Transcript Details
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Survodutide in Obesity: Insights from SYNCHRONIZE-1

Announcer:
This is *Diabetes Discourse* on ReachMD. On this episode, Dr. Carel le Roux will share efficacy and safety results from the SYNCHRONIZE-1 trial, which he presented at the 2026 American Diabetes Association Scientific Sessions. Dr. Le Roux is the Director of the Metabolic Medicine Group and a Professor of Chemical Pathology in the School of Medicine at University College Dublin. Let's hear from him now.

Dr. Le Roux:
More than 700 patients were taken, and all these patients had obesity, but they did not have type 2 diabetes. Some patients went on to have a placebo treatment that involved diet and exercise. Another group went on to a survodutide titration program, and they ended at 3.6 milligrams. The final group went on the same titration schedule, but they ended with six milligrams. And then the patients were followed for 76 weeks.

We had percentage weight loss in the six-milligram group up to 16 percent, and we also had 85 percent of patients who achieved more than five percent weight loss. So that together tells us that this was a positive study.

There was a large number of side effects in the study. What stands out, however, is that the patients treated with the 3.6-milligram arm as well as the 6-milligram arm had vomiting rates as high as 40 percent, and that is higher than expected. Now, to try to understand that, we went back to the clinical trial design. When we set out, the idea was to be very rigid, and that allows us to have rigorous data collection and data that we can interpret in a very rigorous way. But in this attempt to be very rigid with the trial design, I think we didn't respect the peptide enough. And what I mean by that is patients were started on the lower dose and may have felt a little bit nauseous, but they were forced to increase after four weeks. And then they felt moderately nauseous, but they were forced to increase after four weeks to the next level. That's called forced titration, and that's very common in these clinical trials because we want people to go up and reach the top dose. But in this instance, this led to a large number of patients having side effects such as nausea and vomiting. We also had a large number of patients who couldn't continue with the study—23 percent. And to try to understand that, I think you need to interpret that within the context of the very rigid trial design.

This SYNCHRONIZE-1 study is part of a package. We have SYNCHRONIZE-1 with people who do not have type 2 diabetes, SYNCHRONIZE-2 with people who do have type 2 diabetes, and SYNCHRONIZE-Cardiovascular Outcomes with people with existing cardiovascular disease. And we learned from this, and we were able to implement the changes in the cardiovascular outcome study to allow much more dose flexibility.

So ultimately, we see that there's nothing new that we haven't seen before. There were no other safety signals. I think it's also important that we differentiate between tolerability—nausea and vomiting, which is very unpleasant—and safety, which is untoward, unexpected severe adverse events. And there was no difference between the placebo arm having severe adverse events and the active treatment arms. There was also no difference in death; there were no deaths in any of the arms.

The really exciting data of SYNCHRONIZE-1 was not the weight loss; it was actually the metabolic health gains. So we see that there was an improvement in glycemia and in blood pressure, but there was a 63 percent reduction in fat in the liver. So imagine you had 16 percent weight loss, but 25 percent reduction in subcutaneous fat, 34 percent reduction in visceral fat, and 63 percent reduction in liver fat. So ultimately, patients are losing much more fat than lean mass. So that's a positive thing because we also see very impressive improvements in functionality, but I think that it points to the improvement in liver health. That's also why we had the SYNCHRONIZE-Metabolic Dysfunction-Associated Steatotic Liver Disease study. And we also have a big program called LIVERAGE, which is

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specifically studying survodutide within the context of patients with metabolic-associated steatohepatitis. So I think the health gains are going to be first recognized in the liver, but also other health gains that we hope will translate to improvement in cardiac health as well.

Announcer:
That was Dr. Carel le Roux discussing key findings from the SYNCHRONIZE-1 trial in patients with obesity. To access this and other episodes in this series, visit *Diabetes Discourse* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!

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