

# Transfemoral TAVI using the self-expanding ACURATE neo prosthesis: one-year outcomes of the multicentre “CE-approval cohort”



Helge Möllmann<sup>1,2\*</sup>, MD; Thomas Walther<sup>3</sup>, MD; Dimytri Siqueira<sup>4</sup>, MD; Patrick Diemert<sup>5</sup>, MD; Hendrik Treede<sup>6</sup>, MD; Eberhard Grube<sup>7</sup>, MD; Georg Nickenig<sup>7</sup>, MD; Stephan Baldus<sup>8</sup>, MD; Tanja Rudolph<sup>8</sup>, MD; Toru Kuratani<sup>9</sup>, MD; Yoshiki Sawa<sup>10</sup>, MD; Joerg Kempfert<sup>3,11</sup>, MD; Won-Keun Kim<sup>1,3</sup>, MD; Alexandre Abizaid<sup>4,12</sup>, MD

1. Department of Cardiology, Kerckhoff Heart and Lung Center, Bad Nauheim, Germany; 2. Department of Internal Medicine-I, Cardiology, St. Johannes-Hospital, Dortmund, Germany; 3. Department of Cardiac Surgery, Kerckhoff Heart and Lung Center, Bad Nauheim, Germany; 4. Instituto Dante Pazzanese de Cardiologia, Sao Paulo, Brazil; 5. Department of Cardiology, University Heart Center Hamburg, Hamburg, Germany, and Medizinische Klinik II, Westküstenklinikum, Heide, Germany; 6. Department of Cardiovascular Surgery, University Heart Center Hamburg, Hamburg, Germany, and Department of Cardiac Surgery, Mid-German Heart Center, University Hospital Halle, Halle, Germany; 7. Department of Cardiology, University Hospital Bonn, Bonn, Germany; 8. Department of Cardiology, Heart Center, University Hospital Cologne, Cologne, Germany; 9. Department of Minimally Invasive Cardiovascular Medicine, Osaka University Graduate School of Medicine, Osaka, Japan; 10. Department of Cardiovascular Surgery, Osaka University Graduate School of Medicine, Osaka, Japan; 11. Department of Cardiothoracic and Vascular Surgery, German Heart Center, Berlin, Germany; 12. Hospital Albert Einstein, Sao Paulo, Brazil

## KEYWORDS

- aortic stenosis
- death
- femoral
- stroke
- transcatheter aortic valve implantation

## Abstract

**Aims:** The aim of this study was to assess the safety and performance of the ACURATE neo transcatheter heart valve and its transfemoral delivery system.

**Methods and results:** The prospective, multicentre “CE-approval cohort” consists of a prospective series of the first 89 patients implanted with the ACURATE neo prosthesis. The primary endpoint was all-cause mortality at 30 days. Mean patient age was 83.7±4.4 years and logistic EuroSCORE I was 26.5±7.7%. Procedural success was obtained in 84 patients (94.4%). At 30 days, three patients had died, and two major strokes and one reintervention for a ventricular septal defect occurred, leading to a major adverse cardiac and cerebrovascular event (MACCE) rate of 6.7%. Eight patients (10.3%) received a permanent pacemaker. At one year, 20 patients (22.5%) had died and the MACCE rate was 27%. Effective orifice area was 1.76±0.34 cm<sup>2</sup>, and mean gradient 7.5±2.8 mmHg. Only three patients (4.5%) had moderate paravalvular regurgitation. NYHA Class III/IV was present in 94.4% of patients at baseline, in 9.9% at 30 days and in 4.5% at one year post procedure.

**Conclusions:** This first-in-human experience with a novel self-expanding heart valve showed low rates of procedural mortality, major stroke and pacemaker implantation, and good performance outcomes.

\*Corresponding author: Klinik für Innere Medizin I, St.-Johannes Hospital, Johannesstraße 9-13, 44137 Dortmund, Germany. E-mail: helge.moellmann@joho-dortmund.de

## Abbreviations

<b>EOA</b>	effective orifice area
<b>MACCE</b>	major adverse cardiac and cerebrovascular events
<b>NYHA</b>	New York Heart Association
<b>TAVI</b>	transcatheter aortic valve implantation

## Introduction

Transcatheter aortic heart valve implantation (TAVI) has become an established treatment option for high-risk patients with aortic stenosis. Randomised controlled trials with early-generation self-expanding and balloon-expandable devices have shown non-inferiority or even superiority in comparison to surgical aortic valve replacement, but were associated with higher rates of new pacemaker implantations and moderate to severe paravalvular regurgitation, the latter being associated with an increased mortality risk<sup>1-3</sup>.

Newer-generation devices have been developed to address these limitations, such as the self-expanding ACURATE TA™ prosthesis (Symetis SA, Ecublens, Switzerland) for transapical delivery. The prosthesis has specific design features to allow easy and intuitive implantation and has shown low pacemaker and paravalvular regurgitation rates in clinical trials and registries<sup>4,5</sup>. The encouraging results led to the development of the ACURATE neo™ prosthesis (Symetis) (**Figure 1**), translating the key features of the ACURATE TA into a transfemoral platform. Specifically, flexible stabilisation arches allow axial self-alignment, the upper crown allows supra-annular anchoring and captures the native leaflets, hence mitigating the risk of coronary obstruction and paravalvular regurgitation, the lower crown has minimal left ventricular outflow tract protrusion, hence avoiding interference with the conduction system, and the pericardial skirt acts as a seal against paravalvular regurgitation. Additionally, the BioFix™ (Symetis) anticalcification treatment will support the long-term durability of the valve. The ACURATE neo prosthesis has supra-annular leaflets, which allow a large effective orifice area (EOA) and low gradients. With the exception of the CoreValve® Evolut™ R prosthesis (Medtronic, Minneapolis, MN, USA), other transcatheter aortic bioprostheses are placed intra-annularly. The ACURATE TF delivery system is compatible with 15 Fr expandable sheaths and one 8 Fr rigid sheath and has a very flexible shaft facilitating easy tracking even in tortuous aortic anatomy<sup>6,7</sup>.

It was the aim of the “CE-approval cohort” study to assess the safety and performance of this novel device in high-risk patients treated for severe aortic stenosis. Data of this cohort led to CE certification in Europe in September 2014.

## Methods

### STUDY DESIGN AND POPULATION

The study population consisted of the first 89 patients treated with the ACURATE neo prosthesis from January 2012 to October 2013, prior to its commercialisation.

The main inclusion criteria were: severe aortic stenosis characterised by a mean aortic gradient >40 mmHg, or peak jet velocity >4.0 m/s, or aortic valve area of <1.0 cm<sup>2</sup>, age ≥75 years, logistic



**Figure 1.** The ACURATE neo prosthesis. Stabilisation arches allow axial self-alignment of the prosthesis, the upper crown allows supra-annular anchoring and the lower crown is designed for minimal protrusion in the left ventricular outflow tract. The skirt acts against paravalvular leakage.

EuroSCORE I ≥20%, New York Heart Association (NYHA) functional Class >II, aortic annulus diameter ≥21 mm and ≤27 mm, and signed informed consent. The main exclusion criteria were: unicuspid or bicuspid aortic valve, extreme eccentricity of calcification, severe mitral regurgitation (>2+), pre-existing prosthetic heart valve or ring, left ventricular ejection fraction <30%. The full list of inclusion and exclusion criteria is provided at [clinicaltrials.gov](http://clinicaltrials.gov) #NCT03003650. Follow-up occurred at discharge or seven days (whichever occurred first), at 30 days and one-year post procedure and included NYHA classification, National Institutes of Health Stroke Scale and mini mental state exam assessments, blood draw and echocardiography. Patients were not regularly assessed by a neurologist.

The study was conducted according to the Declaration of Helsinki, and approved by the local ethics committees and competent authorities; all patients provided written informed consent prior to any study procedure. No echocardiographic core laboratory was used. Except for the first-in-human cohort and the Japanese cohort, monitoring included 100% source document verification, and an independent clinical events committee adjudicated all deaths and major adverse cardiac and cerebrovascular events (MACCE).

### STUDY DEVICE AND PROCEDURE

The ACURATE neo aortic bioprosthesis with its ACURATE TF delivery system has been described previously<sup>6,7</sup>. In brief, it has a self-expanding nitinol frame with porcine pericardial leaflets in the supra-annular position. In order to obtain stable positioning and anchoring together with some self-alignment, the valve opens from top to bottom, unsheathing first the upper crown, then the stabilisation arches and, in a second step, the lower crown to anchor the device inside the annulus. The prosthesis is partially repositionable. The ACURATE neo prosthesis is available in sizes

S, M, and L, which correspond to diameters of 23, 25 and 27 mm, respectively, and allows treating aortic annulus diameters from 21 to 27 mm. At the time of the study, the system was used with either an 18 Fr or a 20 Fr introducer sheath. Predilatation was mandatory and post-dilatation was left to the discretion of the implanting physician. The recommended medication regime was acetylsalicylic acid lifelong, and dual antiplatelet therapy with clopidogrel 75 mg/day for six months post procedure.

## ENDPOINTS AND DEFINITIONS

The primary endpoint was all-cause mortality at 30-day follow-up. Secondary endpoints were: MACCE at 30 days and at one year, defined as death, myocardial infarction, reintervention and stroke; functional improvement from baseline as per NYHA functional classification at 30 days and one year; procedural success defined as complete deployment, normal coronary perfusion, paravalvular or central leak <grade 3, mean gradient <20 mmHg, EOA  $\geq 0.9$  cm<sup>2</sup>, no migration or dislodgement of the prosthesis, no impairment of the mitral valve and no reintervention. Standardised endpoints according to the Valve Academic Research Consortium guidelines were used to adjudicate clinical events<sup>8</sup>. The following data points were analysed to assess the performance of the study device: EOA, mean transvalvular aortic gradient, paravalvular and central regurgitation, and valve function and morphology.

## STATISTICAL ANALYSIS

No formal sample size calculation was conducted. Patients who received a prosthesis other than the study valve (e.g., conversion to open heart, valve-in-valve) were excluded from echocardiographic follow-up, but included in safety assessments. For quantitative variables, means and standard deviations (SD) were calculated, and for categorical data absolute and relative frequencies. The Wilcoxon signed-rank test and paired t-test were applied for comparison; p-values of <0.05 represent significance. Data analysis was performed using SAS, Version 9.3 (SAS Institute, Cary, NC, USA).

## Results

The “TF 89 cohort” consisted of the first 89 patients implanted with the ACURATE neo prosthesis. Clinical follow-up compliance at 30 days and one year was 100%.

Patients were 83.7 $\pm$ 4.4 years old with a logistic EuroSCORE I of 26.5 $\pm$ 7.7% and an STS score of 6.8 $\pm$ 4.1%. Patients had several comorbidities; nearly half of the patients had coronary artery disease (47.2%), renal disease (42.7%), or arrhythmias (41.6%) (**Table 1**). The procedure was performed under general anaesthesia. Predilatation was performed in all but one patient; 34 patients (38.2%) received a prosthesis size S, 35 (39.3%) size M and 20 (22.5%) size L. Post-dilatation was performed in 43 patients (48.3%). Time from femoral insertion of the delivery system to withdrawal post implant was 6:32 $\pm$ 2:50 minutes, and the total procedure time was 66 $\pm$ 28 minutes. The procedure was performed successfully in 84 patients (94.4%). In three patients, a valve-in-valve procedure was required (two for dislodgement

**Table 1. Baseline and procedural characteristics.**

Baseline	N=89
Age, years	83.7 $\pm$ 4.4
Female	58 (65.2)
Logistic EuroSCORE I, %	26.5 $\pm$ 7.7
STS score, %	6.8 $\pm$ 4.1
Diabetes	23 (25.8)
Renal disease*	38 (42.7)
Atrial fibrillation at baseline ECG (n=86)	20 (23.3)
Cancer	11 (13.5)
Coronary artery disease	42 (47.2)
Previous myocardial infarction	6 (6.7)
Previous coronary artery bypass graft	19 (21.3)
Previous percutaneous coronary intervention	21 (23.6)
Permanent pacemaker prior to procedure	11 (12.4)
*Site reported, without formal definition or threshold.	

during retrieval with subsequent suboptimal implantation height and one for a low implant), two of whom received a Medtronic CoreValve prosthesis and one an Edwards SAPIEN XT prosthesis (Edwards Lifesciences, Irvine, CA, USA). One aortic rupture due to post-dilatation occurred, which was detected post procedure; the patient subsequently died. One conversion to surgery occurred due to leaflet damage of the prosthesis following overinflation of the valvuloplasty balloon during post-dilatation. This patient died on day 2 post procedure. During enrolment, the delivery system was optimised to facilitate positioning and simplify retrieval. The last 34 patients were treated with the novel device iteration; none of them experienced a valve-in-valve procedure. No coronary obstruction or impairment of the mitral valve was observed.

All-cause mortality at 30 days was 3.4% (n=3). Aside from the two deaths mentioned above, the third death at 30 days was caused by a third-degree AV block. Further, two major strokes and one reintervention for a ventricular septal defect occurred, leading to a MACCE rate of 6.7% (**Table 2**). The ventricular septal defect was treated with reconstruction of the myocardium and pericardial patch which required the prosthesis to be removed and replaced by a surgical aortic valve on day 17 post procedure. The patient was discharged in a stable condition 13 days later. Excluding patients with prior pacemaker, the 30-day pacemaker rate was 10.3% (8/78). Between 30 days and one year, 17 additional deaths occurred. Causes were unknown in two, sudden death in two, neurological events in two, and cardiac decompensation in one patient, infection/sepsis in five patients, respiratory events in two patients, and trauma, cancer, and renal failure in one patient each.

Follow-up echocardiography data were available for 82 patients at 30 days and for 66 patients at one year. The EOA improved from 0.67 $\pm$ 0.17 cm<sup>2</sup> preoperatively to 1.77 $\pm$ 0.32 cm<sup>2</sup> at 30 days and remained constant at one year (**Table 3, Figure 2**). Moderate paravalvular regurgitation was observed in four patients at 30 days

**Table 2. Clinical outcomes at 30 days and 1 year.**

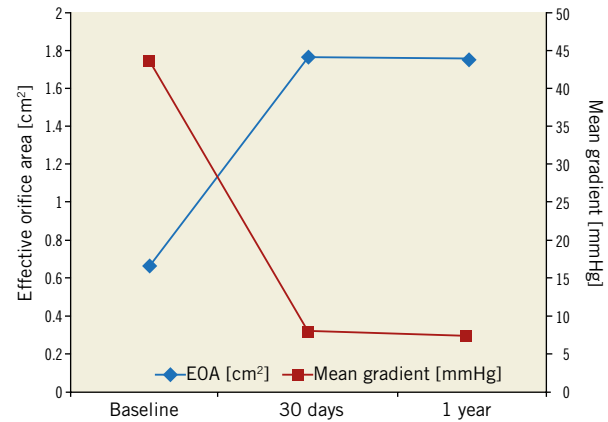
	30 days	1 year
Mortality	3 (3.4)	20 (22.5)
Cardiovascular	3 (3.4)	14 (15.7)
Non-cardiovascular	0 (0.0)	6 (6.7)
Myocardial infarction	0 (0.0)	1 (1.1)
Stroke major	2 (2.2)	6 (6.7)
Life-threatening or disabling bleeding	4 (4.5)	–
AKI stage 3	3 (3.4)	–
Major vascular complication	3 (3.4)	–
Other TAVI-related complications post procedure*	1 (1.1)	1 (1.1)
New permanent pacemaker (n=78) <sup>†</sup>	8 (10.3)	9 (11.5)
Early safety <sup>‡</sup>	14 (15.7)	–
Freedom from MACCE	83 (93.3)	65 (73.0)

Data are presented as n (%). \* Ventricular septal defect. <sup>†</sup>Patients with prior pacemaker implantation were excluded. <sup>‡</sup>A composite of all-cause mortality, major stroke, life-threatening (or disabling) bleeding, AKI – stage 3 (including renal replacement therapy), periprocedural myocardial infarction, major vascular complication, and reintervention. AKI: acute kidney injury; MACCE: major adverse cardiac and cerebrovascular events (a composite of death, stroke, myocardial infarction and reintervention); TAVI: transcatheter aortic valve implantation

and in three patients at one year. NYHA class improved in nearly all patients, with 95.5% of patients being in NYHA Class I or II at 12 months (**Figure 3**).

## Discussion

The main finding of this CE-approval cohort of 89 patients is that transfemoral TAVI with the novel ACURATE neo transcatheter heart valve and its delivery system is safe and effective. Even though this series (a) included an elderly high-risk population with an average age of 83.7 years and a logistic EuroSCORE I of 26.5%, (b) included first-in-human use and best practices on how to implant this prosthesis via the transfemoral approach needed to be established, and (c) included device iterations, outcomes are very good and comparable to other contemporary transcatheter



**Figure 2. Echocardiographic parameters at baseline and follow-up.** Data are available for 82 patients at 30 days and 66 patients at one year. The EOA increased significantly from baseline to 30 days ( $p < 0.0001$ ); the mean gradient decreased significantly ( $p < 0.0001$ ). Values remained stable between 30 days and one year ( $p = 0.24$  for EOA and  $p = 0.28$  for mean gradient). EOA: effective orifice area

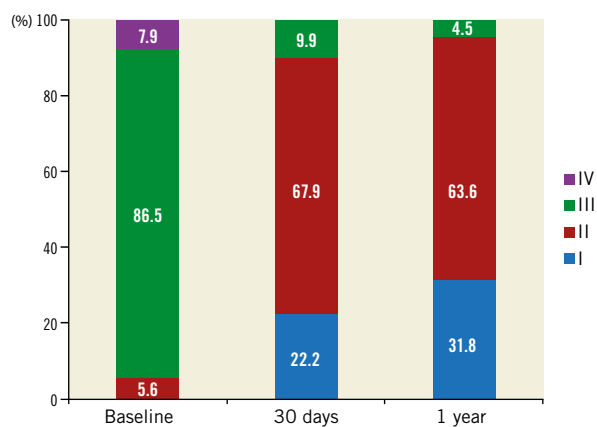
heart valve prostheses. The encouraging results in this early phase are most likely attributed to the self-seating, self-sealing design of the prosthesis, as the top-down deployment leads to a stable, easy implantation in the correct anatomic position<sup>6,7</sup>.

This is particularly important as previous experiences gained from first-in-human use or with similar devices were available for devices such as the the CoreValve Evolut R<sup>9,10</sup>, the Direct Flow Medical valve (Direct Flow Medical, Santa Rosa, CA, USA)<sup>11</sup>, the LOTUS™ valve (Boston Scientific, Marlborough, MA, USA)<sup>12</sup>, the Portico™ valve (St. Jude Medical, St. Paul, MN, USA)<sup>13,14</sup>, and the SAPIEN 3 prosthesis (Edwards Lifesciences)<sup>15</sup>. The total procedure time of 66±28 minutes with 6:32±2:50 minutes from time of femoral insertion of the delivery system to withdrawal post implant underlines the intuitive use of the device. In contrast, procedure times around 1.5 hours were reported for several novel next-generation devices, such as for the Direct Flow Medical

**Table 3. Echocardiographic assessments.**

	Unpaired			Paired	
	Baseline N=89	30 days* N=82	1 year N=66	30 days N=66	1 year N=66
Effective orifice area, cm <sup>2</sup>	0.67±0.17	1.77±0.32	1.76±0.34	1.82±0.32	1.76±0.34
Mean gradient, mmHg	43.6±17.1	8.0±2.9	7.5±2.8	7.9±2.9	7.5±2.8
LVEF	56.1±12.7	60.8±10.1	61.5±8.5	60.7±9.9	61.5±8.5
Central leak	0: none/trace	NA	79 (96.3)	63 (95.5)	64 (97.0)
	1+: mild		3 (3.7)	3 (4.5)	2 (3.0)
Paravalvular leak	0: none/trace	NA	25 (30.5)	20 (30.3)	29 (43.9)
	1+: mild		53 (64.6)	43 (65.2)	34 (51.5)
	2+: moderate		4 (4.9)	3 (4.5)	3 (4.5)

Data are presented as mean±SD or n (%). \* No assessment in 3 patients with valve-in-valve, 1 patient with conversion to surgery, and 3 patients who died up to 30 days. If 30-day echo was not available, discharge echo was used instead. LVEF: left ventricular ejection fraction; NA: not assessed



**Figure 3.** NYHA classification at baseline, 30 days and one year: NYHA class improved significantly from baseline to 30 days ( $p<0.0001$ ); no significant difference was observed from 30 days to one year ( $p=0.307$ ). NYHA: New York Heart Association

multicentre experience<sup>16</sup>, the CoreValve Evolut CE-mark study<sup>9</sup>, and the REPRIS II study<sup>17</sup>.

Three valve-in-valve procedures due to dislodgement during retrieval and malpositioning occurred. As a matter of fact, the risk of valve migration during retrieval of the delivery catheter has been an issue for most self-expanding TAVR devices; however, the final versions of the ACURATE neo and its ACURATE TF delivery system appear to have adequately addressed this issue<sup>7</sup>; positioning became easier and no valve-in-valve procedure occurred in the last 34 patients enrolled.

The mortality of 3.4% at 30 days is lower than in first-generation devices with a pooled 30-day mortality of 7.8% (1.7-14.3%)<sup>18</sup> and comparable to recent reports of next-generation devices ranging from 0% to 4.2%<sup>9,15-17,19-21</sup>. Moreover, two of the three deaths occurred due to intraprocedural complications which are expected to diminish with the updated delivery system and increased operator experience with this device. In contrast, the one-year mortality appears to be higher than in recent studies. Notably, complications associated with increased mortality such as paravalvular regurgitation, acute kidney injury, periprocedural myocardial infarction and major stroke<sup>22,23</sup> were low so that it is likely that the one-year mortality was rather related to the severe comorbidities, reflected by a considerably higher logistic EuroSCORE I in comparison to other studies (26.5% versus 15.1% to 24.7%)<sup>9,15,16,24,25</sup>. In general, it seems that nowadays, with refined procedures and devices, risk scores – reflecting the comorbidities of the patients – are less relevant for predicting procedural outcomes and are rather relevant in predicting midterm outcomes<sup>22,23</sup>. This assumption is confirmed by a recent single-centre study that implanted the ACURATE neo in patients with a substantially lower EuroSCORE I (15.1% compared to 26.5% in our series), reporting a one-year mortality of only 5.2%<sup>26</sup>.

Despite a rather high post-dilatation rate of 48.3% related to the relatively low radial force of the frame of the prosthesis, only two major strokes occurred. Considering that high-intensity transient

signals are mainly observed during valve positioning and implantation<sup>27</sup>, and first-in-human series generally require more manipulation contributing to the higher risk for cerebrovascular events in the first half of centres' experiences<sup>28</sup>, this outcome is encouraging.

The pacemaker rate of 10.3% at 30 days is consistent with those observed for the ACURATE TA prosthesis used for transapical access which ranged between 7.5% and 10.2%<sup>4,5</sup>. It compares well to those observed for first-generation devices (3.4-50.0%, pooled estimate 13.9%)<sup>18</sup>, the LOTUS prosthesis (28.6%)<sup>17</sup>, and the CoreValve Evolut R, Direct Flow, Portico and SAPIEN 3 prostheses which range from 9.5% to 17.1%<sup>9,15,16,20,24,25</sup>. Of note, the values mentioned refer to the overall study population, whereas the 10.3% event rate in our series refers to patients without a prior pacemaker (using the same calculation, our pacemaker rate would be 9.0%).

The large effective orifice area of  $1.77\pm 0.32$  cm<sup>2</sup> and the single-digit mean gradient reflect the true supra-annular design of the valve. With the caveat that echocardiographic parameters are site reported, only four patients (4.9%) had moderate paravalvular regurgitation and none severe, which is lower than observed for the first-generation devices which ranged from 0% to 30% with a pooled estimate of 7.4%<sup>1,2,21</sup>, and comparable to recent reports of next-generation prostheses (1% to 3.8%)<sup>9,15-17,20,24,25</sup>. Echocardiographic outcomes were sustained at one year.

## Limitations

This CE-approval cohort has several limitations. The low patient number and lack of randomisation hamper comparisons to other devices. Echocardiographic data are site reported with no echocardiographic core laboratory being used. As enrolment started in January 2012, only VARC-1 criteria were applied<sup>8</sup>. The strength of the present study is that all patients returned for follow-up assessment. Data on a larger patient number, long-term data and ultimately randomised controlled data comparing different transcatheter heart valves will be necessary to provide further evidence of the usefulness of this device.

## Conclusions

In this first-in-human experience in high-risk elderly patients with severe aortic stenosis, the novel ACURATE neo transcatheter heart valve system has shown a low rate of procedural mortality, major stroke and pacemaker implantation, and good performance outcomes. Specific design features contributing to an “ease of implantation” might have positively affected the outcomes in this early series.

## Impact on daily practice

We report the first one-year multicentre outcomes of the second-generation self-expanding ACURATE neo transcatheter heart valve. Specific design features allow an easy and intuitive implantation of the prosthesis. In this early series, transfemoral TAVI with the ACURATE neo resulted in good safety and performance outcomes, reflecting the ease of use of the device.

## Acknowledgements

We thank W.D. Weaver, A.P. Kappetein, F.W.A. Verheugt, J.G.P. Tijssen, S. Bailey and M. Gorman for their participation in the data monitoring committee, Beatrix Doerr, consultant medical writer, for editorial assistance, and Samuel Copt, consultant statistician, for statistical analysis.

## Funding

This work was funded by Symetis SA, Ecublens, Switzerland.

## Conflict of interest statement

H. Möllmann and W.K. Kim are proctors for Symetis and St. Jude Medical. D. Siqueira is a proctor for Symetis. P. Diemert is a proctor for Symetis and receives lecture fees. H. Treede is a proctor and advisor for Symetis. T. Rudolph is a proctor for Symetis and has received speaker's honoraria. J. Kempfert is proctor for Symetis, Edwards and Medtronic. The other authors have no conflicts of interest to declare.

## References

- Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, Gleason TG, Buchbinder M, Hermiller J Jr, Kleiman NS, Chetcuti S, Heiser J, Merhi W, Zorn G, Tadros P, Robinson N, Petrossian G, Hughes GC, Harrison JK, Conte J, Maini B, Mumtaz M, Chenoweth S, Oh JK; U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med*. 2014;370:1790-8.
- Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med*. 2011;364:2187-98.
- Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM, Webb JG, Douglas PS, Anderson WN, Blackstone EH, Kodali SK, Makkar RR, Fontana GP, Kapadia S, Bavaria J, Hahn RT, Thourani VH, Babaliaros V, Pichard A, Herrmann HC, Brown DL, Williams M, Akin J, Davidson MJ, Svensson LG; PARTNER 1 trial investigators. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet*. 2015;385:2477-84.
- Kempfert J, Treede H, Rastan AJ, Schönburg M, Thielmann M, Sorg S, Mohr FW, Walther T. Transapical aortic valve implantation using a new self-expandable bioprosthesis (ACURATE TA): 6-month outcomes. *Eur J Cardiothorac Surg*. 2013;43:52-6.
- Kempfert J, Holzhey D, Hofmann S, Girdauskas E, Treede H, Schrüfel H, Thielmann M, Walther T. First registry results from the newly approved ACURATE TA™ TAVI system†. *Eur J Cardiothorac Surg*. 2015;48:137-41.
- Möllmann H, Diemert P, Grube E, Baldus S, Kempfert J, Abizaid A. Symetis ACURATE TF™ aortic bioprosthesis. *EuroIntervention*. 2013;9 Suppl:S107-10.
- Schäfer U, Conradi L, Diemert P, Deuschl F, Schofer N, Seiffert M, Lubos E, Schirmer J, Reichenspurner H, Blankenberg S, Treede H. Symetis ACURATE TAVI: review of the technology, developments and current data with this self-expanding transcatheter heart valve. *Minerva Cardioangiol*. 2015;63:359-69.
- Leon MB, Piazza N, Nikolsky E, Blackstone EH, Cutlip DE, Kappetein AP, Krucoff MW, Mack M, Mehran R, Miller C, Morel MA, Petersen J, Popma JJ, Takkenberg JJ, Vahanian A, van Es GA, Vranckx P, Webb JG, Windecker S, Serruys PW. Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium. *Eur Heart J*. 2011;32:205-17.
- Manoharan G, Walton AS, Brecker SJ, Pasupati S, Blackman DJ, Qiao H, Meredith IT. Treatment of Symptomatic Severe Aortic Stenosis With a Novel Resheathable Supra-Annular Self-Expanding Transcatheter Aortic Valve System. *JACC Cardiovasc Interv*. 2015;8:1359-67.
- Piazza N, Martucci G, Lachapelle K, de Varennes B, Bilodeau L, Buihieu J, Mylotte D. First-in-human experience with the Medtronic CoreValve Evolut R. *EuroIntervention*. 2014;9:1260-3.
- Treede H, Tubler T, Reichenspurner H, Grube E, Pascotto A, Franzen O, Mueller R, Low R, Bolling SF, Meinertz T, Schofer J. Six-month results of a repositionable and retrievable pericardial valve for transcatheter aortic valve replacement: the Direct Flow Medical aortic valve. *J Thorac Cardiovasc Surg*. 2010;140:897-903.
- Meredith IT, Worthley SG, Whitbourn RJ, Antonis P, Montarello JK, Newcomb AE, Lockwood S, Haratani N, Allocco DJ, Dawkins KD. Transfemoral aortic valve replacement with the repositionable Lotus Valve System in high surgical risk patients: the REPRISSE I study. *EuroIntervention*. 2014;9:1264-70.
- Manoharan G, Spence MS, Rodés-Cabau J, Webb JG. St Jude Medical Portico valve. *EuroIntervention*. 2012;8 Suppl Q:Q97-101.
- Willson AB, Rodés-Cabau J, Wood DA, Leipsic J, Cheung A, Toggweiler S, Binder RK, Freeman M, DeLarochelière R, Moss R, Nombela-Franco L, Dumont E, Szummer K, Fontana GP, Makkar R, Webb JG. Transcatheter aortic valve replacement with the St. Jude Medical Portico valve: first-in-human experience. *J Am Coll Cardiol*. 2012;60:581-6.
- Webb J, Gerosa G, Lefèvre T, Leipsic J, Spence M, Thomas M, Thielmann M, Treede H, Wendler O, Walther T. Multicenter evaluation of a next-generation balloon-expandable transcatheter aortic valve. *J Am Coll Cardiol*. 2014;64:2235-43.
- Naber CK, Pyxaras SA, Ince H, Latib A, Frambach P, den Heijer P, Wagner D, Butter C, Colombo A, Kische S. Real-world multicentre experience with the Direct Flow Medical repositionable and retrievable transcatheter aortic valve implantation system for the treatment of high-risk patients with severe aortic stenosis. *EuroIntervention*. 2016;11:e1314-20.
- Meredith Am IT, Walters DL, Dumonteil N, Worthley SG, Tchetché D, Manoharan G, Blackman DJ, Rioufol G, Hildick-Smith D, Whitbourn RJ, Lefèvre T, Lange R, Müller R, Redwood S, Allocco DJ, Dawkins KD. Transcatheter aortic valve replacement

for severe symptomatic aortic stenosis using a repositionable valve system: 30-day primary endpoint results from the REPRISE II study. *J Am Coll Cardiol*. 2014;64:1339-48.

18. G n reux P, Head SJ, Van Mieghem NM, Kodali S, Kirtane AJ, Xu K, Smith C, Serruys PW, Kappetein AP, Leon MB. Clinical outcomes after transcatheter aortic valve replacement using valve academic research consortium definitions: a weighted meta-analysis of 3,519 patients from 16 studies. *J Am Coll Cardiol*. 2012;59:2317-26.

19. Schofer J, Nietlisbach F, Bijuklic K, Colombo A, Gatto F, De Marco F, Mangieri A, Hansen L, Bruschi G, Ruparelia N, Rie  FC, Maisano F, Latib A. Transfemoral Implantation of a Fully Repositionable and Retrievable Transcatheter Valve for Noncalcified Pure Aortic Regurgitation. *JACC Cardiovasc Interv*. 2015;8:1842-9.

20. Herrmann HC, Thourani VH, Kodali SK, Makkar RR, Szeto WY, Anwaruddin S, Desai N, Lim S, Malaisrie SC, Kereiakes DJ, Ramee S, Greason KL, Kapadia S, Babaliaros V, Hahn RT, Pibarot P, Weissman NJ, Leipsic J, Whisenant BK, Webb JG, Mack MJ, Leon MB; PARTNER Investigators. One-Year Clinical Outcomes With SAPIEN 3 Transcatheter Aortic Valve Replacement in High-Risk and Inoperable Patients With Severe Aortic Stenosis. *Circulation*. 2016;134:130-40.

21. Athappan G, Gajulapalli RD, Tuzcu ME, Svensson LG, Kapadia SR. A systematic review on the safety of second-generation transcatheter aortic valves. *EuroIntervention*. 2016;11:1034-43.

22. Collas VM, Dubois C, Legrand V, Kefer J, De Bruyne B, Dens J, Rodrigus IE, Herijgers P, Bosmans JM; Belgian TAVI Registry Participants. Midterm clinical outcome following Edwards SAPIEN or Medtronic Corevalve transcatheter aortic valve implantation (TAVI): Results of the Belgian TAVI registry. *Catheter Cardiovasc Interv*. 2015;86:528-35.

23. Linke A, Wenaweser P, Gerckens U, Tamburino C, Bosmans J, Bleiziffer S, Blackman D, Sch fer U, M ller R, Sievert H,

Sondergaard L, Klugmann S, Hoffmann R, Tchetch  D, Colombo A, Legrand VM, Bedogni F, lePrince P, Schuler G, Mazzitelli D, Eftychiou C, Frerker C, Boekstegers P, Windecker S, Mohr FW, Woitek F, Lange R, Bauernschmitt R, Brecker S; ADVANCE study Investigators. Treatment of aortic stenosis with a self-expanding transcatheter valve: the International Multi-centre ADVANCE Study. *Eur Heart J*. 2014;35:2672-84.

24. Schofer J, Colombo A, Klugmann S, Fajadet J, DeMarco F, Tch tch  D, Maisano F, Bruschi G, Latib A, Bijuklic K, Weissman N, Low R, Thomas M, Young C, Redwood S, Mullen M, Yap J, Grube E, Nickenig G, Sinning JM, Hauptmann KE, Friedrich I, Lauterbach M, Schmoeckel M, Davidson C, Lef vre T. Prospective multicenter evaluation of the direct flow medical transcatheter aortic valve. *J Am Coll Cardiol*. 2014;63:763-8.

25. Manoharan G, Linke A, Moellmann H, Redwood S, Frerker C, Kovac J, Walther T. Multicentre clinical study evaluating a novel resheathable annular functioning self-expanding transcatheter aortic valve system: safety and performance results at 30 days with the Portico system. *EuroIntervention*. 2016;12:768-74.

26. Hamm K, Reents W, Zacher M, Kerber S, Diegeler A, Schieffer B, Barth S. Transcatheter aortic valve implantation using the ACURATE TA and ACURATE neo valves: a four-year single-centre experience. *EuroIntervention*. 2017;13:53-9.

27. Kahlert P, Al-Rashid F, D ttger P, Mori K, Plicht B, Wendt D, Bergmann L, Kottenberg E, Schlamann M, Mummel P, Holle D, Thielmann M, Jakob HG, Konorza T, Heusch G, Erbel R, Eggebrecht H. Cerebral embolization during transcatheter aortic valve implantation: a transcranial Doppler study. *Circulation*. 2012;126:1245-55.

28. Auffret V, Regueiro A, Del Trigo M, Abdul-Jawad Altisent O, Campelo-Parada F, Chiche O, Puri R, Rod s-Cabau J. Predictors of Early Cerebrovascular Events in Patients With Aortic Stenosis Undergoing Transcatheter Aortic Valve Replacement. *J Am Coll Cardiol*. 2016;68:673-84.