**Title: TCT 22: RADIANCE II Pivotal Trial: Paradise Renal Denervation System in Pts With Hypertension**

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**Dr Ajay Kirtane**

" - Hi, my name is Ajay Kirtane. I'm an Interventional Cardiologist at Columbia University Medical Centre, New York Presbyterian Hospital in New York. We'll be talking a little bit about the RADIANCE II late-breaking clinical trial that's being presented at the TCT meeting in 2022 in Boston.

What is the background to this study?

Renal denervation has been investigated with the goal of reducing blood pressure as an adjunct to medications and lifestyle modification. The goal of the RADIANCE II study was to extend prior findings and to determine whether renal denervation compared to a sham procedure could lower blood pressure effectively and safely.

Can you please tell us about the Paradise system?

The Paradise System employs ultrasound-based sonication to interrupt renal nerve signalling. There's a cooling balloon that is inserted into the artery, and that cooling balloon protects the luminal surface, preventing damage at that area. And the ultrasonication balloon is used to create sonication or heating of the renal nerves at the depth of one to six millimetres beyond the artery itself. By doing that, we can interrupt renal nerve singling and therefore decrease blood pressure, however not causing arterial damage at the same time.

What was the study design and inclusion criteria?

This was a study that sought to enrol patients with uncontrolled blood pressure. These patients had either been on medicines in the past or were currently on medicines but yet could safely discontinue all medications. So this was in effect, an off-med study design. The idea was to discontinue those medications safely, although blood pressure certainly was elevated within the trial, and then to determine if renal denervation compared with the sham procedure could effectively lower blood pressure at a primary endpoint of two months, or actually three months after medicine discontinuation.

What are the key findings?

So, the key findings from this study are that we did enrol patients with blood pressures that were elevated on average about 150 systolic. Most of them were able to safely come off of medications for that short term time period to be able to test in a pure way the efficacy of denervation versus sham. Of course there were patients who did have elevated blood pressures, they were then rescued and taken out of the study. After randomization, we randomised in a two-to-one fashion patients to denervation versus sham in a total of 224 patients. And what we showed is that renal denervation was able to lower blood pressure to a greater extent than the sham procedure. When we looked at daytime ambulatory systolic blood pressure, this was a difference of 6.3 millimetres of mercury between the two study groups. In fact, the denervation group was dropped by almost eight millimetres of mercury from baseline, and very consistent effects were seen when looking at home blood pressure, office blood pressure, 24-hour blood pressure, nighttime blood pressure, and even diastolic blood pressures within the trial. In addition, what we found is that this was done safely. There were no adverse safety events seen in either arm. And importantly, where you started off in terms of your blood pressure was associated with the magnitude of drop in the denervation arm specifically. And so, while many people say 6.3 millimetres of mercury versus sham is not that great an effect, it all always depends on where you start off. And for patients that start off even higher, there was a greater drop in blood pressure seen. For those patients who started off closer to 140 or so there was less of a blood pressure drop seen, therefore not seeing a safety signal of dropping blood pressure too much.

In what situations would you recommend the use of this product?

Well, data from this study is still preliminary because it's only out to two months, so definitive at the primary endpoint ascertainment of two months, but preliminary in the clinical sense just because we need longer term durability and safety data in that regard. We have published on some of these data from prior trials, but with this trial study, specifically patients will be followed out to five years to determine the durability and safety of this procedure. I think when those things are likely established, then at that point, the idea would be when would we consider this for our patients? And my sense is is that there are many patients that are still uncontrolled despite best efforts at medical therapies and lifestyle modification. There are other patients who simply don't tolerate medications or don't want to take them. And so for those types of patients, my sense is that this will be something that will be approved and able to be implemented in the clinical armamentarium for physicians aiming to seek better control of their blood pressure, of their patient's blood pressure, which I think is a good thing given that we know that blood pressure is associated with so many deleterious consequences down the road.

What is next in the story of renal denervation?

Well, for me, I think what's next in this story is combining these data across data sets, and that's something that we're working on. In addition, I do think that with the completion of IDE trials for device approval that we will be seeing device approvals in the next one to two years, with not just this device, but other devices as well. And when that happens, we then have to figure out what's the best way to implement these types of therapies and for our patients. Again, this has to be on top of previously established and less invasive therapy such as lifestyle modification and medication. So, that's first and foremost. Additionally, we have to be vigilant about diagnosing secondary causes of hypertension. So, that also has to be comprehensive, but overall for patients and for physicians I think this is good news, because it's always better to add tools to the toolbox and then to figure out when to use the appropriate tool for the appropriate patient.”