Kathryn Kennedy:	00:00	So thank you so much Dr. Lopes for taking some time to talk to us today about your presentation at TCT out in San Diego. Tell me, to start off with, what is atorvastatin and what is it used for?
Renato Lopes:	00:12	So, atorvastatin is one of this class of drugs called statins. Which the main goal is to reduce the LDL cholesterol and has been proven to be a very effective drug in preventing cardiovascular events for patients where the LDL is high, where the cholesterol is high, but also in patients who have high cardiovascular risk, such as post-myocardial infarction. So in patients, for example, who have a recent myocardial infarction, we know that statins can prevent recurrence of future events. So less myocardial infarction's, less death, less stroke and so forth.
Kathryn Kennedy:	01:05	So tell me, this is related to the original SECURE-PCI trial. Can we revisit, for a moment, the findings of that trial?
Renato Lopes:	01:13	Yes, so with statins, again, it's a class of drug that is known to reduce cholesterol and is using the chronic statin for patients clinically for lifelong treatment. However, there are also some studies, especially some mechanistic studies trying to demonstrate that statins has also other types of effects, other than just lipid lowering. So there are hypotheses that statins can, for example, reduce the level of inflammation, stabilize the plaque, the arteriosclerotic plaque in the coronary, has antithrombotic effect, has a vasodilator effect. So there's all these other effects of statins that are so-called pleiotropic effects. And these are effects that statins could potentially do irrespective of LDL and cholesterol lowering. And because of that we wanted to test this hypothesis. So we wanted to test, if we give a loading dose of statins in patients presenting with an acute coronary syndrome, before and after a percutaneous coronary intervention, so before and after PCI, compared to placebo, if that strategy of loading those statins, only two doses, have an impact in reducing cardiovascular events. So again, it's only testing the pleiotropic effect because it's only two doses within 24 hours so whatever happened, is not related to lipid lowering because there is not enough time to lower the lipids only in 24 hours. So that was the rationale for testing the strategy in this large trial that we called SECURE-PCI.
Kathryn Kennedy:	03:15	So how does what you presented today, at TCT, build on SECURE-PCI? What was the purpose of this new trial?
Renato Lopes:	03:22	Yeah, so in the main trial we show that these loading doses of atorvastatin in the general ACS patients, did not improve clinical outcomes. However, we did identify a subgroup of patients

where it seems that there is a benefit and those are patients undergoing PCI. So, this was shown in prior studies done by us. But in this study that we presented at TCT, we wanted to look at the impact of the timing, so if there is really this potential benefit of statins pre- and post-PCI, we wanted to look at the impact of the timing of giving the statins. Is there any difference between giving statins one hour before the PCI, or two hours, or four hours, or six hours? So different timing of the statin administration before the procedure. So, this was the focus of the study that we presented at TCT.

Kathryn Kennedy:	04:24	And what were the findings?

Renato Lopes:	04:27	So the findings were that timing really does not matter. We did not find any significant interaction between timing and treatment effect for patients undergoing PCI. So in other words, we look at patients receiving statins one hour before PCI, two hours, four hours, and six hours, or twelve hours and the results were very consistent. Irrespective of when statins were given. In other words, in patients undergoing PCI, there is a 28% reduction in cardiovascular events at 30 days and this effect is irrespective of timing of statin administration.

Kathryn Kennedy:	05:15	So when you come away with a finding that that timing isn't important in the treatment of fact, what does that mean for clinical care? What does this mean for providers and for patients?

Renato Lopes:	05:27	Yeah, so that's a very good question. Basically ... remember in the trial everybody, most patients received statins within 12 hours. So, we look at really the difference in timing between one, two, three, up to twelve hours. So it's not that timing does not matter, because we tested an acute loading dose, but we didn't show that it matters in terms of one versus three versus six hours. But based on that, what we proposed based on the current knowledge and based on our general findings, is that because we are going to give statins no matter what for these patient, at least by the time of discharge, and we showed a potential beneficial effect of almost 30% reduction in cardiovascular events, why not just give statins, this loading dose early on, as early as possible, before PCI, with the objective to improve short term clinical outcomes? So I think that's how we basically interpret it. That we think that with our results, based on the other amount of literature that we have in the field, that we have now enough information that when patients present with an ACS, particularly with a ST elevation myocardial infarction, because that's where we found a more pronounced treatment effect, is the patient with ST elevation

myocardial infarction. So when a patient presents with that, we should then provide statins, a loading dose statin as early as possible, before PCI, because this might improve outcomes in this population.

Kathryn Kennedy:	07:13	Wonderful, well thank you for sharing that. How was your presentation received today? Were there interesting comments or questions that came out of it?

Renato Lopes:	07:21	Yeah, I think, we have a large panel with nine, ten people, and they were very intrigued and very interested with the results. They really believed that this is the largest trial in the field and was an important piece of information that was missing for us to be more confident to actually provide this strategy of early statins administration for patients with ACS, and there were a couple of good questions in terms of what ... people asked how are the mechanism of the benefits? Because if it's not through lipid lowering, and again, the answer to that is exactly the hypothesis that we had initially, which is the pleiotropic effect of statins, something else other than lowering the lipids, such as anti-inflammation effect, or vasodilator effect, or antithrombotic effect, or even antifibrinolytic effect. So there are some studies eluding to a fibrinolytic effect of statins. So, all these other so-called pleiotropic effects, are probably the mechanism of our findings. Why we found that only two doses were beneficial for these patients.

Renato Lopes:	08:41	And then the other good question that came out was, if there was any difference in patients who were already taking statins at home versus those who are not so-called statins naïve. And basically, what we showed is that there was no difference. The benefits were there in both patients that were statin naïve but also in patients who were already taking statins at home, that we also reloaded with the strategy in the trial also benefit from that strategy. So no difference between statin status before getting to the trial. So those are the two more important questions that we got in the presentation.

Kathryn Kennedy:	9:23	It sounds like a lot of good science being presented at the conference this year. And I'm glad that the DCRI and that you were a part of it. Thank you so much, again Dr. Lopes, for taking the time to speak with us today and for sharing knowledge with the world.

Renato Lopes:	9:36	My pleasure and you're absolutely right the TCT was a great meeting, we had a lot of important studies such as the one that I just described. Several faculty and fellows from DCRI in major sessions, in major presentations, advancing the knowledge and

fulfilling our mission. Which is not just generate the knowledge, but really disseminate that through the world.

Kathryn Kennedy:	9:58	Thank you again, Dr. Lopes.

Renato Lopes:	9:59	Thank you very much.