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### Overcoming Obesity: Insights from the SURMOUNT-4 Trial

#### Dr. Buse:

Welcome to *Diabetes Discourse* on ReachMD. I'm Dr. John Buse, and joining us to talk about the SURMOUNT-4 study focusing on tirzepatide for maintenance of weight loss in adults with obesity is Dr. Lou Aronne. He's the Sanford I. Weill Professor of Metabolic Research and Professor of Clinical Medicine at Weill Cornell Medical College in New York and a former President of the Obesity Society.

Lou, thanks so much for speaking with me today.

#### Dr. Aronne:

Thank you for having me, John. It's a pleasure.

#### Dr. Buse:

Obesity has become the big medical story for the last couple of years, especially since therapies like semaglutide and tirzepatide have become available. So to start us off, Lou, what are the biggest conceptual issues that all healthcare providers should keep in mind when thinking about obesity?

#### Dr. Aronne:

Well, that's a great question, John. But I think that the single most important point is that obesity is a disease, and many people can't get their head around it. Both doctors and patients just can't seem to believe that, but that is critical for understanding why we need a medication to treat what looks like a behavioral problem, people just eating too much. If you look at the science, it tells us that in the process of gaining weight, damage occurs to critical parts of the brain that regulate weight. That is why it's hard to lose weight, not because people don't want to lose weight, not because they can't concentrate on it, not because they're lazy, slothful, or any of the terms that have been used to denigrate people with obesity. It's that something physical has changed in their brain that makes them resistant to the hormones that regulate weight, and as a result, their metabolism may be a little bit slow, their appetite is a little bit high, and their weight continues to increase over time.

#### Dr. Buse:

There's been a huge amount of publications on obesity management approaches, particularly leveraging the GLP-1 system. And in particular, your team's publication of the SURMOUNT-4 study I think will be viewed as a landmark paper in obesity management. Can you tell us a bit about the key design features of the study?

#### Dr. Aronne:

Sure. The SURMOUNT-4 study was a trial of tirzepatide, which is a dual GLP-1/GIP agonist. And GLP-1 and GIP are released when you eat food, so they simulate the effect of eating food. Now there are many other hormones, but one of the reasons we think that hormones like this work is because it's kind of like you're eating food.

But the SURMOUNT-4 trial was a study to see what happens when you stop taking a very effective medicine like tirzepatide. So what we did was to take several 100 research subjects with obesity, and their average BMI was 37, like most of our trials, so they were close to needing bariatric surgery, and we gave them the highest dose of tirzepatide they wanted to take, either 10 or 15 milligrams, and what we saw was that 92 percent of people wanted to take 15 milligrams and only 8 percent took 10 milligrams. Over a 9-month period of time, the average weight loss of that group was 20.9 percent, really a fantastic result, because we know that weight continues to be lost well after nine months.

At that point, we randomized the subjects in the trial to either going on a placebo and continuing the behavioral intervention, which is a part of all of our research trials, or staying on the medicine for another year. The subjects who were on the behavioral program and the placebo regained a significant amount of weight. If you look at it compared to their original weight, they gained about 1 percent of their original weight per month, and so at the end of the trial, they were down about 9 percent, so they got to about 21 percent and then they gained 12 percent of their original weight back over that one-year period of time, as they were still down by 9 percent. The group that continued the medication continued to lose weight. They lost another 4.5, 5 percent, so they lost over 25 percent of their body weight. So it was 25 percent in that group, 9 percent in the other group, so it shows that we can get exceptionally good weight loss by continuing to use tirzepatide over a prolonged period of time.

If we stop it, people will start regaining weight at a rate of about 1 percent of their initial weight per month. And, interestingly, some of the benefit was retained in the people who stopped the drug. So a year later, there was still some metabolic benefit remaining, not as much as I would have liked to have seen, but people still had some benefit. And if you look at a 9 percent weight loss, that's still better than much of what we've been able to do in the past, and again, it's after a year of not taking the medication.

**Dr. Buse:**

For those just tuning in, you're listening to *Diabetes Discourse* on ReachMD. I'm Dr. John Buse, and today I'm speaking with Dr. Lou Aronne about the SURMOUNT-4 study.

You had people take the drug for nine months. They lost 21 percent. They stopped taking the drug for a year. They gained most of the weight back, but they still had lost 9 percent, which is impressive. Would you recommend that as a treatment paradigm: the idea of taking the drug and then stopping the drug and then maybe taking the drug again and stopping the drug?

**Dr. Aronne:**

I wouldn't recommend stopping it for a year, but I think it gives us some hope that a treatment paradigm where it's used intermittently rather than every single week for the rest of your life is probably going to turn out to be reasonable. And as we get longer-acting medications, I think that this trend is going to continue.

**Dr. Buse:**

And based on all these results, what's the bottom line for clinicians from SURMOUNT-4? Obviously, we don't want people cycling off these drugs. But what should the take-home message be?

**Dr. Aronne:**

I think the idea that obesity is a chronic disease and it needs chronic treatment. I'm still amazed when I hear physicians say, "Oh, what do you do when you stop the medicine?" "Okay, you're going to give that to the patient for a year or two. And then what do you do after that?" And my response is "What do you do when you stop someone's insulin? What do you do when you stop someone's blood pressure medicines?" I mean, when you look at the chronic disease paradigm, I want doctors and patients to understand that that is not a realistic expectation. I just heard from someone recently who stopped taking medication for months and his weight was stable, and then he started to get hungry again. He restarted the medication, and his weight went back down. Those things are possible in some people, but it's not like that's going to happen. That should not be an expectation.

**Dr. Buse:**

So you are a former president of the Obesity Society. My understanding is that there is a certification pathway to becoming an obesity medicine specialist and that through the Obesity Society, you've had basically a 15-fold increase in the number of obesity medicine-certified people. Can you tell the audience a bit about what the obesity study can do for them and how they may want to be involved if they're interested in obesity management as a focus of their practice?

**Dr. Aronne:**

Back in the late 2000s—2007, 2008—Dr. Bob Kushner, who was also a President of the Obesity Society, and myself thought that it would be a good idea to start a board of obesity medicine and to develop an academic infrastructure so that people who wanted to specialize in this field could get certified so that a credential certifying minimal competence could be achieved and that could identify them as someone who had this interest. There is no clinical component to certification in obesity medicine. It's a classroom education, which can be achieved at the Obesity Society. The Obesity Medicine Association runs courses. So it's certification that you've had education, that you've passed an exam, and it's meant to signify people who have spent the time to learn more than the average physician about obesity and its treatment.

And something that is very gratifying when you start a board—like, you could start a board, but will people come to get certified? And the number of people who are now certified has increased, as you pointed out, dramatically, more than 15-fold. Initially, it was about 500. It's now 8,200 and increasing dramatically. In the past year, it's increased by 1,500 physicians. So what it's telling us is that

physicians of all types: internal medicine, primary care, but also pediatricians, surgeons, and OBGYNs are very, very interested in obesity and its treatment and recognize that they need more education in order to manage their patients appropriately.

**Dr. Buse:**

I have to say that people in our healthcare system that have availed themselves of this course and passed the exam, it's really very impressive how it's upgraded their skills in obesity management. So kudos to you and the Obesity Society for setting this up. Anything else you want to tell our audience before I let you go today?

**Dr. Aronne:**

The Obesity Society is there to educate physicians and researchers about the latest in obesity, its management, and research going on around the world, so very important organization. I've been a member since the 1980s, and we're seeing steady increases. For years, people ignored obesity and the whole academic area, but it is now the fastest-growing area. It's a very, very exciting time, so I would welcome primary care physicians and other clinicians who have an interest in obesity to look into the various organizations, primarily the Obesity Society but also the Obesity Medicine Association, where you can feel at home and where you can find people who also are interested in treating obesity.

I think that NPs and PAs will be playing a bigger and bigger role in the field. There are certifications for them, not through the American Board of Obesity Medicine, but typically through their organizations and certification processes. But I believe that nurse practitioners and PAs are going to play a greater and greater role in treating patients in the years to come.

**Dr. Buse:**

This has been a really interesting conversation. I'd like to thank my guest, Dr. Lou Aronne, for sharing his insights on the SURMOUNT-4 study and letting us know about the Obesity Society and the Obesity Medicine Association.

Lou, it was great speaking with you today.

**Dr. Aronne:**

Thanks a lot, John.

**Dr. Buse:**

For ReachMD, I'm Dr. John Buse. To access this and other episodes from our series, visit *Diabetes Discourse* at ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.