**Title: LINC 23: LIFE-BTK: Esprit BTK System in Narrowed Infrapopliteal Lesions**

**Participants: Dr Sahil Parikh**

**Date: 22/06/2023**

**Dr Sahil Parikh**

" My name is Sahil Parikh. I’m an interventional cardiologist and an Associate Professor of Medicine at Columbia University Irving Medical Centre in New York City. Today we're going to be talking about the Life BTK clinical trial. It’s a trial of a bioresorbable scaffold or below-the-knee intervention.

**Importance of this trial**

So, patients who need treatment of arteries below the knee are usually those who have a condition called chronic limb-threatening ischemia, in which case they have limb-threatening reduction of blood flow. So far in contemporary treatment with these patients, they’re at very high risk for amputation, for unsuccessful restoring blood flow to their limbs. And we've had limited options for minimally invasive treatment. In fact, most of the treatments have been predominantly balloon angioplasty without the benefit of additional medical treatment that is embedded into the device. So, for example, in the arteries of the heart, the standard of care treatment now is a coronary drug-eluting stent, which not only can expand and hold open the artery, but it can also reduce the risk of scar tissue formation in the arteries of the lower extremity, in the femoral artery, basically in the thigh. We have a variety of medical therapies that are conjoined with interventional techniques like drug-coated balloons as well as drug-eluting stents, but in the below knee circulation so far there's been yet to be a successful clinical trial showing that we can improve the long-term outcomes with a medicated device. And so, this is, I guess, the next great hope in that field in that we are combining two unique technologies. One is a scaffold that's entirely made from a polymer. That means that it can be expanded like one would a stent. But it will biologically be reabsorbed over the course of 36 months and eventually there’ll be no scaffold left behind. And over that first year, roughly, of the device’s implantation life, it will elute a drug called everolimus, which is the most found drug used in coronary drug-eluting stents. And then obviously, the combined hope is that we can maintain the artery open for a long enough period that patients who have limb-threatening ischemia can get over whatever issue they have and then not only reduce their likelihood of a long-term amputation, but also improve their quality of life.

**The Esprit BTK Device and its Unique Features**

Well, I think that it's important, obviously, for anybody who is not familiar with the field to recognize that these are some of the most complex patients that are cared for in cardiovascular medicine, the patients who have chronic limb threatening ischemia have a very high morbid profile, where they have a high burden of risk factors, and they have a very high mortality. And this trial was no different. We enrolled patients who were 70% diabetic, virtually all were hypertensive with hyperlipidaemia and the majority have had prior peripheral arterial disease and/or coronary heart disease. And so, you can imagine that this is a very complex patient population. And the fact that we were able to rigorously study and apply the most, I think, appropriate standards to the conduct of the trial and the primary endpoints should suggest to others that it's possible to rigorously study new technologies in this patient population and that these data will therefore be the underpinnings for how we treat patients going forward. So, we're very proud of that and we’re obviously looking forward to making a significant contribution to the field.

**Study Design and Patient Population**

Right, so the most important data that we’ve just released is the full study design. But the patient population are patients who have peripheral artery disease specifically with below-the-knee arterial narrowing and those include specifically disease that extends no more than 17cm in total in any single vessel in the below-knee arteries. And those patients were randomized two to one to having either treatment with the Esprit bioresorbable scaffold or balloon angioplasty. The patients, because they have below knee disease, have severe arterial insufficiency and the clinical syndromes are patients who have either rest pain, so called Rutherford four patients, or patients with minor tissue loss ulcerations typically at the distal perfusion territories of the feet. So that's a Rutherford five. So, Rutherford four and five patients randomized two to one, to get an Esprit BTK which is the scaffold versus the standard of care currently, which is balloon angioplasty.

**Focus of the Trial**

The key sort of focus areas of the presentation was to identify that we're using a composite endpoint that's going to look at a composite of freedom from amputation as well as patency used to use a doppler ultrasound technique. So, one of the big challenges in all the trials that have been done so far is that they have not been able to demonstrate either freedom or reduction in amputation rates or that they have good long-term patency. In other words, that the vessel stays open for a long enough period to affect a good result. So, all the trials essentially have used this composite strategy where they're looking for both the scaffold to stay open as well as for the patient to have a good clinical outcome. So, we are doing the same thing in combining these two sorts of components of the primary endpoint. But the wrinkle that's new in this trial is that we're using binary restenosis. It had been felt to be very difficult previously to get adequate ultrasound images to assess patency using a binary restenosis approach. Most of the trials so far have looked at whether the arteries open or closed. In other words, is there flow visualized or not? This takes that one step further and really looks to see if the stent or scaffold is open. Is there more than 50% renarrowing? And that's what binary restenosis means. And we've realized that this kind of level of accuracy and detail is achievable with ultrasound if you are very fastidious about it. So, the clinical trial design is novel. The safety endpoint is one that's used standardly in most of these other trials, which is major adverse limb events or perioperative death within 30 days. And again, from a clinical standpoint, so far, no device has passed this sort of type of rigorous clinical trial design demonstrating either a composite efficacy endpoint of patency, plus some measure of limb salvage versus plain old balloon angioplasty. So, we're excited that this trial may have the opportunity to be the first of its kind to show that a new drug-eluting device can pass this rigorous standard.

**Next Steps**

So yeah, we're very excited about the conduct of this trial. This is a global trial that enrolled261 patients across the United States, Australia, New Zealand, and Asia Pacific. And so, it's a vast trial that was very complicated in a very sick patient population that was coincidentally initiated during the pandemic. And so, we're not only delighted, but we’re also ecstatic that we were able to completely enrol the trial. And now we're at the very tail end of the follow up period, which is a twelve-month primary endpoint. And so, we expect that this summer, by the end of the summer we'll have the final data and should be able to present and publish our findings in the fall. So, we'll look forward to presenting these data, hopefully, this fall to tell everybody about whether we were successful or not.”