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Exploring A New Anti-Obesity Treatment

Dr. Buse:
Obesity is one of the major drivers of poor health outcomes in the United States and around the world. Recently, a new treatment for obesity, semaglutide 2.4 mg, has been approved by the US Food and Drug Administration, and new data comparing semaglutide to liraglutide may impact the future of the anti-obesity market.

Welcome to *Diabetes Discourse* on ReachMD. I'm Dr. John Buse. And joining me today is the lead author from the STEP 8 randomized clinical trial, Dr. Domenica Rubino. Dr. Rubino is the Director of the Washington Center for Weight Management and Research in Arlington, Virginia.

Dr. Rubino, thanks for joining me today.

Dr. Rubino:
Hi, John. Thanks for having me.

Dr. Buse:
Well, let's start with some background. What does the anti-obesity treatment landscape look like currently?

Dr. Rubino:
Well, you know, John, I've been in this field for about 20 years plus, and it's actually looking more promising. In the early days, we had very little, and now with the expansion into the gastrointestinal hormones, our understanding that, uh, neuroendocrine space from the GI tract and the signaling to the brain I think is going to open up a lot of different possibilities, so I have a lot more hope

Dr. Buse:
Now let's dive into your study. Why did you and your colleagues decide to look at semaglutide compared to liraglutide? And what were some of your primary objectives?

Dr. Rubino:
Yeah. You know, it's interesting, because I know people say it's very unusual to compare two drugs from a same company, but I think they wanted to get a better understanding within the GLP-1 group is do we see those differences. You know, how does it really hold up? Is there something unique about semaglutide, you know, based on the STEP trials, based on phase II, that may be different compared to liraglutide. And, fundamentally, the study really was to focus on sema versus liraglutide, which is why in the studies it's, it's pooled placebo. Right? We've had a lot of questions about that. Why didn't we have a crossover study? Because it's the one thing that the study did not really examine is how does an individual respond differently to each of those drugs.

So it really is important, you know, with phase II trials for semaglutide—which, I participated in as well—we saw what we've been seeing in the STEP trials is that the average person who has semaglutide or takes semaglutide they're much more likely to lose substantive weight. Right? They're more likely to lose the weight that we like to see for people to help their comorbidities, not just cardiometabolic but structural impact on liver, etc., and so it really was an interesting study to take 2 drugs within the same drug class and compare them.

Dr. Buse:
What were the key findings from your study?

Dr. Rubino:
The key findings from the study were that the subjects that were exposed to semaglutide 2.4, when they looked at categorical weight loss, nearly—a little bit over 70 percent of people who received semaglutide actually lost more than 10 percent, but when we look at categorical weight loss of 15 percent and 20 percent, then you were looking at more than 50 percent were able to lose 15 percent of their baseline body weight, and nearly 40 percent were able to lose 20 percent of their body weight or more, similar to what we saw in the STEP trials. When you compare it with liraglutide, it was a small percentage.

I think there's 2 ways to look at this data. First of all, when you look at both of the GLP-1s, they're successful in some people in reaching these higher levels of weight loss, which we need for the comorbidities that are associated with obesity, but we also really saw that there was a greater likelihood for people who received semaglutide to actually reach those goals, and this is an important finding for the physician out there who's trying to help their patient who really does have that level of weight loss and more to lose for their comorbidities.

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. Domenica Rubino about her recent research on anti-obesity medications. So, before that, that little break, you were leading up to the notion of how these findings might actually impact a clinician's approach to treatment. How has it affected your clinical decision-making?

Dr. Rubino:
So, first of all, obviously, you need to look at the situation of someone and look at the comorbidities and, you know, potential contraindications or medications that might interfere. Fundamentally, the economics of the situation is much more important in treating obesity. I mean, not maybe more important, but it's critical, because if people don't have insurance coverage, then that is going to be difficult for them to get the medicine. Even if someone walked in the door and I said, "Hey, you need to lose more than 20 percent of weight, let me give you this drug," the reality is economics. Right? So economics does guide my decision, but if both drugs were covered, typically, I have a discussion with my patients. We talk about each of the medications. We assess whether they have any insurance coverage at all, and then within what is covered, we discuss what are potential side effects, complications, etc., and then we make that decision together of what to do.

I'd say most patients, when they are trying to decide between liraglutide at 3 mg or semaglutide at 2.4 mg, if they're both covered, I would say many folks are going to initially opt to try semaglutide at 2.4, largely because they're more likely to lose greater weight. However, some people who may not tolerate semaglutide may actually tolerate liraglutide. Now, I have some people who like once weekly, and they love that about semaglutide, but I have other people who like to give themselves a daily injection. I'm not sure whether it's like a reminder, part of mindfulness, or maybe even potency; they want to start a little bit lower. So, largely for me, when I work with my patients, it's a discussion, and we decide which way we go, but honestly, it's economic first but most people are really happy with the 2.4.

Dr. Buse:
Yeah. I mean, for me, the thing that's changed is, when we just knew about liraglutide as arguably the most powerful weight loss drug available with average weight loss of 5, 6, 7 percent.—

Dr. Rubino:
Mm-hmm.

Dr. Buse:
—of body weight, people were, were willing to give it a try.

Dr. Rubino:
Mm-hmm.

Dr. Buse:
I think now, for my patients, being able to talk about a drug that's associated with average 15 percent weight change, which means, you know, for most, at least, men, you know, on the order of 30 to 40 pounds—

Dr. Rubino:
Mm-hmm.

Dr. Buse:
—that really grabs people's attention.

Dr. Rubino:

Sure.

Dr. Buse:
So I do think that this trial has changed the landscape of obesity management.

Dr. Rubino:
And, yeah, the landscape has definitely changed because this is the first time we're able to feel pretty confident that in most patients you're going to get at least 10 percent weight loss. Right?

But I think one thing I do want to sort of qualify and throw in there, it's really important to have the conversation with your patients that this is chronic medication. It is a potent suppressor of intake, and it is important to understand they have to commit to it in the sense of they have to understand that this is a daily medication.

And a lot has changed in our understanding of obesity. I mean, if we look back—I mean, at least I can say when I was in medical school, everything was about diet and lifestyle, and it's all a matter of will power. We're so much more sophisticated in understanding these pathways now, but we've got to understand this is not like an infection where you treat it and then you're done. This is long-term, chronic therapy, but for many people it's lifesaving

Dr. Buse:
Yeah. You know, I think that goes back even to the old days of talking about a diet.

Dr. Rubino:
Mm-hmm.

Dr. Buse:
I mean, almost by definition a diet was something that you went on—

Dr. Rubino:
Mm-hmm.

Dr. Buse:
—with the idea that you would eventually go off.

Dr. Rubino:
Go off, yeah.

Dr. Buse:
But the diet shouldn't be something that you go on with the idea that you're going to do it for 3 months either.

Dr. Rubino:
That's true.

Dr. Buse:
I think that's really a critical point. The other thing that I find is that if I really have an in-depth conversation with patients about how these drugs affect, you know, the brain—

Dr. Rubino:
Mm-hmm.

Dr. Buse:
—and enhance satiety, that the key to getting, you know, really nice weight loss is very small portions, eating slowly, being aware of hunger and how, you know, how little hunger people have when they're on these medicines. Just a few bites of food can often be satiating for them but that they need to stop eating, because it's not that they won't be able to eat. They might just throw up if they keep eating beyond satiety.

Dr. Rubino:
Yeah, I think it depends on, it depends on the person. I think if you're starting people on semaglutide or at least the GLP-1s, if you hear yourself sort of say, "Getting a bit full," you have to stop. Now, I would say with semaglutide it's very difficult for the average person to overeat. I mean, one time you overeat, you don't feel good; you actually feel quite sick; you stop, but it's very potent at sort of giving that very strong signal that you stop. And for many of my patients, I would say they actually find that a blessing, because pretty soon you're eating very small portions, but they feel better because they can actually stop. They stop. They don't get seconds.

We've seen a whole spectrum, and I think as a physician who's working with it, you do want to make sure that they're, that they're actually eating adequately too, that they're actually getting enough nutrition, because for some people they actually don't eat much, and so you do need to pay attention to that, making sure that calorie intake is adequate.

Dr. Buse:
Before we close, I'd like to give you the final word. Do you have any other key takeaways that you'd like to share with our audience?

Dr. Rubino:
What I would say is that obviously this drug, semaglutide 2.4, is very promising. I think it's opening up the gateway to us understanding these hormones and how they work with the level of the brain. I mean, we do know that semaglutide decreases intake more than liraglutide.

I guess it's important, I think, just having been in this field for so long to understand that there's individual differences of these medicines. So if someone, say, unfortunately does not respond to semaglutide, don't give up on obesity drugs. Try the different GLP-1s, try the different other anti-obesity medicines, because I think we're still in early stages of understanding who responds to which drug. So, if they don't respond to one, try something else. Don't give up on the treatment of obesity. These medicines are really necessary to help regulate the neuroendocrine protection of weight, and I think what we're learning is this is not just about people's will power. We have to come to a better empathy and understanding of our individual patients that this is a physiological condition that we need to treat and to help them because the body fights very hard at holding on to weight.

Dr. Buse:
With those insights in mind, I want to thank my guest, Dr. Domenica Rubino, for sharing her insights on anti-obesity medications and their impact on patients. Dr. Rubino, thank you for joining us.

Dr. Rubino:
Thanks, John, for having me.

Dr. Buse:
For ReachMD, I'm Dr. John Buse. To access this episode and others from our series, visit reachmd.com/diabetesdiscourse, where you can Be Part of the Knowledge. Thanks for listening.