient.

When implanting the Trifecta GT valve, it is important to implant the valve in accordance with the IFU sizing and handling guidelines.[9-10, 29]

Understanding that clinical decisions are shared between health care providers and patients, please consider the following post-implant:

- Patients should be reminded to seek medical attention with new onset of symptoms such as shortness of breath or fatigue.
- An initial post-procedural transthoracic echocardiogram (TTE) study is recommended for all patients within 1 to 3 months after the implant procedure to evaluate valve hemodynamics and ventricular function.
- Schedule annual follow-up visits beginning 1-year post-implant for clinical evaluation, including TTE to assess transvalvular gradients and valvular regurgitation grade.
- Patients presenting with changes in symptoms (e.g., shortness of breath or fatigue on exertion) or signs (e.g., murmur) indicative of potential SVD should undergo a TTE.
- Patients with evidence of hemodynamically significant SVD should be considered, in consultation with a heart team, for a possible valve intervention with either surgical aortic valve replacement (SAVR) or a transcatheter valve-in-valve intervention depending on individual patient risks and benefits.
- Patients being considered for a valve-in-valve intervention should undergo pre-procedure planning with imaging studies to ensure all potential procedure-related risks such as coronary obstruction are minimized. Additional information regarding future valve-in-valve considerations can be found in the Trifecta GT valve IFU. Please note that the titanium frame of the Trifecta GT valve cannot be fractured using a balloon.

Actions Abbott is Asking You to Take:

- Please consider this information in your practice and share with relevant health care professionals (e.g., cardiac surgeons, cardiologists, primary care physicians) involved in the care of patients implanted with the Trifecta family of valves in your institution.
- Complete and return the provided Acknowledgement Form.
- Report any product incidents, regardless of procedure or patient outcome, to Abbott.

Abbott is working with the FDA on this matter. Report any adverse reactions or quality problems experienced with the use of these products to your local Abbott representative or the customer service department at 1-800-544-1664. Reports may also be sent to the FDA's MedWatch Adverse Event Reporting program by completing Form FDA 3500 online at www.FDA.gov, calling 1-800-FDA-1088 or faxing to 1-800-FDA-0178.

Thank you for your attention to this matter. Abbott is committed to providing high-quality products and partnering with you to ensure the safety of each patient. Please contact your local Abbott representative or the customer service department at 1-800-544-1664 (Option 2) with any questions on this notification.

Sincerely,

Christopher Gallivan
Divisional Vice President, Quality
Abbott Structural Heart

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References

1. Capodanno, Davide, Anna S. Petronio, Bernard Prendergast, Helene Eltchaninoff, Alec Vahanian, Thomas Modine, Patrizio Lancellotti et al. "Standardized definitions of structural deterioration and valve failure in assessing long-term durability of transcatheter and surgical aortic bioprosthetic valves: a consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) endorsed by the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)." European journal of cardio-thoracic surgery 52, no. 3 (2017): 408-417.
2. Cremer, Paul C., L. Leonardo Rodriguez, Brian P. Griffin, Carmela D. Tan, E. Rene Rodriguez, Douglas R. Johnston, Gosta B. Pettersson, and Venu Menon. "Early bioprosthetic valve failure: mechanistic insights via correlation between echocardiographic and operative findings." Journal of the American Society of Echocardiography 28, no. 10 (2015): 1131-1148.
3. Colli, Andrea, Giovanni Marchetto, Stefano Salizzoni, Mauro Rinaldi, Luca Di Marco, Davide Pacini, Roberto Di Bartolomeo et al. "The TRIBECA study:(TRI) fecta (B) ioprosthesis (E) valuation versus (C) arpentier Magna-Ease in (A) ortic position." European Journal of Cardio-Thoracic Surgery 49, no. 2 (2016): 478-485.
4. Phan, Kevin, Hakeem Ha, Steven Phan, Martin Misfeld, Marco Di Eusanio, and Tristan D. Yan. "Early hemodynamic performance of the third generation St Jude Trifecta aortic prosthesis: a systematic review and meta-analysis." The Journal of Thoracic and Cardiovascular Surgery 149, no. 6 (2015): 1567-1575.
5. Goldman, Scott, Anson Cheung, Joseph E. Bavaria, Michael R. Petracek, Mark A. Groh, and Hartzell V. Schaff. "Midterm, multicenter clinical and hemodynamic results for the Trifecta aortic pericardial valve." The Journal of thoracic and cardiovascular surgery 153, no. 3 (2017): 561-569.
6. Tsui, Steven, Michael Rosenbloom, James Abel, Jeffrey Swanson, Axel Haverich, Joseph Zacharias, Gilbert Schorlemmer, Gideon Cohen, Michael Moulton, and Rüdiger Lange. "Eight-year outcomes of aortic valve replacement with the Carpentier-Edwards PERIMOUNT Magna Ease valve." Journal of cardiac surgery (2022).
7. Fallon, John M., Joseph P. DeSimone, J. Matthew Brennan, Sean O'Brien, Dylan P. Thibault, Anthony W. DiScipio, Philippe Pibarot, Jeffrey P. Jacobs, and David J. Malenka. "The incidence and consequence of prosthesis-patient mismatch after surgical aortic valve replacement." The Annals of thoracic surgery 106, no. 1 (2018): 14-22.
8. Mehaffey, J. Hunter, Robert B. Hawkins, Zachary K. Wegermann, Maria V. Grau-Sepulveda, John M. Fallon, J. Matthew Brennan, Vinod H. Thourani, Vinay Badhwar, and Gorav Ailawadi. "Aortic annular enlargement in the elderly: short and long-term outcomes in the United States." The Annals of Thoracic Surgery 112, no. 4 (2021): 1160-1166.
9. Trifecta GT IFU.
10. Goldman, Scott. "Bigger valve size is not always better." The Journal of thoracic and cardiovascular surgery 154, no. 3 (2017): 820-821.

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Appendix A, Literature Review References

11. Yount, Kenan W., Robert B. Hawkins, J. Hunter Mehaffey, Nicholas R. Teman, Leora T. Yarboro, John A. Kern, and Gorav Ailawadi. "Aortic valve biologic protheses: A cohort comparison of premature valve failure." Journal of Cardiac Surgery 37, no. 5 (2022): 1224-1229.
12. Suzuki, Ryo, Toshiro Ito, Masato Suzuki, Shunsuke Ohori, Ryo Takayanagi, and Shiro Miura. "Trifecta versus Perimount Magna Ease aortic valves: Failure mechanisms." Asian Cardiovascular and Thoracic Annals (2022): 02184923221100994.
13. Yongue, Camille, Diana C. Lopez, Edward G. Soltesz, Eric E. Roselli, Faisal G. Bakaeen, A. Marc Gillinov, Gösta B. Pettersson et al. "Durability and performance of 2298 Trifecta aortic valve prostheses: a propensity-matched analysis." The Annals of Thoracic Surgery 111, no. 4 (2021): 1198-1205.
14. Mortelé, Augustijn, Alexander Dereu, Thierry Bové, and Katrien François. "Mid-term clinical and haemodynamic results after aortic valve replacement with the Trifecta bioprosthesis." Interactive cardiovascular and thoracic surgery 34, no. 1 (2022): 16-25.
15. Rubens, Fraser D., Janet Ngu, Anahita Malvea, Steven J. Samuels, and Ian G. Burwash. "Early midterm results after valve replacement with contemporary pericardial prostheses for severe aortic stenosis." The Annals of Thoracic Surgery 112, no. 1 (2021): 99-107.
16. Krishnamoorthy, Bhuvaneswari, William R. Critchley, Nehru Devan, James Barnard, Issac Kadir, Stuart W. Grant, and Rajamiyer V. Venkateswaran. "Low Incidence of Structural Valve Degeneration With the Trifecta Aortic Valve Bioprosthesis." (2021).
17. Stubeda, Herman, Hashem Aliter, Ryan A. Gainer, Chris Theriault, Steve Doucette, and Gregory M. Hirsch. "Six-year follow-up of aortic valve reoperation rates: Carpentier-Edwards Perimount versus St. Jude Medical Trifecta." Journal of Cardiac Surgery 35, no. 12 (2020): 3347-3353.
18. Werner, Paul, Jasmin Gritsch, Sabine Scherzer, Christoph Gross, Marco Russo, Iuliana Coti, Alfred Kocher, Guenther Laufer, and Martin Andreas. "Structural valve deterioration after aortic valve replacement with the Trifecta valve." Interactive cardiovascular and thoracic surgery 32, no. 1 (2021): 39-46.
19. Wakami, Tatsuto, Shigeki Koizumi, and Tadaaki Koyama. "Is Trifecta safe for small valve size from mid-term outcome?." (2022).
20. Lam, Ka Yan, Bart Koene, Naomi Timmermans, Mohamed Soliman-Hamad, and Albert van Straten. "Reintervention after aortic valve replacement: comparison of 3 aortic bioprostheses." The Annals of Thoracic Surgery 110, no. 2 (2020): 615-621.
21. Lehmann, Sven, Khalil Jawad, Maja T. Dieterlen, Alexandro Hoyer, Jens Garbade, Piroze Davierwala, and Michael A. Borger. "Durability and clinical experience using a bovine pericardial prosthetic aortic valve." The Journal of Thoracic and Cardiovascular Surgery 161, no. 5 (2021): 1742-1749.
22. Fard, Amir, Zahid Mahmood, Sukumaran Nair, Kasra Shaikhrezai, and Nawwar Al-Attar. "Analysis of incidence and reasons for re-intervention after aortic valve replacement using the Trifecta aortic bioprosthesis." Current Problems in Cardiology (2022): 101125.
23. Fukuhara, Shinichi, and Lise Tchouta. "Early Trifecta Failure Is More Evident After Propensity Matching: Reply." The Annals of Thoracic Surgery 110, no. 3 (2020): 1093-1094.
24. Fukuhara, Shinichi, Suzuna Shiomi, Bo Yang, Karen Kim, Steven F. Bolling, Jonathan Haft, Paul Tang et al. "Early structural valve degeneration of Trifecta bioprosthesis." The Annals of Thoracic Surgery 109, no. 3 (2020): 720-727.
25. Wakami, Tatsuto, Shigeki Koizumi, and Tadaaki Koyama. "Impact of postoperative patient-prosthesis mismatch as a risk factor for early structural valve deterioration after aortic valve replacement with Trifecta bioprosthesis." Journal of Cardiothoracic Surgery 17, no. 1 (2022): 1-8.
26. Biancari, Fausto, Antti Valtola, Tatu Juvonen, Annastiina Husso, Sebastian Dahlbacka, Teemu Laakso, Maina P. Jalava et al. "Trifecta versus perimount magna ease aortic valve prostheses." The Annals of thoracic surgery 110, no. 3 (2020): 879-888.
27. Werner, Paul, Iuliana Coti, Alexandra Kaider, Jasmin Gritsch, Markus Mach, Alfred Kocher, Guenther Laufer, and Martin Andreas. "Long-term durability after surgical aortic valve replacement with the Trifecta and the Intuity valve—a comparative analysis." European Journal of Cardio-Thoracic Surgery 61, no. 2 (2022): 416-424.
28. Lange, Rüdiger, Zahra Alalawi, Stephanie Voss, Johannes Boehm, Markus Krane, and Keti Vitanova. "Different rates of bioprosthetic aortic valve failure with Perimount™ and Trifecta™ bioprostheses." Frontiers in Cardiovascular Medicine 8 (2022): 2097.
29. Escalera, Alain, Isaac Pascual, Daniel Hernandez-Vaquero, Francesco Formica, Julio Casares, Rocio Diaz, Ruben Alvarez et al. "Association of the Surgical Technique With the Structural Valve Deterioration of a Bioprosthesis: A Prospective Cohort Study." In Seminars in Thoracic and Cardiovascular Surgery. WB Saunders, 2022.
30. Kattach, Hassan, Benoy N. Shah, Stephen Harden, Clifford W. Barlow, Szabolcs Miskolczi, Theodore Velissaris, and Sunil K. Ohri. "Premature structural failure of Trifecta bioprosthesis in midterm follow-up: a single-center study." The Annals of Thoracic Surgery 112, no. 5 (2021): 1424-1431.
31. Malvindi, Pietro Giorgio, Hassan Kattach, Suvitesh Luthra, and Sunil Ohri. "Modes of failure of Trifecta aortic valve prosthesis." Interactive CardioVascular and Thoracic Surgery 35, no. 2 (2022): ivac086.