RESILIENCE Study Design Clinical Summary:

Study Design of the Prospective Non-Randomized Single Arm Multicenter Evaluation of the Durability of Aortic Bioprosthetic Valves with RESILIA Tissue in Subjects under 65 Years Old (RESILIENCE Trial)

Pibarot P., et al., Structural Heart 2020. DOI: 10.1080/24748706.2019.1686554

Inspiring Results

Objective

To determine the time to valve failure due to valve deterioration requiring re-intervention, as well as to collect/investigate early potential predictors of valve durability (e.g. calcification and hemodynamic deterioration) in RESILIA aortic tissue valves.

Key Points

- The RESILIENCE trial is the first prospective study to associate both clinical and imaging definitions of SVD with long-term (11 years) bioprosthetic valve durability
- The primary outcome is the occurrence of valve re-intervention or death related to SVD for RESILIA tissue valves for patients <65 years of age
- The secondary outcomes are the volume of valve leaflet calcification measured by CT and the occurrence of hemodynamic SVD measured by TTE

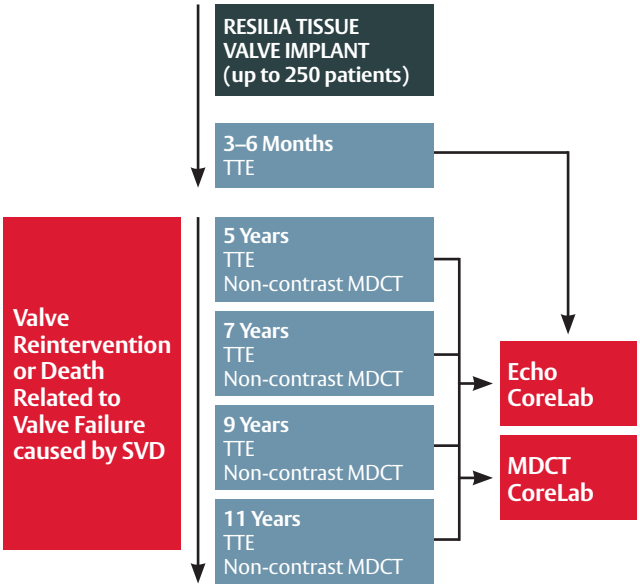
Methods

- Multicenter, prospective, non-randomized, single-arm, observational trial
- Up to 250 patients who previously underwent SAVR with a RESILIA tissue valve will be enrolled at up to 15 investigational centers across the United States and Europe
  - Includes patients <65 years old; this is a population that is at high risk to develop SVD
  - First patient enrolled on November 21, 2018
  - Anticipated 3 year enrollment period
- Patients undergo a TTE and non-contrast CT at 5, 7, 9, and 11 years post-valve implant (Figure 1)
- The definition proposed by Dvir et al. includes four stages: Stage 0: no SVD; Stage 1: Morphological SVD; Stage 2: Moderate hemodynamic SVD; and Stage 3: Severe hemodynamic SVD (Table 1)

Results

- Echocardiography and CT Core Laboratories will be responsible for independently evaluating TTEs and CTs submitted by trial sites and will report upon the primary and secondary outcomes of the trial
- The morphology and mobility of the bioprosthetic valve leaflets will be visually assessed in multiple views by 2D echocardiography
- Non-contrast CT images will be acquired using a 64 slice or dual-source scanner
  - Valve leaflet calcification will be measured by the volumetric method that identifies calcium within the valve leaflets
  - The total volume of calcification over the 3 valve leaflets will be calculated and expressed in mm^3

Figure 1. Study flow chart. CT: computed tomography; TTE: transthoracic echocardiography.



Trial limitations

- A limitation of this trial is that there is no comparative arm with non-RESILIA tissue valves

Conclusion

The RESILIENCE trial is the first prospective study that uses both clinical and imaging definitions of SVD to provide a comprehensive description of all stages of SVD and determine the long-term durability of the RESILIA tissue in a aortic valve.

Edwards

Table 1. Primary and Secondary Outcomes of the RESILIENCE trial.

Trial Outcomes	Definition
Secondary outcome: Valve leaflet calcification by non-contrast CT	
	Volume of valve leaflet calcification (in mm^3) Percentage of patients with detectable calcification
Secondary outcome: Hemodynamic valve deterioration by TTE	
Stage 1 Morphological SVD	Morphological abnormalities of bioprosthetic valve leaflets (leaflet thickening, fibro-calcific remodeling, restricted opening) compatible with SVD with absence of HVD.
Stage 2 Moderate hemodynamic SVD	Morphological abnormalities of bioprosthetic valve leaflets (leaflet thickening, fibro-calcific remodeling, restricted opening, tear, perforation) compatible with SVD with moderate valve hemodynamic deterioration from baseline (3–6 months post-implant), defined as an increase in mean gradient ≥10 mmHg with concomitant decrease in valve EOA of >0.3 cm^2 or at least 1 grade new onset or worsening of trans-prosthetic regurgitation with final grade of moderate regurgitation.
Stage 3 Severe hemodynamic SVD	Morphological abnormalities of bioprosthetic valve leaflets (leaflet thickening, fibro-calcific remodeling, restricted opening, tear, perforation) compatible with SVD with severe valve hemodynamic deterioration from baseline (3–6 months post-implant), defined as an increase in mean gradient ≥20 mmHg with concomitant decrease in valve EOA of >0.6 cm^2 or at least 2 grades new onset or worsening of trans-prosthetic regurgitation with final grade of severe regurgitation.
Primary outcome: Valve failure due to SVD	
	Valve re-intervention or confirmed study valve-related death

Notes. HVD, hemodynamic valve deterioration; SVD, structural valve deterioration.

Edwards Lifesciences • One Edwards Way, Irvine CA 92614 USA • edwards.com

Edwards