# Inspire

## Your latest news on RESILIA tissue

Newsletter #5 – July 2023

Life$^{R}$

Life to the power of RESILIA

A promise of freedom. That's the power of RESILIA tissue.

Edwards

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**In this issue**



We hope you enjoy this issue of *Inspire*. Want to read more about the COMMENCE 7-year data? Visit **info@edwards.com/C7YA-EU or scan the QR code.**

FRONT COVER IMAGE:
ISTOCK.COM/DEJAN_DUNDJERSKI

# Introduction

We are delighted to announce that **200,000 patients** worldwide have now received an INSPIRIS RESILIA valve, making it the market-leading valve.

By choosing the INSPIRIS RESILIA valve, patients and their Heart Teams are helping to plan for the patients' future. This is particularly important for patients younger than 60 years, who tend to experience accelerated structural valve deterioration (SVD) due, in part, to calcification.[1,2] For them, bioprosthetic valve durability relative to life expectancy is a concern.[1]

The INSPIRIS RESILIA valve is an enhanced tissue valve designed with the future in mind, featuring:

- Edwards Integrity Preservation technology to minimise calcification[3,4]
- VFit technology* – fluoroscopically visible size markers and an expansion zone – to facilitate potential future valve-in-valve procedures[3]

Help your patients meet the future confidently with the INSPIRIS RESILIA valve.

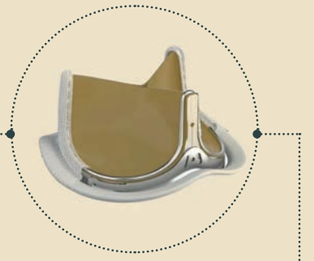
**INSPIRIS RESILIA valve is based on the trusted and proven design features on the Carpentier-Edwards PERIMOUNT and PERIMOUNT Magna Ease valves**

**Durability features**

Anti-calcification with residual aldehyde targeting that may allow valve to last longer†

**VFit technology with the exclusive expansion zone**

Technology designed to enable potential valve-in-valve procedures in the future*



**Based on the trusted PERIMOUNT platform**

Same leaflet design and wireform with enhanced RESILIA tissue

*Refer to device 'Instructions for Use' for important warnings related to VFit technology. These features have not been evaluated in clinical studies to establish the safety and effectiveness of the model 11500A for use in valve-in-valve procedures. VFit technology is available on sizes 19–25 mm.

†No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients

# RESILIA tissue demonstrates good durability in the longest follow-up to date

Beaver T *et al.* AATS Annual Meeting, 6–9 May 2023, Los Angeles, CA, USA.

As mentioned on page 2, tissue valve durability is of paramount importance as bioprosthetic aortic valve replacement (AVR) extends to younger patients.

COMMENCE is an FDA IDE trial, now in the post-approval phase, exploring the outcomes of AVR with bioprostheses using RESILIA tissue. The trial enrolled approximately 700 patients with up to 10 years' follow-up across 27 clinical sites in the USA and Europe.

Dr Beaver presented 7-year follow-up data from the COMMENCE trial at the recent American Association for Thoracic Surgery (AATS) meeting. As the follow-up time in this study advances beyond the mid-term period, direct and indirect measures of RESILIA tissue valve safety and efficacy will be highlighted.[5]

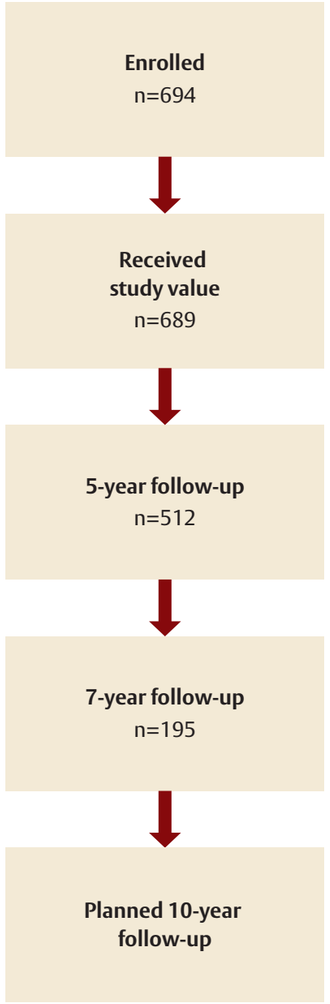
Of the 512 patients who completed the 5-year follow-up, 225 reconsented for extended follow up, with a mean (± standard deviation [SD]) age of 65.1 ± 10.9 years and a mean STS risk score of 2.1 ± 2.1%. A total of 195 patients completed the 7-year follow-up.

All safety endpoints were adjudicated by an independent clinical events committee and were as defined by Akins *et al*.[6]

Haemodynamic performance was evaluated by an independent echocardiographic core laboratory.[5]

**Patient demographics**

| | Full cohort | 7-year re-consented cohort |
|---|---|---|
| **Mean age** | 66.9 ± 11.6 years | 65.1 ± 10.9 years |
| **NYHA II and III** | 50% and 24% respectively | 43% and 19% respectively |
| **Male** | 71.8% | 76.9% |






These 7-year results from the COMMENCE aortic trial indicate a favourable safety profile and strong haemodynamic performance for a bioprosthetic valve with RESILIA tissue.

The 7-year data from the COMMENCE aortic trial represents the longest follow-up after AVR with RESILIA tissue in a large IDE trial utilising an independent clinical events committee and an echocardiography core laboratory. Ongoing follow up out to 10 years will continue to evaluate the long-term safety and effectiveness of this bioprosthetic valve with RESILIA tissue.

**Safety outcomes at 7 years**

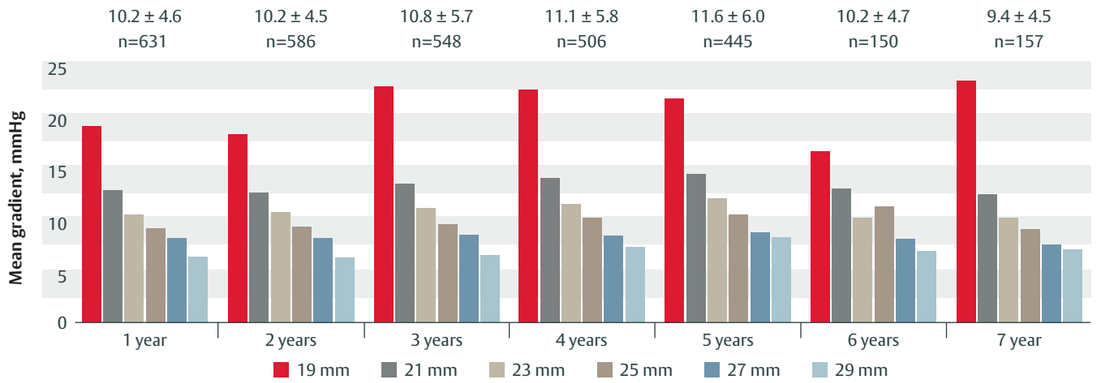
**85.4%**
Freedom from all-cause mortality
(95% CI 82.2–88.7%)

**99.3%**
Freedom from SVD
(95% CI 98.3–100.0%)

**97.2%**
Freedom from reoperation
(95% CI 95.5–99.0%)

**99.5%**
Freedom from major paravalvular regurgitation
(95% CI 99.0–100.0%)

**Haemodynamic performance remained stable over 7 years – echo-derived mean gradients**



# Investigator perspective on the COMMENCE Trial 7-year data

Dr Joseph Bavaria is co-director of the Penn Aorta Center at the University of Pennsylvania and, throughout his career, has completed more than 7,000 valve procedures. Dr Bavaria has worked for nearly 20 years to advance the field of bicuspid aortic valve repair and is a significant participant in the COMMENCE trial.

Professor Michael Borger is the Director of the University Clinic for Cardiac Surgery at the Leipzig Heart Center – one of the largest cardiac centres in Europe. Prof. Borger's interests include surgical management of aortic valve disease, and he is an investigator on the COMMENCE trial.

At the recent AATS meeting, we caught up with Dr Bavaria and Prof. Borger to discuss the recent data from the COMMENCE trial.

**Q. Could you remind us what COMMENCE is about?**

**A.** [*Joseph Bavaria*] The COMMENCE trial is a standard FDA IDE trial carried out in centres across the USA and Canada. It is the largest and most expansive trial looking at RESILIA technology to date with 696 patients recruited, including approximately 250 with bicuspid aortic valves (BAVs).

The trial started in 2013 and recruited until 2016, with the 7-year follow-up data just released.

**Q. Could you tell us more about the specific study population – were they traditional patients?**

**A.** [*Michael Borger*] The COMMENCE trial is different to most bioprosthetic AVR studies, not only because of the unique tissue treatment platform, but also because the patients are being followed up carefully with a standard echocardiographic protocol.

Importantly, the patient population age is lower than that of most bioprosthetic aortic valve studies, with a mean age of just under 67 years. Indeed, for the 7-year data, the average age is just 65 years. For the subset of patients with BAVs, the mean age is even younger, at around 57 years of age. The younger the patients, the earlier their bioprostheses tend to fail, which is why the COMMENCE data for patients with BAVs are so interesting.

This is probably the lowest average age for a surgical trial in 25 years, with the choice of valve decided by the clinician along with patient preference. This reflects the reality that bioprosthetic valves are increasingly being requested by younger patients. This also illustrates the trust that clinicians have in this new valve platform, based on the well-known Carpentier-Edwards PERIMOUNT Magna Ease valve, together with RESILIA preservation technology that has demonstrated better anti-calcification in preclinical studies than anything we have seen before.

It is noteworthy that concomitant procedures were allowed in this trial. Despite this, we had excellent perioperative outcomes and long-term survival – 85.4% at 7 years.

**Q. We are here to discuss the 7-year results, but could you briefly comment on the 5-year data?**

**A.** [*JB*] The recently published 5-year data were spectacular, probably the best data that have ever been published on any tissue valve, with no SVD in a group of patients with an average age of 66.9 years and an STS score of 2.3%. This is a powerful study and we are very pleased with the data.

**Q. We would like to get your clinical opinion on the COMMENCE 7-year data – what were the most remarkable data presented?**

**A.** [*JB/MB*] The most striking thing about the 7-year data is that there were only two cases of SVD in the entire data set of over 200 patients, ([*MB*] which translates to a Kaplan–Meier freedom from SVD of 99.3%). These are outstanding data in a very well-monitored and tight clinical trial.

[*MB*] Additionally, mean gradient and effective orifice area (EOA) haven't changed, which is reassuring for the long-term haemodynamic performance of this valve.

[*JB*] Again, it is important to consider that the age of the patient population was just 65 years – these are the kind of data that will end up impacting treatment guidelines.

Even rates of intravalvular leak were very low, which is important as this is the first marker for SVD.

**Q. Could you expand on your comment about guidelines?**

**A.** [*JB*] From the perspective of the American Heart Association/American College of Cardiology, there was strong evidence to guide recommendations for patients under the age of 50 year and over the age of 65 years, but there was a grey area between the ages of 50 to 65. I think that data like these coming from the COMMENCE trial over the next decade will provide evidential support to push that grey area more towards tissue valves in these patients.

[*MB*] For guidelines, we need high-quality data, which we are getting from the COMMENCE trial – we have a patient population where we would expect a higher incidence of SVD and we have an adjudicated core echo laboratory closely monitoring echocardiographic findings, so this will inform guidelines.

Of course, this is not a randomised trial, but it certainly reflects the reality that we see on a daily basis.

**Q. What do you think these data are telling us in terms of both guidelines and lifetime management?**

**A.** [*MB*] The COMMENCE data will inform us on lifetime management in two important ways; the first, is that we are seeing very low rates of paravalvular leak (PVL; 0.7%), which is much lower than we are currently seeing with transcatheter aortic valve replacement (TAVR).

Secondly, there are many different lifetime management options for younger patients who do not want a mechanical valve, including SAVR and then valve-in-valve. There is even a suggestion to do TAVR first and then SAVR – but the mortality rates for this option are double what you would normally expect for this patient population.[10,11] These data, combined with the excellent COMMENCE data, are likely to result in more clinicians favouring SAVR with a RESILIA tissue valve as the index procedure in younger patients.

[*JB*] Importantly, a lot of 25–29 mm valves were implanted in the COMMENCE trial. This will have a significant impact on lifetime management as it will allow a larger valve-in-valve bioprosthesis to be implanted in the future – with no PVL. It's striking that any PVL seen (2.5%) was mild, with no moderate or severe leak.

**Q. Are you looking forward to seeing the 10-year results?**

**A.** [*JB*] The 10-year data will be interesting as, historically, with most bioprostheses, SVD increases around the 7–8-year mark, but so far we have seen very good results at 5 and 7 years – probably better than any other FDA IDE trial.

**Q. What is the role of the cardiac surgeon in getting access to new innovations?**

**A.** [*JB*] From a cardiac surgery perspective, access to innovations is incredibly important – cardiac surgery is a very device-specific and innovation-dependent field and we need cardiac surgeons to be involved in clinical trials.

[*MB*] Not all innovations are the same – the innovative technology we are seeing with the COMMENCE trial is based on a previously proven platform, from a company that has been an expert in the field for 50 years. This is different to a completely new design or approach and will undoubtedly lead to better long-term outcomes for our patients.

# Encouraging results on the durability of RESILIA tissue valves at 5 years *versus* contemporary tissue valves

Bartus K *et al. J Comp Eff Res.* 2023; 12: e220180.

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| Why is this study interesting?[7] | What are the study limitations?[7] |
|---|---|
| Propensity score matched analysis with variables selected based on published literature | The COMMENCE and PARTNER IIA trials were conducted independently and not designed to be compared. After propensity score-matching some significant differences remained |
| Comparison of RESILIA tissue valves in a modern cohort of SAVR patients whose valve composition represents a strong set of bioprostheses comprising 82% Edwards valves | As data become available beyond 5 years, future analyses will be needed to confirm the findings of this study |
| VARC-3 definition of HVD | Some other components of valve failure are not captured by SVD-related HVD |

From a propensity score-matched analysis after **5 years** follow-up:

Significantly lower **SVD-related haemodynamic valve deterioration** (HVD) for RESILIA tissue valves than contemporary valves.[7]

Bartus *et al*. compared 5-year SVD-related HVD between the COMMENCE trial and the surgical AVR (SAVR) arm of the PARTNER II, cohort A trial.[6] The SAVR arm of the PARTNER IIA trial is a modern contemporary cohort of patients undergoing SAVR, with the Carpentier-Edwards PERIMOUNT, Magna and Magna Ease valves comprising over 80% of the valves used in this cohort.[7]

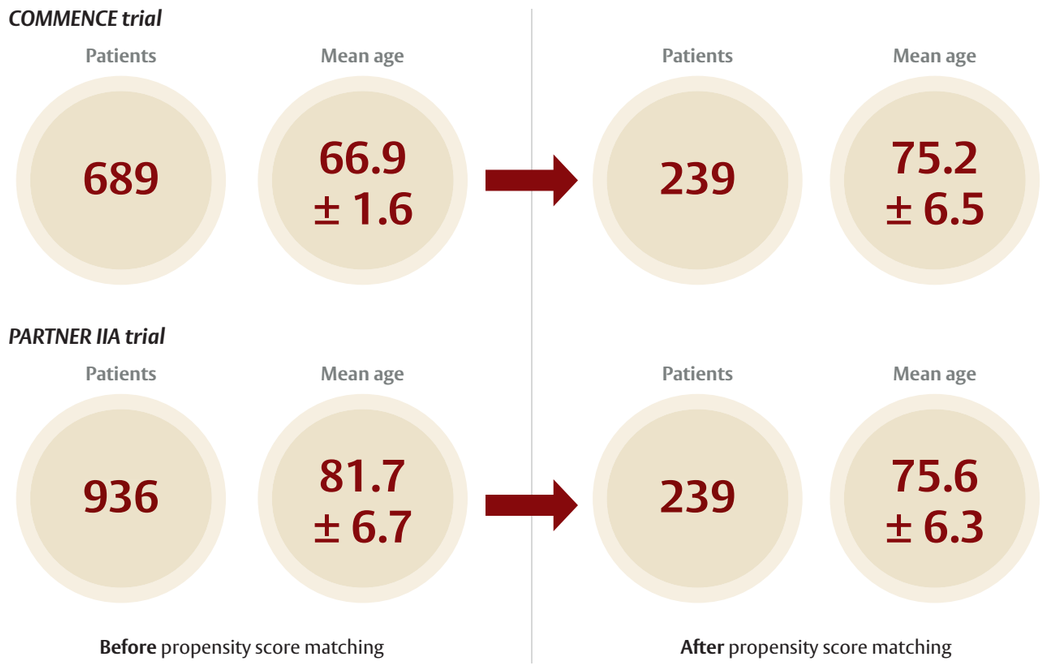
Propensity score matching was used to identify a meaningful number of patients matched to multiple baseline characteristics reported to impact structural valve deterioration, with 239 propensity score-matched pairs used in the analysis. The primary outcome was SVD-related HVD stage ≥2, as defined using Valve Academic Research Consortium-3 (VARC-3) guidelines:

- Increase in mean gradient **≥10 mmHg** + Final mean gradient **≥20 mmHg**.[7]

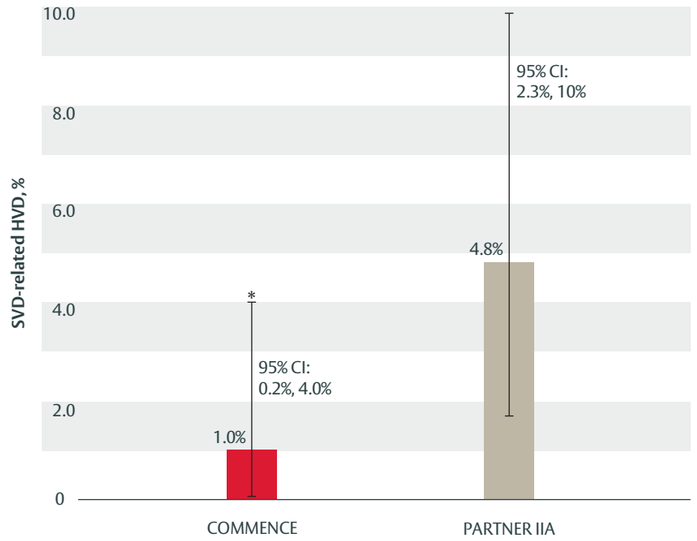
**These results are encouraging for the durability of RESILIA-tissue heart valves. Although, broader and longer-term data are needed, this is a signal for enhanced durability compared to other commercially available valves**



**Patient characteristics**




**After propensity-score matching, SVD-related HVD was significantly lower in the COMMENCE sub-cohort than the PARTNER IIA SAVR sub-cohort.**




*Lower-bound HR: 1.15, p=0.03.
Error bars represent 95% CI.

*The RESILIA tissue valve demonstrated significantly reduced SVD-related HVD compared with contemporary bioprostheses in this analysis.*

# Favourable mid-term results for the INSPIRIS RESILIA valve in Japanese patients

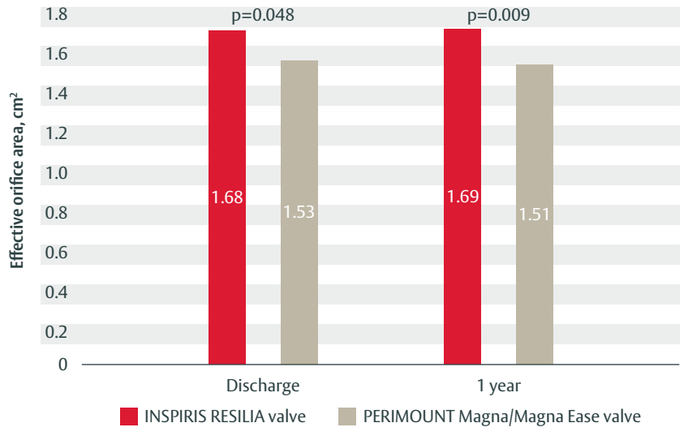
Maeda K *et al. J Cardiol*. 2023; doi: 10.1016/j.jjcc.2023.05.012.

The INSPIRIS RESILIA valve is one of the main bioprosthetic valves used for SAVR in Japan, but few studies have reported the valve's mid-term safety and efficacy in Japanese patients.

However, recently published data from Koichi Maeda, at Osaka University Graduate School of Medicine, and colleagues shows that the INSPIRIS RESILIA valve has comparable mid-term haemodynamics to earlier generation valves from the Carpentier-Edwards PERIMOUNT valve family.

The team evaluated early and mid-term results from 66 patients (mean age 74 years) who underwent isolated SAVR with the INSPIRIS RESILIA valve at five cardiovascular centres in Japan. In hospital mortality was 1.5%, and freedom from all-cause mortality was 95.2% at 1 year, remaining unchanged to 3 years. No SVD was noted during follow-up (mean 640 days).

The patients were propensity score-matched with patients who underwent the same procedure with the PERIMOUNT Magna or Magna Ease valves, and valve haemodynamics were compared. While no significant differences in peak velocity or mean gradient were observed at discharge, EOA was significantly larger in patients with an INSPIRIS RESILIA valve than in those with a PERIMOUNT Magna or Magna Ease valve (1.68 ± 0.38 $cm^2$ *vs* 1.53 ± 0.41 $cm^2$, p=0.048). In addition, patient–prosthesis mismatch (PPM) at discharge was significantly lower in the INSPIRIS RESILIA valve group (11.8% *vs* 36.4%, p=0.004). The differences in EOA and PPM remained significant at 1-year follow-up.






# Hot off the press

Francica A *et al. J Clin Med.* 2023; **12:** 2077.

In *Inspire* issue 3 last year, we reported data from a propensity-matched analysis of the INSPIRIS RESILIA valve and the PERIMOUNT Magna Ease valve, as presented by Alessandra Francica at EACTS 2022. We are delighted to see the full study has now been reported in the *Journal of Clinical Medicine.*

As a reminder, the mid-term efficacy of the INSPIRIS RESILIA valve in patients younger than 70 years was comparable to that of the PERIMOUNT Magna Ease valve.

Propensity score matched analysis of 122 pairs showed no significant differences between the valves:

**Peri-procedural data:**

| Magna Ease | | INSPIRIS RESILIA |
|---|---|---|
| 0.0% | **Periprocedural mortality** | 0.0% |
| 0.8% | **Stroke** | 0.8% |
| 3.3% | **Definitive pacemaker** | 1.6% |
| 2.0% | **Surgical revision for bleeding** | 0.8% |

- Mean gradient of **12.8 ± 5.2** mmHg at 3 years for INSPIRIS RESILIA and **12.2 ± 7.9** mmHg for Magna Ease
- Steady **left ventricular reverse remodelling** over time seen in both groups
- **0% SVD** for INSPIRIS RESILIA and **3.3% SVD** for Magna Ease at 3 years

In patients aged < 70 years, this safety and efficacy outcomes of the INSPIRIS RESILIA valve were comparable to the excellent outcomes in the established Magna Ease valve.

## References:


1. Bourguignon T, Bouquiaux-Stablo AL, Candolfi P *et al*. Very long-term outcomes of the Carpentier-Edwards PERIMOUNT valve in aortic position. *Ann Thorac Surg.* 2015; **99:** 831–7.

2. Xue Y, Kossar AP, Abramov A *et al*. Age-related enhanced degeneration of bioprosthetic valves due to leaflet calcification, tissue crosslinking, and structural changes. *Cardiovasc Res.* 2023; **119:** 302–15.

3. Edwards Lifesciences. INSPIRIS RESILIA Aortic Valve. Instructions for Use.

4. Tod TJ and Dove JS. The association of bound aldehyde content with bioprosthetic tissue calcification. *J Mater Sci Mater Med.* 2016; **27:** 8.

5. Beaver T, Bavaria JE, Griffith B *et al*. Seven-year outcomes following aortic valve replacement with a novel tissue bioprosthesis. AATS Annual Meeting, 6–9 May 2023, Los Angeles, CA, USA.

6. Akins CW, Miller DC, Turina MI *et al*. Guidelines for reporting mortality and morbidity after cardiac valve interventions. *J Thorac Cardiovasc Surg*. 2008; **135:** 732–8.

7. Bartus K, Bavaria JE, Thourani VH *et al*. Structural hemodynamic valve deterioration durability of RESILIA-tissue versus contemporary aortic bioprostheses. *J Comp Eff Res*. 2023; **12:** e220180.

8. Maeda K, Shimamura K, Yoshioka D *et al*. Midterm outcomes after surgical aortic valve replacement with the INSPIRIS RESILIA from a multicenter AVR registry. *J Cardiol*. 2023; doi:10.1016/j.jjcc.2023.05.012.

9. Francica A, Tonelli F, Rossetti C *et al*. PERIMOUNT MAGNA Ease vs. INSPIRIS RESILIA valve: A PS-matched analysis of the hemodynamic performances in patients below 70 years of age. *J Clin Med*. 2023; **12:** 2077.

10. Hawkins RB, Deeb GM, Sukul D *et al*. Redo surgical aortic valve replacement after prior transcatheter versus surgical aortic valve replacement. *JACC Cardiovasc Interv*. 2023; **16:** 942–53.

11. Tang GHL, Zaid S, Kleiman NS *et al*. Explant vs redo-TAVR after transcatheter valve failure: Mid-term outcomes from the EXPLANTORREDO-TAVR international registry. *JACC Cardiovasc Interv*. 2023; **16:** 927–41.


**Important safety information:**

**No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients. Based on bench data. Refer to device Instructions for Use for important warnings related to VFit technology. These features have not been evaluated in clinical studies to establish the safety and effectiveness of the model 11500A for use in valve-in-valve procedures. VFit technology is available on sizes 19–25 mm.**

**Medical device for professional use. For a listing of indications, contraindications, precautions, warnings, and potential adverse events, please refer to the Instructions for Use (consult eifu.edwards.com where applicable).**

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