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News We're Watching: TCT Yields More Encouraging Results For TAVR; HeartPoint Resets Trial Plans, Butterfly Tries Brain-Interface Tech

by Reed Miller

Clinical trial results announced at the Transcatheter Therapeutics conference in San Francisco headlined the medtech research and development news last week. Noteworthy "commercial" developments in late October include iCad's decision to sell its Xoft brachytherapy business to Elekta and Butterfly Network's plans to work with Forest Neurotech on brain-computer interfaces.

Long-Term Data Support Durability Of Edwards' And Medtronic's TAVR Systems

Long-term results from two major clinical trials support transcatheter aortic valve replacement (TAVR) as an alternative to surgery, even in patients at low risk for surgical complications.

Edwards Lifesciences' Sapien line of balloon-expandable TAVR and *Medtronic*'s CoreValve line of self-expanding TAVR systems are already approved by the US Food and Drug Administration for high-risk, intermediate-risk, and low-risk patients, as defined by the *risk score system created by the Society of Thoracic Surgeons*.

Everything else being equal, *patients would prefer TAVR to surgery because the post-procedure recovery is shorter and easier*, so TAVR will continue to take *market share* from surgical valves if it can continue to show durable benefits in randomized trials comparing TAVR to surgery in the low-risk group. (Also see "*Abbott Becomes Third US TAVR Competitor With Portico Approval*" - Medtech Insight, 20 Sep, 2021.)

Four-year outcomes from the *Evolut Low-Risk trial*, comparing Medtronic's TAVR systems to surgical aortic valve replacement in low-risk patients were presented by Michael Reardon of Houston Methodist Hospital at the Transcatheter Therapeutics (TCT) conference in San Francisco on 23 October.

> *"Believers in both valves will find reasons for comfort though, and as a result we would not anticipate a meaningful change in market share." – Margaret Kaczor Andrew*

The trial randomized 1,414 low-risk patients with severe aortic stenosis to surgical valve replacement or TAVR with a Medtronic Evolut R, Evolut Pro, or CoreValve system. At four years, the combined rate of death or disabling stroke was 10.7% in the TAVR group versus 14.1% in the surgery group and the absolute difference between treatment arms for this primary endpoint continued to increase over time. The composite of all-cause mortality, disabling stroke, or aortic valve rehospitalization was 18.0% with TAVR and 22.4% with surgery.

At the same conference, Martin Leon of Columbia University *presented five-year results* from the *PARTNER 3* trial. PARTNER 3 randomized about 1,000 low-risk patients with aortic stenosis to surgical valve replacement or TAVR with Edwards' Sapien 3 or Sapien 3 Ultra. The results are also published in *The New England Journal of Medicine*.

The trial had two primary endpoints: a composite of death, stroke, or rehospitalization related to the valve, the procedure, or heart failure; and a hierarchical composite of death, disabling stroke, nondisabling stroke, and rehospitalization measured in days. There was no significant between-group difference in the two primary composite outcomes.

The indicators of valve-durability showed no differences between the two groups. Structural valve deterioration was rare in both the TAVR and surgery groups – 1.4% vs. 2.0%, respectively. Only about 3% of patients in both groups needed a reintervention during the five-year follow-up period.

Edwards and Medtronic dominate the *$5.1bn global TAVR market*. Edwards has about 70% of the market and Medtronic is a distant second with about 27% of the market. Abbott, Boston Scientific and a few players are working on catching up to the established players. (Also see "*Minute Insight: Abbott Rolls Out Navitor Next-Gen TAVR System To Catch Up To Medtronic And Edwards*" - Medtech Insight, 25 Jan, 2023.)

The implications of these results on the TAVR market are hard to predict, because the results of the two trials cannot be compared directly because of differences in the blood-thinner medications the patients were using and because of the influence of COVID-19 on patient follow-up.

"It is difficult and perhaps misleading to try to compare the two trials directly," BTIG analyst Marie Thibault wrote on 25 October. "We do expect doctors to engage with both companies and try to understand the nuances."

Margaret Kaczor Andrew of William Blain Equity Research wrote, "The absolute performance of both valves was comparable in the TAVR arms (10.7% and 8.0% at four years). Believers in both valves will find reasons for comfort though, and as a result we would not anticipate a meaningful change in market share."

HeartPoint Set To Start Clinical Trial Of Pulmonary Stent In Pediatric Patients

HeartPoint Global's Intellistent for interventional adjustment of pulmonary blood flow in patients with congenital heart defects, won the Shark Tank Innovation Competition at the TCT conference in San Francisco on 25 October.

The TCT Shark Tank Innovation Competition is a partnership between TCT's organizer, the Cardiovascular Research Foundation, and the Jon DeHaan Foundation. The competition was adjudicated by a panel of multidisciplinary experts. For winning the competition, HeartPoint will get $200,000 and the Jon DeHaan Foundation Award for Innovation in Cardiology.

Over 170 companies applied to the competition and Intellistent won against five other finalists. The criteria for selection were: unmet clinical need, technology differentiation, intellectual property viability, biological proof of concept, regulatory pathway, and commercialization potential.

Intellistent is a catheter-implanted, adjustable multi-lumen stent that reproduces the effects of surgical pulmonary artery banding in people with congenital heart defects that cause blood to shunt from the left to the right side of the heart.

> *"We [have] just a simple technology that is proven to work." – Seth Bogner*

“We are so grateful that we were chosen, not only because of our innovations, but because the [panelists] see things the way we do. These are some of the leading interventional cardiologists in the world,” HeartPoint CEO Seth Bogner told *Medtech Insight*. “We [have] just a simple technology that was proven to work.”

The company expects it could help treat a variety of cardiac problems, but the company is going to focus on treating infants and children with advanced left ventricle dilated cardiomyopathy.

About 20% of newborns have some kind of congenital heart disease. Bogner emphasized that Intellistent could eventually help the millions of children with congenital heart defects in developing countries, including many who are currently undiagnosed or untreated.

Proof-of-concept research led by Elna Amin of the University of California – San Francisco showed that Intellistent may be a less-invasive alternative to surgery as a bridge to transplant in these pediatric patients.

HeartPoint was set to begin first-in-human trials in the Ukraine last year, but those plans fell through because of the ongoing war in that country. (Also see "*Cardio Catch-Up: Arga, HeartPoint Plan First-In-Human Trials Of Novel Devices; Medtronic And Edwards Announce Product Launches, And More*" - Medtech Insight, 29 Aug, 2022.)

The company hopes to begin international clinical trials in the next few months, Bogner said.

“We [will do] a couple of proof-of-concept cases. Then we're going to go into an up-to-30 patient trial, which will be international, and then [we will do] whatever the FDA tells us to do,” he said. The company hopes the FDA will grant breakthrough status to Intellistent in order to expedite its path to the market.

HeartPoint is partnering with Meditrial, a contract research organization to start first-in-human clinical trials in the US, central Asia and Indonesia.

“[They] helped us focus on the indication and doing everything we need to do to get the necessary pieces we’re missing,” he said.

In the longer-term, the company expects to license its technology to other companies to develop the technology to treat other kinds of congenital heart defects. “This is what the interventionalists have all been waiting for: something that is adjustable. And it’s simple to adjust and the procedure itself is very easy for the interventionalists to do.”

AGENT IDE Trial Supports Boston Scientific's Agent DCB

One-year results from the 480 patients in the *AGENT IDE* clinical trial showed *Boston Scientific*'s Agent drug-coated balloon (DCB) is more effective than uncoated angioplasty balloons for treating in-stent restenosis.

The trial randomized a total of 600 patients with in-stent restenosis of a previously treated lesion of up to 26 mm in length to treatment with Agent DCB or a regular uncoated angioplasty balloon. About 44% of the patients in the trial had multiple stents in the target lesion and 51% were diabetic.

Robert Yeh of Beth Israel Deaconess Medical Center in Boston presented the results at the TCT meeting on 25 October.

The primary endpoint was target lesion failure (TLF) at 12 months; The TLF rate was 17.9% in the the group treated with the Agent DCB and 28.7% in the control group treated with a regular angioplasty balloon – a 38% relative risk reduction. There were zero definite/probable cases of stent thrombosis in patients treated with the Agent DCB.

Agent DCB was approved in Japan in 2023 and received a CE mark in 2014 for the treatment of patients with in-stent restenosis and previously untreated small vessel coronary disease. So far, it has been used in about 100,000 cases, according to the company.

The US FDA granted Agent DCB *its breakthrough device designation* in 2021 and these results from AGENT IDE will support the company's PMA for Agent DCB.

LIFE BTK Results Show Abbott's Esprit BTK Slows Progression of PAD.

The *LIFE BTK* trial of Abbott's Esprit BTK everolimus-eluting peripheral scaffold in patients with critical-limb ischemia met both of its primary safety and effectiveness endpoints.

Esprit BTK is a scaffold with 99-micron thick struts made of poly-L-lactide, a semi-crystalline bioresorbable polymer engineered to resist vessel recoil and deliver drugs. The scaffold is uniformly coated with poly-D L-lactide to control the release of everolimus, a cytostatic drug that prevents restenosis as the vessel wall heals. (Also see "*Abbott Launches Trial Of First-Of-A-Kind Resorbable Scaffold For Critical Limb Ischemia*" - Medtech Insight, 7 Sep, 2020.)

LIFE BTK is a randomized trial comparing Esprit BTK to percutaneous transluminal balloon angioplasty in 261 patients with critical limb ischemia and up to two lesions in their infrapopliteal lesions.

Ramon Varcoe of the Prince Of Wales Hospital in Sydney presented one-year results from LIFE BTK at the TCT meeting on 25 October. The results are also published in *The New England Journal of Medicine*.

Nearly 75% of patients treated with Esprit BTK were free of one of the efficacy clinical events – total obstruction of the target vessel, narrowing of the target lesion, major amputation or repeat interventions of the target lesion – versus 43.7% in the control group.

Abbott will submit these results to the US FDA to support a PMA for Esprit BTK; FDA granted Esprit BTK its *breakthrough designation* in 2020.

Butterfly Signs Deal With Forest To Develop Brain Ultrasound

Handheld-ultrasound developer *Butterfly Network* entered into a five-year agreement with *Forest Neurotech* to co-develop a minimally invasive device for imaging and stimulating the brain with ultrasound.

The agreement includes $20m to be paid to Butterfly for annual licensing, chip purchases, services and milestone payments and additional revenue for every unit sold upon commercialization. The company received $3.5m upon signing the agreement.

Forest Neurotech is part of the Convergent Research incubator for "ambitious scientific non-profits."

"We opened our imaging platform for co-development to encourage and expedite innovation that captures the full potential of Butterfly's disruptive chip technology through new applications and in adjacent markets," said Butterfly CEO Joseph DeVivo.

Butterfly's ultrasound-on-chip technology Butterfly iQ became the first FDA-cleared ultrasound-on-a-chip-based imaging device in 2017. It is supported by a growing suite of artificial intelligence software to make ultrasound imaging easier-to-use and more powerful.

"By the end of 2024/2025, we will start building new markets that nobody else can compete in, markets where patients can leverage ultrasound at home," DeVivo said in a recent interview with *Medtech Insight*. (Also see "*After Floating To Butterfly Network, CEO DeVivo Is Ready To Sting Like A Bee*" - Medtech Insight, 9 Oct, 2023.)

Elekta Buys iCad's Xoft Brachytherapy Business

Elekta will acquire the Xoft brachytherapy business from *iCAD* for $5.5m plus assumed liabilities, the companies announced on 23 October. The deal will close in early November.

“We have been in the process of exploring strategic options for the Xoft business that would accelerate the accessibility of this technology and provide more focus and synergies to its growth,” said iCad CEO Dana Brown.

Stockholm-based Elekta bills itself as the world leader in brachytherapy to treat cancer. Xoft markets the Accent electronic brachytherapy (eBx) system to precisely target cancer with a miniaturized low-energy X-ray source instead of a radioactive isotope.

Accent is FDA-cleared, CE-marked and installed in 120 sites in 16 countries. So far, Xoft has primarily marketed it for breast cancer, non-melanoma skin cancer, and gynecological cancers, but it could eventually be suitable for other indications.

John Lapré, the president of brachy and neuro solutions at Elekta, said, “We will be able to provide a wider range of radiation therapy options that are tailored to the specific needs and preferences of the clinics we support, while helping to reduce their operational costs – since no extensive shielding is needed – and minimize their logistical challenges such as importing radioactive material.”