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ORIGINAL RESEARCH

Thirty-day outcomes of a novel biomimetic balloon-expandable transcatheter heart valve in patients with small aortic annuli

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ABSTRACT

BACKGROUND: Transcatheter aortic valve implantation (TAVI) in patients with small aortic annuli (SAA) is associated with an increased risk of prosthesis-patient mismatch (PPM).

AIMS: This study assesses the 30-day performance of the novel, balloon-expandable DurAVR transcatheter heart valve (THV), which features a unique single-piece biomimetic leaflet design, in patients with SAA.

METHODS: This pooled analysis derived from first-in-human and early feasibility studies includes all patients with SAA (defined as an aortic annular area from 346 to 452 mm²) treated with the Small size DurAVR THV. The mean computed tomography (CT)-derived aortic annulus area was 404 ± 37 mm², with an average diameter of 22.7 ± 1.0 mm. Outcomes at 30 days, including PPM, were evaluated per Valve Academic Research Consortium-3 (VARC-3) criteria, with independent adjudication of clinical events and core laboratory analysis of post-implant transthoracic echocardiograms.

RESULTS: Amongst 100 patients (mean age 77.0 ± 7.3 years; 78% female; mean Society of Thoracic Surgeons [STS] score 4.7 ± 4.0%) treated with the DurAVR THV, the overall technical success rate was 93%. At 30 days, device success was achieved in 91% of patients, with no reported deaths and a stroke rate of 2%. Echocardiographic haemodynamic assessment showed a mean transprosthetic gradient of 8.2 ± 3.1 mmHg, a mean effective orifice area of 2.2 ± 0.3 cm², and a doppler velocity index of 0.60 ± 0.10. The incidence of moderate or greater PPM was 3%, and no patients experienced more than mild paravalvular leak. The rate of new permanent pacemaker implantation was 6%.

CONCLUSIONS: In patients with SAA, the DurAVR THV demonstrated promising clinical and echocardiographic outcomes at 30 days. Longer-term follow-up in larger cohorts is needed to confirm these encouraging early results.

KEYWORDS: Transcatheter aortic valve, small annulus, biomimetic leaflets, early outcomes

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Short title: Biomimetic Balloon-expandable Transcatheter heart valve in small aortic annuli

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Keywords: Transcatheter aortic valve, small annulus, biomimetic leaflets, early outcomes

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STRUCTURED ABSTRACT

Background. Transcatheter aortic valve implantation (TAVI) in patients with small aortic annuli (SAA) is associated with an increased risk of prosthesis-patient mismatch (PPM).

Aims. This study assesses the 30-day performance of the novel, balloon-expandable DurAVR transcatheter heart valve (THV), which features a unique single-piece biomimetic leaflet design, in patients with SAA.

Methods. This pooled analysis derived from first-in-human and early feasibility studies includes all patients with SAA (defined as an aortic annular area from 346 to 452 mm^2) treated with the Small size DurAVR THV. The mean computed tomography (CT)-derived aortic annulus area was 404 ± 37 mm^2, with an average diameter of 22.7 ± 1.0 mm. Outcomes at 30 days, including PPM, were evaluated per Valve Academic Research Consortium-3 (VARC-3) criteria, with independent adjudication of clinical events and core laboratory analysis of post-implant transthoracic echocardiograms.

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Conclusions. In patients with SAA, the DurAVR THV demonstrated promising clinical and echocardiographic outcomes at 30 days. Longer-term follow-up in larger cohorts is needed to confirm these encouraging early results.

Abbreviations

AVA	aortic valve area
BMI	body mass index
BVF	bioprosthetic valve failure
CT	computed tomography
DVI	Doppler velocity index
EFS	early feasibility study
EOA	effective orifice area
KCCQ	Kansas City cardiomyopathy questionnaire
NYHA	New York Health Association
PPM	prosthesis-patient mismatch
SAA	small aortic annulus
TAV	transcatheter aortic valve
TAVI	transcatheter aortic valve implantation
TEE	transesophageal echocardiography
THV	transcatheter heart valve
TTE	transthoracic echocardiography

INTRODUCTION

As transcatheter aortic valve implantation (TAVI) increasingly extends to younger patients with longer life expectancies, factors such as hemodynamic valve performance, valve durability, and the feasibility for re-intervention becomes even more critical [1]. Patients with small aortic annuli (SAA) undergoing TAVI often encounter suboptimal results, including elevated transprosthetic gradients, increased prosthesis-patient mismatch (PPM), and early bioprosthetic valve failure (BVF) [2–5]. These outcomes can be influenced by the design of the transcatheter aortic valve (TAV), particularly differences in leaflet position, whether supra-annular or intra-annular, and leaflet design. However, existing data on this topic remain conflicting [5–11].

The DurAVR Transcatheter Heart Valve (THV, Anteris Technologies, MN, USA) is a novel, balloon-expandable valve featuring a unique, first-of-its-kind single-piece biomimetic leaflet design. Early experience from first-in-human and early feasibility studies have demonstrated promising results [12]. In this study, we report the procedural and 30-day clinical and haemodynamic outcomes for patients with SAA who underwent TAVI with the DurAVR THV.

METHODS

Study cohort

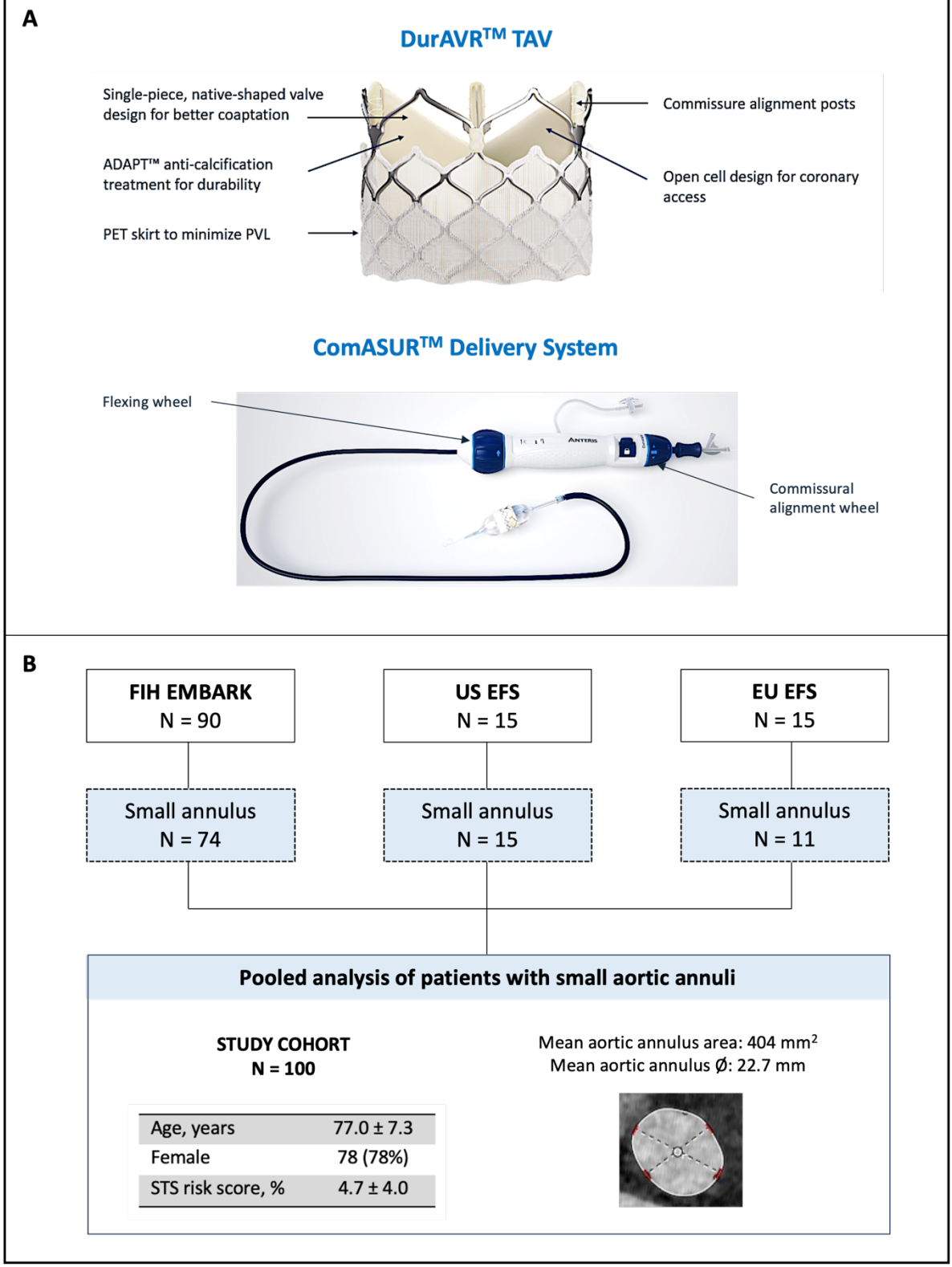
All patients with severe aortic stenosis and a small aortic annulus (SAA), defined as a computed tomography (CT) based aortic annular area of 346-452 mm^2, who participated in the DurAVR First-in-Human Study (EMBARK, NCT05182307), United States Early Feasibility Study (US-EFS, NCT05712161) and European Early Feasibility Study (EU-EFS, NTC06510855), were pooled together to constitute the study population for this analysis. The EMBARK First-in-Human study was a prospective, single-arm, single-center study enrolling 90 patients from November 2021 to May 2025. The US-EFS was a prospective, single-arm study enrolling 15 patients across four sites between August and October 2023. The EU-EFS was a prospective, single-arm study enrolling 15 patients at a single-center between January and June 2025. The study protocols were approved by national regulatory authorities and the institutional ethical committees at the participating sites, and informed consent was obtained from all patients. Inclusion and exclusion criteria are detailed in **Supplementary Table 1**.

Device description

The DurAVR THV features a balloon-expandable stent frame encompassing a single-piece of bovine pericardial tissue molded into a tri-leaflet configuration to mimic native aortic valve geometry **(Figure 1)**. The bovine pericardium is treated with a proprietary ADAPT anti-calcification tissue engineering process, developed to reduce the antigens responsible for inflammation and calcification [13]. This process enhances leaflet elasticity and strength, resulting in a valve performance comparable to healthy native leaflets [14]. The DurAVR stent frame consists of a top row of large open cells for ease of coronary access, radiopaque markers to facilitate valve positioning and commissural alignment and a polyethylene terephthalate (PET) skirt to minimize paravalvular leak (PVL). The DurAVR THV is

crimped onto a balloon-expandable catheter and delivered via the transfemoral ComASUR Delivery System. The system comprises a flexible steering catheter and a commissural wheel that enables 1:1 rotational torque, facilitating patient-specific commissural alignment.

Figure 1. DurAVR™ TAV and study cohort



Implant procedure

Patient eligibility for DurAVR THV implantation was determined by the respective Heart Teams at each site and the study screening committees. All patients received a DurAVR THV Small valve, suitable for treatment of native aortic annuli with an area-derived diameter of 21 to 24 mm and aortic annulus area of 346 to 452 mm^2. The valve was deployed under fluoroscopic guidance during rapid pacing. Post-deployment assessments included stent frame expansion by fluoroscopy, hemodynamic function, and detection of aortic regurgitation. The overall procedural approach, including decisions regarding pre- or post-dilatation, use of cerebral embolic protection devices, vascular access closure methods, and post-procedural anti-platelet or anti-thrombotic therapy, were left to the discretion of the operator.

Data collection

Prospective data on baseline demographics, procedural details, and 30-day follow-up results were collected. An independent clinical event committee verified all events in the EFS studies, while independent physician adjudication was performed for the EMBARK study. Symptoms and quality of life were assessed at baseline and 30 days post-procedure using the New York Heart Association (NYHA) classification and the Kansas City Cardiomyopathy Questionnaire (KCCQ).

Transthoracic echocardiography (TTE) was performed at baseline and 30 days after the procedure, with images analysed by dedicated core laboratories for the EMBARK (Acudoc Swedish Echo Core Lab, Acudoc Clinical Physiology Laboratories, Stockholm, Sweden) and US-EFS and EU-EFS cohorts (Cardiovascular Research Foundation, New York, USA). Aortic stenosis severity was determined using mean gradient, peak velocity, and aortic valve area (AVA). Post-procedure valve hemodynamics included measurements of transprosthetic gradient, effective orifice area (EOA), and doppler velocity index (DVI). Prosthesis-patient mismatch (PPM) severity was classified according to Valve Academic Research Consortium (VARC)-3 criteria: in patients with a body mass index (BMI) <30 kg/m^2, moderate PPM was defined as an indexed EOA of 0.66 - 0.85 cm^2/m^2 and severe PPM was defined as ≤ 0.65

cm^2/m^2; in patients with a BMI ≥30 kg/m^2, moderate PPM was defined as an indexed EOA of 0.56 - 0.70 cm^2/m^2 and severe PPM was defined as ≤ 0.55 cm^2/m^2 [15]. Prosthetic aortic valve regurgitation (central and paravalvular) was graded per VARC-3 classification: none/trace, mild, moderate, or severe.

Study endpoints

All study endpoints were reported in accordance with VARC-3 criteria [15]. Technical success, assessed immediately upon exiting the procedure room, was defined as: the absence of mortality, successful vascular access, proper delivery and deployment of the device, retrieval of the delivery system, correct positioning of a single prosthetic valve into the proper anatomical location, and absence of surgical or other interventions related to the device or major vascular, access-related, or cardiac structural complications. Safety endpoints were reported as per VARC-3 criteria. Clinical efficacy at 30 days was defined as the absence of all-cause mortality, stroke, hospitalization related to the procedure or valve, and less than 10 points decline in the overall KCCQ score from baseline, nor worsening NYHA class.

Statistical analysis

Patient demographics, device performance, risk factors, and clinical outcomes were summarized using descriptive statistics. Continuous variables are expressed as means with standard deviations, while categorical variables are presented as counts and proportions. All analysis were performed using SPSS version 30 (IBM, USA).

RESULTS

Baseline characteristics

A total of 100 patients with SAA, derived from the EMBARK (n=74), US-EFS (n=15), and EU-EFS (n=11) cohorts, were included for analysis. Baseline characteristics are summarized in **Table 1**, with individual cohort details available in **Supplementary Table 2**. The mean age was 77.0 ± 7.3 years, 78% were female and the overall mean Society of Thoracic Surgeons (STS) risk score was 4.7% ± 4.0%. 91% of patients had a tricuspid aortic valve and 9% had a type 1 bicuspid aortic valve phenotype (8 patients with left-right fusion and one patient with non-right fusion). The CT-based mean aortic annulus area was 404 ± 37 mm^2, with an average annulus diameter of 22.7 ± 1.0 mm. Baseline mean aortic valve gradients were 48.1 ± 17.0 mmHg and left ventricular ejection fraction (LVEF) was 58%.

Procedural outcomes

Procedural data and outcomes are summarized in **Table 2** and **Supplementary Table 3**. In the initial EMBARK study, most procedures (69%) were performed under general anaesthesia with transesophageal echocardiography (TEE) guidance. In contrast, in the more recent EU-EFS study a minimalist approach using local anaesthesia and sedation was successfully adopted in 100% of procedures. Transfemoral access route was utilised for 94% of cases while transaortic and transcarotid access routes were used in 5% and 1% of cases, respectively. Pre-dilatation was performed in 57% of procedures, while post-dilatation was noted in 8% of procedures.

The overall VARC-3 defined technical success rate was 93%. Peri-procedural complications were only encountered in the first-in-human EMBARK cohort, reflecting early device and operator experience **(Supplementary Table 4)**. Subsequent refinements to the valve design, compliance of the inflation balloon, delivery system and expandable sheath profile were implemented. In the last 50 consecutive

implants, including the US-EFS and EU-EFS cohorts, no major peri-procedural complications occurred, reflecting a technical success rate of 100% **(Table 2).**

Thirty-day clinical outcomes

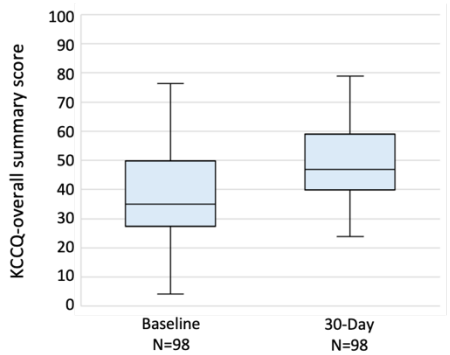
Complete 30-day follow-up was achieved in all patients. **(Figure 2)** There were no deaths, and two patients experienced a stroke. Major vascular complications and bleeding (type 2-4) occurred in 5% and 7% of patients, respectively. Notably, none of these complications were observed in the US/EU-EFS cohorts. The overall rate of new permanent pacemaker implantation was 6%. Patients showed marked symptomatic improvement, with the KCCQ score increasing by 12 points from baseline. Additionally, 70% of patients reported an improvement in NYHA classification as early as 30 days.

Figure 2. 30-day clinical outcomes

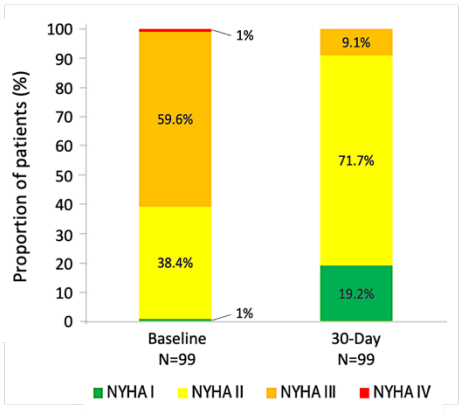
Early safety – at 30 days (VARC-3)	
All-cause mortality	0
Stroke	2/100 (2%)
Disabling stroke	2/100 (2%)
Non-disabling stroke	0
Myocardial Infarction	0
Vascular complication	
Minor	6/100 (6%)
Major	5/100 (5%)
Bleeding, type 2-4	7/100 (7%)
Acute kidney injury, stage 3-4	0
Permanent pacemaker implantation	6/100 (6%)
Surgery or intervention related to the device	0

Clinical efficacy – at 30 days (VARC-3)§	
Freedom from all-cause mortality	100/100 (100%)
Freedom from stroke	98/100 (98%)
Freedom from procedure- or valve-related hospitalization	96/100 (96%)
Freedom from KCCQ overall summary score decline from baseline of > 10 points or worsening NYHA class	94/98 (96%)

KCCQ score



NYHA class



Valve performance

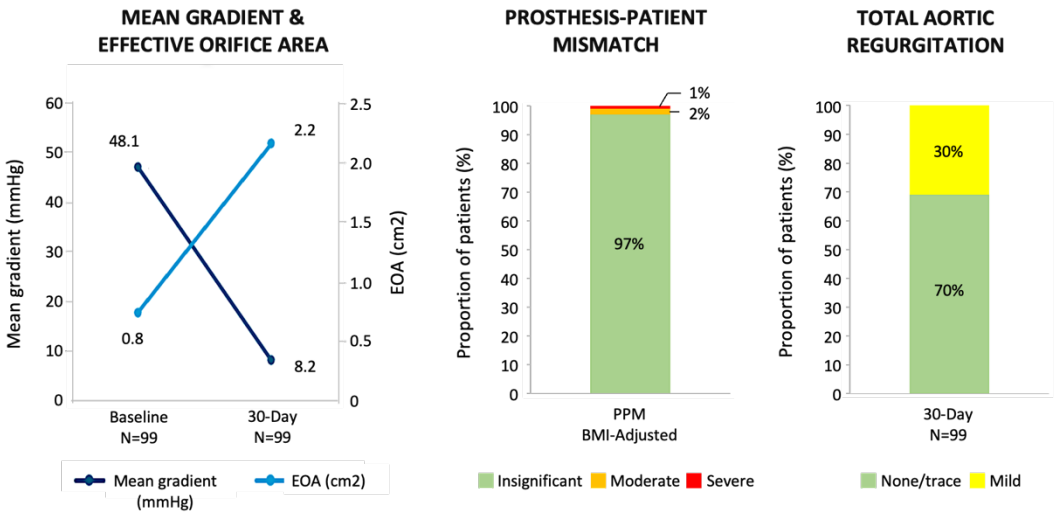
Device success per VARC-3 criteria was achieved in 91% of patients. **(Figure 3)** One patient developed a late external iliac artery thrombosis requiring vascular intervention and one other patient exhibited a residual mean transprosthetic gradient > 20 mmHg, attributed to leaflet thrombosis detected on

post-TAVI CT imaging. At 30 days, the mean transprosthetic gradient was 8.2 ± 3.1 mmHg, with a mean EOA of 2.2 ± 0.3 cm², and mean Doppler Velocity Index of 0.60 ± 0.10. The incidence of moderate and severe PPM was 2% and 1%, respectively. No patients had greater than mild paravalvular leak (PVL).

Figure 3. 30-day device success and valve performance

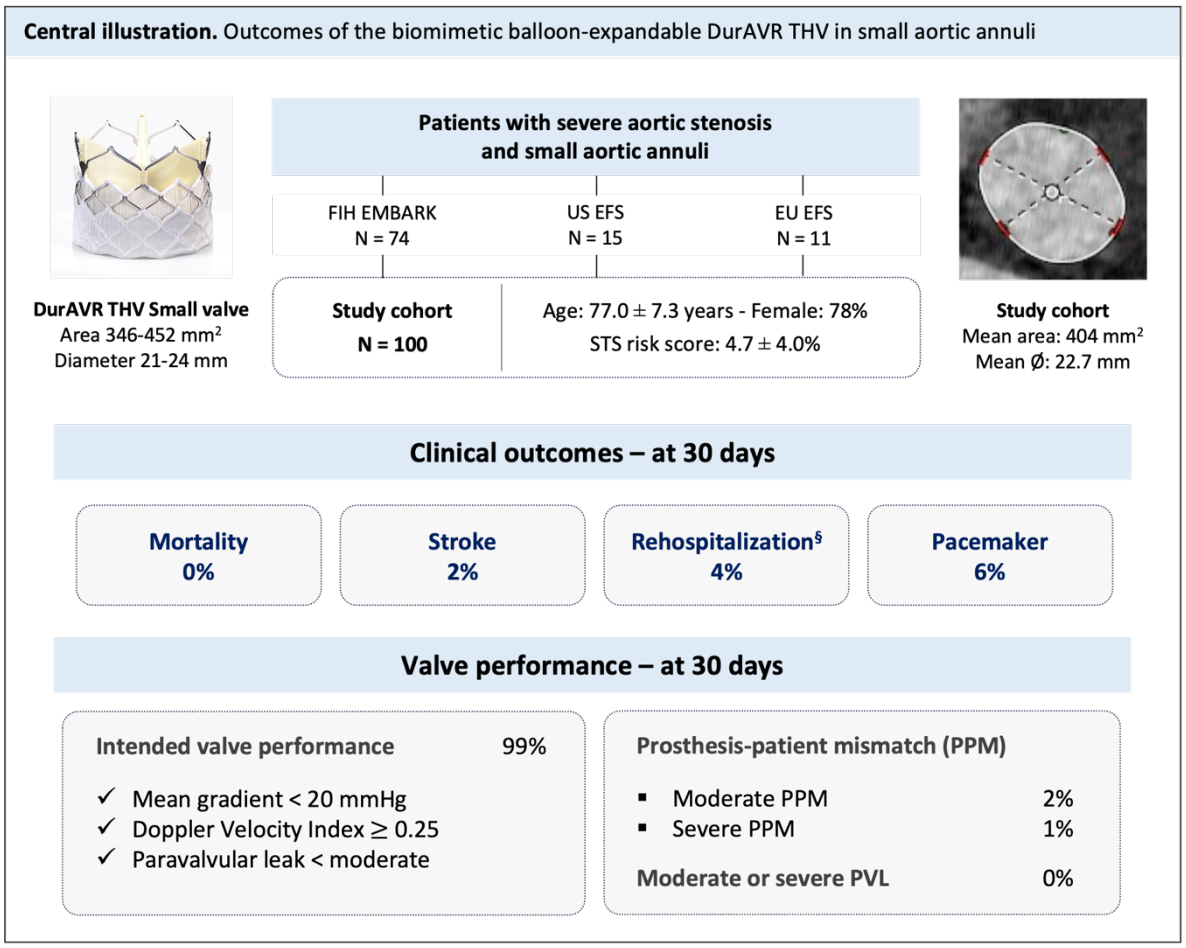
Device success – at 30 days (VARC-3)	
Device success (VARC-3)	91/100 (91%)
Technical success	93/100 (93%)
Freedom from mortality	100/100 (100%)
Freedom from surgery or intervention related to the device or to a major vascular or access-related or cardiac structural complication	99/100 (99%)
Intended valve performance (mean gradient < 20 mmHg, DVI ≥ 0.25 and paravalvular leak < moderate)	98/99 (99%)

Valve performance – at 30 days (VARC-3)



DISCUSSION

This is the largest study to date reporting on clinical and echocardiographic outcomes following implantation of the novel biomimetic balloon-expandable DurAVR THV. Among 100 patients with small aortic annuli (SAA), we observed: (1) a high rate of VARC-3 defined technical success (93%), early clinical safety and efficacy; (2) favourable core-lab assessed echocardiographic hemodynamic outcomes, including low mean transprosthetic gradients (8.2 ± 3.1 mmHg), a large EOA (2.2 ± 0.3 cm^2), only 3% of patients with moderate or greater PPM, and no cases of greater than mild PVL; and (3) a permanent pacemaker implantation rate of 6%. **(Central Illustration)** It should be noted that these outcomes were derived from a mixed cohort, including first-in-human and early feasibility studies. In more recent US-EFS and EU-EFS cohorts, the DurAVR THV system demonstrated a 100% technical success rate, which compares favourably with current generation TAVI systems when treating patients with SAA.



Challenges of small aortic annuli

Surgical aortic valve replacement (SAVR) in patients with SAA often results in high postoperative mean transprosthetic gradients, smaller EOAs, and a higher incidence of PPM, factors linked to increased all-cause and cardiovascular mortality, heart failure hospitalizations, and bioprosthetic valve degeneration (BVD) [16–18]. Similarly, TAVI outcomes are affected by the presence of SAA, which is associated with higher residual gradients, increased PPM, and poorer clinical outcomes [6,19,20]. Data from the STS/ACC TVT registry showed that among 62,125 patients who underwent TAVI between 2014 and 2017, the incidence of moderate and severe PPM was 25% and 12%, respectively, and this was linked with increased mortality risk (HR 1.19, 95% CI: 1.09–1.31, p<0.001) and heart failure hospitalization (HR 1.12, 95% CI: 1.02–1.24, p<0.001) at one-year follow-up [2]. Furthermore, the European Valve Durability TAVI registry noted higher rates of structural valve deterioration (SVD) at a median follow-up of 6.1 years with smaller TAVs (HR 4.8, 95% CI: 2.42–9.60, p<0.001) [21].

Impact of transcatheter aortic valve design

Not all TAVI devices perform equally in patients with SAA; outcomes vary significantly based on the valve design. The retrospective multicenter TAVI-SMALL 2 registry, involving 1,378 patients with SAA, reported that self-expanding valves (SEV) compared to balloon-expandable valves (BEV) were associated with lower mean transprosthetic gradients (8.0 ± 4.1 vs. 13.6 ± 4.7 mmHg; p<0.001) and lower rates of PPM (4.6% vs. 8.7%) [7]. Similarly, the BERN TAVI registry, after propensity-matching 723 patients with SAA, reported severe PPM in 19.7% with SEV vs. 51.8% with BEV [9]. These findings have been consistent across studies involving both older and newer-generation TAVs as well as in patients with extra-small annuli [8,11]. The SMART trial, a randomized controlled trial comparing SAA patients receiving Evolut™ (SEV, Medtronic, MN, USA) or SAPIEN™ (BEV, Edwards Lifesciences, CA, USA), demonstrated that SEV implantation was associated with a significantly lower incidence of mean transprosthetic gradients ≥20 mmHg (3.2% vs. 32.2%), reduced moderate or greater PPM (11.2% vs. 35.3%, p<0.001), and subsequently, lower rates of SVD (3.5% vs. 32.8%) and BVD (10.2% vs. 43.3%) at one year [5]. However, these hemodynamic advantages of SEV come with trade-offs, including higher rates of PVL and permanent pacemaker implantation [7,9,11].

DurAVR THV for small aortic annuli

In this study, we demonstrated that the balloon-expandable DurAVR THV in patients with SAA exhibits favourable hemodynamic valve performance. Specifically, low mean transprosthetic gradients (8.2 ± 3.1 mmHg), high EOAs (2.2 ± 0.3 cm^2), and a very low incidence of moderate (2%) and severe (1%) PPM was observed. Additionally, the rates of core-lab assessed PVL were minimal, with no patients experiencing more than mild PVL. The need for new permanent pacemaker implantation was only 6%. This early experience suggests that the combination of BEV-like performance—characterized by high device success and low pacemaker implantation rates— alongside SEV-like hemodynamics, makes the DurAVR THV an attractive new option for patients with SAA. The favourable hemodynamic profile may

be attributed to its innovative biomimetic leaflet design. The DurAVR THV leaflets are made from a single piece of bovine pericardial tissue, treated with the proprietary ADAPT anti-calcification tissue engineering process and shaped to mimic a native aortic valve. This design results in a longer leaflet coaptation length (~7 mm), allowing the valve to replicate the natural geometry and kinematics of a native aortic valve. In contrast, conventional TAVs have three separate leaflets sutured to the stent frame, often leading to smaller orifice areas and abnormal blood flow patterns in the ascending aorta. [22]

Cardiac magnetic resonance flow studies support these findings, demonstrating that DurAVR THV restores near-normal laminar flow in the aorta, comparable to healthy valves [12]. Further research is needed to determine what impact restoration of laminar flow can have on left ventricular mass regression, often impaired in SAA patients with PPM, and risk of neo-sinus or leaflet thrombosis. [23] These factors could influence long-term durability of the valve, especially as TAVI is increasingly used in younger patients with longer life expectancy, where considerations such as coronary re-access and the feasibility of redo-TAVI are crucial for lifelong management. Patients with small aortic roots are at higher risk for challenging coronary access or redo-interventions and the short-frame design and ability to achieve patient-specific commissural alignment represent significant advantages of the DurAVR THV.

Limitations

Several limitations should be acknowledged. First, the small sample size included both very early first-in-human procedures and more recent implants, reflecting a learning curve and device improvements over time. This progression is evident in the better safety profile and technical success observed in the EFS cohorts compared to the EMBARK cohort. Second, this report describes hemodynamic performance at 30 days post-procedure; longer-term data are needed to confirm valve durability. Lastly, without a comparator group, it is difficult to directly compare DurAVR THV performance to that

of other current generation TAVs. However, this will be addressed in the upcoming PARADIGM randomized controlled trial (NCT07194265), which will compare DurAVR THV with commercially available TAV systems in a broad patient population with severe aortic stenosis.

CONCLUSIONS

The biomimetic balloon-expandable DurAVR THV demonstrated high rates of technical and device success, along with favourable hemodynamic outcomes at 30 days, including a low incidence of PPM in patients with SAA. Further studies are necessary to confirm its long-term durability.

IMPACT ON DAILY PRACTICE

The DurAVR transcatheter heart valve (THV) is a balloon-expandable valve, featuring a single-piece biomimetic leaflet design, which was associated with favourable 30-day haemodynamic performance in patients with small aortic annuli. Ongoing randomized controlled trials will further evaluate DurAVR THV advantages compared to current generation TAVs and explore how its biomimetic design might improve patient outcomes.

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FIGURE LEGENDS

Figure 1. DurAVR THV and study cohort. (A) The DurAVR transcatheter heart valve (THV) is a short-frame, balloon-expandable valve featuring a novel single-leaflet, native-shaped biomimetic leaflet design that replicates native aortic valve leaflets. The valve is delivered using the dedicated ComASUR delivery system, which permits active patient-specific commissural alignment. **(B)** The study cohort comprises all patients with a small aortic annulus treated in the first-in-human and early feasibility studies. THV, transcatheter heart valve; PET, polyethylene terephthalate; PVL, paravalvular leak; STS, Society of Thoracic Surgeons.

Figure 2. 30-day clinical outcomes. High clinical safety, clinical efficacy, and improvement in symptoms were observed at 30-days following DurAVR THV implantation in patients with small aortic annuli. Paired analysis for KCCQ and NYHA scores. [§]modified VARC-3 definition. KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA, New York Heart Association; VARC, Valve Academy Research Consortium.

Figure 3. 30-day device success and valve performance. DurAVR THV demonstrated high device success and favourable hemodynamic outcomes at 30-days post-procedure in patients with small aortic annuli. DVI, Doppler velocity index; EOA, effective orifice area; PPM, prosthesis-patient mismatch; VARC, Valve Academy Research Consortium.

Central Illustration. Outcomes of the biomimetic balloon-expandable DurAVR THV in small aortic annuli. VARC-3-defined clinical outcomes and valve performance at 30 days after DurAVR THV implantation in a patient population with small aortic annuli. PPM, prosthesis-patient mismatch; STS,

Society of Thoracic Surgeons; TAV, transcatheter aortic valve. §procedure- and valve-related hospitalization.

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Table 1. Baseline characteristics

	N = 100
Clinical variables	
Age, years	*77.0 ± 7.3*
Female	*78 (78%)*
Body Mass Index, kg/m²	*28.6 ± 5.1*
Arterial hypertension	*91 (91%)*
Diabetes mellitus	*33 (33%)*
Coronary artery disease	*60 (60%)*
Previous myocardial infarction	*12 (12%)*
Previous PCI	*36 (36%)*
Previous CABG	*7 (7%)*
Peripheral arterial disease	*2 (2%)*
Atrial fibrillation	*12 (12%)*
Previous stroke	*1 (1%)*
Renal insufficiency or failure	*56 (56%)*
Chronic obstructive pulmonary disease	*3 (3%)*
Previous pacemaker	*6 (6%)*
STS risk score, %	*4.7 ± 4.0*
NYHA class III or IV	*61 (61%)*
KCCQ overall summary score	*40.7 ± 20.4*
Baseline echocardiographic data	
Left ventricular ejection fraction, %	*58.0 ± 7.0*
Mean transvalvular gradient, mmHg	*48.1 ± 17.0*
Peak transvalvular gradient, mmHg	*78.3 ± 26.8*
Aortic valve area, cm²	*0.8 ± 0.2*
Aortic regurgitation ≥ moderate, %	*6/99 (6%)*
Mitral regurgitation ≥ moderate, %	*10/97 (11%)*
Baseline CT data	
Aortic annulus area, mm²	*404 ± 37*

Aortic annulus perimeter, mm	*72.0 ± 3.5*
Aortic annulus mean diameter, mm	*22.7 ± 1.0*
Sinotubular junction diameter, mm	*27.3 ± 2.6*
Left coronary artery height, mm	*13.2 ± 2.8*
Right coronary artery height, mm	*16.4 ± 2.8*

Values are expressed as mean ± SD, n (%) or n/N (%).

CABG, coronary artery bypass grafting; CT, computed tomography; KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STS, Society of Thoracic Surgeons.

Table 2

Table 2. Procedural characteristics and technical success

	N = 100
Procedural characteristics	
Anaesthesia type	
General anaesthesia	69 (69%)
Conscious sedation/local anaesthesia	31 (31%)
Transfemoral access and delivery	94 (94%)
DurAVR THV Small valve size	100 (100%)
Pre-dilatation	57 (57%)
Post-dilatation	8/95 (8%)
Cerebral embolic protection device	26 (26%)
Procedural time, min	24.3 ± 20.8
Fluoroscopy time, min	18.5 ± 8.9
Use of contrast dye, ml	91.2 ± 31.2
Technical success (VARC-3)	
Freedom from mortality	100 (100%)
Successful access, delivery of the device, and retrieval of the delivery system	100 (100%)
Correct positioning of a single THV into the proper anatomical location	98 (98%)
Freedom from surgery or intervention related to the device or to a major vascular or access-related, or cardiac structural complication	95 (95%)
Technical success at exit from procedure room	93 (93%)
FIH-EMBARK cohort - early experience	67/74 (91%)
US/EU-EFS cohort - latter experience	26/26 (100%)

Values are presented as mean ± SD, n (%). EFS, early feasibility study; FIH, first-in-human; THV, transcatheter heart valve; VARC, Valve Academic Research Consortium.

Supplementary Table 1. Inclusion and exclusion criteria for study cohorts

EMBARK, First-in-human

Inclusion Criteria

Subjects are eligible for entry in this study if ALL the following conditions are met:

1. Symptomatic, severe aortic stenosis*
2. Eligible for delivery of the DurAVR THV
3. Anatomy appropriate to accommodate safe placement of DurAVR THV (as per instructions for use)
4. Understands the study requirements and the treatment procedures and provides written informed consent
5. Subject agrees to complete all required scheduled follow-up visits

*Critical aortic valve area defined as an initial aortic valve area of ≤ 1.0 cm2 OR aortic valve area index < 0.6 cm^2/m^2 AND, in presence of left ventricular function (LVEF > 40%):

   a. Mean gradient ≥40mmHg OR
   b. Vmax≥ 4m/sec OR
   c. DVI ≤ 0.25

Exclusion Criteria

Subjects are eligible for entry in this study if NONE of the following conditions are met:

Anatomical

1. Anatomy precluding safe placement of DurAVR™ THV
2. Pre-existing prosthetic heart valve in any position
3. Congenital unicuspid or bicuspid aortic valve with no raphe (Sievers classification type 0)
4. Severe aortic regurgitation
5. Severe mitral or severe tricuspid regurgitation requiring intervention.
6. Moderate to severe mitral stenosis
7. Hypertrophic obstructive cardiomyopathy
8. Echocardiographic evidence of intracardiac mass, thrombus or vegetation requiring treatment.
9. Severe basal septal hypertrophy with outflow gradient

Clinical

1. Evidence of an acute myocardial infarction ≤ 30 days before the intended treatment
2. Determined inoperable/ineligible for surgery by the Heart Team
3. Any percutaneous coronary or peripheral interventional procedure performed within 30 days prior to the index procedure
4. Blood dyscrasias as defined: leukopenia (WBC < 1000 mm3), thrombocytopenia (platelet count <50,000 cells/mm3), history of bleeding diathesis or coagulopathy, or hypercoagulable states
5. Untreated clinically significant Coronary Artery Disease (CAD) requiring revascularization

6. Cardiogenic shock manifested by low cardiac output, vasopressor dependence, or mechanical hemodynamic support
7. Need for emergency surgery for any reason
8. Ventricular dysfunction with left ventricular ejection fraction (LVEF) ≤ 30% as measured by resting echocardiogram
9. Recent (within 6 months) cerebrovascular accident (CVA) or transient ischaemic attack (TIA)
10. Symptomatic carotid or vertebral artery disease
11. End stage renal disease requiring chronic dialysis or creatinine clearance < 20 cc/min
12. GI bleeding within the past 3 months
13. A known hypersensitivity or contraindication to any of the following which cannot be adequately pre-medicated: aspirin, heparin, nitinol (titanium or nickel), ticlopidine and clopidogrel, contrast media
14. Ongoing sepsis, including active endocarditis (Duke Criteria)
15. Subject refuses a blood transfusion
16. Life expectancy < 12 months due to associated non-cardiac co-morbid conditions
17. Other medical, social or psychological conditions that in the opinion of an Investigator precludes the subject from appropriate consent
18. Severe dementia (resulting in either inability to provide informed consent for the trial/procedure, prevents independent lifestyle outside of a chronic care facility, or will fundamentally complicate rehabilitation from the procedure or compliance with followup visits).
19. Currently participating in an investigational drug or another investigational device trial
20. Subject belongs to a vulnerable population (Vulnerable subject populations are defined as individuals with mental disability, persons in nursing homes, children, impoverished persons, homeless persons, nomads, refugees, and those permanently incapable of giving informed consent. Vulnerable populations also may include members of a group with a hierarchial structure such as university students, subordinate hospital and laboratory personnel, employees of the Sponsor, members of the armed forces, and persons kept in detention).

US Early Feasibility Study

Inclusion Criteria

1. Symptomatic, severe native aortic stenosis in subjects 65 years or older
2. Requires aortic valve replacement and is indicated for TAVR as determined by the Heart Team (composed of an experienced interventional cardiologist and an experienced cardiac surgeon)
3. Eligible for transfemoral delivery of the DurAVR™ THV
4. Anatomy appropriate to accommodate safe placement of DurAVR™ THV (Preprocedural measurements by TTE and CT required: aortic annulus diameter 21-23 mm by CT)
5. Understands the study requirements and the treatment procedures and provides written informed consent
6. Subject agrees to complete all required scheduled follow-up visits.

Exclusion Criteria

1. Anatomy precluding safe placement of DurAVR™ THV

2. Pre-existing prosthetic heart valve in any position
3. Unicuspid or bicuspid aortic valve
4. Severe aortic regurgitation
5. Severe mitral or severe tricuspid regurgitation requiring intervention.
6. Moderate to severe mitral stenosis.
7. Hypertrophic obstructive cardiomyopathy
8. Echocardiographic evidence of intracardiac mass, thrombus or vegetation requiring treatment.
9. Severe basal septal hypertrophy with outflow gradient
10. Evidence of an acute myocardial infarction ≤ 30 days before the intended treatment.
11. Determined inoperable/ineligible for surgery by the Heart Team
12. Any percutaneous coronary or peripheral interventional procedure performed within 30 days prior to the index procedure
13. Blood dyscrasias as defined: leukopenia (WBC < 1000 mm3), thrombocytopenia (platelet count < 50,000 cells/mm3), history of bleeding diathesis or coagulopathy, or hypercoagulable states
14. Untreated clinically significant Coronary Artery Disease (CAD) requiring revascularization
15. Cardiogenic shock manifested by low cardiac output, vasopressor dependence, or mechanical hemodynamic support
16. Need for emergency surgery for any reason
17. Ventricular dysfunction with left ventricular ejection fraction (LVEF) < 30% as measured by resting echocardiogram
18. Recent (within 6 months) cerebrovascular accident (CVA) or transient ischemic attack (TIA).
19. Symptomatic carotid or vertebral artery disease
20. End stage renal disease requiring chronic dialysis or creatinine clearance < 20 cc/min.
21. GI bleeding within the past 3 months
22. A known hypersensitivity or contraindication to any of the following which cannot be adequately pre-medicated: aspirin, heparin, nitinol (titanium or nickel), ticlopidine and clopidogrel, contrast media
23. Ongoing sepsis, including active endocarditis (Duke Criteria) [49]
24. Subject refuses a blood transfusion
25. Life expectancy < 12 months due to associated non-cardiac co-morbid conditions
26. Other medical, social, or psychological conditions that in the opinion of an Investigator precludes the subject from appropriate consent
27. Severe dementia (resulting in either inability to provide informed consent for the trial/procedure, prevents independent lifestyle outside of a chronic care facility, or will fundamentally complicate rehabilitation from the procedure or compliance with follow-up visits)
28. Currently participating in an investigational drug or another investigational device trial
29. Subject is contraindicated for MDCT or MRI Scans.
30. Subject belongs to a vulnerable population (Vulnerable subject populations are defined as individuals with mental disability, persons in nursing homes, children, impoverished persons, homeless persons, nomads, refugees, and those permanently incapable of giving informed consent. Vulnerable populations also may include members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel, employees of the Sponsor, members of the armed forces, and persons kept in detention).

European Early Feasibility Study

Inclusion Criteria

1. Symptomatic, severe native aortic stenosis or severe degeneration of surgically implanted aortic bioprosthetic valve in subjects 18 years or older.
2. Requires aortic valve replacement and is indicated for TAVR as determined by the Heart Team
3. Eligible for transfemoral delivery of the DurAVR™ THV
4. Anatomy appropriate to accommodate safe placement of DurAVR™ THV
5. Understands the study requirements and the treatment procedures and provides written informed consent
6. Subject agrees to complete all required scheduled follow-up visits.

Exclusion Criteria

1. Anatomy precluding safe placement of DurAVR™ THV
2. Pre-existing prosthetic mitral or tricuspid valve
3. Unicuspid, bicuspid or non-calcified aortic valve
4. Severe mitral or severe tricuspid regurgitation requiring intervention
5. Moderate to severe mitral stenosis
6. Hypertrophic obstructive cardiomyopathy
7. Echocardiographic evidence of intracardiac mass, thrombus or vegetation requiring treatment
8. Evidence of an acute myocardial infarction ≤ 30 days before the intended treatment
9. Any percutaneous coronary or peripheral interventional procedure performed within 30 days prior to the index procedure
10. Recent (within 6 months) cerebrovascular accident (CVA) or transient ischemic attack (TIA)
11. End-stage renal disease requiring chronic dialysis or creatinine clearance < 20 cc/min
12. GI bleeding within the past 3 months
13. Ongoing sepsis (including active endocarditis) or endocarditis in the last 3 months
14. Life expectancy < 12 months due to associated non-cardiac co-morbid conditions

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Supplementary Table 2. Baseline characteristics

	Total (N = 100)	EMBARK (N = 74)	US EFS (N = 15)	EU EFS (N = 11)
Clinical variables				
Age, years	*77.0 ± 7.3*	*76.0 ± 7.4*	*81.1 ± 7.2*	*78.0 ± 5.1*
Female	*78/100 (78%)*	*61/74 (82%)*	*10/15 (66%)*	*7/11 (64%)*
Body Mass Index, kg/m²	*28.6 ± 5.1*	*29.5 ± 5.2*	*26.2 ± 4.4*	*25.6 ± 3.4*
Body Surface Area, m²	*1.81 ± 0.17*	*1.82 ± 0.17*	*1.77 ± 0.20*	*1.82 ± 0.13*
Arterial hypertension	*91/100 (91%)*	*74/74 (100%)*	*13/15 (87%)*	*4/11 (36%)*
Diabetes mellitus	*33/100 (33%)*	*22/74 (30%)*	*7/15 (47%)*	*4/11 (36%)*
Coronary artery disease	*60/100 (60%)*	*52/74 (70%)*	*8/15 (53%)*	*0/11 (0%)*
Previous PCI	*36/100 (36%)*	*34/74 (46%)*	*2/15 (13%)*	*0/11 (0%)*
Previous myocardial infarction	*12/100 (12%)*	*10/74 (14%)*	*2/15 (13%)*	*0/11 (0%)*
Previous CABG	*7/100 (7%)*	*7/74 (9%)*	*0/15 (0%)*	*0/11 (0%*
Previous stroke	*1/100 (1%)*	*1/74 (1%)*	*0/15 (0%)*	*0/11 (0%)*
Peripheral arterial disease	*2/100 (2%)*	*1/74 (1%)*	*1/15 (7%)*	*0/11 (0%)*
Atrial fibrillation	*12/100 (12%)*	*5/74 (7%)*	*6/15 (40%)*	*1/11 (9%)*
Renal insufficiency or failure	*56/100 (56%)*	*50/74 (68%)*	*6/15 (40%)*	*0/11 (0%)*
Chronic obstructive pulmonary disease	*3/100 (3%)*	*1/74 (1%)*	*1/15 (7%)*	*1/11 (9%)*
Previous pacemaker	*6/100 (6%)*	*5/74 (7%)*	*0/15 (0%)*	*1/11 (9%)*
STS risk score, %	*4.68 ± 3.96*	*4.76 ± 3.91*	*5.78 ± 4.84*	*2.63 ± 3.98*
NYHA class III or IV	*61/100 (61%)*	*52/74 (70%)*	*7/15 (47%)*	*2/11 (18%)*
KCCQ overall summary score	*40.7 ± 20.4*	*31.8 ± 11.0*	*70.2 ± 23.6*	*59.9 ± 12.6*
Baseline echocardiographic data				
Left ventricular ejection fraction, %	*58.1 ± 6.9*	*58.1 ± 7.3*	*56.1 ± 5.8*	*59.8 ± 5.4*
Mean transvalvular gradient, mmHg	*47.8 ± 16.9*	*51.6 ± 17.2*	*32.6 ± 9.9*	*44.0 ± 8.9*
Peak AV gradient, mmHg	*78.0 ± 26.7*	*84.4 ± 27.4*	*54.9 ± 14.5*	*68.0 ± 12.2*
Aortic valve area, cm²	*0.75± 0.16*	*0.75 ± 0.19*	*0.76 ± 0.13*	*0.76 ± 0.11*
Aortic regurgitation ≥ moderate, %	*6/99 (6%)*	*5/74 (7%)*	*1/14 (7%)*	*0/11 (0%)*
Mitral regurgitation ≥ moderate, %	*10/97 (11%)*	*6/74 (8%)*	*4/13 (31%)*	*1/10 (10%)*
Baseline CT data				
Aortic annulus area, mm²	*404 ± 37*	*400 ± 38*	*410 ± 35*	*420 ± 26*
Aortic annulus perimeter, mm	*72.0 ± 3.5*	*71.6 ± 3.6*	*73.2 ± 2.9*	*73.6 ± 2.7*

Aortic annulus mean diameter, mm	*22.7 ± 1.0*	*22.6 ± 1.0*	*22.8 ± 1.0*	*23.1 ± 0.7*
Sinotubular junction diameter, mm	*27.3 ± 2.6*	*27.4 ± 2.7*	*27.6± 2.4*	*26.5 ± 1.9*
Left coronary artery height, mm	*13.2 ± 2.8*	*13.4 ± 2.8*	*Not Available*	*12.3 ± 2.7*
Right coronary artery height, mm	*16.4 ± 2.8*	*16.6 ± 2.8*	*Not Available*	*15.4 ± 2.6*

CABG, coronary artery bypass grafting; KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STS, Society of Thoracic Surgeons.
Baseline echocardiographic are core lab adjudicated.

Supplementary Table 3. Procedural characteristics and technical success for all study cohorts

	Total (N = 100)	**EMBARK (N = 74)**	**US EFS (N = 15)**	**EU EFS (N = 11)**
Procedural characteristics				
Anaesthesia type				
General anaesthesia	69/100 (69%)	66/74 (89%)	3/15 (20%)	0/11 (0%)
Conscious sedation	31 / 100 (31%)	8/74 (11%)	12/15 (80%)	11/11 (100%)
Access and delivery				
Transfemoral	94/100 (94%)	68/74 (92%)	15/15 (100%)	11/11 (100%)
Transaortic	5/100 (5%)	5/74 (7%)	0/15 (0%)	0/11 (0%)
Transcarotid	1/100 (1%)	1/74 (1%)	0/15 (0%)	0/11 (0%)
DurAVR THV Small valve	100/100 (100%)	74/74 (100%)	15/15 (100%)	11/11 (100%)
Pre-dilatation	57/100 (57%)	31/74 (42%)	15/15 (100%)	11/11 (100%)
Post-dilatation	8/96 (8%)	2/70 (3%)	4/15 (27%)	2/11 (18%)
Cerebral embolic protection	26/100 (26%)	16/74 (22%)	10/15 (67%)	0/11 (0%)
Implantation duration, min	24.3 ± 20.8	23.0 ± 20.2	23.5 ± 27.0	33.9 ± 13.1
Fluoroscopy time, min	18.5 ± 8.9	17.0 ± 6.9	27.5 ± 13.1	16.5 ± 6.9
Use of contrast dye, ml	91.2 ± 31.2	96.8 ± 25.5	63.5 ± 34.7	91.1 ± 42.5
Technical outcomes (VARC-3)				
Technical success at exit from procedure room	93/100 (93%)	67/74 (91%)	15/15 (100%)	11/11 (100%)

Freedom from mortality	100/100 (100%)	74/74 (100%)	15/15 (100%)	11/11 (100%)
Successful access, delivery of the device, and retrieval of the delivery system	100/100 (100%)	74/74 (100%)	15/15 (100%)	11/11 (100%)
Correct positioning of a single prosthetic heart valve into the proper anatomical location	98/100 (98%)	72/74 (97%)[1]	15/15 (100%)	11/11 (100%)
Freedom from surgery or intervention related to the device or to a major vascular or access-related, or cardiac structural complication	95/100 (95%)	69/74 (92%)[2]	15/15 (100%)	11/11 (100%)

Supplementary Table 4. Summary of major peri-procedural complications encountered

Complication	Cohort	Detail	Management	Patient outcome
Valve embolization	EMBARK FIH	Manufacturing defect on delivery balloon resulted in aortic embolization	Percutaneously managed with implantation of second valve	Alive
Valve embolization	EMBARK FIH	Loss of pacing capture during valve deployment resulting in aortic embolization	Percutaneously managed with implantation of second valve	Alive
Aortic pseudoaneurysm	EMBARK	Post-dilatation for paravalvular leak	Conservatively managed	Alive

& dissection	FIH	resulted in aortic dissection and pseudoaneurysm formation.	with no progression or symptoms	
Pericardial tamponade	EMBARK FIH	Right ventricular perforation secondary to ventricular pacing wire in elderly highly co-morbid patient	Percutaneous management and drainage of pericardial effusion.	Alive
Vascular access-site dissection	EMBARK FIH	Flow-limiting dissection of femoral vascular access site	Percutaneously managed with covered stent	Alive
Vascular access-site dissection	EMBARK FIH	Flow-limiting dissection of femoral vascular access site	Percutaneously managed with covered stent	Alive
Vascular access-site bleeding	EMBARK FIH	Major bleeding of femoral vascular access site	Percutaneously managed with covered stent	Alive