Title: CIRSE 23: SAVE: Sirolimus-eluting Balloon for Failed AV Fistula
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Dr Konstantinos Katsanos

"I'm Dr. Konstantinos Kasanos. I'm a consultant associate professor of Interventional Radiology, and I'm speaking to you from Patras, Greece.

Rationale behind the study

So, CIRSE 2023. We are presenting and announcing completion of enrollment of a very important Pilot randomized controlled study looking at the novel innovative sirolimus-coated balloon angioplasty in the setting for the indication of failing hemodialysis access. This is all about investigating in a pilot setting the first evidence of efficacy of a sirolimus-eluting device for high-grade stenosed arteriovenous fistulas in a patient population suffering from hemodialysis.

SELUTION SLR DEB

So the drug-coated balloons have been designed. Most of the current evidence and most of the commercial devices have to do with paclitaxel-coated balloons. Like everybody knows, we have a few new balloons on the market and one of the most innovative technologies has to do with the application of sirolimus-coated balloon technologies. Contrary to paclitaxel, there has been a lot of evidence and there has been a lot of controversy about the safety and efficacy of paclitaxel. So now we are moving on to testing new devices like the sirolimus one, the one on question, this is from MedAlliance. It's called the SELUTION device. And this is a sirolimus-coated balloon catheter, which is basically a technology where the sirolimus is intermixed with a biodegradable polymer on top of the balloon. Now, there are some key differences here compared to the well-known paclitaxel ones. First, sirolimus is a completely different agent. It is mostly cytostatic compared to cytotoxic paclitaxel. And this technology with the biodegradable polymer is quite interesting as it has completely

different pharmacokinetics and drug transfer properties and bioavailability at the vessel wall. To explain a little bit further, first of all, there is a lot more of the drug being applied to the vessel wall, contrary to the paclitaxel ones, where most of the drug might escape in the microcirculation. Second, because of this combination with this biodegradable polymer, there is sustained delivery and sustained bioavailability of sirolimus into the vessel into the site of treatment, approximately out to two to three months' time. So basically, completely different medication, completely different drug transfer technology, and sustained prolonged availability into the vessel wall.

Patient Population and Study Design

As we said at the beginning, those are new technologies. A number of studies have started to investigate those technologies. This particular study had to do with the failing hemodialysis access. So this had to do with patients suffering from stenosed, failing arteriovenous fistulas in the upper or lower arm, but don't continue doing hemodialysis properly. So the main indication was a failing dialysis access and high-grade stenosis in hemodialysis patient population. As you might note from our CIRSE presentation, the baseline demographics and patient characteristics were very well balanced between the two patient arms. And the design had the following overall design, the following over our treatment allocation in total, it was powered on primary patency and we allocated randomly 84 patients between the two treatment arms. In the control arm, only a plain high-pressure balloon angioplasty was applied to treat the stenosis and in the active interventional arm the SELUTION sirolimus-coated balloon was applied on top of the high-grade balloon angioplasty for the anti-stenotic treatment. Now this was the random allocation at this point. Of course, I would like to thank my co-investigators. This was a multi-center multinational randomized study. There were three centers overall our center in Patras with my co-investigators, Professor Kanabatidis and Professor Kitu and of course myself. Then we had Athens with Professor Burnjos and Professor Speopros who also contributed a significant portion of the patients. And then we also had the team from Singapore with Professor Chong and Dr. Tang who also contributed a number of patients.

The design of the study again has been powered on primary patency. So basically after the patients have been treated and again we are very happy to announce the completion of enrollment of the study with very well-balanced procedural and baseline characteristics. Then we would be working on the primary endpoint. And this is I think what makes the study very interesting because we had a number of important methods applied here working on the efficacy of those devices. So first, primary patency will be checked at six months' time. So hopefully enrollment was completed August 2023. So six months out from today we would be working on the primary endpoints study we also looked at quantitative vessel angiography. So we are checking in a quantitative manner how much will the site of treatment become stenosed again? And also we have functional parameters being measured, like, for example, the flow rate measurements. How much blood flow does the fistula supply, which is the functional equivalent of any kind, for example, of perfusion analysis, in other kind of vascular indications. So different methods being applied. Primary endpoint is the primary patency and again pilot randomized the application of the sirolimus-coated balloon versus the non-drug treatment.

Take-Home Messages

This study was quite slow to enroll because of the COVID situation over the past years. Still, with the help of my very helpful and important co-investigators we managed to complete the enrollment of this very important pilot randomized study. Overall the device showed 100% efficacy. All patients in both arms managed to resume hemodialysis. We had no issues with applying the technology and overall the immediate procedural outcomes showed very significant improvement both of angiographic outcomes of immediate procedural flow rate measurements and successful resumption of hemodialysis. So the first take-home message I think is clearly that the technology can be applied safely and effectively in this diverse patient population who suffer usually from a myriad of baseline comorbidities. And I will also point out that the recruitment of the study was very well-balanced and split between both upper arm brachiocephalic and lower arm radiocephalic fistulas and those might be very important subgroup analysis to look into the future. The other second important message is that hopefully

within six months' time we will be able to check whether the device was effective in improving primary patency of the patients. And I think this is a very important and very sort of interesting pending question in light of the competing paclitaxel-coated balloon technologies.

Additional Comments?

On top of the primary endpoint. We are very interested on the outcomes of the study because this is the first randomized study with the paclitaxel-coated balloon technology in the hemodialysis fistulas and our methods are combining both angiographic and functional measurements. So, for example, we are very keen to correlate primary patency and angiographic improvement, if any, with the corresponding flow rate measurements. We are very curious to see whether any improvement in the flow rate measurements are actually corresponding to better patient outcomes. So we have a number of different methods also introduced into the design of this randomized study, but have not been applied in similar studies previously. And we are very interested and curious to see how this might relate also to the results of this novel sirolimus-coated balloon."