Evaluate Vantage

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ACC 2023 – the market tries to take Medtronic’s pulse

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Being first does not always mean a clear win.

Medtronic is on track to have the first pulsed field ablation catheter approved in the US, after yesterday’s success in the pivotal trial of its PulseSelect device. Expectations are enormous for pulsed field technology, with some believing that it could completely replace the more dangerous ablation techniques in current use. But Medtronic’s stock closed down 2%.

The problem seems to be that it is difficult to put the data into context, since the few trials of similar technologies that have read out have very different designs. The uncertainty about PulseSelect’s commercial potential might only clear after more easily comparable US trials of rival devices report.

PulseSelect delivers pulsed electric fields that interrupt the irregular electrical pathways in the heart that trigger atrial fibrillation (AF). Traditional methods of ablation use temperature to ablate, or scar, the atrial tissue to break up the electrical signals; radiofrequency devices use heat and cryoablation devices freeze the heart. Pulsed field ablation is thought to pose less risk of damaging surrounding structures.

Successful AF

Pulsed AF recruited 300 drug-refractory, recurrent AF patients, equally split between those who had paroxysmal AF and those with persistent AF. Data were presented at the American College of Cardiology’s annual meeting in New Orleans, and simultaneously published in Circulation.

The main readout of the uncontrolled trial concerned safety, and this was an incontrovertible hit, with only one primary safety endpoint event in each cohort. A cerebrovascular accident occurred on the same day as the procedure in a patient with paroxysmal AF, causing left lower leg numbness and mild dysphasia; it was resolving by the trial’s end. And a patient with persistent AF had pericardial effusion requiring drainage.

This gives a primary safety adverse event rate of 0.7%, which Medtronic calls one of the lowest adverse event rates ever seen in an FDA trial for AF ablation, or in any multicentre pulsed field ablation trial.

Efficacy was also respectable. 66.2% of paroxysmal AF patients were free from a composite of acute procedural failure, arrhythmia recurrence, repeat ablation, direct current cardioversion, left atrial surgery, or antiarrhythmic drug escalation. This was evaluated for nine months following a three-month blanking period, during which efficacy was not measured, immediately after the procedure.

The rate among patients with the persistent form of the condition was 55.1%. These figures exceeded the prespecified performance goals of at least 50% and at least 40% in the paroxysmal and persistent cohorts respectively.

Freedom from atrial arrhythmia recurrence at 12 months was 70% in the paroxysmal and 62% in the persistent cohort.

Compare and contrast

Medtronic stated that it had re-analysed its own data using the outcomes used in other PFA studies, “and found the Pulsed AF outcomes to be higher when using those metrics”.

The main comparator used was Boston Scientific’s Manifest assessment of its pulsed field catheter Farapulse. Post-hoc Medtronic analyses of the Pulsed-AF data using the monitoring protocol and endpoints of Manifest gave efficacy figures of 91.3% and 86.3% for the paroxysmal and persistent cohorts respectively, the company said.

The figures for the Farapulse device given in Manifest itself were respectively 73.4% and 58.2% for paroxysmal and persistent.

But Manifest was a European postmarket registry rather than a more rigorous clinical trial with FDA buy-in, and thus the comparison is far from conclusive. Farapulse’s pivotal US trials, Advent in paroxysmal AF and Advantage AF in persistent patients, should report this year and next respectively.

The other player here is Johnson & Johnson, via its electrophysiology subsidiary Biosense Webster. Interim data from the Inspire trial, in paroxysmal patients, gave an efficacy figure of 70.9%. Medtronic also analysed the data from the paroxysmal cohort of Pulsed AF using Inspire’s criteria, reporting identical efficacy of 70.9%.

Both Stifel and Wells Fargo analysts believe, after speaking with electrophysiologists, that pulsed field technology could completely replace cryoablation as an AF therapy within five years of approval. Medtronic plans to price PulseSelect at a premium to existing AF devices and is confident of an easy path to reimbursement.

But J&J and Boston Scientific are not far behind – and it seems that the battle will play out in the market rather than in the clinic.