TAVI*talk*

DESIGNING THE FUTURE OF TAVI — A Technology-Focused Edition: The SAPIEN 3 Valve

Inside **TAVI***talk*

ADDITIONAL PHYSICIAN TESTIMONIALS:

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(Kerckhoff Heart Center, Bad Nauheim, Germany)

Philipp Kahlert *(West German Heart Center, Essen, Germany)*

Addressing Critical Needs— A Shared Vision with Heart Teams

Jean-Luc Lemercier
Vice President, Transcatheter Heart Valves Europe
Edwards Lifesciences

TAVI's rapid evolution has made it one of the most exciting developments in the treatment of valvular heart disease. As one of the leaders in this field, it is our duty to maintain the pace of innovation. While additional treatment options for patients remain important, so too do refinements that can meaningfully improve outcomes.

The Edwards SAPIEN 3 valve is a case in point. Recently approved for use in Europe, Edwards' most advanced transcatheter valve reflects our strategy of using innovation to service continual enhancement in clinical outcomes. Its design has the potential to reduce paravalvular leak and vascular complications.

We look forward to working with you to bring the Edwards SAPIEN 3 valve to your clinical practice and patient care. •

Clinical Trial Update
The Edwards SAPIEN 3 Valve CE Mark Trial Overview
Study design, patients, early observations

Thomas Walther Kerckhoff Heart Center Cardiac Surgery Clinic, Bad Nauheim, Germany

John Webb St. Paul's Hospital, Department of Cardiology, Vancouver, BC, Canada

The SAPIEN 3 CE Mark Trial is a non-randomized, prospective, multicentred study designed to assess the safety and device success of the Edwards SAPIEN 3 valve and the Edwards Commander and Edwards Certitude delivery systems in patients with symptomatic, severe aortic stenosis who are indicated for surgical aortic valve replacement (SAVR). Initial enrollment consisted of 50 high-risk patients. The subsequent 100 patients enrolled could have an

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Edwards Lifesciences v. Boston Scientific Scimed
IPR2017-00060, U.S. Patent 8,992,608
Exhibit 2038

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intermediate- or high-risk profile. Phases 1 and 2 of the SAPIEN 3 CE Mark Trial have successfully completed enrollment (see Figure 1).

One hundred and fifty patients were recruited in 20 sites across France, Germany, Italy, Spain, the UK and Canada. The study was initiated in January 2013, and patient inclusion for Phases 1 and 2 was finished by November 2013. Patients are being treated via a transfemoral, transapical or transaortic approach. Follow-up is scheduled at 30 days, 1 year, and annually thereafter up to 5 years.

The SAPIEN 3 valve (see Figure 2) was available in sizes of 23, 26 and 29 mm. The SAPIEN 3 valve is inserted using the Edwards Commander delivery system (14F or 16F eSheath-compatible) or the Edwards Certitude delivery system (18F or 21F sheath-compatible).

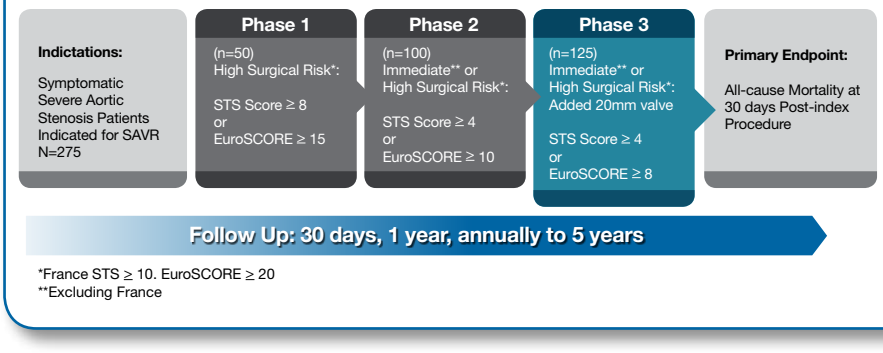
The **primary endpoint** of the SAPIEN 3 valve CE Mark Trial study is all-cause mortality at 30 days post-index procedure.

Secondary endpoints are device success according to VARC 2 as a composite of no procedural mortality, correct positioning of a single prosthetic heart valve into the proper anatomical location and performance of the prosthetic heart valve (no valve-patient mismatch, mean aortic valve gradient < 20 mmHg or peak velocity < 3 m/s and no moderate or severe prosthetic valve regurgitation).

Safety outcomes according to VARC 2 are a composite safety endpoint covering stroke, major vascular complications, life-threatening bleeding, acute kidney injury, myocardial infarction or new conduction abnormalities. Clinical efficacy is assessed by means of a composite clinical efficacy endpoint based on need for rehospitalization for cardiac causes, NYHA class, 6-minute walk test, quality of life, total valvular regurgitation and length of stay in ICU and hospital for the total index procedure.

Hemodynamic performance is assessed by echo as follows: paravalvular and total regurgitation, effective orifice area

The SAPIEN 3 CE Mark Trial



Progress of SAPIEN 3 CE Mark Trial.

mean transvalvular gradient, LV ejection fraction or structural valve deterioration. Clinical data on the initial commercial experience with the SAPIEN 3 valve will be captured in the SOURCE 3 Registry. Phase 3 of the trial is currently enrolling patients suitable for a 20 mm valve and patients of intermediate risk. •

Conclusions – The SAPIEN 3 Trial

- Outcomes at 30 days were excellent.
- Transfemoral (TF) SAPIEN 3 valve implantation was associated with a very low mortality of 2.1%, stroke of 1.0%, and very few access-site complications.
- TF implantation was associated with a very low mortality of 1.1% in the valve implant population.
- 99.3% of valves were implanted at the intended location — due to precise SAPIEN 3 positioning.
- 96.6% of patients had ≤ mild PVL. There was no severe PVL.
- Post-implant maneuvers were rarely needed despite reduced oversizing - Procedural post-dilatation (3.3%), valve-in-valve implants (0%)
- The SAPIEN 3 valve may enable treatment of intermediate-risk patients with aortic stenosis.

For more information on the conclusion of the SAPIEN 3 Trial, please visit

THE SAPIEN 3 TRIAL

SAPIEN 3 Valve: Excellent Early Clinical Experience

Danny Dvir St Paul's Hospital, Vancouver, BC, Canada
(Presented at TCT 2013, San Francisco)

The SAPIEN 3 valve with the low-profile Edwards Commander and Edwards Certitude delivery systems incorporates features intended to facilitate accurate positioning and improve paravalvular sealing. We have reported our preliminary clinical experience with the SAPIEN 3 valve in two Canadian medical

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Positive clinical experience

"Our experience with the SAPIEN 3 valve was quite positive for transfemoral and transapical implantation when starting the study early in 2013. None of our initial 15 patients who were included in the clinical trial in January and February 2013 have had any clinically relevant aortic incompetence (Figure 2)."

Thomas Walther, Jörg Kempfert, Helge Möllmann
Kerckhoff Heart Center, Cardiac Surgery Clinic, Bad Nauheim, Germany
TAVI Team

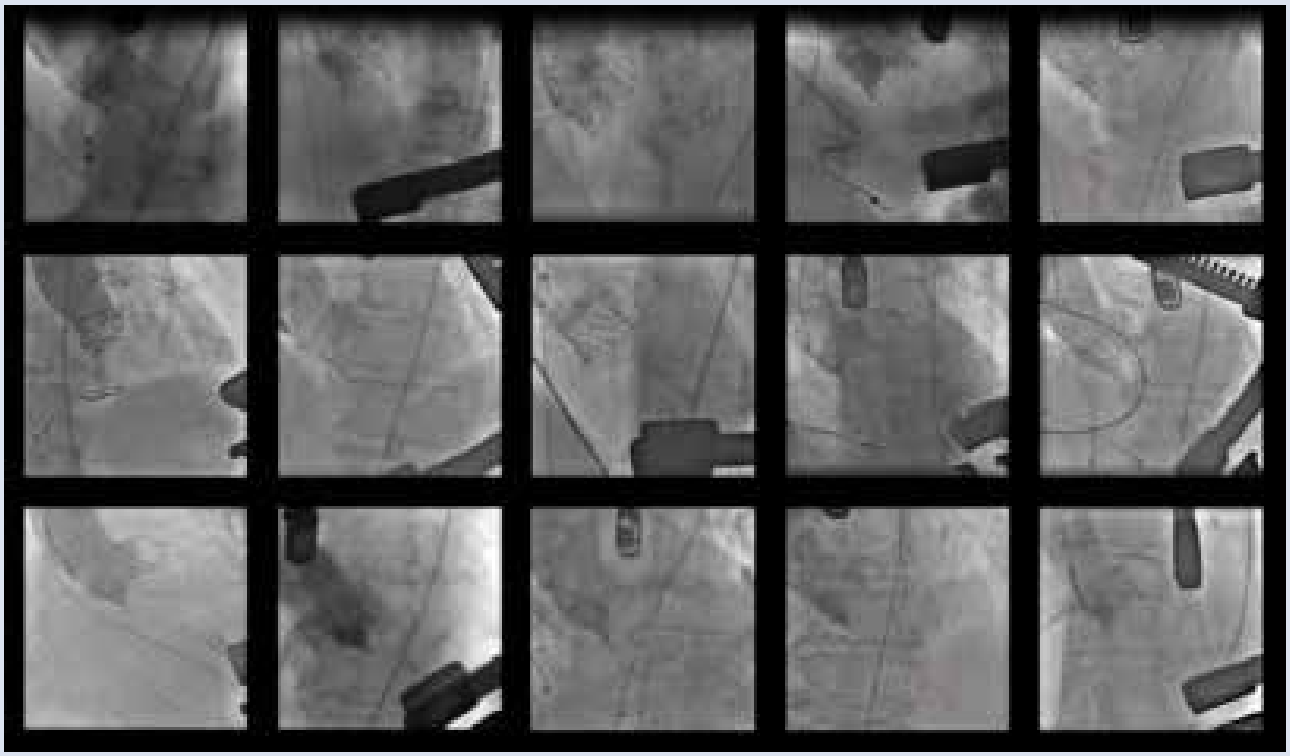
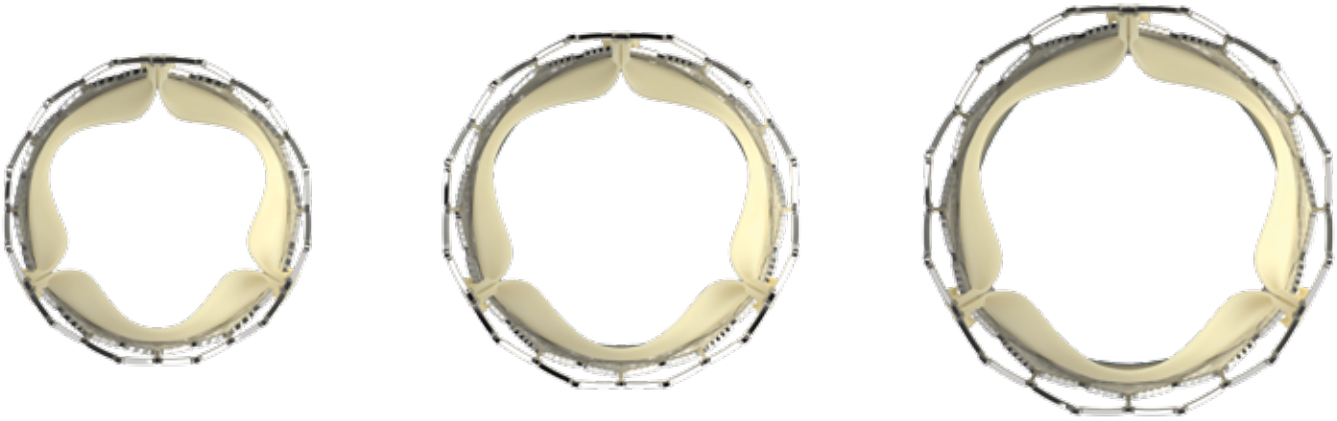


Figure 2. Initial 15 patients showed no aortic regurgitation.



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Holger Schröfel
TAVI Team Karlsruhe,
Cardiac Surgery Clinic Karlsruhe,
Germany

The TAVI Team in Karlsruhe has implanted more than 1.600 transcatheter valves since April 2008. In the summer of 2013 we had the opportunity to test the newly developed SAPIEN 3 valve as part of the CE Mark Trial. The most obvious changes you will notice are the new stent geometry and the innovative outer skirt which is designed to dramatically reduce PV leaks. The implantation starts, as usual, with the positioning of the valve in the perpendicular oriented aortic root. For this, the new valve positioning marker (in the middle of the balloon) is very useful. The SAPIEN 3 valve should be positioned with the centre marker at the insertion point of the leaflets (Figure 3). The biggest difference in implanting the SAPIEN 3 valve is the new stent design: the stent clearly shortens during deployment (personal

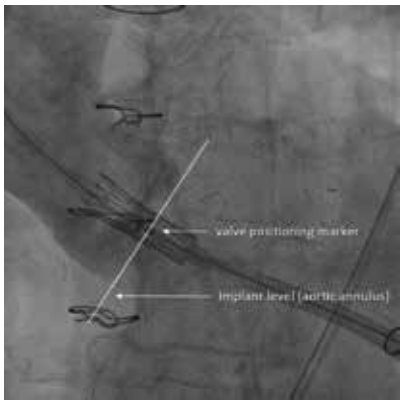

Figure 3. Positioning: Align the centre marker of the valve at the insertion point of the native valve leaflets as visualized under fluoroscopy.

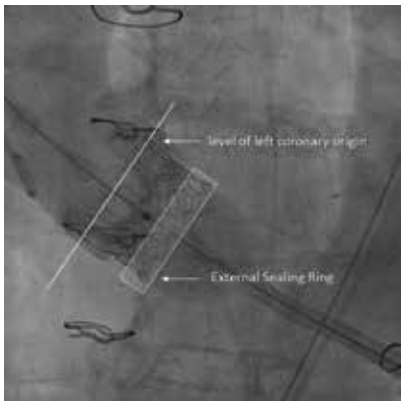

Figure 4: Implant result: Confirmed placement of the SAPIEN 3 valve with the external sealing ring below the native annulus.

Experience in 34 Consecutive Patients — an Interview with Dr. Achim Büttner on Behalf of the TAVI Heart Team

University Heart Center Freiburg/Bad Krozingen

In February and March 2014, the SAPIEN 3 Transcatheter Heart Valve (THV) was implanted in 34 consecutive TAVI patients at our centre. All had symptomatic severe aortic stenosis and were treated via femoral arterial access.

Patient characteristics

- Mean age was 83.8±5.0 years
- Multidetector computed tomography (MDCT) estimated aortic annular area 457±59 mm²
- Area derived annular diameter 24.0±1.5 mm
- Doppler-echo mean pressure gradient 46±15 mmHg
- Calculated aortic valve area 0.8±0.2 cm²

5 patients received a 23 mm valve, 22 patients received a 26 mm valve and 7 patients received a 29 mm valve. Valve implantation using slow initial inflation was successful in all 34 cases. No balloon pre-dilatation was performed in the last 23 cases and we had no difficulties in crossing the native valve or fine-positioning the THV. Paravalvular leakage (PVL) was less than mild in all cases (no PVL in 65%, trace in 35%). No post-dilatations were performed.

There were no major vascular complications (focal femoral artery stent implantation in two patients). The post-transcatheter aortic valve replacement MDCT showed consistently symmetrical and circular valves and the Doppler-echo mean pressure gradient at discharge was 9.9±2.9 mmHg.

Conclusion:
The SAPIEN 3 valve and delivery system could facilitate fully percutaneous implantation in a broader range of patients with the potential to provide more accurate positioning and less paravalvular regurgitation.

Was the implant procedure faster or more efficient than previously? If so, in what way?
The design of the Edwards Commander delivery system is a step forward and makes the procedure less traumatic and faster to do. The reduced profile of the valve and the added distal flex of the delivery system seems to reduce the risk of vascular complications and eases positioning of the THV in the native aortic valve. Our initial experience showed that implantation of the SAPIEN 3 THV is feasible without balloon pre-dilatation.

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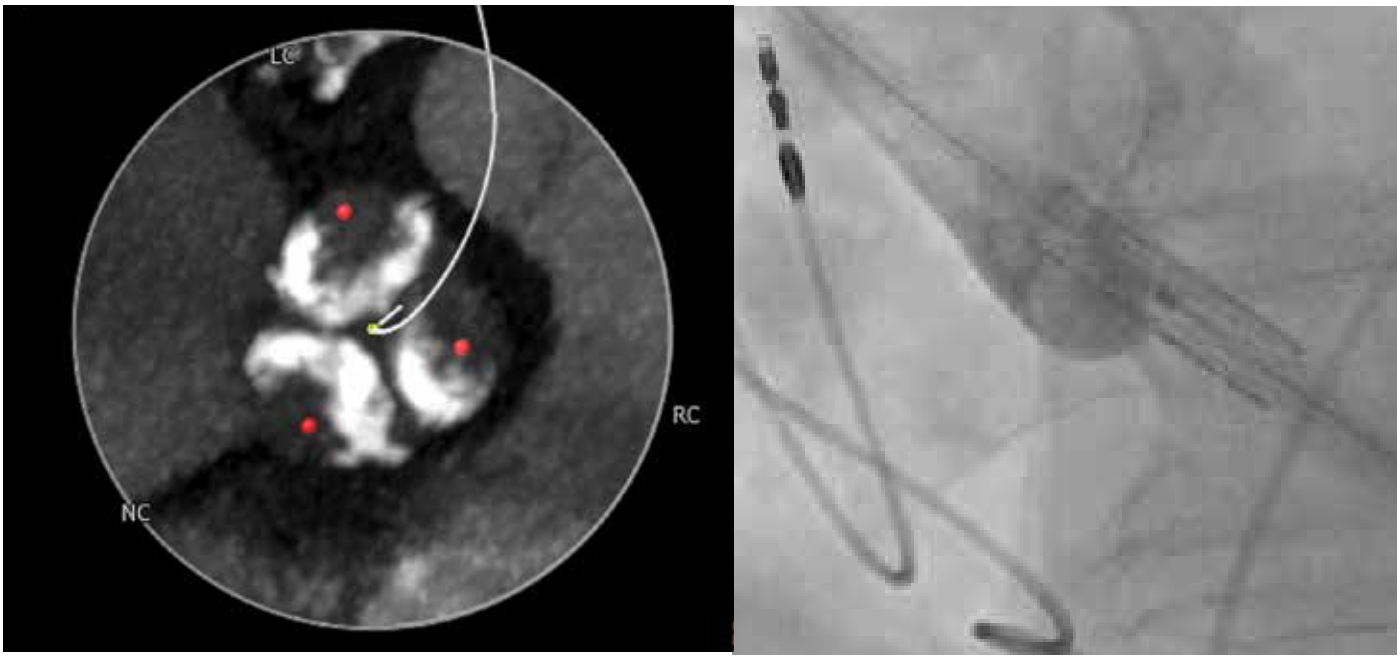

Figure 5. CT view of valvular calcification pattern and positioning of the SAPIEN 3 valve before deployment under fluoroscopic view.

Case 2: 81-year-old patient, transfemoral SAPIEN 3 valve implantation

This 81-year-old lady was admitted to our hospital with a history of syncope and exertional angina. Angiography ruled out coronary artery disease, but echocardiography revealed high grade aortic stenosis with a gradient of 91/43 mmHg and an effective orifice area of 0.7 cm^2. Our patient had a history of allergic asthma that was intermittently treated with steroids; otherwise the medical history was without significance. However, because the patient appeared frail with reduced grip-strength and mobility, the Heart Team selected transfemoral (TF) TAVI rather than surgical aortic valve replacement. Computed tomography showed a tricuspid aortic valve with eccentric calcification (Figure 6). The aortic annulus diameter was 20 mm on TOE and 21 mm by CT (perimeter-derived effective annulus diameter). The aorta, iliac and femoral vessels did not show any significant calcification, but the diameters of the common femoral arteries were quite narrow with only 0.6 cm on the left side and 0.7 cm on the right side. We decided on a 23 mm SAPIEN 3 valve using the 14F expandable Edwards Commander delivery system. With this significantly downsized delivery system, transfemoral access did not present a problem in spite of the narrow femoral arteries.

This was one of our first cases with the SAPIEN 3 valve, and we were very mindful of the asymmetric foreshortening of the stent during valve deployment. It is quite essential for the implanter to be aware that the lower stent part of the SAPIEN 3 valve will show a higher degree of foreshortening compared to the upper half of the stent. During our first SAPIEN 3 valve cases we quickly learned that you can have very predictable results with the SAPIEN 3 valve if you follow three important rules:

1. Start with the middle positioning marker at the insertion point of the leaflets.
2. Use nominal volume for deployment
3. Perform a very slow inflation with a bolus of contrast to correct for implantation height, if necessary.

In our case, we had an excellent result without the need for post-dilatation and without paravalvular leakage despite the eccentric calcification (see Figure 6). The transvalvular gradient was 9/4 mmHg, and the calculated aortic orifice area was 1.9 cm^2. The patient was extubated on the OR table immediately after the procedure and showed an uneventful postoperative course. The SAPIEN 3 valves allow for predictable and precise placement which is key to shorter procedures and, more importantly, to fewer maneuvers and manipulations within the native valve. This is important as the number of maneuvers has been associated with stroke.[3]

In summary: With the new SAPIEN 3 valve we have consistently achieved good implantation results with a remarkably low rate of paravalvular leakage. The downsizing of both TA and TF delivery systems is a significant advantage. There are some important changes in the implantation technique compared to the SAPIEN XT valve that implanters need to be aware of, especially in regard to the need for fewer maneuvers, the future potential of deploying valve without prior BAV and predictable deployment. However, if these steps are properly applied, the SAPIEN 3 valve implantation is very straightforward and reliable. •

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