SAPIEN 3 versus Myval transcatheter heart valves for transcatheter aortic valve implantation (COMPARE-TAVI 1): a multicentre, randomised, non-inferiority trial

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Summary

Background Transcatheter aortic valve implantation (TAVI) is a guideline-directed treatment for severe aortic stenosis and degenerated aortic bioprostheses. When new transcatheter heart valve (THV) platforms for TAVI are launched, they should be compared with best-in-practice contemporary THVs for their short-term and long-term performance. The COMPARE-TAVI 1 trial was designed to provide a head-to-head comparison of the SAPIEN 3 or SAPIEN 3 Ultra THVs and the Myval or Myval Octacor THVs.

Methods This multicentre, all-comers, randomised, non-inferiority trial was done at three university hospitals in Denmark. Eligible patients were aged 18 years or older, scheduled for transfemoral TAVI, and eligible for treatment with SAPIEN 3 THVs or Myval THVs. Patients were randomly assigned (1:1) to treatment with SAPIEN 3 (29 mm diameter) or SAPIEN 3 Ultra (20 mm, 23 mm, or 26 mm diameter) THVs or Myval or Myval Octacor THVs (20–32 mm diameter). The TAVI procedure was performed according to local practice and under local anaesthesia unless leaflet laceration was performed. The primary endpoint was a composite of death, stroke, moderate or severe aortic regurgitation, or moderate or severe haemodynamic THV deterioration at 1 year according to Third Valve Academic Research Consortium criteria. All patients assigned to THV treatment were included in the intention-to-treat analysis, and all patients who were treated as randomly assigned were included in the per-protocol analysis. With an expected event rate of 13%, the prespecified non-inferiority margin was 5·3%. This trial is registered with ClinicalTrials.gov, NCT04443023, and is closed to accrual.

Findings Between June 15, 2020, and Nov 3, 2023, 1031 patients were enrolled. Enrolment was paused twice because of patent-related legal proceedings. Of 1031 patients, 517 patients were randomly assigned to SAPIEN 3 THVs and 514 to Myval THVs. The median patient age was 81·6 years (IQR 77·6–85·0), and 415 (40%) of 1031 patients were female and 616 (60%) were male. The primary endpoint occurred in 67 (13%) of 517 patients randomly assigned to SAPIEN 3 THVs versus 71 (14%) of 514 patients randomly assigned to Myval THVs (risk difference –0·9% [one-sided upper 95% CI 4·4%]; $p_{non\text{-}inferiority}$=0·019).

Interpretation Myval THVs were non-inferior to SAPIEN 3 THVs in terms of a 1-year composite endpoint of death, stroke, moderate or severe aortic regurgitation, or moderate or severe haemodynamic THV deterioration.

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Introduction

Aortic stenosis is the most prevalent valvular disease in high-income countries, and the prognosis for untreated severe aortic stenosis is poor.[1] Transcatheter aortic valve implantation (TAVI), a minimally invasive procedure in which a transcatheter heart valve (THV) is implanted,[2,3] is being increasingly used to treat severe aortic stenosis, not just in patients ineligible for surgical aortic valve replacement[4] and those at high surgical risk,[5] but also in those with intermediate[6] or low surgical risk.[7,8] New THVs are frequently launched and used in clinical practice although data on short-term performance are scarce and long-term data are absent. Ideally, new THVs should be compared with best-in-practice contemporary THVs. The COMPARE-TAVI trial was designed to provide a large-scale, head-to-head comparison of the SAPIEN 3 or SAPIEN 3 Ultra THVs versus the Myval or Myval Octacor THVs in an all-comers setting, reflecting routine daily use of THVs in the general population treated with TAVI and focusing on intermediate-term and long-term performance and durability.[9]

Methods

Study design and participants

COMPARE-TAVI 1 trial was a multicentre, randomised, non-inferiority trial done at three university hospitals in

Research in context

Evidence before this study

When launching new transcatheter heart valves (THVs), they should be compared head-to-head with best-in-practice contemporary THVs. We searched PubMed from database inception to Dec 19, 2024, with the search term "Myval", for previously published data on head-to-head comparisons of the Myval THV series (Myval or Myval Octacor THV) with other THVs and identified 87 papers mentioning Myval. Before the start of the COMPARE-TAVI 1 trial on June 15, 2020, no previous head-to-head comparisons between the contemporary THVs and the newer generation THV series (eg, Myval) had been performed. In 2024, the LANDMARK trial showed non-inferiority of Myval compared with contemporary THVs (SAPIEN 3 and Evolut) at 30 days, but 1-year data from the trial have not yet been reported.

Added value of this study

COMPARE-TAVI 1 is the first trial comparing SAPIEN 3 and Myval THVs at 1 year and the largest comparison of any THVs to date. Myval THVs were found to be non-inferior to SAPIEN 3 THVs for the 1-year primary composite endpoint but were associated with an increased risk of need for pacemaker implantation. The differences observed in individual components of the primary endpoint, as well as in secondary endpoints, might reflect the different technology on which the two balloon-expandable THVs are based.

Implications of all the available evidence

The safety and efficacy of new THVs should be compared with that of best-in-practice, contemporary THVs. To our knowledge, Myval is the first THV showing non-inferiority with SAPIEN 3 THVs at 1 year, although it increases the risk of first-time pacemaker implantation, which requires further evaluation. Follow-up will clarify whether differences in secondary outcomes affect prognosis, whether short-term differences in effective orifice area translate to differences in long-term durability, and whether these two balloon-expandable THV series perform differently in those with small aortic valve annuli and in female patients.

Denmark: Aarhus University Hospital, Odense University Hospital, and Aalborg University Hospital. The rationale and design of the COMPARE-TAVI trial are detailed in a previous publication.[9] The comparison of the SAPIEN 3 or SAPIEN 3 Ultra THV series and the Myval or Myval Octacor THV series was initially denoted as cohort B but is herein referred to as COMPARE-TAVI 1 because it is the first COMPARE-TAVI cohort in which inclusion was finalised.[9] The Ethics Committee for the Central Denmark Region granted ethics approval on March 3, 2018 (1–10–72–389–17). Amendments were filed when new head-to-head comparisons were launched. COMPARE-TAVI 1 was approved by The Ethics Committee for the Central Denmark Region on April 23, 2020 (protocol amendment 2). Additional amendment approval requests were filed for substudies incorporating multislice CT and cardiac MRI during follow-up, for changes in patient consent forms (when stating the funding source), and for protocol changes to adhere to the third Valve Academic Research Consortium (VARC-3) criteria. The Danish protocol (version 6.5.2023; amendment 10) was approved by The Ethics Committee for the Central Denmark Region on May 30, 2023. The English translation of the protocol incorporates approved substudies (appendix pp 2–12). This study is registered with ClinicalTrials.gov, NCT04443023, and is closed to accrual.

See Online for appendix

Eligible sites were required to perform at least 75 TAVI procedures per year and operators were required to have implanted at least 15 of each THV.[9] Aarhus University Hospital, Odense University Hospital, and Aalborg University Hospital (appendix p 1) provide open-heart surgery and had a TAVI volume in 2020 of 295, 200, and 122 procedures, respectively. Eligible patients were older than 18 years, scheduled for transfemoral TAVI, and eligible for treatment with the SAPIEN 3 or Myval THVs.[9] The study was intended as an all-comers trial, and centres prioritised inclusion of all eligible patients regardless of anatomy (eg, tricuspid, bicuspid, or valve-in-valve) or timing of the procedure (eg, elective, subacute, or in-hospital). Patients with large aortic annuli suitable for treatment with Myval XL valves (30·5 mm and 32·0 mm diameter) were eligible for inclusion if the TAVI team also found them eligible for treatment with a SAPIEN 3 (29·0 mm diameter) THV. All participants provided written informed consent.

Randomisation and masking

Patients were randomly assigned (1:1) to the SAPIEN 3 THVs or Myval THVs by treating physicians using a web-based system (corolog.net) with block permutation (block sizes 2–6), stratified by centre and sex. Masking of physicians and patients was not possible. Randomisation occurred as close as possible to the procedure, preferably after arrival at the catheterisation laboratory. After randomisation, patients were removed from the study only if they withdrew consent.

Procedures

Patients were scheduled for treatment with SAPIEN 3 (29 mm diameter) or SAPIEN 3 Ultra (20 mm, 23 mm, or 26 mm diameter) THVs (Edwards Lifesciences, Irvine, CA, USA) or Myval or Myval Octacor THVs (20–32 mm diameter; Meril Life Sciences, Vapi, India). The TAVI procedure was performed according to local practice and under local anaesthesia, unless leaflet laceration was performed in which case general anaesthesia was used.[10] After the Myval Octacor valve was introduced in the trial,

operators attempted to align all transcatheter heart valves used in the trial relative to the left main coronary artery. To achieve this, they adjusted the position of one of the valve's commissural posts (the neo-commissure) before implantation. For the Myval Octacor valve, the neocommisure was positioned 120° from the left main coronary artery takeoff, measured from the baseline multislice CT, whereas for the SAPIEN valves, it was aligned at the 1200 h position.

Clinical follow-up, including echocardiography, was scheduled at 30 days and at 1, 3, 5, and 10 years. Echocardiography was performed according to a standardised protocol (appendix pp 13–19), and echocardiography results were reviewed centrally by a core site (Odense University Hospital). Echocardiography images were transmitted to the core laboratory at Odense University Hospital and assigned to five readers (NSBM and four others) that included highly experienced research fellows and a cardiologist with level 3 certification in echocardiography. The images were subsequently verified by the core laboratory director. Before initiation of the study, all core laboratory members underwent a pairwise comparison of 25 cases for variables included in the electronic case report form. Echocardiography images were analysed using Viewpoint 6 (GE Healthcare, Horten, Norway) and IntelliSpace Cardiovascular (Philips Healthcare Best, Netherlands). Clinical data, including sex, were collected from Danish electronic patient files. Data on race and ethnicity were not collected because these are not routinely included in Danish electronic patient files.

The left ventricular outflow tract diameter was measured from outer edge to outer edge of the THV frame.[11] At clinical follow-up, study nurses assessed and reported events (endpoints) in an electronic case report form and screened patients' electronic medical records for events. Events were monitored according to a separate monitoring plan (appendix pp 20–27) by trained monitors who also had access to patients' electronic medical records. Two neurologists adjudicated all strokes and transitory ischaemic attacks reported in patient records during admission and follow-up. Because routine neurological examinations were not included in the study, only clinically reported events were adjudicated. Two cardiologists adjudicated bleeding events in the following cases: death during the procedure, tamponade, conversion to surgery, surgery or endovascular intervention at access site, vascular complications including annulus rupture, drop in haemoglobin concentration of 1·86 mmol/L or more, or transfusion of 2 units or more of blood. The cardiologists also adjudicated all reported readmissions for congestive heart failure, endocarditis, and acute myocardial infarction. The adjudication committees were given access to electronic patient records and all available imaging data. Classification was done in accordance with the VARC-3 criteria. If adjudicated events were downgraded to non-events, the hospitals and monitors were informed to ensure that follow-up for relevant events continued. Vital status was updated daily in the electronic patient records,[10] and sites and monitors checked vital status at 1 year.

Outcomes

Individual endpoints are listed below and presented according to the original study plan, except for first-time pacemaker implantation.[9] We initially planned to include prophylactic (within 1 month before TAVI) pacemakers in the secondary efficacy endpoint, but the steering committee decided to adhere to the VARC-3 criteria[12] and include only pacemakers implanted after TAVI; data for prophylactic pacemakers are presented separately. Following their publication in 2021, VARC-3 criteria were also used for other endpoints as possible.

The primary endpoint was a composite of all-cause death, stroke, moderate or severe aortic regurgitation, or moderate or severe haemodynamic THV deterioration at 1 year according to the VARC-3 criteria.[12] Separate analyses of each component of the primary outcome were conducted to elucidate their contributions to the primary endpoint.[9] Secondary endpoints, subject to Bonferroni correction, as predefined in the methods paper we published previously,[9] were the proportion of patients with successful implantation of the chosen valve (defined as no need for more than one THV, no change to an unplanned THV during the procedure, and no conversion to surgery or procedure-related death), pacemaker implantation (defined as first-time pacemaker implantation within 1 year after TAVI in patients without a previous pacemaker), and TAVI-related complications (defined as conversion to open surgery during implantation, unplanned use of cardiopulmonary support, coronary artery obstruction, ventricular septal perforation, mitral valve apparatus damage or dysfunction, cardiac tamponade, valve embolisation, valve migration or need for TAVI-in-TAVI deployment, annulus rupture, aortic rupture or perforation, aortic dissection, or shunts other than ventricular septum defects). Endpoints related to the multislice CT and cardiac MRI substudies, valve thrombosis, and degree of aortic regurgitation and gradients according to annular calcium on multislice CT, and 3-year, 5-year, and 10-year findings are planned to be published separately (appendix p 5).

Exploratory secondary endpoints were endocarditis according to VARC-3 criteria at 30 days and 1 year, reoperation (TAVI, surgical aortic valve replacement, or balloon aortic valvuloplasty) at 30 days and 1 year, readmission for congestive heart failure according to VARC-3 criteria at 30 days and 1 year, readmission for acute myocardial infarction according to VARC-3 criteria at 30 days and 1 year, percutaneous coronary intervention or coronary artery bypass grafting (not scheduled before TAVI) at 30 days and 1 year, newly diagnosed atrial

fibrillation or flutter at 30 days and 1 year, 6-min walk test at 30 days and 1 year, VARC-3 bleeding type 2, 3, or 4 at 30 days, major vascular access site and access-related complications resulting in endovascular or open surgery at 30 days, acute kidney injury of stage 2 or worse (increase in renal creatinine level ≥200% or dialysis) at 30 days, and moderate or severe patient–prosthesis mismatch at 30 days. Patient–prosthesis mismatch was defined as an effective orifice area indexed to body surface area of 0·70 cm²/m² or less with a BMI of 30 kg/m² or higher, or 0·85 cm²/m² or less with a BMI of less than 30 kg/m², according to VARC-3 criteria.

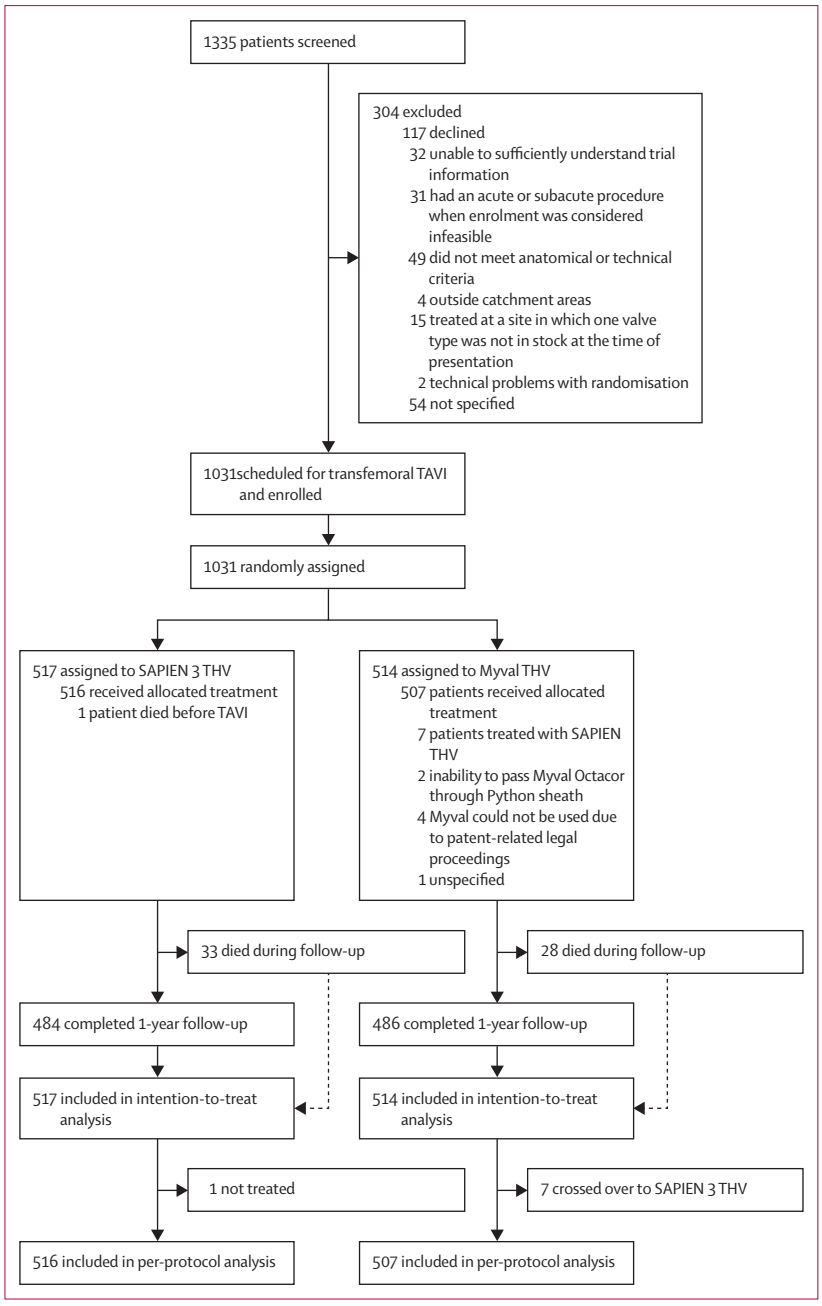

Figure 1: **Trial profile**
TAVI=transcatheter aortic valve implantation. THV=transcatheter heart valve.

Statistical analysis

Continuous outcomes are presented as median (IQR) with specification of valid cases and were compared with the non-parametric Wilcoxon rank-sum test. THV sizes are also presented as mean (SD). Categorical outcomes are presented as total numbers per valid cases and percentages and were compared with the Chi-square test or Fisher's exact test.

Time-to-event outcomes were analysed using the Kaplan–Meier method for all-cause mortality, with comparisons made using the log-rank test. For other time-to-event outcomes, Aalen–Johansen analyses were used to account for competing risk, such as death. For participants with an event, the event date was based on the first event occurrence. For participants without an event, the date of censoring was 1 year after TAVI unless the patient was withdrawn early from the study, in which case the date of withdrawal was used. The risk difference between treatment groups was calculated along with the corresponding 95% CI. A one-sided 95% CI is presented for the primary composite endpoint, and two-sided 95% CIs are presented for each component of the primary endpoint, as well as for secondary and exploratory endpoints. For the primary outcome, a one-sided Farrington–Manning test was used to assess non-inferiority. For all other outcomes, including individual components of the primary endpoint, a two-sided Wald test was used.

The non-inferiority assumption was tested at a one-sided significance level of α=0·05 and with a power of 0·80. The non-inferiority margin was dependent on the final event rate. A prespecified non-inferiority margin of 4·5% was chosen for a 9% event rate and was increased to 5·3% for a 13% event rate, and when allowing for a 5% dropout the total sample size was set to 1062 patients. With no dropout, a sample size of only 1002 patients would have been needed.[9] Non-inferiority was established if the upper limit of the one-sided 95% CI of the risk difference did not cross the prespecified non-inferiority margin. The analysis of the primary composite endpoint was performed according to the intention-to-treat principle, but per-protocol analyses were also conducted if crossover occurred, as prespecified in the methods paper we published previously.[9] All patients assigned to THV treatment were included in the intention-to-treat analysis, and all patients who were treated as randomly assigned were included in the per-protocol analysis. Non-inferiority was declared only if both analyses supported the same conclusion. If non-inferiority was demonstrated for the primary composite endpoint, a gate-keeping strategy with a split α was used to test for superiority of the primary composite endpoint (α=0·025) and three secondary safety and efficacy endpoints (Bonferroni

correction α=0·025/3 for each endpoint). All other secondary outcomes were considered exploratory (hypothesis-generating) and were not subjected to Bonferroni correction.[13–15] A complete case analysis of the primary composite endpoint was also performed, limited to patients who had paired 1-year and 1-month echocardiography for evaluation of haemodynamic THV deterioration, or who already had fulfilled one of the three other components of the composite endpoint (death, stroke, or moderate or severe aortic regurgitation). No subgroup analyses were planned.

To account for potential missing death and stroke data, admissions and vital status were updated daily in the Danish Civil Registration System and the Danish National Patient Registry and were available in electronic medical records in Denmark.[16,17] The most recently available echocardiography images were used to ascertain the degree of aortic regurgitation (at 1 year, 30 days, or post-procedure) to account for potential missing aortic regurgitation data. To account for potential missing data on haemodynamic THV deterioration, deterioration was assessed only if 1-year echocardiograms were available for comparison with either a 30-day (first choice) or post-procedure echocardiogram; otherwise, the patient was classified as having no documented haemodynamic THV deterioration at 1 year.

Statistical analyses were done using Stata/SE, version 18. An independent data and safety monitoring board, comprising two cardiologists, an epidemiologist, and a statistician, reported no safety issues and recommended that trial inclusion continued on Aug 23, 2023, when 575 patients had reached 1-year follow-up.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between June 15, 2020, and Nov 3, 2023, 1335 patients were screened, and 1031 patients were enrolled (figure 1). Enrolment was paused from Feb 17, 2021, to March 28, 2021, and from Aug 31, 2021, to Aug 22, 2022, because of patent-related legal proceedings. Although the planned sample size of 1062 patients had not been reached, the statistical power was deemed to be sufficient because of an absence of withdrawal or emigration; therefore, the steering committee ended enrolment on Nov 3, 2023. No patients emigrated out of Denmark within 1 year. Of 1031 patients, 517 patients were randomly assigned to SAPIEN 3 THVs and 514 to Myval THVs. The median patient age was 81·6 years (IQR 77·6–85·0), and 415 (40%) of 1031 patients were female and 616 (60%) were male (table 1). Median Society of Thoracic Surgeons (STS) score was 2·3 (IQR 1·6–3·7), 98 (10%) of 1031 patients had bicuspid anatomy (all Sievers type 1), 40 (4%) of 1031 patients had a valve-in-valve procedure, and 103 (10%) of 1030 patients had acute or subacute TAVI performed.

Ten (2%) of 507 Myval THVs were Myval XL (30·5 mm and 32 mm; appendix p 28). Median delay from randomisation to treatment was 50 min (IQR 31–1313; table 2). Among enrolled patients, one patient was never

	SAPIEN 3 THVs (n=517)	Myval THVs (n=514)
Age, years	81·1 (77·5–84·8)	81·9 (77·8–85·2)
Sex		
Female	207 (40%)	208 (40%)
Male	310 (60%)	306 (60%)
Disease history		
Diabetes	122 (24%)	102 (20%)
Hypertension	387/516 (75%)	391 (76%)
Atrial fibrillation or atrial flutter	210 (41%)	167 (32%)
Ischaemic heart disease	87/443 (20%)	84/446 (19%)
Pacemaker implantation	49 (9%)	59 (11%)
Pacemaker implantation ≤1 month before TAVI	5 (1%)	10 (2%)
ECG findings		
No bundle branch block	398/506 (79%)	420/503 (83%)
Left bundle branch block	54/506 (11%)	39/503 (8%)
Right bundle branch block	48/506 (9%)	36/503 (7%)
Right bundle branch block plus LAH	6/506 (1%)	8/503 (2%)
New York Heart Association class		
I	43/515 (8%)	46 (9%)
II	262/515 (51%)	268 (52%)
III	204/515 (40%)	192 (37%)
IV	6/515 (1%)	8 (2%)
EuroSCORE II	2·6% (1·7–4·3%)	2·5% (1·5–4·3%)
STS-PROM	2·4% (1·6–3·5%)	2·3% (1·6–3·8%)
<2%	202 (39%)	215 (42%)
2% to <4%	209 (40%)	180 (35%)
4% to <8%	77 (15%)	81 (16%)
≥8%	29 (6%)	38 (7%)
6-min walk test, m	330 (240–406); n=344	320 (240–395); n=345
Left ventricular ejection fraction	56% (47–63%); n=515	58% (47–66%)
Peak gradient, mm Hg	73 (59–88); n=516	72 (59–87); n=510
Mean gradient, mm Hg	46 (37–56); n=516	47 (38–57); n=509
Aortic valve area, cm^2	0·7 (0·6–0·8); n=514	0·7 (0·6–0·9); n=506
Valve anatomy		
Tricuspid native valve	447 (86%)	446 (87%)
Bicuspid native valve	50 (10%)	48 (9%)
Valve-in-valve	20 (4%)	20 (4%)
Aortic annulus measurement if not valve-in-valve		
Area, mm^2	485 (415–550); n=497	472 (415–531); n=494
Small annuli (area ≤430 mm^2)	155/497 (31%)	151/494 (31%)
Average diameter, mm	25·0 (23·1–26·6); n=494	24·9 (23·1–26·3); n=492
Perimeter, mm	80 (74–85); n=497	79 (74–83); n=493

Data are median (IQR), n (%), or n/N (%) unless otherwise specified. ECG=electrocardiogram. EuroSCORE II=European System for Cardiac Operative Risk Evaluation. LAH=left anterior hemiblock. STS-PROM=Society of Thoracic Surgeons Predicted Risk of Mortality. TAVI=transcatheter aortic valve implantation. THV=transcatheter heart valve.

Table 1: **Patient baseline characteristics**

treated because of severe bleeding resulting in cancellation of TAVI. A SAPIEN 3 THV was implanted in seven (1%) of 514 patients randomly assigned to treatment with the Myval THVs due to inability to pass a Myval Octacor THV through the Python sheath (two patients), unavailability of Myval THVs because of patent-related legal issues (four patients), or unknown reason (one patient). Predilatation before TAVI was required in fewer patients treated with SAPIEN 3 THVs (107 [21%] of 516) than in patients treated with Myval THVs (230 [45%] of 514; table 2). For patients treated with Myval THVs, predilatation was required less often with Myval implantation (37 [20%] of 183 patients) than with Myval Octacor (191 [59%] of 324 patients; p<0·0001). The degree of oversizing calculated as the nominal area of the THV divided by the annulus area (excluding valve-in-valve procedures) was 6·3% (496 patients) for the SAPIEN 3 THVs and 7·5% (494 patients) for the Myval THVs (p=0·025).

SAPIEN 3 THVs were associated with fewer first-time pacemaker implantations at 30 days, but smaller effective orifice area for all THV sizes (table 3) and total range of annulus area (appendix pp 29–30), as well as with higher peak and mean gradients. Length of hospital stay was significantly longer in patients with new pacemaker implantation during admission than in patients with previous pacemaker or no need for pacemaker implantation during admission (table 2).

The primary composite endpoint occurred in 67 (13%) of 517 patients randomly designed to SAPIEN 3 THVs and in 71 (14%) of 514 patients randomly designed to Myval THVs, showing non-inferiority of Myval THVs versus SAPIEN 3 THVs (risk difference –0·9% [one-sided upper 95% CI –4·4]; $p_{non\text{-}inferiority}$=0·019; figures 2, 3). These findings were supported by per-protocol analyses, with primary endpoints occurring in 66 (13%) of 516 patients treated with SAPIEN 3 THVs and in 71 (14%) of 507 patients treated with Myval THVs (risk difference –1·2% [one-sided upper 95% CI 4·7]; $p_{non\text{-}inferiority}$=0·029; figure 3). The complete case analysis showed similar results (figure 3). In post-hoc analyses, superiority of the SAPIEN 3 THVs for the primary endpoint were not shown in the intention-to-treat analysis (p=0·69) or per-protocol analysis (p=0·57). For individual components of the primary outcome, less moderate or severe aortic regurgitation was observed with SAPIEN 3 THVs (six [1%] of 511 patients) than with Myval THVs (20 [4%] of 509) at 1 year (p=0·0051; figure 3). Of 26 patients with moderate or severe aortic regurgitation, the dominant cause was paravalvular leakage in 24 (92%) patients and central THV regurgitation in two (8%) patients. Data on no or trace, mild, moderate, and severe aortic regurgitation are provided in the appendix (p 31). Echocardiograms for evaluation of aortic regurgitation were available for 1020 (99%) of 1030 patients. Among these patients, 1-year echocardiograms were used for 957 (94%) of 1020 patients, 1-month echocardiograms for 48 (5%) patients, and post-procedure echocardiograms for ten (1%) patients.

Death and stroke during follow-up are presented in the appendix (pp 32–33). Among Bonferroni-corrected

	SAPIEN 3 THVs (n=517)	Myval THVs (n=514)	p value
TAVI performed	516 (<100%)	514 (100%)	0·32
Timing of procedure	..	..	0·21
Elective	460/516 (89%)	467 (91%)	..
Subacute (≤2 weeks)	38/516 (7%)	25 (5%)	..
Acute or in-hospital	18/516 (3%)	22 (4%)	..
Time from randomisation to TAVI, min	51 (30–1315); n=516	50 (32–1313)	0·60
Valve implanted	..	..	<0·0001
SAPIEN 3	516/516 (100%)	7 (1%)	..
Myval	..	183 (36%)	..
Myval Octacor	..	324 (63%)	..
Mean THV diameter, mm	25·6 (2·3); n=516	25·4 (2·2)	..
Median THV diameter, mm	26 (23–26); n=516	26 (24·5–27·5)	0·18
Procedure time, min	34 (25–49); n=516	38 (30–51)	<0·0001
Fluoroscopy time, min	9 (7–14); n=516	10 (7–13)	0·44
X-ray exposure, Gy/cm²	14 (9–22); n=515	14 (9–23)	0·71
Contrast agent used, mL	60 (50–80); n=516	60 (50–80)	0·68
Predilatation performed	107/516 (21%)	230 (45%)	<0·0001
Postdilatation performed	59/516 (11%)	68 (13%)	0·38
Complications during procedure	39/516 (8%)	50 (10%)	0·22
Death	2/516 (<1%)	2 (<1%)	1·00
Stroke	1/516 (<1%)	2 (<1%)	0·56
Need for pacemaker implantation (temporary or permanent)	20/516 (4%)	30 (6%)	0·14
Pericardiocentesis	11/516 (2%)	6 (1%)	0·22
Annulus rupture	5/516 (1%)	1 (<1%)	0·10
Aortic perforation or dissection	3/516 (1%)	5 (1%)	0·47
Valve embolisation or migration	1/516 (<1%)	1 (<1%)	1·00
Conversion to open surgery	4/516 (1%)	1 (<1%)	0·18
Non-planned use of CPS	2/516 (<1%)	0	0·16
Conversion to alternative access	0/516	1 (<1%)	0·32
Coronary artery obstruction	2/516 (<1%)	2 (<1%)	1·00
Need for TAVI-in-TAVI	1/516 (<1%)	1 (<1%)	1·00
Simultaneous PCI	10/506 (2%)	14 (3%)	0·40
Unplanned	4/516 (1%)	4 (1%)	1·00
Length of hospital stay, days	2·1 (1·2–3·1)	2·2 (1·6–4·0)	0·0006
Length of hospital stay if no pacemaker implanted before or during admission	2·1 (1·2–3·0); n=433	2·1 (1·2–3·1); n=394	0·063
Length of hospital stay if previous pacemaker implanted	1·3 (1·1–2·1); n=49	2·1 (1·2–3·1); n=59	0·037
Length of hospital stay if new pacemaker implanted during admission	4·6 (3·0–8·0); n=34	6·1 (4·0–8·9); n=61	0·18
Medical treatment at discharge	..	..	0·018
No antiplatelets or anticoagulants	0/515	3/513 (1%)	..
Single antiplatelet	281/515 (55%)	320/513 (62%)	..
Dual antiplatelets	29/515 (6%)	23/513 (4%)	..
Anticoagulants with or without an antiplatelet	205/515 (40%)	167/513 (33%)	..

Data are n (%), n/N (%), and median (IQR) unless specified otherwise. CPS=cardiopulmonary support. PCI=percutaneous coronary intervention. TAVI=transcatheter aortic valve implantation. THV=transcatheter heart valve.

Table 2: **Procedural and in-hospital characteristics**

secondary endpoints, no difference was observed in patients with TAVI-related complications or patients with successful TAVI procedures, but fewer first-time pacemaker implantations were required in patients treated with SAPIEN 3 (56 [12%] of 468) than with Myval (95 [21%] of 455) THVs at 1 year (p=0·0002; figure 3). Patients treated with Myval Octacor THVs had the highest rates of first-time pacemakers (post-hoc analysis, appendix p 34). The exploratory secondary endpoints indicated higher rates of moderate or severe patient–prosthesis mismatch in patients treated with SAPIEN 3 THVs, but higher rates of first-time atrial fibrillation and more VARC-3 type 2 and 3 bleeding in patients treated with the Myval THVs (figure 3). No patients were treated with coronary artery bypass grafting following TAVI. At 1 year, patients treated with SAPIEN 3 THVs walked a median of 330 m (IQR 240–406) on the 6-min walk test, whereas patients treated with Myval THVs walked 320 m (240–395; p=0·43).

Discussion

This multicentre, randomised, non-inferiority trial found that Myval THVs were non-inferior to SAPIEN 3 THVs for the 1-year composite outcome, but they were associated with a greater risk of need for first-time pacemaker implantation at 1 year. The non-inferiority margin used in this trial is the smallest to date in any head-to-head comparison of THVs (ie, 5·3% for the observed event rate of 13%).[9,18–21] By comparison, in the SCOPE-1 trial,[18] the ACURATE THV was not found to be non-inferior to the SAPIEN 3 THV, and SAPIEN 3 THV was found to be superior to the ACURATE THV despite the higher non-inferiority margin of 7·7%. In the SCOPE-2 trial,[19] non-inferiority was not established with ACURATE when compared with Evolut, with a non-inferiority margin of 6·0%. The Portico THV was compared with contemporary THVs in the PORTICO-IDE study,[20] and non-inferiority was demonstrated with a non-inferiority margin of 8·5% for the 30-day primary safety outcome and 8·0% for the 1-year primary efficacy outcome. In the LANDMARK trial comparing Myval THVs with contemporary THVs (SAPIEN 3 or Evolut), the non-inferiority margin was set to 10·44%.[21] LANDMARK, like many previous head-to-head comparisons of THVs, focused on 30-day outcomes.[18,21] It used a seven-component composite endpoint, resulting in higher event rates, and justified use of a higher non-inferiority margin. The LANDMARK trial also demonstrated non-inferiority of Myval THVs to contemporary THVs.[21] However, the LANDMARK trial has not reached 1-year follow-up for all patients. COMPARE-TAVI 1 therefore provides the most robust data available to date on intermediate follow-up in patients treated with Myval or Myval Octacor THVs and will also be the first study to provide long-term data. However, pooled analyses of the LANDMARK trial and COMPARE-TAVI 1 trial will not only help to understand long-term durability and monitor hard endpoints for both THV series but will also explore whether the observed differences in secondary outcomes might affect the hard endpoints. Furthermore, pooled analyses would clarify whether outcomes differ between first-generation and second-generation Myval THVs and SAPIEN 3 THVs, given that the LANDMARK trial used

	SAPIEN 3 THVs (n=517)	Myval THVs (n=514)	p value
30-day clinical follow-up			
Death	6 (1%)	9 (2%)	0·43
Stroke	13 (3%)	18 (4%)	0·35
Moderate or severe aortic regurgitation	3/511 (1%)	11/509 (2%)	0·031
Newly diagnosed atrial fibrillation*	13/307 (4%)	26/347 (7%)	0·079
New pacemaker implantation†	49/468 (10%)	88/455 (19%)	0·0002
New York Heart Association class	..	..	0·019
I	345/501 (69%)	322/502 (64%)	..
II	116/501 (23%)	154/502 (31%)	..
III	36/501 (7%)	25/502 (5%)	..
IV	4/501 (1%)	1/502 (<1%)	..
6-min walk test, m	393 (300–453); n=294	390 (315–443); n=288	0·79
Left ventricle ejection fraction	61% (53–68%); n=496	62% (53–69%); n=499	0·55
Mean gradient, mm Hg	11 (8–14); n=497	9 (7–11); n=496	<0·0001
Mean gradient ≥20 mm Hg	30/497 (6%)	13/496 (3%)	0·0082
Peak gradient, mm Hg	19 (15–24); n=497	16 (12–20); n=496	<0·0001
Effective orifice area, cm²	1·7 (1·4–2·1); n=496	1·9 (1·6–2·3); n=494	<0·0001
Medical treatment	..	..	0·22
No antiplatelets or anticoagulants	9/506 (2%)	10/504 (2%)	..
Single antiplatelet	241/506 (48%)	272/504 (54%)	..
Dual antiplatelets	35/506 (7%)	32/504 (6%)	..
Anticoagulants with or without an antiplatelet	221/506 (44%)	190/504 (38%)	..
1-year clinical follow-up‡			
New York Heart Association class	..	..	0·82
I	337/484 (70%)	348/485 (72%)	..
II	115/484 (24%)	110/485 (23%)	..
III	30/484 (6%)	26/485 (5%)	..
IV	2/484 (<1%)	1/485 (<1%)	..
Left ventricle ejection fraction	63% (54–69%); n=488	62% (55–68%); n=488	0·27
Mean gradient, mm Hg	10 (8–14); n=487	9 (7–12); n=488	<0·0001
Mean gradient ≥20 mm Hg	33/487 (7%)	18/488 (4%)	0·030
Peak gradient, mm Hg	19 (14–23); n=487	16 (12–21); n=488	<0·0001
Effective orifice area, cm²	1·8 (1·5–2·2); n=486	2·0 (1·6–2·3); n=486	<0·0001
Medical treatment	..	..	0·48
No antiplatelets or anticoagulants	21/481 (4%)	14/483 (3%)	..
Single antiplatelet	251/481 (52%)	269/483 (56%)	..
Dual antiplatelets	2/481 (<1%)	3/483 (1%)	..
Anticoagulants with or without an antiplatelet	207/481 (43%)	197/483 (41%)	..

Data are n (%), n/N (%), and median (IQR) unless specified otherwise. THV=transcatheter heart valve. *In patients without previous atrial fibrillation or atrial flutter. †In patients without previous pacemaker. ‡Haemodynamic data based on 1-year echocardiogram or, if not available, on the latest echocardiogram before 1 year.

Table 3: **Clinical follow-up data**

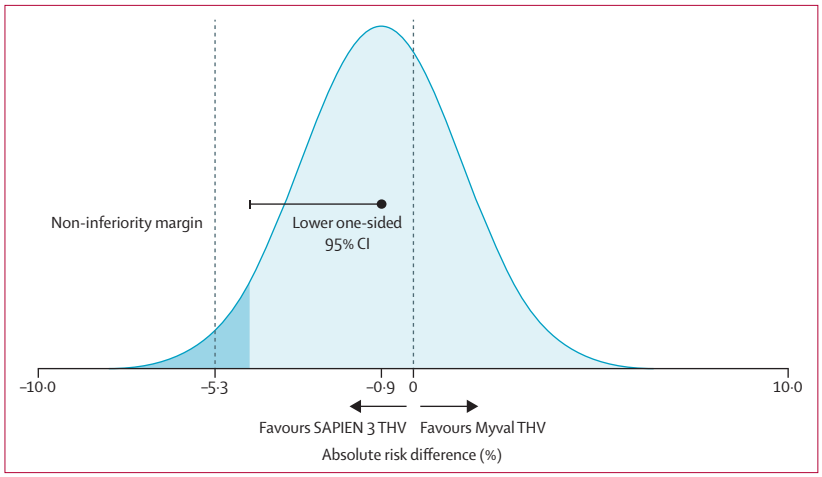

Figure 2: **Probability distribution of the absolute risk difference for the primary endpoint with SAPIEN 3 versus Myval THVs**
THV=transcatheter heart valve.

predominantly Myval THVs, whereas COMPARE-TAVI 1 used Myval Octacor THVs in 63% of cases.[21]

In COMPARE-TAVI 1, we decided to include only death, stroke, moderate or severe aortic regurgitation, and moderate or severe haemodynamic THV deterioration in the composite primary endpoint. Which individual components to include in a composite primary endpoint will always be a matter of debate, but mortality and stroke are prioritised in most trials, as recommended by the VARC-3 criteria.[12] Inclusion of moderate or severe aortic regurgitation was reasonable because this endpoint has been associated with unfavourable clinical outcomes, and statistically significant differences in paravalvular leakage have been observed in previous comparisons of THVs.[18–20] Finally, haemodynamic THV deterioration is important as TAVI treatment is increasingly recommended for patients at low surgical risk with long life expectancy, and using THVs with the longest durability might mitigate the risk of TAVI-in-TAVI procedures in the future. Because haemodynamic THV deterioration according to VARC-3 cannot be evaluated until after 1 year, we considered a 1-year composite endpoint to be ideal. In previous trials, the primary endpoint included even more components, which allowed higher event rates to be reached and justified higher non-inferiority margins. However, a non-inferiority margin should be clinically relevant. Using multiple components to justify a higher non-inferiority margin might not be ideal because it risks diluting differences in crucial endpoints, such as mortality, as non-fatal components tend to be more prevalent in the final analysis.

The Bonferroni-corrected secondary outcomes indicated that the SAPIEN 3 and Myval THVs were similar in terms of TAVI complications and technical success. We focused on cardiac-related technical success and found rates to be similar or even lower than those previously reported.[22] The elevated risk of first-time pacemaker implantation with Myval THVs, also compared with previous reports, requires further evaluation.[21] Despite the use of similar balloon expandable technologies, differences in design and implantation techniques might result in higher pacemaker implantation rates with Myval THVs than with SAPIEN 3 THVs. More first-time pacemakers were implanted in patients who received Octacor Myval THVs than in patients who received Myval THVs, which explains some of the increased pacemaker rates in COMPARE-TAVI 1 compared with the LANDMARK trial that mainly used first-generation Myval THVs. The differences in pacemaker rates might be associated with variations in the design of skirts used, delivery systems leading to deeper implants, implantation balloons, or increased oversizing with Myval THVs than SAPIEN 3 THVs. Differences in oversizing were not reflected in the similar median and mean THV sizes observed between groups but were supported by the higher oversizing observed in patients treated with Myval than SAPIEN 3 when comparing the nominal size of the THV implanted with the annulus area (7·5% *vs* 6·3%). However, this modest difference seems unlikely to explain the nearly doubled risk of need for pacemaker with Myval versus SAPIEN 3 THVs. A multislice CT substudy will provide data on expansion of THV frames, eccentricity, and implantation depth. If these features do not differ, then there could be a type I error or a high impact on the outflow tract by the skirt or trauma from the inflation balloon with Myval THVs.

Because this study was not powered to analyse the exploratory secondary endpoints, the related findings should be interpreted with caution as hypothesis-generating only. Fewer patients treated with SAPIEN 3 THVs were diagnosed with atrial fibrillation than patients treated with Myval THVs, which might have been associated with the higher rate of pacemaker implantations in those treated with Myval THVs because more atrial fibrillation was detected by the devices or the devices induced atrial fibrillation. These findings warrant further investigation to clarify whether a causal relation might exist. Among other exploratory endpoints, haemodynamic outcomes appeared to favour Myval THVs. For example, effective orifice area was higher, and moderate or severe patient–prosthesis mismatch rates were lower with Myval THVs than with SAPIEN 3 THVs. Assessing whether patient–prosthesis mismatch rates are lower with Myval THVs or SAPIEN 3 THVs and translating these findings into differences in haemodynamic THV deterioration during long-term follow-up is of great interest. Given that THVs with the same mean sizes were implanted, different valve designs should enable a larger effective leaflet opening in the Myval THV series than the SAPIEN 3 THV series. Notably, SAPIEN 3 THVs with Resilia technology were not available during the study periods. A direct

comparison with SAPIEN 3 Ultra Resilia might have yielded different findings, given that the newest Resilia technology has been associated with higher effective orifice area than have SAPIEN 3 THVs without Resilia technology.[23] The better haemodynamic observed with Resilia technology has been explained by different solutions for attachment of the leaflets to the stent frame; this aspect might also apply to the Myval THV design. Moreover, use of intermediate sizing might also affect haemodynamic (eg, nine sizes in the Myval THV series were used and only four were available in the SAPIEN 3 THV series), and underfilling of the inflation device when implanting valves might cause more pinwheeling in the SAPIEN 3 THV series.[24] Although patient–prosthesis mismatch might be associated with outcomes and valve durability, such an association remains to be documented and is at present debatable according to registry data.[25,26] Long-term data from COMPARE-TAVI 1

	SAPIEN 3 THV series Number of events/ number of patients (%)	Myval THV series Number of events/ number of patients (%)	Risk difference % (95% CI)	p value
Primary endpoints				
Primary composite endpoint at 1 year	67/517 (13%)	71/514 (14%)	−0·9% (−4·4 to NA)	0·019
Primary composite endpoint, per protocol at 1 year	66/516 (13%)	71/507 (14%)	−1·2% (−4·7 to NA)	0·029
Primary composite endpoint, complete case at 1 year	67/503 (13%)	71/502 (14%)	−0·8% (−4·4 to NA)	0·020
Individual components of primary endpoint				
All-cause death at 30 days	6/517 (1%)	9/514 (2%)	−0·6% (−2·1 to 0·9)	0·43
All-cause death at 1 year	33/517 (6%)	28/514 (5%)	0·9% (−1·9 to 3·8)	0·52
Stroke at 30 days	13/517 (3%)	18/514 (4%	−1·0% (−3·1 to 1·1)	0·35
Stroke at 1 year	24/517 (5%)	26/514 (5%)	−0·4% (−3·0 to 2·2)	0·76
Fatal	1/517 (<1%)	3/514 (1%)	−0·4% (−1·1 to 0·4)	0·31
With sequelae	7/517 (1%)	5/514 (1%)	0·4% (−0·9 to 1·7)	0·57
Without sequelae	16/517 (3%)	18/514 (4%)	−0·4% (−2·6 to 1·8)	0·71
Moderate or severe aortic regurgitation at 30 days	3/511 (1%)	11/509 (2%)	−1·6% (−3·0 to −0·1)	0·031
Moderate or severe aortic regurgitation at 1 year	6/511 (1%)	20/509 (4%)	−2·8% (−4·7 to −0·8)	0·0051
Moderate or severe haemodynamic THV deterioration at 1 year	10/474 (2%)	5/474 (1%)	1·1% (−0·5 to 2·6)	0·19
Secondary endpoints, Bonferroni corrected				
TAVI-related complications, procedural	17/516 (3%)	14/514 (3%)	0·6% (−1·5 to 2·7)	0·59
Successful implantation of planned THV, procedural	508/516 (98%)	507/514 (99%)	−0·2% (−1·7 to 1·3)	0·80
New pacemaker at 1 year	56/468 (12%)	95/455 (21%)	−8·9% (−13·7 to −4·2)	0·00024
Exploratory secondary endpoints				
New pacemaker implantation at 30 days	49/468 (10%)	88/455 (19%)	−8·9% (−13·4 to −4·3)	0·00014
Endocarditis at 30 days	0/517 (0%)	1/514 (<1%)	0·2% (−0·2 to 0·6)	0·32
Endocarditis at 1 year	9/517 (2%)	7/514 (1%)	0·4% (−1·1 to 1·9)	0·62
Reoperation (TAVI, SAVR, BAV) at 30 days	3/517 (1%)	1/514 (<1%)	0·4% (−0·4 to 1·1)	0·32
Reoperation (TAVI, SAVR, BAV) at 1 year	5/517 (1%)	3/514 (1%)	0·4% (−0·7 to 1·5)	0·48
Readmission with congestive heart failure at 30 days	0/517 (0%)	2/514 (<1%)	0·4% (−0·1 to 0·9)	0·16
Readmission with congestive heart failure at 1 year	8/517 (2%)	10/514 (2%)	−0·4% (−2·0 to 1·2)	0·63
Acute myocardial infarction at 30 days	2/517 (<1%)	1/514 (<1%)	0·2% (−0·5 to 0·8)	0·57
Acute myocardial infarction at 1 year	6/517 (1%)	2/514 (<1%)	0·8% (−0·3 to 1·8)	0·16
PCI not scheduled before TAVI at 30 days	5/517 (1%)	6/514 (1%)	−0·2% (−1·5 to 1·1)	0·75
PCI not scheduled before TAVI at 1 year	11/517 (2%)	9/514 (2%)	0·4% (−1·3 to 2·1)	0·66
Newly diagnosed atrial fibrillation at 30 days	13/307 (4%)	26/347 (7%)	−3·3% (−6·8 to 0·3)	0·074
Newly diagnosed atrial fibrillation at 1 year	25/307 (8%)	47/347 (14%)	−5·4% (−10·1 to −0·7)	0·025
Moderate or severe PPM at 30 days	152/510 (30%)	98/506 (19%)	10·4% (5·2 to 15·7)	<0·0001
Endovascular or open surgery, access site at 30 days	10/517 (2%)	18/514 (4%)	−1·6% (−3·6 to 0·4)	0·12
VARC-3 bleeding type 2, 3, or 4 at 30 days	65/517 (13%)	112/514 (22%)	−9·2 (−13·8 to −4·6)	<0·0001
VARC-2 bleeding type 4 at 30 days	5/517 (1%)	4/514 (1%)	0·2% (−0·9 to 1·3)	0·74
VARC-3 bleeding type 3 at 30 days	19/517 (4%)	32/514 (6%)	−2·6% (−5·2 to 0·1)	0·059
VARC-3 bleeding type 2 at 30 days	41/517 (8%)	76/514 (15%)	−6·9% (−10·7 to −3·0)	0·00049
Stage 2 AKI at 30 days	6/439 (1%)	7/449 (2%)	−0·2% (−1·8 to 1·4)	0·81

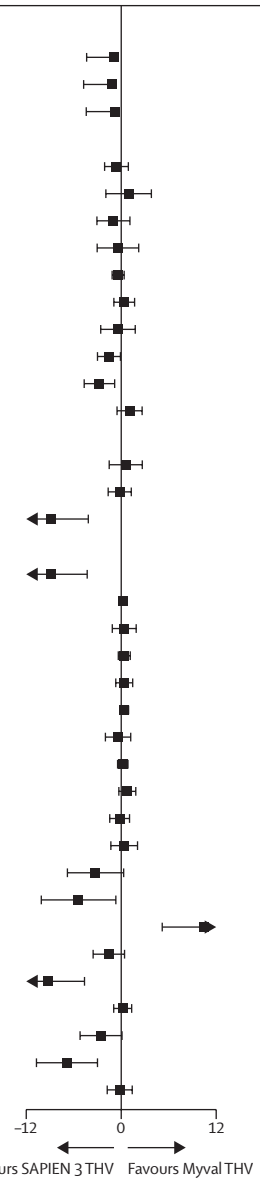

Figure 3: **Analyses of primary composite endpoint, secondary Bonferroni-corrected endpoints, and secondary exploratory endpoints**
All 95% CI and p values are two-sided, except those relating to the primary, non-inferiority analyses (one-sided). AKI=acute kidney injury. BAV=balloon aortic valvuloplasty. NA=not available. PCI=percutaneous coronary intervention. PPM=patient–prosthesis mismatch. SAVR=surgical aortic valve replacement. TAVI=transcatheter aortic valve implantation. THV=transcatheter heart valve. VARC-3=Third Valve Academic Research Consortium criteria.

might elucidate the effect of patient–prosthesis mismatch on mortality and reinterventions. The finding of more moderate or severe aortic regurgitation with Myval THVs than SAPIEN 3 THVs, despite the opportunity for more precise sizing and a higher average degree of oversizing with Myval THVs, might indicate that the skirt used for the SAPIEN 3 THVs provides better sealing against paravalvular leakage. Among other exploratory secondary endpoints, SAPIEN 3 THVs were favourable in terms of bleeding events. The higher rate of bleeding events in patients treated with Myval THVs than with SAPIEN 3 THVs was probably associated with the access site (ie, from bleeding around or oozing from the sheath), as initially reported by participating centres after the launch of Myval THVs. Although non-inferiority was demonstrated for the primary endpoint, the secondary endpoints and differences in procedural and in-hospital characteristics indicated that the SAPIEN 3 and Myval THV series are truly different technologies. Longer-term follow-up and additional analyses will provide valuable knowledge regarding whether the differences observed affect long-term prognosis.

There are notable limitations to this trial. We used a one-sided α of 5% in the non-inferiority analysis, which might be too high because it increases the risk of falsely claiming non-inferiority. However, this level is consistent with the level used in previous device trials.[27–29] For the secondary exploratory endpoints, a risk of type I error might exist due to multiple testing.[30] The change in the non-inferiority margin due to a higher-than-expected event rate also could increase the risk of falsely claiming non-inferiority. An absolute non-inferiority margin was chosen when the trial was originally designed. However, the steering committee decided to adjust the margin when the blinded event rate became higher than anticipated. Although a relative non-inferiority margin would have been preferable from the beginning, the change was made based on blinded event rates as recommended.[29,31] Even with an unchanged non-inferiority margin, the Myval THV series would have shown non-inferiority in the intention-to-treat analysis. Documenting the level of overfilling and underfilling of inflation devices during implantation would have been of interest to fully understand the degree of oversizing of the THVs. However, these data were not registered in the electronic case report form. There are no data on depth of THV implantation, which will be evaluated in a multislice CT substudy using patient multislice CT scans. We also did not report cardiac death—only all-cause mortality, which we believe is recorded without bias. Although operators and patients were not masked to randomisation, we do not believe this has affected the primary outcome. No statistical analysis plan was established before the initiation of the study. No subgroup analyses based on sex were planned but, for long-term follow-up, these analyses will be prioritised to understand if the larger effective orifice area achieved with Myval THVs affects THV durability and could be beneficial for female patients.

To our knowledge, COMPARE-TAVI 1 is the first all-comers trial to perform a head-to-head comparison of the SAPIEN 3 or SAPIEN 3 Ultra and Myval or Myval Octacor THVs with 1-year follow-up. This trial differs from previous head-to-head comparisons of THVs in several important aspects. Firstly, this trial was investigator-initiated and provides the largest randomised comparison of any two THVs to date. Secondly, it was a true all-comers trial with high rates of inclusion; 1031 (77%) of 1335 of patients treated during enrolment were randomly assigned. In previous trials, information on the proportion of patients randomly assigned to the total number treated is sparse or absent.[18–21] The average monthly inclusion rate of approximately one patient per centre in most previous trials suggests that none have been true all-comers trials.[9,18–21] Thirdly, our study showed that most patients were eligible for treatment with balloon-expandable technology. Even patients with bicuspid anatomy and requiring valve-in-valve procedures, as well as patients treated acutely and subacutely were included; by contrast, most previous head-to-head comparisons have imposed numerous exclusion criteria.[18–20] Moreover, very few patients who were asked to participate did not consent. Fourthly, the COMPARE-TAVI 1 findings, as well as its future long-term outcomes, might be generalisable to day-to-day clinical practice at medium-to-high volume centres. Lastly, most patients in this study had an STS score below 4, such as those included in the PARTNER 3 trial,[7] and approximately 40% had an STS score below 2. Accordingly, our future long-term follow-up data might provide important information regarding outcomes in these patients at low risk.

Contributors

CJT designed the study and was responsible for ethics approval, regulatory board approvals, and funding. HN, PF, EHC, MT, and TT contributed to study design. CJT and JH managed the data. All authors participated in study conduct. BLN was responsible for the multislice CT core laboratory. JSD and NSBM were responsible for the echocardiography core laboratory. CJT, LP, and JH accessed and verified the data. CJT and LP conducted the statistical analyses. CJT, HN, PF, HTS, and TT drafted the initial manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

CJT reports institutional research grants from Meril Life Sciences, the Danish Heart Foundation, Vingmed Denmark, and the Central Denmark Region for the conduct of the COMPARE-TAVI 1 trial; proctor fees from Meril Life Sciences; and lecture fees from Edwards Lifesciences, Meril Life Sciences, Terumo, and Medtronic. PF reports proctor fees from Meril Life Sciences; lecture fees from Edwards Lifesciences, Meril Life Sciences, and Boston Scientific; and support for meeting attendance from Edwards Lifesciences and Meril Life Sciences. JSD reports travel support for meeting attendance from Edwards Life Sciences. TT reports lecture fees from Terumo and Chiesi; and travel support for meeting attendance from Chiesi. JE reports advisory board participation for Boston Scientific. BLN reports institutional research grants from the Novo Nordisk Foundation. EHC reports institutional research grants from Abbott; proctor fees from Edwards Lifesciences, Meril Life Sciences, Boston Scientific, and Abbott; and lecture fees from

Edwards Life Sciences, Meril Lifesciences, Boston Scientific, and Abbott. HN reports institutional research grants from Meril Life Sciences and Vingmed Denmark, and lecture fees from Edwards Lifesciences and Meril Life Sciences. All other authors declare no competing interests.

Data sharing

All study-related documents will be made available on request to the corresponding author (chriterk@rm.dk). Individual data collected for the study will be made available for collaborative pooled analyses provided relevant contracts and data sharing agreements are made. Only anonymised data will be shared.

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