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AHA 2022 – History repeats for Medtronic

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The company's renal denervation system has failed in a crucial late-stage trial, just as an earlier version did eight years ago.

It's 2014 all over again for Medtronic. Long-awaited data on Symplicity Spyral, its renal denervation system, are a bust. This is a distressing echo of what happened when an earlier iteration, called Symplicity, failed in its US approval trial, forcing the technology into a sort of developmental purgatory from which it only emerged three years later.

Medtronic filed Spyral with the FDA yesterday despite the trial failure, and is extremely bullish on the hypertension device's commercial potential. But shareholders were plainly disappointed, with the stock down 6% in early trade.

Downward Spyral

Yesterday's data, presented as a late-breaker at the AHA meeting, came from the Spyral HTN-On Med study, in patients taking antihypertensive drugs. On the primary endpoint, 24-hour ambulatory systolic blood pressure at six months, treated patients had a reduction of 6.5mmHg, versus 4.5mmHg for the sham-treated control group. The difference did not hit significance, with a p value of 0.119.

An important secondary, office blood pressure reduction, was hit with significance – though this can be only nominal, since the primary analysis failed.

The company principally blamed medication use for the study's failure. Among the expansion cohort – the patients enrolled after the study was enlarged from its pilot phase – 22% of the patients in the sham group had an escalation of medication number or dose by six months, the company said, compared with only 2% of the patients in the treatment group.

Discussing the results at the AHA congress, Ajay Kirtane of the Columbia University Medical Center, agreed, saying that the effects within the denervation arm were consistent with prior trials in the space, but that the sham group varied more than expected.

Medtronic is keeping its hopes up for approval and widespread use based on one vital fact: On Med was not the pivotal study of Spyral. That trial was Off Med, which came in positive back in 2020. The group opted to wait for the On Med data before filing, as this setting better represented the real-world population.

Investors are doubtless wondering whether management regrets that decision.

Approval, reimbursement, adoption

The next question for the company is whether the FDA will call an adcom to investigate Spyral's approvability. On a webcast last night Medtronic said it expected to hear from the agency on this point in the next quarter.

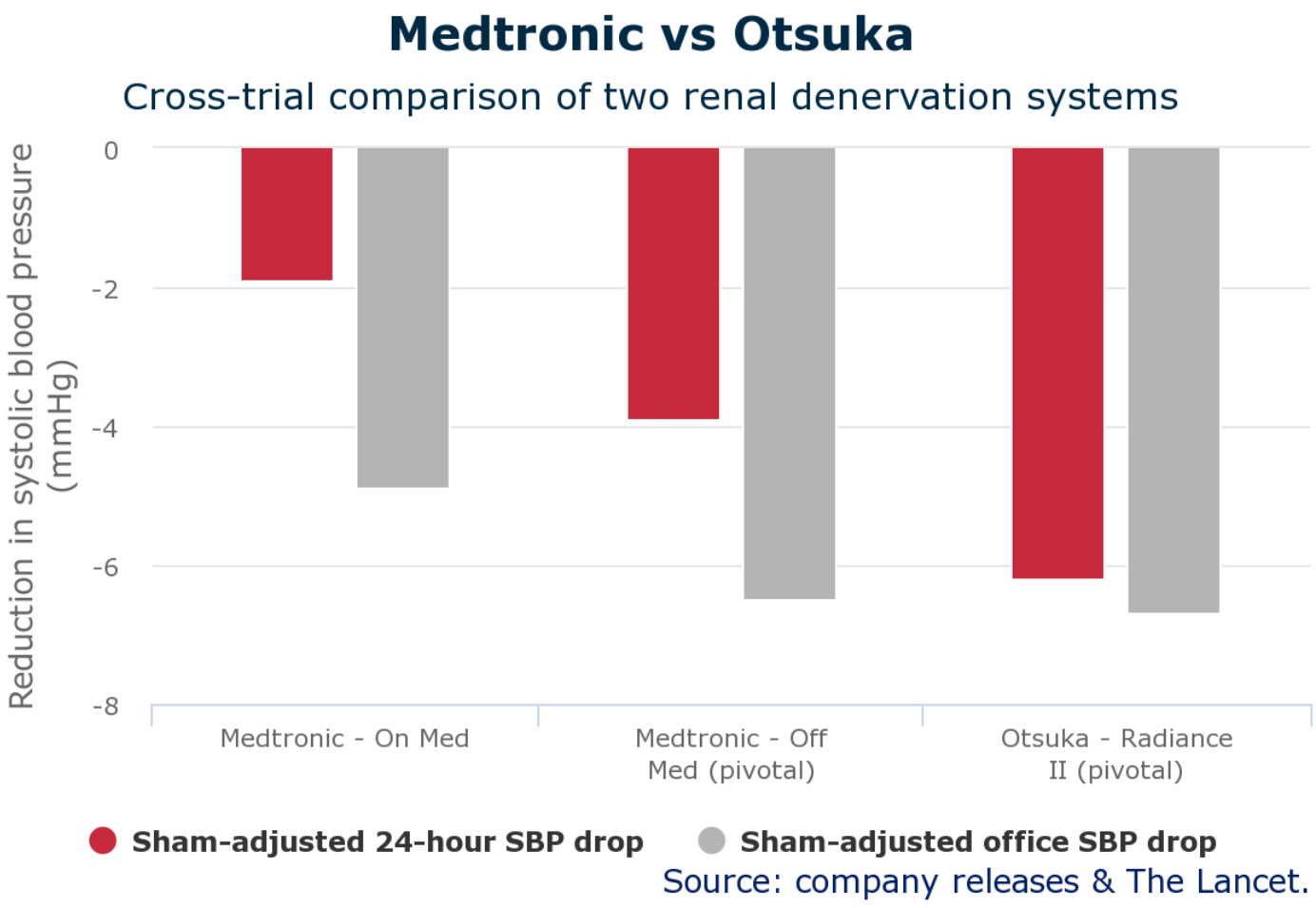
Panel or no panel, Medtronic is confident of approval, and Dr Kirtane also believes in the device. "In Spyral HTN-On Med, my conclusion from seeing this data are that despite missing the primary study endpoint, and when taken in conjunction with the Off Med data, no medications in the background, this trial in my mind confirms that radiofrequency renal denervation lowers blood pressure," he said.

Beyond the FDA, however, lies reimbursement and uptake. Medtronic said it would approach private payers in the US one by one, but that Medicare reimbursement could come around a year after approval.

It also plans a vast charm offensive aimed at cardiologists. Knowing that incorporation into medical guidelines is crucial to ramping decent sales of a new tech, Medtronic aims to "mobilise" doctors to support the therapy. But the most important European organisation in this field, the European Society of Cardiology, does not recommend renal denervation outside clinical trials, and will not update its guidelines until 2024 at the earliest.

Medtronic says that, should Spyral capture just 1% of the treatment-resistant hypertension market, sales would top $1bn.

But the company will have to battle a competitor – one arguably better positioned – for this market. Otsuka's renal denervation device, Paradise, hit its pivotal goal nicely in the summer and might be a more popular choice among cardiologists. No wonder Medtronic is so keen to discuss the vast size of the potential market.



The graph above shows data from the On Med and Off Med trials of Medtronic's Symplicity Spyral device at 6mth and 3mth respectively, and from the Radiance II trial of Otsuka's Paradise device at 2mth.

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