Title: AGENT IDE: AGENT Paclitaxel Coated Balloon Angioplasty for In-Stent Restenosis
Participants: Dr Robert W Yeh
Date: 26th October 2023

Dr Robert W Yeh

"My name is Robert Yeh. I'm a professor of medicine at Harvard Medical School and the section chief of interventional cardiology at Beth Israel Deaconess Medical Centre. We'll be talking about the Agent IDE trial of a drug-eluting balloon versus conventional angioplasty for patients with coronary instant restenosis.

Unmet Needs of ISR Patients

In-stent restenosis is quite common still, despite the advances in drug-eluting stents. In a recent analysis that we participated in, 10% or more of all PCIs done in the United States are for in-stent restenosis. And these patients commonly undergo restenting and have extraordinarily high rates of recurrent events after that. And some of these events are not benign. In fact, a large proportion of these events, a significant proportion of these events actually are unstable presentations with non-ST elevation, myocardial infarctions, unstable angina, and we just have limited options to treat these patients, particularly after they've had one or two stents put in the same artery where we have just balloon angioplasty or the need to put in yet an additional layer of metal, which is sometimes not optimal for the patient.

Unique Features of the AGENT Balloon

The agent balloon is a paclitaxel-coated balloon angioplasty catheter. The balloon catheter itself is a highly deliverable, highly pushable catheter, so it's easy to deliver it into previously placed stents. And then paclitaxel itself is a particularly good drug for this indication and for this use, which is to be able to apply a drug that stays in the vessel wall after a short application or balloon inflation. It's very distinct from the properties that one requires for a stent or a drug-eluting stent. Paclitaxel itself is lipophilic. It tends to stay within tissue once delivered even for a 32nd or 1 minute inflation. And that's where

you want it to stay so it can do the work that it needs to do. And in this formulation of paclitaxel on the AGENT balloon, it is sort of, for lack of a better word, a sticky crystalline structure that tends to embed quite well in a low-dose formulation into the vessel wall.

Patient Population and Study Design

The AGENT IDE trial was a randomised trial. Randomization occurred in a two-to-one ratio with every two patients allocated to receive the paclitaxel-eluding balloon versus one patient allocated to receive conventional balloon angioplasty. Patients who were randomised were those who had instant restenosis of a native coronary vessel of diameter between two and four millimetres and a lesion length of less than 26 millimetres. Patients had to be treated successfully with a residual diameter stenosis of less than 50%, and at that point, they were randomised to either the agent balloon or conventional balloon angioplasty.

Primary Outcomes

Well, the primary outcomes were the composite endpoint of target lesion failure at one year, which was the combination of ischemia-driven target vessel revascularization, ischemia-driven target lesion revascularization, target vessel myocardial infarction, or cardiac death. And in the primary analysis, patients treated with the paclitaxel-coated balloon agent paclitaxel balloon had a reduction in the primary endpoint by ten percentage points. So, the POBA arm or the conventional angioplasty arm had an event rate at one year of 28.7% compared to 17.9% receiving the agent drug code to balloon. It was a highly significant p-value of 0.63. In addition, looking at the component endpoints, ischemia-driven target lesion revascularization was reduced by about 50% with treatment with the paclitaxel balloon. In addition, target vessel myocardial infarction was also reduced by 50%. And finally, stent thrombosis occurred in no patients receiving the paclitaxel-eluting balloon, but it occurred in six patients receiving conventional balloon angioplasty. So, we think these results were highly favourable for the Agent balloon, really demonstrating that the balloon itself is highly effective, certainly much more effective than conventional balloon angioplasty for our patient population.

Take-Home Messages

Well, I think the real take-home message is that we now have a device, hopefully soon in the United States, which will be able to be an excellent alternative to placement of an additional drug-eluting balloon. Certainly, an alternative that is superior clearly to conventional balloon angioplasty for patients with ISR. We think this is going to be an extraordinarily welcome occurrence in the United States. In the United States, this trial enrolled much faster than anticipated. That's rare even during a post-COVID period where we were enrolling patients so quickly. And that reflects really the enthusiasm and the clinical need for a device for practitioners in the United States who have not had a coronary eluting balloon at their disposal.

Further Study Required

Well, I think this is just the beginning. We have many other potential applications of drug-coated balloons. ISR is one of them. But we have long diffuse vessel disease, we have small vessels, treatment with bifurcations, treatment of native coronary vessels that have not been previously stented. So, I think that all these questions remain for the application of drug-eluting balloons in the coronary circulation. Of course, we want to dive more deeply into the analysis of the subgroup populations within the agent trial itself. And there's an additional set of patients who are enrolled. So, this total sample size ultimately of the trial will be 600 patients. And I'm just reporting now the first 480, which were the original design of the trial. This was a joint effort in partnership with Boston Scientific, my study co-chair, Dr. Ajay Kirtane, and an incredibly talented and diverse steering committee. So, I think a lot of people's hard work went into pulling off a very successful trial and everybody is quite proud of the work."