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Beyond A1c: Practical Strategies for Managing Obesity in Patients with T2D

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Beyond A1c: Practical Strategies for Managing Obesity in Patients with Type 2 Diabetes” is provided by Prova Education.

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Dr. Ryan:
There are now multiple medical therapies available to achieve weight loss in patients with type 2 diabetes. But who’s the right patient? When should these therapies be started? And what are the right combinations and intensification strategies to sustain meaningful weight loss that can lower the risk of complications?

This is CME on ReachMD, and we’re going to answer these very important questions. I am Donna Ryan, Professor Emerita at the Pennington Biomedical Research Center.

Dr. Frias:
And I’m Juan Frias. I am an endocrinologist and Medical Director of Velocity Clinical Research in Los Angeles, California.

Dr. Ryan:
Let’s get started with a case. Let’s meet Estelle, who was recently diagnosed with type 2 diabetes. She’s 46 years old with a BMI of 34. Her A1c is 7.4. Triglycerides are over 150. She has a low HDL, and her blood pressure is 140/90. She has a history of chronic knee pain and mild depression. Her multiple attempts at diet and lifestyle modification have been unsuccessful, and she has shown a progressive history of increasing body weight over time. She’s a mom of 2, with a son who’s a sophomore in high school and a daughter getting ready to go to college. She and her husband just celebrated their 25th wedding anniversary.

A lot to unpack there, Juan, so let’s start with this. Is Estelle the type of patient who you would consider putting on a GLP-1 or a GLP-1/GIP receptor agonist [RA] right away? Or would you start her on metformin and see where that leads you?

Dr. Frias:
Yeah, great question, and I think the answer is, absolutely, I would think about putting a patient like this on a GLP-1 receptor agonist or a dual GIP/GLP-1 receptor agonist right away unless there was some contraindication which I’m not seeing here. She is an ideal patient for this type of therapy. She is obese, she’s been having progressive increases in body weight, and she has many complications of obesity. Her diabetes is not well controlled. She’s got borderline hypertension, if not hypertension. She’s got dyslipidemia. She has mild depression as well. She has osteoarthritis. So, so much could be helped in a patient like Estelle with weight loss, and today we have agents that can address the glycemia and many other issues, including weight reduction, for type 2 diabetes, so I think we need to be more aggressive in using these therapies in the appropriate patient, and I think she’s certainly an appropriate patient for this.

Dr. Ryan:
The main reason that we’re emphasizing weight management early in this patient is it can have such a big effect over the long term in

patients with type 2 diabetes. It's a way to intervene now that has an impact much later. And look, this patient has a lot of living left to do.

Dr. Frias:
I agree that she's a very appropriate patient for this type of therapy. So she is an ideal patient, but before we talk about what drug combination would be best for her, we also want to improve her quality of life, right, Donna? So what are your thoughts on that, as far as quality of life in a patient like this?

Dr. Ryan:
You know, Juan, the real reason for initiating weight management in patients with type 2 diabetes is because it can have such a powerful impact on the course of the disease, and so I think it takes you out of the usual chronic disease model, where we're just starting metformin and we'll slowly add a DPP-4 inhibitor. This really is intended to move patients upstream in the course of the disease and have impacts not just on glycemia targets, but to get patients perhaps even into normal glycemia and improve all the complications and comorbidities that are associated with type 2 diabetes. But look, it is not something that I can do by myself. The patient has to be involved. It's always a case of shared decision-making. The person who has to make the lifestyle changes is the patient.

Dr. Frias:
And the other, last point I'll make – and you've mentioned this so many times, Donna – is just how important quality of life is, and anecdotally, we certainly see improvements in quality of life and patients just feeling better when they lose this degree of body weight. And we've also seen it in the clinical trials through patient-reported outcomes questionnaires, as well.

Dr. Ryan:
Ok, Juan. Don't look now, but Estelle is in your office. How do you decide which drug combination is the right one to start with? Can you share what you've been doing in your own practice?

Dr. Frias:
So we have a lot of options, but she's a patient that I would either put on a GLP-1 receptor agonist or a dual, GIP/GLP-1 receptor agonist. So the GLP-1 receptor agonists have been around, the first one in 2004. They help increase insulin secretion. They reduce glucagon secretion, and they have very important central effects of GLP-1 receptors in areas of the brain that are intricately involved in energy balance, in food intake and satiety, even in energy expenditure. So working centrally, they reduce appetite primarily and cause reductions in body weight. And now, more recently, we've moved into the so-called unimolecular multi-agonists, or dual agonists, like tirzepatide, which is a single molecule with GIP, which is the second incretin hormone, and GLP-1 receptor agonism. So they stimulate both of these receptors, and by doing so, what we've seen in the clinical trials, is cause even more, or greater, reduction in hemoglobin A1c with greater weight reduction than the selective GLP-1 receptor agonists, such as dulaglutide and semaglutide. And we've seen this in clinical trials.

With tirzepatide, the dual agonist, in the study called SURPASS-2, we looked directly at tirzepatide versus semaglutide 1 mg once weekly and saw even greater reductions in A1c with the 3 doses of tirzepatide, 5, 10, and 15 mg, and greater body weight reductions. And with both of these classes of agents you have positive improvements in blood pressure, in lipids as well, and with the selective GLP-1 receptor agonists, such as dulaglutide and semaglutide, proven cardiovascular benefit. And the cardiovascular outcomes trial for tirzepatide is ongoing, though it's been proven to be safe from a cardiovascular perspective. So my go-to in a patient like Estelle would be either a GLP-1 receptor agonist or a GIP/GLP-1 dual agonist. An SGLT2 inhibitor may be good as well, certainly, but we want an agent that can help with glycemia and significantly reduce her body weight, as that is one of her key concerns and one of her key health issues.

So, Donna, part of the challenge is setting expectations up front for patients. So what do you tell patients with regards to their targets, either for weight and/or for glycemia? And how do you get them sort of in the right frame of mind, if you will?

Dr. Ryan:
Yeah, you know, I think about weight loss goals in terms of percentage, because I know that 5% will give me a certain amount of benefits, 10% more benefit, and 15% the greatest. So patients don't think in percentage, though. Patients think in terms of pounds. So when I talk to patients, I talk about pounds. And then, you know, for patients, the whole purpose of setting a goal, I believe, is to monitor weight and see how it's going over time. So part of that is managing weight loss expectations. You know, all over the internet, you see these rapid weight loss claims, and it actually is not a rapid process. So one thing I like to do is to use the weight loss predictors, the body weight predictor by the NIH, or Pennington has one; they're available online. And what they do is they give patients an idea of how the weight loss trajectory is going to be.

For those just tuning in, you're listening to CME on ReachMD. I'm Donna Ryan, and here with me today is Dr. Juan Frias. Together, we're exploring the right combinations of therapy to achieve both weight loss and glycemic control in patients with obesity and type 2

diabetes.

Okay, let's move on to some rapid-fire questions. I'm going to throw some scenarios at you to see how you'd handle them. Are you ready?

Dr. Frias:
Ready. Let's do it.

Dr. Ryan:
Okay. So Estelle responds well to therapy. How long do patients need to stay on a GLP-1 or GLP-1/GIP RA?

Dr. Frias:
Yeah, so generally the plateau, if we look at clinical trials, on average anyway – and everyone's an individual – but will be somewhere around a year or maybe a little after a year. And patients need to stay on these medications for the effect to continue, for them not to regain the weight. So in general, I think it needs to be explained to the patient that this is a chronic disease and will require chronic therapy.

Dr. Ryan:
Very good. What if it works too well, and Estelle begins to lose too much weight? What do you do then?

Dr. Frias:
Well, that's not an uncommon problem, where patients start losing too much weight and either get below a safe BMI or actually they just don't want to lose so much weight, and they're having issues with their loss of appetite. So in those cases, I think we're very fortunate to have various doses of these medications, whether it's a selective GLP-1 receptor agonist or the dual agonist, tirzepatide. So I would initiate by de-escalating the dose, or reducing the dose, see how the patient does with that, and if needed, reducing the dose further. And that usually works for the patient.

Dr. Ryan:
Great. Now we've gotten Estelle's A1c down to 6.5, but the weight still isn't where we want it. Do you adjust anything with the GLP-1 or GLP-1/GIP RA?

Dr. Frias:
I would. In the tirzepatide trial, as you see, a very clear, in all of the studies, dose-response relationship between the dose and the reduction in body weight. So I would, again, in general, go ahead and increase the dose and see how the patient responded to that increase despite the fact that they were at a good A1c, because again, we're dealing with a lot of different issues here, not just the glucose.

Dr. Ryan:
Okay, let's say you put Estelle on a GLP-1 receptor agonist, and it doesn't work out as planned. Do you switch? And if so, what do you change out?

Dr. Frias:
You know, safety is of the utmost importance, but I think we could try to switch them, for example, from dulaglutide to semaglutide or from either of the selective GLP-1 receptor agonists to a dual agonist, tirzepatide. And then see how they do if they've sort of stalled.

Dr. Ryan:
You know, bariatric surgery has been our most effective and most durable option for weight loss, and it has been associated with reduction in cardiovascular events and mortality. So when should we consider surgery for this patient?

Dr. Frias:
Certainly, in my patients, and this goes almost straight from the guidelines, with BMIs of over 40 – and I have patients with BMIs, you know, 45, 50, and above – particularly if they're just not responding to pharmacotherapy. But even patients with lower BMIs who have a lot of cardiovascular risk factors or other metabolic disorders, which most of them do, I think should be candidates if they don't respond well to today's therapies.

Dr. Ryan:
You know, Juan, this has been a fantastic and practical conversation. But before we wrap up, I'm going to give you the opportunity for a take-home message that you'd like to share with our audience.

Dr. Frias:
Absolutely. So I think we're in a great place today in the management of type 2 diabetes. We've come a long way. Our focus, clearly, on

glucose is critically important, but we need to be thinking about the extra glycemic effects of our medications, particularly the effect on body weight, as losing weight not only has an important effect on glucose, but on so many other of the complications of obesity. So I think we need to act sooner, and we need to use these agents in the appropriate patients as soon as possible, basically.

Dr. Ryan:
You know, you and I were both at ADA this year, and we remarked on the enthusiasm there was for weight management as a pathway to better diabetes management. And it's all because we finally have some tools in our toolbox to help our patients lose weight and get better chronic disease management. So I think it's important for everybody who's listening to us to think about what they can do to help their patients by using these tools as part of good diabetes management.

Unfortunately, that's a wrap. I want to thank our audience for listening in and offer a special thank you to you, Juan Frias, for sharing all of your valuable insights and expertise. It was great diving into this topic with you. Thank you.

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