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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 mm^2 to 452 mm^2) treated with the small-sized DurAVR THV. The mean computed tomography (CT)-derived aortic annulus area was 404±37 mm^2, with a mean diameter of 22.7±1.0 mm. Outcomes at 30 days, including PPM, were evaluated per Valve Academic Research Consortium 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 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 cm^2, 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: biomimetic leaflets; early outcomes; small annulus; transcatheter aortic valve

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As transcatheter aortic valve implantation (TAVI) increasingly extends to younger patients with longer life expectancies, factors such as haemodynamic valve performance, valve durability, and the feasibility for reintervention become 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) 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 (EFS) 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.

Editorial, see page e131

Impact on daily practice

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

Methods

STUDY COHORT

All patients with severe aortic stenosis and an 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; ClinicalTrials.gov: NCT05182307), United States Early Feasibility Study (US-EFS; NCT05712161) and European Early Feasibility Study (EU-EFS; NCT06510855) were pooled together to constitute the study population for this analysis. The EMBARK First-in-Human study was a prospective, single-arm, single-centre study enrolling 90 patients from November 2021 to May 2025. The US-EFS was a prospective, single-arm study enrolling 15 patients across 4 sites between August and October 2023. The EU-EFS was a prospective, single-arm study enrolling 15 patients at a single centre 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 moulded into a trileaflet configuration to mimic native aortic valve geometry **(Figure 1)**. The bovine pericardium is treated with a proprietary ADAPT anticalcification tissue engineering process, which was 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 minimise paravalvular leak (PVL). The DurAVR THV is crimped onto a balloon-expandable catheter and delivered via the transfemoral ComASUR Delivery System (Anteris Technologies). The system comprises a flexible steering catheter and a commissural wheel that enables 1:1 rotational torque, facilitating patient-specific commissural alignment.

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 small DurAVR THV, suitable for treatment of native aortic annuli with an area-derived diameter of 21-24 mm and aortic annulus area of 346-452 mm^2. The valve was deployed under fluoroscopic guidance during rapid pacing. Post-deployment assessments included stent frame expansion by fluoroscopy, haemodynamic 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 postprocedural antiplatelet or antithrombotic therapy, was 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,

Abbreviations

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

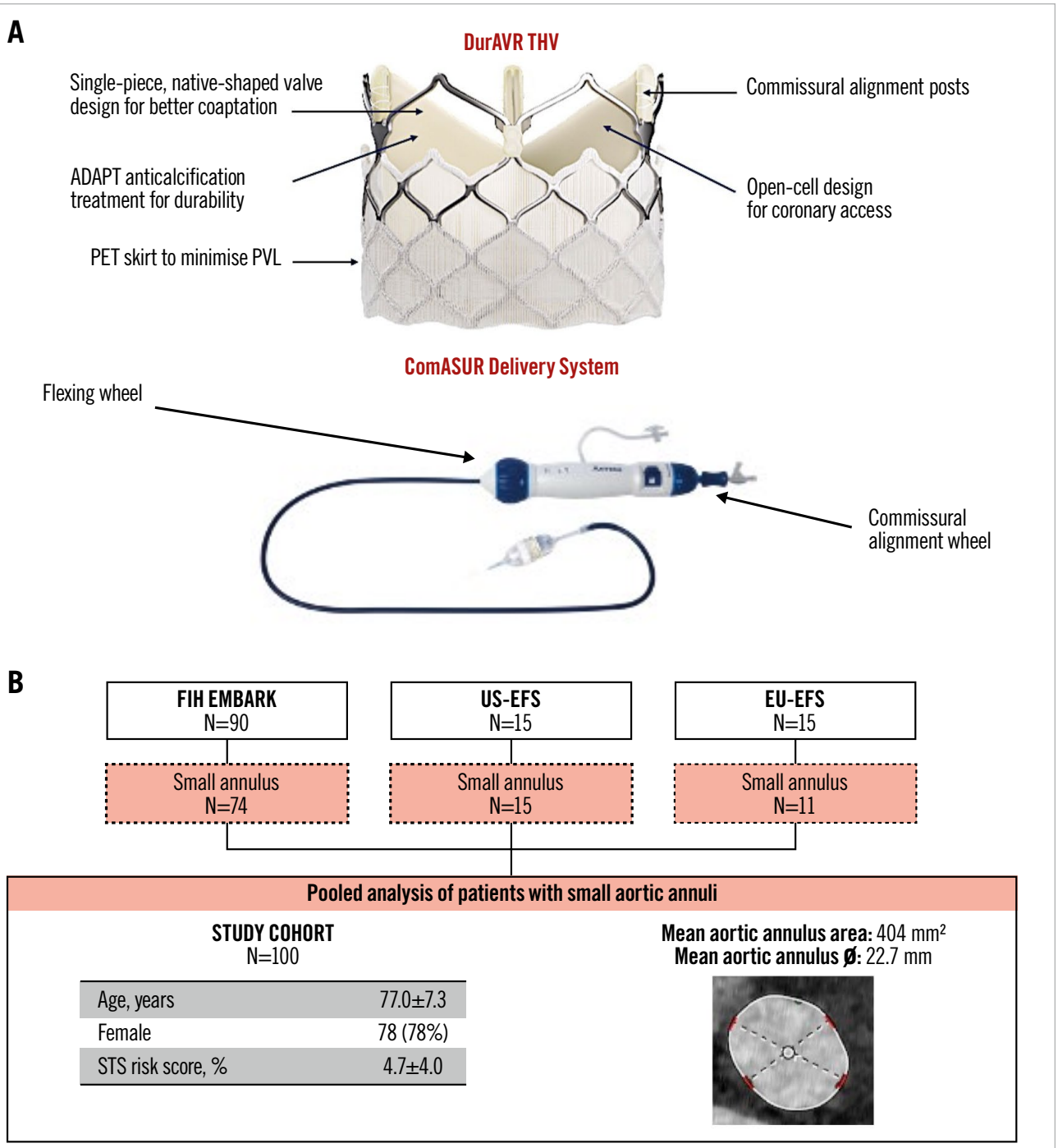


Figure 1. *DurAVR THV and study cohort. A) The DurAVR transcatheter heart valve (THV) is a short-frame, balloon-expandable valve featuring a novel single-leaflet, native-shaped biomimetic leaflet design that replicates native aortic valve leaflets. The valve is delivered using the dedicated ComASUR Delivery 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. EFS: early feasibility study; EU: European; FIH: first-in-human; PET: polyethylene terephthalate; PVL: paravalvular leak; STS: Society of Thoracic Surgeons*

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, NY, USA). Aortic stenosis severity was determined using the mean gradient, peak velocity, and aortic valve area (AVA). Post-procedure valve haemodynamics included measurements of transprosthetic gradient, effective orifice area (EOA), and Doppler velocity index (DVI). PPM severity was classified according to Valve Academic Research Consortium 3 (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, hospitalisation related to the procedure or valve; a decline of less than 10 points in the overall KCCQ score from baseline; and no worsening of NYHA Class.

STATISTICAL ANALYSIS

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

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 summarised 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%. A total of 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 1 patient with non-right fusion). The CT-based mean aortic annulus area was 404±37 mm^2, with a mean annulus diameter of 22.7±1.0 mm. The baseline mean aortic valve gradient was 48.1±17.0 mmHg and left ventricular ejection fraction (LVEF) was 58.0±7.0%.

PROCEDURAL OUTCOMES

Procedural data and outcomes are summarised in **Table 2** and **Supplementary Table 3**. In the initial EMBARK study, most procedures (69%) were performed under general anaesthesia with transoesophageal echocardiography (TOE) 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. The transfemoral access route was utilised for 94% of cases, while transaortic and transcarotid access routes were used in 5% and 1% of cases, respectively. Predilatation 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%. Periprocedural complications were only encountered in

Table 1. Baseline characteristics.

	N=100
Clinical variables	
Age, years	77.0±7.3
Female	78 (78)
Body mass index, kg/m^2	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, cm^2	0.8±0.2
Aortic regurgitation ≥moderate, %	6/99 (6)
Mitral regurgitation ≥moderate, %	10/97 (11)
Baseline CT data	
Aortic annulus area, mm^2	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; SD: standard deviation; STS: Society of Thoracic Surgeons

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)
Predilatation	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, 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 – later experience	26/26 (100)

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

the EMBARK first-in-human cohort, reflecting early device and operator experience **(Supplementary Table 4)**. Subsequent refinements to the valve design, compliance of the inflation balloon, the delivery system, and the expandable sheath profile were implemented. In the last 50 consecutive implants, including the US-EFS and EU-EFS cohorts, no major periprocedural 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 2 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.

VALVE PERFORMANCE

Device success per VARC-3 criteria was achieved in 91% of patients **(Figure 3)**. One patient developed a late external iliac artery thrombus 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 cm^2, and mean DVI of 0.60±0.10. The incidences of moderate and severe PPM were 2% and 1%, respectively. No patients had greater than mild PVL.

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 SAA, we observed (1) a high rate of VARC-3-defined technical success (93%) and early clinical safety and efficacy; (2) favourable core-lab-assessed echocardiographic haemodynamic 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 in patients with SAA often results in high postoperative mean transprosthetic gradients, small EOAs, and a high incidence of PPM, factors linked to increased all-cause and cardiovascular mortality, heart failure hospitalisations, and bioprosthetic valve degeneration

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 hospitalisation	96/100 (96%)
Freedom from KCCQ overall summary score decline from baseline of >10 points or worsening NYHA Class	94/98 (96%)

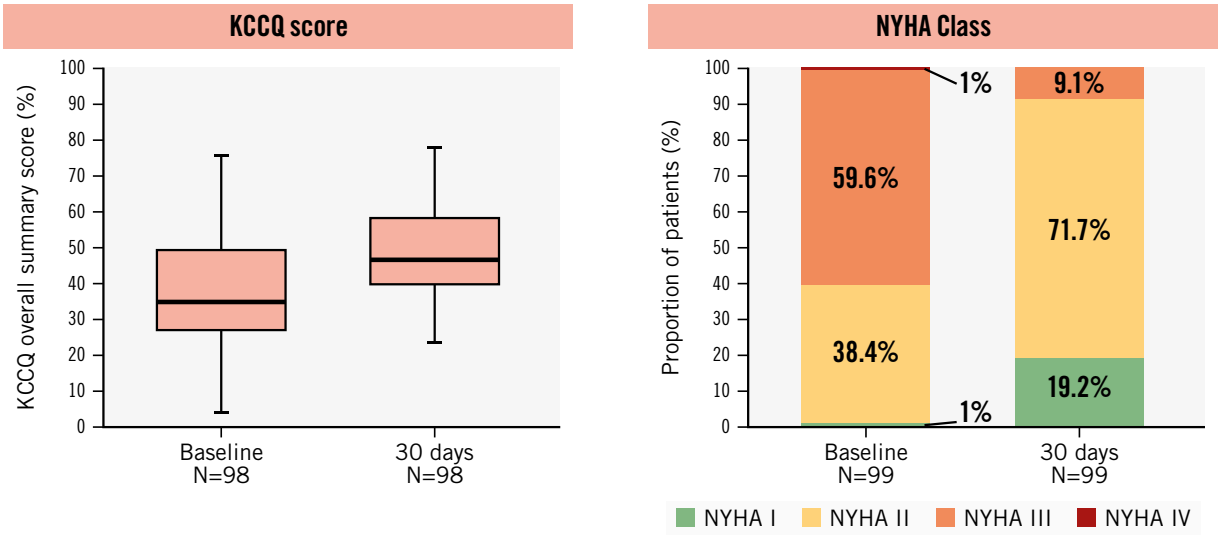


Figure 2. *Thirty-day clinical outcomes. High clinical safety, clinical efficacy, and improvement in symptoms were observed at 30 days following DurAVR THV implantation in patients with small aortic annuli. Paired analysis for KCCQ and NYHA scores. §Modified VARC-3 definition. KCCQ: Kansas City Cardiomyopathy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

(BVD)[16-18]. Similarly, TAVI outcomes are affected by the presence of SAA, which are associated with higher residual gradients, increased PPM, and poorer clinical outcomes[6,19,20]. Data from the STS/ACC Transcatheter Valve Therapy (TVT) Registry showed that among 62,125 patients who underwent TAVI between 2014 and 2017, the incidences of moderate and severe PPM were 25% and 12%, respectively, and these were linked with increased mortality risk (hazard ratio [HR] 1.19, 95% confidence interval [CI]: 1.09-1.31; p<0.001) and heart failure hospitalisation (HR 1.12, 95% CI: 1.02-1.24; p<0.001) at 1-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

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, 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)

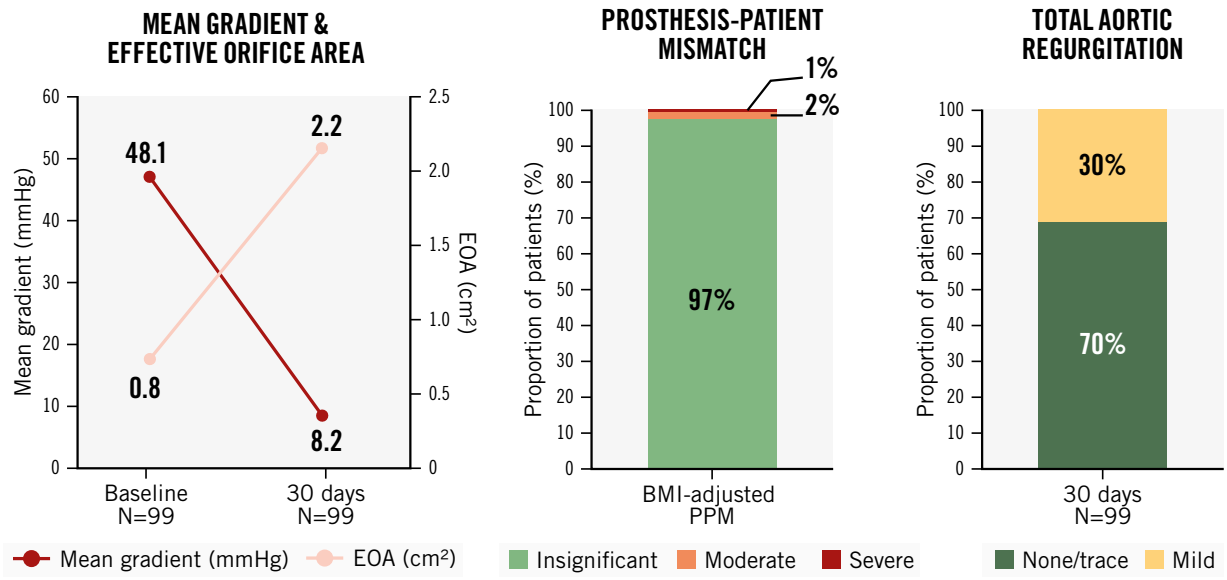


Figure 3. *Thirty-day device success and valve performance. The DurAVR THV demonstrated high device success and favourable haemodynamic outcomes at 30 days post-procedure in patients with small aortic annuli. BMI: body mass index; DVI: Doppler velocity index; EOA: effective orifice area; PPM: prosthesis-patient mismatch; THV: transcatheter heart valve; VARC: Valve Academic Research Consortium*

retrospective multicentre TAVI-SMALL 2 registry, involving 1,378 patients with SAA, reported that self-expanding valves (SEVs), compared to balloon-expandable valves (BEVs), were associated with lower mean transprosthetic gradients (8.0±4.1 mmHg 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 SEVs versus 51.8% with BEVs[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 randomised controlled trial comparing SAA patients receiving Evolut (SEV; Medtronic) or SAPIEN (BEV; Edwards Lifesciences) valves, 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 1 year[5]. However, these haemodynamic advantages of SEVs 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 exhibits favourable haemodynamic valve performance in patients with SAA. Specifically, low mean transprosthetic gradients (8.2±3.1 mmHg), high EOAs (2.2±0.3 cm²), and very low incidences of moderate (2%) and severe (1%) PPM were 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 – characterised by high device success and low pacemaker implantation rates – alongside SEV-like haemodynamics makes the DurAVR THV an attractive new option for patients with SAA. The favourable haemodynamic 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 anticalcification 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

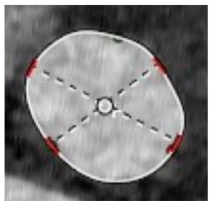
EuroIntervention — Central Illustration

Outcomes of the biomimetic balloon-expandable DurAVR THV in small aortic annuli.

Small DurAVR THV
Area: 346-452 mm²
Diameter: 21-24 mm

Patients with severe aortic stenosis and small aortic annuli

FIH EMBARK N=74	US-EFS N=15	EU-EFS N=11
Study cohort N=100	Age: 77.0±7.3 years; female: 78% STS risk score: 4.7±4.0%	



Study cohort
Mean area: 404 mm²
Mean Ø: 22.7 mm

Clinical outcomes at 30 days

Mortality	Stroke	Rehospitalisation§	Pacemaker
0%	2%	4%	6%

Valve performance at 30 days

Intended valve performance	99%
✓ Mean gradient <20 mmHg	
✓ Doppler velocity index ≥0.25	
✓ Paravalvular leak <moderate	

Prosthesis-patient mismatch	
• Moderate PPM	2%
• Severe PPM	1%
Moderate or severe PVL	**0%**

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VARC-3-defined clinical outcomes and valve performance at 30 days after DurAVR THV implantation in a patient population with small aortic annuli. §Procedure- and valve-related hospitalisations. PPM: prosthesis-patient mismatch; STS: Society of Thoracic Surgeons; THV: transcatheter heart valve; VARC: Valve Academic Research Consortium

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 the impact that restoration of laminar flow can have on left ventricular mass regression, which is often impaired in SAA patients with PPM, and the risk of neosinus or leaflet thrombosis[23]. These factors could influence the long-term durability of the valve, especially as TAVI is increasingly used in younger patients with longer life expectancy, where considerations such as coronary reaccess 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 haemodynamic 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 randomised controlled trial (ClinicalTrials: NCT07194265), which will compare the 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 haemodynamic outcomes at 30 days, including a low incidence of PPM in patients with SAA. Further studies are necessary to confirm its long-term durability.

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Conflict of interest statement

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Supplementary data

Supplementary Table 1. Inclusion and exclusion criteria for study cohorts.

Supplementary Table 2. Baseline characteristics.

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

Supplementary Table 4. Summary of major periprocedural complications encountered.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-25-01106

Supplementary data

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/m^2	28.6 ± 5.1	29.5 ± 5.2	26.2 ± 4.4	25.6 ± 3.4
Body Surface Area, m^2	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, cm^2	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, mm^2	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 periprocedural 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 & dissection	EMBARK FIH	Post-dilatation for paravalvular leak resulted in aortic dissection and pseudoaneurysm formation.	Conservatively managed with no progression or symptoms	Alive
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