www.medscape.org

This article is a CME / ABIM MOC / CE certified activity. To earn credit for this activity visit: http://www.medscape.org/viewarticle/970215

Supported by an independent educational grant from
Eli Lilly and Company

The New Side of Incretin-Based Therapy in Type 2 Diabetes: Exploring Advances From EASD 2021 CME / ABIM MOC / CE

Carol Wysham, MD; Stefano Del Prato, MD; Juan Pablo Frias, MD

Posted: 3/15/2022

Educational Impact Challenge

Clinician Handout

The goal of this activity for primary care providers (PCPs) is to improve the knowledge and awareness of emerging dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 receptor agonist (GLP-1 RA) therapies and their mechanism of action, the clinical data on their glycemic and extra-glycemic effects, particularly on weight loss, and their potential effectiveness/benefits in T2D management as they progress through development.

The goal of this activity for diabetologists/endocrinologists is to increase clinical understanding of emerging dual GIP and GLP-1 RA therapies and implications of clinical data on their glycemic and extra-glycemic effects, particularly on weight loss, and improve clinical appreciation of how these agents may potentially fit into T2D management as they progress through development.

Before you begin this activity, please assess your clinical knowledge by completing this brief survey. Answering these questions again after the activity will allow you to see what you learned and to compare your answers with those of your peers.

Educational Impact Challenge

What did you learn from this activity? Please click on the "Next" button to proceed to a brief survey to see how your knowledge improved after the education. You can also see how your answers compare with those of your peers.

Educational Impact Challenge

Activity Transcript

Carol Wysham, MD: Hello, I'm Carol Wysham, Clinical Professor of Medicine at the University of Washington in Spokane, Washington. Welcome to this program titled “The New Side of Incretin Based Therapies in Type 2 Diabetes: Exploring Advances from EASD 2021.” Joining me today are Stefano Del Prato, who is professor of Endocrinology and Metabolism at the University of Pisa School of Medicine in Pisa, Italy. Welcome Stefano.

Stefano Del Prato, MD: Hello.

Dr Wysham: And also Juan Pablo Frias, who is the Medical Director and Principal Investigator at Velocity Clinical Research in Los Angeles, California. Thank you for joining us in our discussion today Juan.

Juan Pablo Frias, MD: Thank you

Dr Wysham: It's actually hard to believe that the newest class of anti-hyperglycemic agents, the GLP-1 receptor agonist were approved by the US FDA in 2005. Since then, there have been development of daily and now weekly versions of GLP-1 receptor agonist therapy, and the demonstration that they are the most efficacious agents that lowering HbA1c. Yet, we still have patients using GLP-1 receptor agonists, even the most potent ones, who fail to achieve glycemic control. Thus, we need new strategies, new therapies, as well as the identification of appropriate use of our current therapies to help improve glycemic control in our patients.

What we understand now is GLP-1 is an incretin therapy, but it's only one of many incretins, that is, hormones released by the intestinal cells in response to food intake. Of these hormones, GIP plays a very significant role in postprandial glucose control. As you can see, the GIP contributes about 45% of the postprandial insulin release in normal individuals, whereas glucose itself contributes about 26% of the insulin, and GLP-1 about 29%. So taken together, GLP-1 and GIP contributed about 75% of the postprandial insulin secretion. Now, we have robust agents in GLP-1 [receptor agonists], but can we harness the impact of GIP in order to improve glucose control in our patients with diabetes?

Clinical Animation: An emerging target for the treatment of type 2 diabetes are the GIP receptors. GIP receptor agonism reduces food intake, nausea, body weight and increases glucagon. In subcutaneous white adipose tissue, GIP increases lipid buffering capacity and reduces inflammatory immune cell infiltration. Combining GIP with GLP-1 can produce synergistic effects in controlling glucose and lipids in type 2 diabetes.

The safety and efficacy of an investigational dual GIP and GLP-1 receptor agonist, called tirzepatide, has been evaluated in the SURPASS clinical trial program. Data from SURPASS 1, 2, 3 and 5, which were monotherapy and comparisons with semaglutide, dulaglutide, and glargine were presented during the 2021 81st Scientific Sessions of the American Diabetes Association.

tirzepatide = Mounjaro; semaglutide = Ozempic, Rybelsus, Wegovy

In SURPASS-2, at 40 weeks, all 3 doses of the once weekly tirzepatide resulted in superior HbA1c reductions from baseline compared with once weekly semaglutide. Up to 86% of patients who received tirzepatide reached an HbA1c goal of less than 7% compared with 79% of participants who received semaglutide. Reductions in body weight with tirzepatide was dose dependent, and all 3 doses were associated with greater weight loss than semaglutide. Of note, in the LOOK AHEAD, a body weight loss of 10% showed impact on cardiovascular outcomes. In addition, despite the slow titration, reductions in fasting glucose levels were nearly identical between the 2 highest doses of tirzepatide. With greater reductions and fasting serum glucose levels, observed and all tirzepatide doses compared with semaglutide.

Dr Wysham: Now I'd like to ask Stefano to review some of the new data on emerging therapies for patients with type 2 diabetes that were presented during the 2021, 57th Annual Meeting of the European Association for the Study of Diabetes. Stefano?

Dr Del Prato: Carol, thank you very much. Thank you. It's a pleasure for me to give you an update and highlight the data that have been presented recently at the ADA and EASD. The SURPASS-3 study was a trial that that evaluated the efficacy and the safety of tirzepatide at 3 different doses, 5, 10, and 15 mg vs insulin degludec. What you can see in the slide here is the overall results of the trial showing what is the main outcome. In other words, a greater ability to improve glycemic control as shown by the significant production in HbA1c as compared with insulin degludec. This has been associated with a significant reduction in a dose dependent manner of bodyweight.

However, what was looked at in the MRI substudy was the liver fat content in a subgroup of the SURPASS-3 population. A total of 296 subjects had been recruited and distributed to the 3 arms with the 3 doses of tirzepatide and the fourth group treated with insulin degludec to the same design that has been used for the main trial. However, all these subjects have been evaluated and investigated using MRI.

The first result that I would like to point out to you is what has been also observed in the main study, which is changes throughout the study in the alanine aminotransferase and aspartate aminotransferase, ALT and AST. And what you can see and what can be appreciated is that a dose dependent reduction in the liver enzymes, although there was also some reduction, particularly when you look at the ALT with insulin degludec. However, the reduction observed with tirzepatide, particularly for the highest of the dose, the 10 and the 15 mg are significantly greater, so suggesting, to some degree, an improvement in liver function that could be also associated with a reduction in the fat content.

As I already mentioned, this has been evaluated using MRI and this is just an example of what can be observed. This was a patient who started with a BMI over 44.8. As a result of treatment with tirzepatide, the BMI dropped to 36.2 kg/m^2, and the body weight went from 134 kg down to 108 kg. But what you can also appreciate here is a significant change in the MRI of the structure and fat content in the liver that was very much reduced, together with an improvement also the glycemic control. So as I said, this is just an example.

But when you do calculate the change from baseline in terms of liver fat content, what has been observed is a significant greater reduction in the fat content using the tirzepatide as compared with insulin degludec.

And when you look in particular at those people who were able to achieve a certain degree of reduction greater than 30%, you can also appreciate that there is a larger number of people achieving that kind of a target in terms of liver fat content. So altogether, these results suggest that tirzepatide together with a reduction in the body weight may also have a quite a positive effect in reducing the fat content in the liver, which we have learned over the past few years to be another potential important factor that can contribute to complications of diabetes, and in particular, cardiovascular complication.

Dr Wysham: Great, thank you very much for that very interesting information Stefano.

Clinical Animation: At EASD 2021, Stefano presented data from the SURPASS-4 trial. In this clinical trial, tirzepatide was evaluated vs insulin glargine as add on to 1 up to 3 oral antihyperglycemic medications. That is, metformin, an SGLT2 inhibitor, and or a sulfonylurea in patients with type 2 diabetes and high cardiovascular risk.

Dr Wysham: Stefano, please tell us more about these data.

Dr Del Prato: As you mentioned, SURPASS-4 was designed to evaluate the efficacy and safety of tirzepatide vs insulin glargine. However, it has 3 major characteristics and features as compared with the entire SURPASS program. First of all, as you mentioned, subjects with a greater cardiovascular risk as compared with the entire diabetic population that have been included so far in the SURPASS program was recruited for this specific study. Second, the follow up was longer than. Most of the prior SURPASS trials had a 52 week follow up. Here, the study was extended, and was extended for another reason, and that was, in order to collect as many as possible adjudicated cardiovascular events in order to explore the initial cardiovascular safety of tirzepatide.

And here is some of the demographics of these patients, just to give you an idea what I was referring to and you can see that the vast majority of these individuals had a duration of diabetes that was in the range over 12 years, slightly higher than what has been presented in other trials of the SURPASS program. The HbA1c to start with was in the range of 8.5%, slightly higher than prior observation. And here, what is really unique of SURPASS-4 is the high percentage of people with a history of cardiovascular disease. In fact, 87% of the population had a history of cardiovascular disease. And along with that, 20% of these patients had prior non-proliferative retinopathy, and as you mentioned, a certain number of these people also were on an SGLT2 inhibitor, a sulfonylurea, and metformin. So aligned to also to better observe and get more information about what would be the implication of using tirzepatide in people that are failing multiple oral agents.

And here you can see the main results of the study. As compared with insulin glargine, the 3 doses of tirzepatide was associated with a greater improvement in terms of the HbA1c. But here you can see also that that improvement after the finish of 52 weeks was maintained for the remaining time of the observation, so providing initial information about the durability of the improvement of glycemic control that can be obtained with tirzepatide. It's interesting to see that with the insulin glargine, there was an initial drift upward in terms of the HbA1c. So tirzepatide seems to really provide sustained glycemic control. And the same is true with respect to the body weight, because after the initial body weight reduction, that reduction after the initial year was maintained without no significant changes throughout the remaining time of the observation, which accounts for a significantly greater reduction in body weight with tirzepatide as compared with insulin glargine.

In SURPASS-4 we also looked at the lipid profile, and you can see here a summary graph of the different changes with the 3 doses of tirzepatide with the light blue color, and the dark blue color according to the different doses have been used, and showing that overall, the tirzepatide doses were associated with a greater improvement in the profile, in particular in terms of triglyceride reduction, total cholesterol reduction, increase in HDL cholesterol, reduction in VLDL cholesterol and non HDL cholesterol. Interestingly enough, the triglyceride and non HDL cholesterol reduction was also maintained in the follow up and in the extension of the study.

Tirzepatide was also associated, compared with insulin glargine, with a significant reduction in both systolic and diastolic blood pressure that remained constant throughout the entire period of the follow up extending after the initial 52 weeks.

Also, because of the long duration of the observation of SURPASS-4, we've also looked at the adverse events, and overall it was shown that tirzepatide is mainly associated with a typical adverse event profile typical of a GLP-1 receptor agonist which is diarrhea, nausea, decrease of appetite, vomiting and dyspepsia and with a very similar incidence as other adverse event that has been reported throughout the trials.

And, as I mentioned before, specific attention was paid to collect cardiovascular events. And all these cardio events have been adjudicated. Here is a Kaplan Meier curve for the time to appearance of adjudicated MACE. And what you can see here, once again, is the 3 doses of tirzepatide as compared with glargine. And overall, there was a numerical reduction in terms of the events with tirzepatide as compared with glargine in particular, when you put together all the events in the 3 different arms and 3 different doses of tirzepatide, although this is a just a numerical difference and there is no statistical power, but I think that these data really suggest that in terms of the cardiovascular safety, tirzepatide, is safe with respect to the use of glargine and let me remind you that glargine also is an insulin that have been evaluated and be tested for cardiovascular safety in the ORIGIN trial.

Dr Wysham: Thank you for those very interesting data, Stefano.

Clinical Animation: Across the SURPASS clinical trial program, tirzepatide demonstrated consistent reductions in HbA1c, proportions achieving HbA1c less than 7%, and body weight. The overall safety profile for tirzepatide was consistent with the GLP-1 receptor agonist class. Common adverse events seen in the clinical trials include nausea, diarrhea and vomiting, most of which were mild to moderate and were transient

Dr Wysham: Juan, there are also other therapies and strategies that are being explored for management of patients with type 2 diabetes and obesity. Can you help update us on those?

Dr Frias: Yeah, thank you, Carol and it's a pleasure to be with both you and Stefano for this very interesting program. There's been a lot of work in drug development, not only for type 2 diabetes, but other metabolic conditions, particularly obesity and fatty liver disease. One important trend that we have seen is the study of higher doses of selective GLP-1 receptor agonists that are already available for our patients. So this would be dulaglutide, semaglutide, as well as oral semaglutide.

Dulaglutide was studied at 3.0 and 4.5 mg once weekly vs what was previously the highest dose which is 1.5 mg once weekly in a study called AWARD-11, and actually the higher doses were approved by FDA in September of 2020, and now the higher doses are commercially available.

Semaglutide has also been studied at higher doses in the previous maintenance doses of 0.5 and 1.0 mg once weekly. The SUSTAIN FORTE study which was recently published, looked at 2 mg of once weekly semaglutide for patients with type 2 diabetes, and both in AWARD-11 looking at high dose dulaglutide and SUSTAIN FORTE looking at high dose semaglutide, what was seen was at these higher doses provided greater reduction in HbA1c, so improvements in glycemic control, as well as improvements in weight control compared with the previous high doses or highest maintenance doses of these medications.

The other not yet completed study though, looking at higher doses of GLP-1 receptor agonists that are already approved, is a study that's ongoing called PIONEER PLUS, which is looking at higher doses of once daily oral semaglutide, comparing a 25 and a 50 mg dose once daily with the current highest maintenance dose of 14 mg once daily. Given the weight effects that we see with GLP-1 receptor agonists, recently we had approval of semaglutide at 2.4 mg once weekly for the treatment of overweight and obesity. And there's actually a study looking at oral semaglutide as well with doses as high as 50 mg once daily, a study called the OASIS-1 study, looking again in patients with overweight and obesity, specifically a weight reduction.

They're also triple agonists as well. So looking at agonism of GLP-1, GIP and the glucagon receptor.

A couple of other very interesting developments. One is the once weekly amylin analog called cagrilintide which has been shown to have significant reduction in body weight. This is also being assessed in combination with semaglutide. Again, early studies have shown increased body weight [reduction] with this combination compared with semaglutide alone.

Clinical Animation: Amylin is an amino acid peptide produced by beta cells in the pancreas, and released, along with insulin, in response to nutrient intake. Amylin primarily acts in the hindbrain to regulate appetite and induce satiety.

Also in clinical development, is the basal insulin icodec, a once-weekly basal insulin in combination with once-weekly semaglutide.

Clinical Animation: Modifications to the structure of basal insulin icodec increases its stability and reduces enzymatic degradation, imparts strong and reversible binding to albumin, and contributes to slow receptor-mediated clearance.

And lastly, there's also early phase development of small molecules that are GLP-1 receptor agonist that can be administered once-daily, orally. So a lot going on in both type 2 diabetes or type 2 diabetes and obesity, as well as fatty liver disease. I think it will be very exciting to see how all these programs play out and how ultimately, they may help our patients achieve better control.

Dr Wysham: Juan, thank you for those intriguing data. I'm very interested in the future of these compounds that you that reviewed today.

I'd like to pause and let the audience weigh in on this.

3D Animation: After a meal, incretin hormones are released from cells in the instestines. GLP-1, a 30 amino acid peptide binds to GLP-1 receptors found in the GI tract, pancreas, brain, heart, and kidneys. Unlike GLP-1, GIP receptors are highly expressed on adipocytes. GIP is a 42 amino acid peptide. A major effect of GLP-1 and GIP is to stimulate insulin secretion, contributing to the incretin effect. In type 2 diabetes, the incretin effect is reduced. Dual GIP/GLP-1 receptor agonist have agonist activity at both the GIP and GLP-1 receptors with greater affinity to GIP receptors. This synergy may result in a greater effect on glucose levels and body weight in patients with type 2 diabetes.

Dr Wysham: Juan, tell us a bit more about what we just saw in that 3D animation.

Dr Frias: Yeah, absolutely. As we saw, there are 2 incretin hormones, GIP and GLP-1, and these hormones are very important normally in maintaining glucose and energy homeostasis or metabolism. Actually, both of these have the same function on the pancreatic beta cell, which is to augment glucose stimulated insulin secretion. And, as we also saw in the video, that it's not just the pancreatic beta cells that have these receptors but many cells and other organs and tissues have receptors for either both GIP and GLP-1 or one of the incretin hormone.

Some of the examples of this would be the central nervous system so the CNS or the brain, which has receptors for both the incretins, so GLP-1 and GIP, in areas of the brain that are very involved in appetite and satiety as well; the reason why we get weight loss with these medications, so it's thought that there may be a synergistic effect when we're agonizing if you will, both of these receptors.

On the pancreatic alpha cell which produces and secrete glucagon, you have receptors, certainly GLP-1 receptors and probably GIP receptors as well, but they have sort of differential effects if you will, with GLP-1 reducing glucagon in a glucose dependent manner. And with GIP, particularly during hypoglycemia and euglycemia, increasing glucagon but certainly during hyperglycemia, there is a reduction. In the stomach there are no GIP receptors but you do have GLP-1 receptors which modulate or slow gastric emptying which is very important for postprandial glucose metabolism. I think one of the key aspects of GIP is that the GIP receptor is widely expressed on fat cells or adipocytes and GLP-1 is not, and Carol, you had mentioned this previously. So by stimulating the GIP receptor, you do get mobilization of fat uptake by the fat cells particularly in the postprandial state and then appropriate release of fat during the post absorptive state and this actually reduces some ectopic fat accumulation whether it be in the liver, the skeletal muscle, or actually in the pancreas and potentially in cardiac tissue. And this is very important for sensitizing these tissues and also for the release of adipokines that are insulin sensitizing such as adiponectin. I think we'll be learning more about mechanism of action as time goes on. But certainly very interesting.

Dr Wysham: Thank Juan that's very important. I mean, not only are we looking at HbA1c reduction but we know our patients frequently are obese, have abnormal lipid metabolism and this ectopic fat metabolism. And so these are very exciting data that hopefully will translate to improvement in outcomes as well.

Now, I'm sure our audience would be very interested in hearing your views on the placement of this new class of medication - GIP GLP-1 receptor agonism - in the algorithm for treatment of patients with type 2 diabetes. Stefano, would you like to give us your opinion on where you might see these fit should they be approved?

Dr Del Prato: Carol, this is an interesting question. I could see the placement of these drugs into different stages of the disease. While I'm still remain convinced that good glycemic control is important for people with diabetes in order to reduce the risk of microvascular complication, if this can be combined with quite an effect on body weight and blood pressure and lipids, I will say this to should really be considered very early in the stage of diabetes.

Also, the other thing and we need to have more information on this for sure, but as I mentioned before, tirzepatide is associated with a significant improvement in the cardiovascular risk profile. It has also been associated with a numerical reduction and really I like to underline numerical reduction, which is not the final proof for potential cardiovascular benefit. But, a study is ongoing looking specifically at the potential for cardiovascular protection using tirzepatide. So that study will provide us sufficient evidence if there is some cardiovascular protection. Now you can see also how tirzepatide can be in use for people with a very high cardiovascular risk.

And finally there is the third which, I am sure Juan can surely comment on more than I can, but in obese individuals, we need to consider the potential for increasing the dose or using larger dose that may not be necessarily the dose needed for people with a type 2 diabetes with moderate overweight or morbid obesity. In some of them, that could be very helpful.

Dr Wysham: Thank you, Stefano. Juan, do you have anything to add to that very complete discussion?

Dr Frias: I think the other thing I would add to that it's very nice to have a range of doses as well. If a patient's losing too much weight, I would I have the ability to reduce the dose or I may find patients who are doing perfectly well with the 5 mg dose for example, and I may not need to escalate the dose further. You know quite frankly, I think initially I would probably use it just as I use GLP-1 receptor agonists probably in combination with metformin and an SGLT2 inhibitor. Just based on the fact that it has such robust reduction in HbA1c and body weight, I tend to favor it in patients who are very poorly controlled or and/or who were obese as well. But I think it sort of remains to be seen, we'll see how the insurance coverages too which clearly plays a big role in what we prescribe in the US as well. And Stefano, I mean absolutely, the cardiovascular data will be critical also to determine which patient populations it really fits in the most.

Dr Wysham: Juan, what would you suggest we do with this medication again, should it be approved before the CVOT data are available; if you have a patient with CVD, would you be using this medication?

Dr Frias: That's a great question and potentially I would. We have as you know selective GLP-1 receptor agonists, liraglutide, semaglutide, dulaglutide with proven cardiovascular benefit in patients not only who have pre existing atherosclerotic cardiovascular disease but who are very high risk as well. If I'm going to prescribe a GLP-1 receptor agonist with cardiovascular protection in mind, until I have the cardiovascular data, I would stick to drugs that have proven cardiovascular benefit, so I would stick to the selective GLP-1 receptor agonists. Now that said, if it was a patient that really needed stronger medication with respect to body weight, with respect to HbA1, I can combine it with an SGLT2 inhibitor with proven cardiovascular benefit. Now we don't have data on that but certainly that is an option. I think as with treatment with any medication for patients with type 2 diabetes, we need to individualize.

Dr Wysham: Great, thank you. Those are very important considerations and I think really helps the audience understand how they might look at placement of this medication. Stefano, our colleagues and our patients are often very concerned about hypoglycemia. Can you review the data for hypoglycemia with tirzepatide?

Dr Del Prato: I think this is a very natural concern for whatever glucose lowering agents we would like to consider. And overall, the risk of hypoglycemia that has been associated to tirzepatide is very similar to the one that has been reported with GLP-1 receptor agonists. There's only one difference if I can say, because in SURPASS-4 we monitored hypoglycemia. Now, it was overall, limited but slightly higher that that's been reported in the SURPASS trials. But remember in SURPASS-4, people were allowed to continue their oral agent they were on at the beginning of the trial and we had a significant percentage of people on sulfonylureas. So although the rate of hypoglycemia, severe hypoglycemia was lower with tirzepatide as compared with glargine overall, when we calculated the frequency rate of hypoglycemia according to the current use of sulfonylureas, it turned out that the vast majority if not almost the totality of the hypoglycemic events occur in those people using tirzepatide on top of sulfonylureas. So this is nothing surprising here, this is what we know very well. Sulfonylureas are the driving force for the risk of hypoglycemia in people with type 2 diabetes. But I think that this is important clinical information because it may set some of the recommendation that we may need to take into account when we start using and prescribing tirzepatide on people who are on sulfonylureas.

Dr Wysham: Juan, I'd like to turn to the adverse events that we're seeing in the clinical trials. Can you speak to those and specifically discuss how you might try to mitigate those side effects in your clinical practice?

Dr Frias: Absolutely. As I think was expected and what we saw in the phase 2 clinical trials, the most common adverse events were gastrointestinal in nature, so nausea, vomiting, diarrhea, constipation. As with the selective GLP-1 receptor agonist, the majority of them occurred early in the course of therapy or during the dose escalation periods, and were mild to moderate in severity and tended to dissipate over time. So very similar in nature to the GLP-1 receptor agonists and I certainly don't want to minimize it by any means so it is important to be very proactive with patients as we are with GLP-1 receptor agonists and let them know that these side effects may occur, give them dietary guidance that may help mitigate some of these side effects. Also, the dose escalation scheme that was used in the phase 3 trials really minimized or helped mitigate some of the issues with GI side effects. So that's very slowly escalating, getting to the 15 mg dose after 20 weeks of dose escalation, that also helps to reduce it. And really, there were no other unexpected side effects that we're seeing with respect to pancreatitis, cholecystitis, retinopathy, for example. Blood pressure was reduced, there was the usual increase in pulse as seen with the GLP-1 receptor agonists. So it looks very safe and has a very similar profile to the selective GLP-1 receptor agonists.

Dr Wysham: I might just add that based upon the clinical trials, we had to get patients up to their doses and many of our patients might do fine at a lower dose and not require titration or even to be allowed to back titrate which sometimes was not allowed in the clinical trials. I think we're going to be able to learn more but just as we do with GLP-1 receptor agonists, go slow and find the dose that is tolerated. Thank you for the for those comments.

I'd like to bring this session to a close by just summarizing some of the key takeaways from this program. As we've discussed, there is growing evidence and growing interest to suggest the need to treat obesity as a primary endpoint for patients with diabetes not just the HbA1c because of the importance of management not only of the hyperglycemia and complications of hyperglycemia but also the complications of obesity including cardiovascular disease, NASH and other weight related comorbidities. GLP-1/GIP receptor agonists and other newer agents which target glucose lowering as well as obesity and lipids are under investigation and some of which are very exciting should they come to fruition. With that, I'd like to ask Stefano for any of your closing comments?

Dr Del Prato: Carol, I consider myself to be very fortunate to be living in a time where we had so many opportunities for treating diabetes and to see how new opportunities are becoming available. When we have drugs that can really impact not only glucose control, but the broader range of the cardiovascular profile. I think this is something that we should really consider because this is a novel opportunity.

Dr Wysham: Thank you, and Juan?

Dr Frias: Yes, I would agree. I think these benefits beyond glycemic control are critically important. One point that I'd like to make is just how important in the clinic, simplicity of a regimen is as well. Anything we can do to simplify therapy for the patient will improve adherence and persistence.

Dr Wysham: Stefano and Juan, I really want to thank you for this great discussion. I really enjoyed it today.

Dr Frias: Likewise, thank you, Carol.

Dr Del Prato: Thank you very much, Carol.

Dr Wysham: And, I want to thank the audience for participating in this activity. Please be sure to click on and download the clinician handout to the right of the video player. This will provide supplemental content on emerging treatments for type 2 diabetes. Finally, please continue on to answer the questions that follow and complete the evaluation. Thank you very much.

This program was presented by Medscape Education Global.

This article is a CME / ABIM MOC / CE certified activity. To earn credit for this activity visit: http://www.medscape.org/viewarticle/970215