Title: 3 Trials That Will Change My Practice With Dr Itchhaporia
Participants: Dr Dipti Itchhaporia
Date: 23/11/23

Dr Dipti Itchhaporia

"Hello, I'm Dipti Itchhapporia, I'm past President of ACC and I'm here today at AHA to talk about the top trials that are practice-changing. And I thought that we would cover three trials and of course the first I would have to start with is the SELECT trial.

As you know, there's been a lot of buzz about this trial. As we know, the GLP-1 agonists have shown cardiovascular benefits in patients that are diabetic and that are also overweight. But what this trial showed was that they looked at a reduction in cardiovascular death, in cardiovascular events in patients that are overweight, that have cardiovascular disease, but have no diabetes.

So there was actually quite a bit of buzz about this trial. And what it showed was that patients that were overweight and obese that have preexisting cardiovascular disease actually had a 20% reduction in the three-point MACE cardiovascular death, myocardial infarction and stroke. There were 17,000 patients in this trial with a BMI that was greater than 27. Actually, on the average, the BMI was 33.

And what they show was that the cardiovascular disease and these patients had established cardiovascular disease, so they either had a myocardial infarction, stroke or symptomatic PAD. And these patients got a dose of semaglutide that was titrated up to the maximum dose of 2.4 micrograms and they were then tested against placebo and then showed to have this 20% reduction.

So this is really a very interesting trial because the curve separated almost immediately and the patient, if you looked at just myocardial infarction and all-cause death, there was a 19% reduction. And what we saw was that there was also a decrease 38% in the high-sensitivity CRP.

So I think this is a game changer in how we treat obese patients and I think this is a game changer in terms of just obese management. And so now when we think about obesity and these drugs, the Semiaglutide that GLP-1 agonist, we're thinking of these now as cardiovascular prevention drugs. And not just drugs just to lose weight.

Now, the average weight loss in this trial really was about 8%. I thought it could have been a little bit higher, but it was about 8%. But this trial, I think, is going to make the payers Look at this. And I think we're going to have to look at utilising these drugs and our obese patients with established cardiovascular disease to change their MACE outcomes.

The second trial that I'm going to talk about is the ARIES-HM3 trial and this is the HeartMate Three. And this is really looking at LVAD therapy. I believe this is the first randomised trial on LVAD therapy and as we all know, LVADs are evolving in a very positive manner. There's been so many iterative improvements in the HeartMate and now we have the HeartMate Three pump.

But the thing that still plagues LVAD therapy is these hemocompatibility adverse events. And although some of the iterations in the technology has improved the pump thrombosis rate, the stroke rate, all of that with us using vitamin K antagonist therapy. The question is, what about these non-surgical bleeding risk? We still see a lot of non-surgical bleeding in these patients that increases their mortality.

And we've conventionally always used vitamin K antagonists with aspirin because aspirin was believed to be sort of a withholder or- we felt that we really needed aspirin and that if we didn't have aspirin that these patients wouldn't do well. So this actually tested whether withholding aspirin keeping the vitamin K antagonist, but using placebo versus aspirin.

And how these patients did and what they did is they demonstrated in 628 patients and they used an aspirin dose of 100 milligrammes versus placebo. And what they found was that the placebo was non-inferior to low dose aspirin with regards to the primary composite endpoint of these hemodynamic hemocompatibility adverse events.

And so I think that there was definitely less bleeding, 34% less non-surgical bleeding events, that's 14.5 fewer events per 100 patients that were looked at. And so I think that that made us take a pause and say maybe aspirin is not the therapy that we need, but I think that is truly a game changer because we've always held on to aspirin. And now the question is do we really need to continue to hold on to aspirin in these patients?

The last trial is the ORBITA-2 trial. This has also been a trial that has been very much looked at. As you know, the ORBITA-1 trial looked at PCI sham controlled and looked at that versus medical management, optimal medical management in patients with stable coronary disease.

So in this trial, they actually did quite a few novel things, I think. First of all, they took patients that had single as well as multivessel disease. Remember, the first trial only looked at single vessel patients, this was single vessel versus multivessel disease patients. They had to have symptomatic angina and then these patients and they looked at about 300 patients in multiple sites in the UK.

And what they did was after they had documented symptoms, they did questionnaires and what they did was they randomised these patients, they took them off their antianginal drugs and then they randomised the patients to either sham-controlled placebo versus doing a PCI on their documented ischemic lesions.

And what they demonstrated was that they actually got decrease in angina relief. I mean, they got more angina relief that these patients had increased exercise duration and they had improvement in the Seattle antianginal questionnaire. And so there was a lot of improvement with the PCRR.

So I think in a sham-controlled way we showed that PCI actually can help with angina. Now, I think there's a lot more to unpack in this trial. What's the mechanism? Because there were still quite a few patients that still needed antianginal medications because they had symptoms. What's the mechanism of that?

So I think we're going to be looking at a lot more data. But I think what this trial tells us is that this thought after the first ORBITA trials is no PCI for stable angina patients. I think now we need to include PCI as a discussion with the patient. When we do a discussion with the patient for options, I think PCI certainly has to be at the table because when you talk to what's important to the patients and the quality of life on those patients, PCI may certainly make a difference in their quality of life.

So I think this is something else that we'll have to be looking at more data to be unpacked from this trial."