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September 19, 2012

Therapeutic focus – Transcatheter aortic valves boosted by guidelines

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Since the first approval in 2006, transcatheter heart valves have become widely accepted as a welcome alternative to the chest-cracking open surgery previously required for valvular repair or replacement. Now, for the first time, percutaneous valve replacement using these products is recommended for aortic stenosis, according to official guidelines.

The guidelines, released by the European Society of Cardiology and the European Association for Cardiothoracic Surgery, have enormous power to affect the choices made by interventional cardiologists and their colleagues not just in Europe but all over the world. Only one transcatheter aortic valve is on the market in the US, Edwards Lifesciences' Sapien, but there are a further four in Europe, with another prosthesis, St Jude Medical's Portico, set to gain CE mark – European approval – within a few months.

The use of transcatheter aortic valves is already widespread, but the validation offered by the guidelines will reassure those doctors previously uncertain about the devices' utility.

TAVI

Transcatheter heart valves are threaded through the blood vessels and implanted via either the femoral vein, the subclavian artery beneath the collarbone, the apex of the heart, or directly through the aorta.

The undisputed champion in this area is Californian company Edwards Lifesciences, whose Sapien device was approved for use in Europe five years ago, and in the US late last year.

The other main player in percutaneous heart valves is medtech giant Medtronic, which is pursuing TAVI through its CoreValve prosthesis, launched in Europe in 2007. CoreValve is the only TAVI system approved for three transarterial access options: transfemoral, subclavian and direct aortic. CoreValve is likely to reach the US market in 2014 after its two pivotal US trials read out in January and May next year and could steal market share from Sapien due to the increased access options.

The newest entries to the European market were approved on the same day, just over a year ago. The Acurate TA valve developed by Symetis and German company JenaValve Technology's repositionable and retrievable device, also called JenaValve, bring the total number of TAVI products on the market to five (see table below). These two valves are unlikely to obtain huge market share, but each have innovative structures to aid in correct positioning.

Transcatheter aortic valves on the market

Company	Device Name	Delivery route	FDA Approval	EU Approval (CE Mark)
Edwards Lifesciences	Sapien	Transfemoral and transapical	November 2, 2011	September 30, 2007
Medtronic	CoreValve	Transfemoral, direct aortic and subclavian	-	May 16, 2007
Edwards Lifesciences	Sapien XT	Transfemoral and transapical	-	March 2, 2010
Symetis	Acurate TA	Transapical	-	September 30, 2011
JenaValve	JenaValve	Transapical	-	September 30, 2011

Follow-ups

As for products in R&D, the TAVI pipeline is split between companies who already have a toehold in the market and those trying to break through (see table below).

Edwards is working on its “third-generation” valve, Sapien 3, which like its predecessor may be used for transapical and transfemoral procedure. The company has another contender in Centera, a self-expanding device.

The Centera technology is a departure from current methods in which transcatheter valves are delivered in a collapsed state and expanded with balloons when in position with balloons ; these may be repositioned during the implant procedure if the site in which it is initially deployed is not ideal. Centera may be delivered transfemorally, but is also under investigation for subclavian delivery.

Both Sapien 3 and Centera are to enter CE mark trials this year.

Having established CoreValve as a transfemoral, subclavian and direct aortic product, Medtronic is now making a play for transapical delivery with another valve, the Engager. The self-expanding device is currently in a European pivotal trial due to report in July 2017. In a 30-patient study of Engager, it was placed accurately in 97% of cases, and in 80% of the patients, no more than mild paravalvular leakage was observed.

Symetis is aiming to follow its transapical Acurate TA with a transfemoral equivalent called Acurate TF. Acurate TF is currently in its first trials in humans. This strategy of developing a separate transapical and transfemoral TAVI device is also being pursued by JenaValve, which is developing an as yet-unnamed transfemoral valve.

New players

Of all the valves in R&D, the first to reach market will be St Jude’s Portico, which is likely to obtain CE mark this year. Early clinical data with the product has been positive, with results from the first human trial, in 10 patients, finding only mild paravalvular regurgitation, with most patients graded at none or trivial. A 50-patient European trial will be completed by the end of 2012.

With Medtronic, Edwards and St Jude exploring this area, it is not a surprise to find Boston Scientific treading the path too – the only surprise is that it is so far behind. Boston obtained its Lotus valve through the acquisition of Sadra Medical in November 2010, and is to start a pivotal 120-patient European trial of the device in 2012, with enrolment completion slated for the first half of 2013. It could reach market in Europe in 2013, but US approval is a long way off.

The last company aiming to break into TAVI has a highly unusual technology. Santa Rosa, California-based Direct Flow Medical is developing a metal-free percutaneous aortic valve, which uses an inflatable polyester fabric cuff to anchor it in place. Around 30 patients have now received the valve, and trials in a total of 100 patients are planned.

Innovation is crucial in medical technology, but there is a chance that Direct Flow could pay a price for its inventiveness; such a wildly different design could mean that regulatory authorities will demand trials on a larger scale than those to back more conventional designs.

Edwards currently has 61% of the worldwide TAVI market, according to analysts at Canaccord Genuity, with Medtronic on 35%. Penetration of new products could reduce Edwards’s share to 58% and Medtronic’s to 32% in 2015. With the worldwide market for TAVI devices set to reach $1bn next year and twice that by 2015 according to analysts at Canaccord Genuity, even a small share could be very profitable. But no-one will topple Edwards from the podium any time soon.

Transcatheter aortic valve pipeline				
Company	**Device Name**	**Delivery route**	**Trial ID**	**Reporting date**
St Jude Medical	Portico	Transfemoral	NCT01493284	December 2012
Edwards Lifesciences	Centera	Transfemoral and subclavian	-	-
Edwards Lifesciences	Sapien 3	Transapical	-	-
Medtronic	Engager	Transapical	NCT01348438	July 2017
Symetis	Acurate TF	Transfemoral	-	-
JenaValve	JenaValve (transfemoral)	Transfemoral	-	-
Boston Scientific	Lotus	Transfemoral	NCT01383720	May 2012
			NCT01627691	March 2013
Direct Flow Medical	Percutaneous Aortic Valve (PAV) System	Transfemoral	NCT01475799	No date given

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