A landmark trial in the treatment of severe AS

The recent PARTNER Trial results represent one of the landmark trials of this century, focusing on the treatment of high-risk patients with severe aortic stenosis. New minimally invasive transcatheter approaches, whether delivered transfemorally (retrograde approach) or transapically (antegrade approach), have proven to yield comparable results to conventional aortic valve surgery, a procedure that has been established over five decades, in high-risk elderly patients. The teams of interventional cardiologists and cardiac surgeons have to be congratulated for obtaining excellent outcomes, especially in the short-term with very low 30-day mortality rates, and for reaching the goal of non-inferiority for the primary endpoint of 1-year mortality.

(continued on page 2)
The excellent outcomes of this trial are remarkable, especially in view of the patients’ high-risk profiles. Nineteen of the 25 sites had no prior experience with TAVI procedures before starting this study. Detailed teaching protocols, specific patient screening, regular conference calls with detailed discussions on all specific patient-related aspects, as well as carefully proctored initial implants were clearly key factors for these successes. Guidance by the FDA in the US and study support by the sponsor contributed to these favourable outcomes. Thus, thought-ful and stepwise distribution of new technology seems to be the ideal strategy to obtain meaningful and perfect results.

What can we take out of these results in order to further improve outcomes in European practice? There may also be some good short-term results in Europe, but most centres that have been performing TAVI procedures for several years would not be able to obtain equivalent outcomes given that many of the patients treated in Europe (in an all-comers situation) would have been excluded by The PARTNER Trial design. Thus, some selection bias may have influenced the overall outcomes. As such, a comparison between The PARTNER Trial Cohort A (n = 348) and The SOURCE Registry (n = 1,038) reveals a difference in 30-day mortality rates of 5.4% versus 8.5%. However, at 1 year, mortality rates are almost identical, namely 24.2% versus 25.9%, respectively.*

In summary, during the past few years, TAVI has evolved as a great procedure, using either the transfemoral or the transapical approach in treating high-risk elderly patients with aortic stenosis in a truly minimally invasive manner. In the future, we need to perform the right procedures with the right Heart Teams in order to offer our patients the best options.

THOMAS WALTHER
(continued from page 1)

The PARTNER Trial Cohort A results demonstrate that, even with the first generation of the Edwards SAPIEN valve, outstanding results for transfemoral (TF) and transapical (TA) aortic valve implantation (AVI) can be achieved. For the surgical community, it is reassuring that conventional aortic valve replacement (AVR) is not inferior to TAVI in terms of mortality, even in high-risk patients with aortic stenosis.

Compared to the European experience, it is impressive to see that the 30-day mortality in Cohort A (TF: 3.3%, TA: 3.8%), but also Cohort B (TF: 5%), is lower compared to The SOURCE Registry (TF: 6.3%, TA 10.3%). In fact, Cohort A 30-day mortalities are the lowest reported so far. At present, it remains to be seen if this is a result of the selection process of Cohort A, in which inoperable patients had been excluded, or if it is explained by something else. However, one wonders why this lower 30-day mortality does not translate into lower 1-year mortalities, which are very similar between Cohort A (TF: 22.2%, TA: 29%), Cohort B (50.7%), and The SOURCE Registry (TF: 19.9, TA: 27.9%).

The PARTNER Trial has answered some of the burning questions about transcatheter AVI, however, as is often the case with excellent studies, it also raises new questions. Close cooperation between Heart Teams and different regions will remain key to finding the right answers.

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The lowest reported 30-day mortalities so far

* Percentages represent TF/TA Cohorts combined
As demonstrated by the commentary offered by my esteemed colleagues that you can find throughout this issue of TAVItalk, The PARTNER Trial results from both cohorts of this well-designed trial are impressive. Last September, the results from Cohort B demonstrated the dramatic superiority of TAVI over best medical therapy. The results from Cohort A presented last month at the Annual Scientific Session of the ACC demonstrated equivalence between TAVI and AVR in the high surgical risk patient population. I join in the comments published here and elsewhere that have commended these results, as well as all of those who took part in this exemplary trial. I also appreciate that the results from The PARTNER Trial complement the extensive data sets that we have established in the various large registries here in Europe.

I am honoured to be a guest editor of this issue of TAVItalk with Thomas Walther, who was also an early adopter of TAVI. Although he now works in Bad Nauheim, Germany, I previously had the privilege of working with Prof. Walther when he worked with Prof. Mohr and our Heart Team in Leipzig. To the best of my knowledge, Prof. Walther has performed more transapical TAVI procedures than anyone else in the world, and has been instrumental in driving the transapical technology and learnings. It has been a great honour to be part of this dedicated team of cardiologists and surgeons that has propelled this therapy and built bridges between specialties.

As an early pioneer of angioplasty, it has been gratifying to be involved in the early adoption of TAVI and to see how TAVI has changed the paradigm that was previously established in coronary care. While angioplasty once separated surgeons and cardiologists, it has been rewarding to be part of a therapy that is bringing these two specialties together to offer our patients the very best options for their treatment.

I hope that you enjoy this edition of TAVItalk and continue to share our enthusiasm for this burgeoning technology as we seek to improve the lives of our patients.

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**QUOTABLE**

**Q:** What are your thoughts regarding The PARTNER Trial Cohort A data?

**A:** I was really surprised—in a positive way—to look at The PARTNER Trial data and see the successful translation of new technology into practice with a very low mortality rate. And also, I was surprised by the surgical results. I would have guessed that, in this high-risk group, the outcome would be about 6.5% in the surgical arm, so I was really surprised to see that the transcatheter approach was even better in these early outcomes. I think that’s a very positive message, and it tells us the trial was performed in a very careful manner and that all participants, cardiologists and surgeons, tried to do their best. These are excellent data.

**Q:** What impact do you believe these data will have on TAVI adoption?

**A:** I think this is something that will cause surgeons, who did not look at this high-risk cohort until today, to now be interested in treating these patients who have previously not been operated on in many centres. We need to accept that, especially for the high-risk patients, there is a very suitable alternative that can reduce the surgical trauma and has at least a good short-term result. In Cohort A, we are looking at data out to 12 months and, in some of the patients, we have data out to 24 months. There is no doubt that these data are valid and actually confirm our practice in Europe over the past three to four years. We have very deliberately used these catheter-based techniques in these high-risk patients.
Q: In one sentence, could you describe what the cost-effectiveness results from Cohort B of The PARTNER Trial show?

MR. LAURET: The cost-effectiveness results achieved in inoperable patients are very positive for TAVI. They show two things: the cost is $50,200 (approx. 33,888 €) per additional life year gained and $62,000 (approx. 41,812 €) for each quality adjusted life year (QALY) gained.

When a new technology or therapy gets approved, the first question asked by the payors is if there is value for money with this therapy. One way to answer this question is to first determine if the new therapy is going to provide a better quality of life and clinical benefit for the patients and then determine what is the cost per QALY. In other words, what additional cost is to be invested to gain one additional unit of effectiveness (or QALY) with a new therapy, the definition of QALY being a common measure of benefit that combines quantity and quality of life. The estimated average life expectancy in the TAVI group was 3.1 years and 1.2 years in the control group. This difference of 1.9 years forms the denominator of the cost-effectiveness ratio.

Generally, in the United States, an acceptable cost per QALY is between $50,000 (approx. 33,780 €) and $100,000 (approx. 67,440 €), therefore the results achieved in Cohort B of The PARTNER Trial analysis are well within this range.

Exactly what costs were included for the QALY analysis of Cohort B of The PARTNER Trial?

MR. LAURET: The costs of the TAVI procedure were calculated by multiplying direct measures of resource use (procedure duration, supplies, etc.) by their respective 2010 unit prices. The estimated commercial price for the Edwards SAPIEN valve in the United States and its delivery system was set at $30,000 (approx. 20,232 €) for the purpose of this exercise. All other costs for the index TAVI admissions were calculated by multiplying charges from the hospital bills by hospital and department-specific cost-to-charge ratios. The costs of follow-up hospital admissions for any cause were calculated directly from billing data or, when bills were not available, were based on average Medicare reimbursement.

Additional costs were included for residential care in rehab or skilled nursing facilities, as well as for outpatient visits, emergency room visits, outpatient cardiac testing, and medications.

Can we apply the economic analysis of the results from Cohort B to a European model?

MR. LAURET: Yes, with some modifications due to the fact that patient treatment pathways and treatment costs differ between countries. In Europe, the focus is very much on incremental clinical benefit (ICB) and the additional costs associated. Most of the payors in Europe have requested this kind of analysis for TAVI, well before The PARTNER Trial's Cohort B results became available. This has been key to obtaining reimbursement in most European countries. Still, there is work to be done in other regions, such as the United Kingdom and Belgium.

The only country that is widely using the Incremental Cost-Effectiveness Ratio as a point of reference to determine the

Published Cost Effectiveness Estimates

Source data: Reynolds M. PARTNER B cost-effectiveness analysis. Presented at the 60th Annual American College of Cardiology 2011 meeting, April 3, 2011, New Orleans, LA, USA.
willingness to pay per QALY for a new therapy is the United Kingdom. The United Kingdom has an established practice of health care economics that has been refined over several years. They assess the threshold for cost per QALY at £30,000 (approx. 33,370 € or $49,481).

Does the Cohort B economic analysis of The PARTNER Trial have any usefulness for European reimbursement decisions?

MR. LAURET: When working with the European reimbursement systems, we have been careful to point out that the $62,000 (approx. 41,000 €) is not directly transferable to the European health care systems for several reasons. The cost structures in the United States and Europe are very different (e.g., physicians’ salaries, cost per intensive care unit [ICU] day, etc.). You can still take the length of time in the ICU for the TAVI patients and apply the different cost structures. As an example, the cost per ICU day in the United States is in the region of $2,500 (approx. 1,686 €); in Europe, it is in the region of 1,000 € ($1,482).

We have used the clinical data obtained from Cohort B to populate our cost-effectiveness models using the various European cost structures. With these analyses, we will be able to assess the European cost-effectiveness of TAVI compared to inoperable patients.

How are European countries measuring quality of life?

MR. LAURET: In most countries, when you seek to obtain reimbursement for a new product, the first thing that you have to do is to submit a dossier to the Health Technology Assessment (HTA) groups. There are different tools used by the assessors, such as a detailed questionnaire measuring quality-of-life index. These questions help assess patients’ quality of life by examining factors such as fatigue, limited mobility, whether they are house-bound, their ability to stand, or if they are out of breath, etc. Inoperable patients receiving TAVI are likely to have immediate clinical benefit as a result of improved haemodynamics. They will be far less dependent on supplemental care, enabling greater independence and ability to enjoy life.

Note: All monetary conversions are approximate, based on exchange rates valid May 3–4, 2011.

Patient screening: be careful what you are extrapolating from

Matthew Reynolds, MD, when presenting these data at the ACC, pointed out several important limitations. First, Cohort B still represents early TAVI experience with the technology, procedure, and postoperative management in the United States. The efficiency of care and outcomes for patients may improve with time. Second, the medical management of the control patients in Cohort B may have differed from the care of similar patients in community practice. Finally, Cohort B was a uniquely old and inoperable patient population, and therefore these results cannot be extrapolated to other patient groups. The analysis of the Cohort A data on high-risk patients with severe symptomatic aortic stenosis comparing TAVI to conventional aortic valve replacement is currently being reviewed and will be presented at a future meeting.

Managing patient expectations is key

When evaluating patients with severe aortic stenosis, it is extremely important to review the multitude of options available—including surgery—and to refer them to a hospital where a multidisciplinary Heart Team will review all the information. Managing patients and family expectations is key, as many patients will be better suited to surgical valve replacement—still the gold standard for patients with lower risk profiles. It is difficult for all concerned when a patient arrives with his/her heart set on TAVI and is not a suitable candidate.

PIRAR TORNOS MAS, MD, FESC
Hospital General Universitari Vall d’Hebron, Barcelona, Spain
Former head of the European Society of Cardiology’s Task Force for the management of valvular heart disease
Learning curve in mastering the technique

Q: What impact do you believe these data will have on TAVI?

A: I think cardiologists and surgeons will be convinced that we can use this approach in high-risk patients. This is very important because we can now offer either TAVI or AVR to these patients, and the team can make a decision regarding the optimal approach for a given patient.

Q: Was there anything about the Cohort A data that stood out to you?

A: If we compare the stroke rates, it is higher in the TAVI group compared to aortic valve replacement group. This was a surprise for me because it is not the experience that we have in France, nor in other countries in Europe. Looking at the SOURCE data, for example, there is no difference in terms of strokes between TAVI and surgery. Neurologic events were really captured in this study compared to other studies in Europe where the design was less rigorous than in The PARTNER Trial. This difference in terms of neurologic events is probably related to several things. The first is the learning curve. You need to master the technique to cross the aortic arch with the delivery system, being careful not to damage the internal or external parts of the arch where there is debris that can cause embolisation in the brain. Optimal anticoagulation during the procedure is also a very important issue, as well as the profile of the device, which is clearly better with the next generation valve currently available in Europe compared to The PARTNER Trial.

Cohort A: a testament to surgical skill

Given the enthusiasm around the favourable results of TAVI, as documented by both cohorts in The PARTNER Trial, as well as many other non-randomised studies, what is still unknown is the long-term durability of these new valves and if they will parallel the long-term durability proven in surgical valves.*

In addition, the risk of minor and major neurological events associated with TAVI could be reduced with the use of smaller devices. Embolic protection systems may offer another level of risk reduction, especially in patients with severe calcification of the iliofemoral vessels and aortic arch.

The various risk scores for evaluating surgical candidacy are imperfect, and the lower-than-expected rate of 30-day mortality in patients treated with surgical AVR reported in Cohort A provide further evidence that risk scores may frequently overestimate the predicted surgical risk to the patients. This finding confirms the importance of patient selection in the multidisciplinary team decision-making process and the value of an experienced team. It is also noteworthy that the surgical results in Cohort A were truly exceptional and are a testament to the skill of the surgeons participating in this study.

The non-inferior results of TAVI compared to surgical AVR should be a strong incentive for surgeons to be fully involved in transcatheter procedures, as well as to optimise surgical treatment with new techniques and technologies to offer the best range of therapeutic options for AS patients.

*Seven-year THV durability data for one of Pr. Cribier’s early, very compromised patients, initially treated in September 2003, are on file in Rouen, France. Twenty year surgical valve data are available in the clinical communiqué 20 yr results (AR002835) on file at Edwards LLC.
Definitive results through rigorous design

Survival rates after the onset of symptoms in severe aortic stenosis are dismal, as low as 50% at 2 years and 20% at 5 years. Surgical aortic valve replacement (AVR) is the current standard of care, but it has been estimated that between 30% and 60% of patients do not undergo AVR. The PARTNER Trial (Placement of AoRtic TraNs-cathetER Valves) was initiated to investigate the safety and effectiveness of a less invasive treatment in this population. The world’s first prospective, randomised, and controlled trial for transcatheter aortic valve implantation (TAVI), sets the standard in site selection, case screening, study management, multidisciplinary teamwork, and patient follow-up. Methodology required top-performing surgical capability in order to set the highest possible standard for comparison to TAVI.

THE PARTNER TRIAL CONSISTS OF TWO INDIVIDUALLY POWERED PATIENT COHORTS.

- IN COHORT A, the safety and effectiveness of the balloon-expandable Edwards SAPIEN Transcatheter Heart Valve (THV) was compared to AVR in high-risk patients with severe symptomatic aortic stenosis.

- IN COHORT B, the safety and effectiveness of the balloon-expandable Edwards SAPIEN THV was compared to standard therapy (best medical management) in inoperable patients with severe symptomatic aortic stenosis.
COHORT A

Survival with Edwards SAPIEN THV was equivalent to AVR in high-risk patients

**Primary Endpoint: all-cause mortality at 1 year (ITT)**

![Graph showing mortality rates for Edwards SAPIEN THV and AVR](image)

**Mortality at 1 Year**

- **Edwards SAPIEN THV**
  - Expected 30-day mortality rate: 11.7%
  - Observed 30-day mortality rate: 5.2%
  - O:E ratio = 0.44

- **AVR**
  - Expected 30-day mortality rate: 11.8%
  - Observed 30-day mortality rate: 8.0%
  - O:E ratio = 0.68

**Results for Both Procedures Exceeded Expectations**

- **AVR**
  - Expected 30-day mortality rate: 11.8%
  - Observed 30-day mortality rate: 8.0%
  - O:E ratio = 0.68

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  - Expected 30-day mortality rate: 11.7%
  - Observed 30-day mortality rate: 5.2%
  - O:E ratio = 0.44

**Transfemoral approach equivalent to AVR**

- Transfemoral TAVI subgroup non-inferior to AVR ($P = .002$)

**Transapical approach results**

- While not powered for independent statistical analysis, the transapical TAVI subgroup showed similar results as AVR at 1-year.

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*As-treated (at) analysis. ITT, intent to treat.*

For use outside The United States only | Not intended for general distribution.
**COHORT A**

**Clinical outcomes: High-risk patients**
Both TAVI and AVR were associated with important but different periprocedural hazards.

### Edwards SAPIEN THV:
Statistically higher incidence of all stroke or TIA and major vascular complications

### AVR:
Statistically higher incidence of major bleeding and new atrial fibrillation

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<tr>
<th>Outcome</th>
<th>30 Days</th>
<th>1 Year</th>
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<tr>
<td>All-Cause Mortality</td>
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<td>24.2%</td>
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<td>All Stroke or TIA</td>
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<td>8.3%</td>
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<tr>
<td>Major Stroke</td>
<td>3.8%</td>
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<td>Major Vascular Complications</td>
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<td>Major Bleeding</td>
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<td>New Pacemaker</td>
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<td>Edwards AVR</td>
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AVR and Edwards SAPIEN THV improved haemodynamics and sustained valve performance.

Edwards SAPIEN THV rapidly improved symptoms with results equivalent to AVR at 1 year.

85% of patients in NYHA class I or II at 1 year
Symptom improvement favored Edwards SAPIEN THV at 30 days and was similar to AVR at 1-year
COHORT B

Edwards SAPIEN THV significantly improved survival in inoperable patients

![Graph showing survival rates for Standard Therapy and Edwards THV over time.](image)

- **20%** absolute reduction in mortality⁵
  - Despite expert care and frequent BAV (78.2%), standard therapy failed to alter the dismal natural course of disease⁵,⁶

- **NNT=5**
  - Need to treat just 5 patients with an Edwards SAPIEN THV to save a life⁴

Edwards SAPIEN THV significantly improved symptoms and quality of life

- **75%** of the Edwards SAPIEN THV patients in NYHA class I or II at 1-year⁵
  - Significant improvement observed as early as 30 days (P < .001)⁵

- **25** point treatment effect in KCCQ score⁶
  - 20-point improvement in KCCQ score represents change of large clinical importance⁷

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*NYHA and KCCQ scores of surviving patients only.

BAV, balloon aortic valvuloplasty; KCCQ, Kansas City Cardiomyopathy Questionnaire; MCID, minimum clinically important difference.

References appear on p. 16.
Cohort B of The PARTNER Trial demonstrated that TAVI, using the Edwards SAPIEN valve, achieves a 20% reduction in mortality in patients with severe aortic stenosis who are inoperable. Cohort A of The PARTNER Trial demonstrated similar outcomes in high-risk patients with severe aortic stenosis, whether they underwent conventional surgery or TAVI, but the positive quality-of-life impact was faster with TAVI.

If a patient has aortic stenosis that is considered to be inoperable and you want to increase that patient’s chance of survival in a better clinical condition, TAVI is the best choice. In addition, patients with aortic stenosis at high risk for surgery can be treated either with surgery to replace their damaged valve, or they can have a TAVI. Both treatments are excellent options for severe aortic stenosis.

However, if the patient wants to be restored to a normal activity level in a shorter time, they should undergo TAVI.

TAVI increases the chance of survival if the patient is inoperable.

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**Unprecedented teamwork**

These extraordinary results were accomplished because of an unprecedented teamwork between a cardiologist, cardiac surgeon, and the associated caregivers.

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**The advantages of reduced recovery time**

Cohort B of The PARTNER Trial demonstrated that TAVI, using the Edwards SAPIEN valve, achieves a 20% reduction mortality in patients with severe aortic stenosis who are inoperable. Cohort A of The PARTNER Trial demonstrated similar outcomes in high-risk patients with severe aortic stenosis, whether they underwent conventional surgery or TAVI, but the positive quality-of-life impact was faster with TAVI.

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TAVI increases the chance of survival if the patient is inoperable.

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**Low mortality in both groups was ‘exceptional’**

Q: What are your thoughts regarding The PARTNER Trial Cohort A data?

A: These data are excellent and are of paramount importance for medical history, the history of our patients, as well as the physicians who treat aortic stenosis because this is the first randomised trial comparing a new therapeutic option (TAVI) with the established surgical valve replacement in patients defined as being at high risk for surgery. The global results of both arms of the trial seem not simply good, but excellent. The investigators of The PARTNER Trial did a very good job in treating these high-risk patients. In the real world, patients at high risk for surgery with aortic stenosis usually are very old, very fragile, and have a lot of comorbidities. To obtain low mortality, 3% or 6%, at 30 days in these kinds of patients is exceptional.
Q: What are your thoughts regarding The PARTNER Trial Cohort A data?

A: The most remarkable thing was the performance of the multidisciplinary TAVI and surgical teams. These are the best reported results for transcatheter valve implantation. For 19 of the 26 centres to be doing their first cases within the trial and yet still achieve a 30-day transfemoral mortality of only 3.7% is absolutely remarkable. It should be noted that both the transapical and surgical AVR mortality are remarkably low. Surgeons did brilliantly because, there is no doubt that, this was a very high-risk group of patients.

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Ideal opportunity to compare TAVR to the gold standard

This is the ideal opportunity, because surgical AVR is one of the most effective operations surgeons offer, and TAVR is the most exciting new treatment for aortic stenosis in the past two to three decades. This opens up a new set of patients who may very well benefit as much by TAVR as by the conventional gold standard surgery.

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A ‘remarkable’ performance in a high-risk group of patients

Q: What are your thoughts regarding The PARTNER Trial Cohort A data?

A: The most remarkable thing was the performance of the multidisciplinary TAVI and surgical teams. These are the best reported results for transcatheter valve implantation. For 19 of the 26 centres to be doing their first cases within the trial and yet still achieve a 30-day transfemoral mortality of only 3.7% is absolutely remarkable. It should be noted that both the transapical and surgical AVR mortality are remarkably low. Surgeons did brilliantly because, there is no doubt that, this was a very high-risk group of patients.

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Even with a steep learning curve, TAVI measures up to AVR

My first take on the data is very positive. I think it’s very encouraging because we are looking at two procedures—a well-known, proven technology that has been around for more than 50 years and we are comparing it with a technology that has had less than 10 years since first-in-man (FIM) and less than 5 years in a “real world” post-commercial setting. Essentially, we are testing, in a randomised way, a therapy that is on the steepest part of its learning curve using a first-generation device, and comparing it with a very mature, sophisticated, surgical option that is probably at the plateau of its learning curve for the therapy. The results are encouraging and suggest a very bright future for the TAVI technology.
A clear lesson for the most difficult-to-treat AS patients

We have clearly learned from The PARTNER Trial that, in our most difficult to treat aortic stenosis patients, TAVR is both the new standard-of-care for inoperable patients and an exciting alternative for carefully selected high-risk patients. Based upon the results from the inoperable and high-risk patient cohorts in The PARTNER Trial, balloon-expandable TAVR is now an invaluable new therapy to optimally manage our most difficult aortic stenosis patients.

MARTIN LEON, MD
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New York-Presbyterian Hospital, Columbia University Medical Center
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Co-principal Investigator of The PARTNER Trial

‘Widening the field of effective therapies in high-risk patients with aortic stenosis’

The PARTNER Trial, Cohort B, is a landmark trial in the field of valvular heart disease. It is not only a major step in the evaluation of TAVI, but it is also the first study justifying—with a high level of evidence—the treatment of severe, symptomatic aortic stenosis in high-risk elderly patients. In a paper from the Euro Heart Survey highlighting the insufficient referral of elderly patients with aortic stenosis, we concluded in 2005, “These findings underline particular difficulties regarding decision-making in the elderly, in whom current guidelines provide limited recommendations as a consequence of the low level of evidence from the literature. Randomised trials are unlikely to be conducted in this field…”

This was before TAVI gained wide application, and it illustrates how the evaluation of a new technique may contribute to addressing complex existing issues. There is no doubt that TAVI widens the field of effective therapies in high-risk patients with aortic stenosis. We now have proof of its usefulness in patients who were likely to be undertreated. Given new evidence from The PARTNER Trial, it can be expected that practitioners will become more interested in referring high-risk patients with aortic stenosis.

BERNARD JUNG, MD, PhD
Chairman, European Society of Cardiology, Working Group on Valve Disease Cardiology Department, Bichat Hospital and Paris 7 University
Paris, France

A lower rate of death from any cause at 1-year

On the basis of a rate of death from any cause at 1-year that was 20 percentage points lower with TAVI than with standard therapy, balloon-expandable TAVI should be the new standard of care for patients with aortic stenosis who are not suitable candidates for surgery.

THE PARTNER TRIAL INVESTIGATORS
Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery
Comparing Edwards SAPIEN and Edwards SAPIEN XT Transcatheter Heart Valves

The results of The PARTNER Trial Cohorts A and B validate the balloon-expandable Edwards SAPIEN transcatheter heart valve that Edwards released in late 2007. Since its release, our team of engineers has continued to advance the design of the Edwards’ line of balloon-expandable valves. Utilising clinical feedback and R&D advancements, the Edwards SAPIEN XT valve was released in early 2010. This is the latest generation THV currently available in Europe.

The Edwards SAPIEN valve product line is based upon four key design elements: proven leaflet design, optimal frame height, high radial strength, and predictable valve deployment. These elements went into the original design of the Edwards SAPIEN valve, and were also the core criteria evolving the Edwards SAPIEN XT valve.

**PROVEN LEAFLET DESIGN**

The Edwards line of transcatheter heart valves share many features that are core to Edwards’ long history of tissue valve design. The leaflets are made of bovine pericardial tissue, which has clinically proven long-term durability. The leaflets undergo the Carpentier-Edwards ThermaFix treatment process which is intended to minimise the risk of calcification. The leaflets are all matched for thickness and elasticity to promote consistent leaflet function and coaptation.

One new feature of the Edwards SAPIEN XT valve, compared to the original Edwards SAPIEN valve, is the new leaflet design. This design features a proprietary surgical leaflet shape based upon Edwards’ surgical valves and has been updated for stress distribution, to support valve durability.

**OPTIMAL FRAME HEIGHT**

A significant design criterion for the Edwards transcatheter heart valves was to have a frame height that is designed for proper placement and non-interference with the surrounding anatomy. The Edwards SAPIEN frame is 14 mm (23 mm valve), 16 mm (26 mm valve) and 19 mm (29 mm valve) tall. It is designed to fit within the native annulus, minimising the risk of atrioventricular (AV) block and disruption of mitral leaflet function. It is also designed for placement below coronary arteries, allowing clear access for future percutaneous coronary interventions (PCIs).

The Edwards SAPIEN XT frame had the same design requirement. The Edwards SAPIEN XT frame is 14 mm (23 mm valve), 17 mm (26 mm valve) and 19 mm (29 mm valve) tall.

**Transapical delivery system**

Predictable and precise transcatheter valve deployment

Balloon-expandable valve design facilitates easy positioning with fast, accurate valve deployment for both transfemoral and transapical delivery systems
The Edwards transcatheter heart valves established a new paradigm in valve delivery; one key feature of this was the fact they possess a strong supportive frame with high radial strength. The Edwards SAPIEN frame strength has shown, throughout its high volume of implants, to result in a large effective orifice area, even in heavily calcified annuli. It was designed for reliable deployment with nominal diameter which is necessary for proper leaflet coaptation. This high radial strength results in proper haemodynamics and valve durability.

The Edwards SAPIEN XT frame offers comparable radial strength to the original Edwards SAPIEN frame. This was one of the key design criteria. The new feature of this frame is that it also allows for low profile crimping. In order to combine radial strength with low profile crimping, the Edwards SAPIEN XT frame geometry features fewer rows than the Edwards SAPIEN frame and is made from cobalt chromium rather than stainless steel.

**High Radial Strength**

The Edwards SAPIEN THV was delivered transapically with the Ascendra delivery system and transfemorally with the RetroFlex 3 delivery system. The delivery systems were designed for their means of access and featured balloon-expandable delivery engineered for predictably accurate valve placement. These are the products used in The PARTNER Trial.

The Edwards SAPIEN XT THV is delivered transapically with the Ascendra2 delivery system and transfemorally with the NovaFlex delivery system. Both systems were designed to take advantage of the low-profile crimping frame design to decrease their sheath sizes while maintaining the predictable valve placement, which represent significant steps forward in design evolution.

**Expanded treatment options**

The only commercially available transcatheter aortic valve that treats an annulus size range of 18 to 27 mm.

### Table: Valve Size and Heights

<table>
<thead>
<tr>
<th>Valve size</th>
<th>Edwards SAPIEN valve height</th>
<th>Edwards SAPIEN XT valve height</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 mm</td>
<td>14 mm</td>
<td>14 mm</td>
</tr>
<tr>
<td>26 mm</td>
<td>16 mm</td>
<td>17 mm</td>
</tr>
<tr>
<td>29 mm</td>
<td>n/a</td>
<td>19 mm</td>
</tr>
</tbody>
</table>

**Predictable Valve Deployment**

The Edwards SAPIEN THV is delivered transapically with the Ascendra delivery system and transfemorally with the RetroFlex 3 delivery system. The delivery systems were designed for their means of access and featured balloon-expandable delivery engineered for predictably accurate valve placement. These are the products used in The PARTNER Trial.

The Edwards SAPIEN XT THV is delivered transapically with the Ascendra2 delivery system and transfemorally with the NovaFlex delivery system. Both systems were designed to take advantage of the low-profile crimping frame design to decrease their sheath sizes while maintaining the predictable valve placement, which represent significant steps forward in design evolution.
The ‘Nautilus’: Edwards’ clinical history of TAVI

The ‘Nautilus’ depicts the evolution and momentum of the Edwards Lifesciences global clinical research program for TAVI. In 2010, the results of TRAVERCE, PARTNER EU, The SOURCE Registry, and The PARTNER Trial were all published in peer-reviewed journals. Each study and manuscript reflects upon unique aspects of the TAVI experience, from feasibility through randomised controlled pivotal trials, as well as extensive postmarket surveillance of real-world practice.

Our commitment to continued leadership in clinical research is unwavering. In 2011, we initiated enrolment in four new trials (SOURCE XT, PREMIER [pulmonic] Registry, The PARTNER II Trial, and a Valve-in-Valve study), as well as continued follow-up and publication of results from all of the trials previously reported.

We wish to thank all of our investigators and scientific collaborators, including statisticians, clinical event adjudicators, core laboratories, and thought leaders, for their collective expertise and contributions to these important programs.

References

* Data on file at Edwards Lifesciences LLC.