TRANCRIPT, EP 56: GLP-1s and Neuroendocrine Cancer: What Do We Know?

Jessica Thomas, LCSW, Director of Patient Education at NETRF
GLP-1 medications have transformed the treatment of diabetes and obesity… and their use has exploded. But for people living with neuroendocrine cancer, they've also raised an important question: Are GLP-1s safe if you have neuroendocrine cancer? The answer isn't a simple yes or no. Researchers have discovered that some neuroendocrine tumors express the GLP-1 receptor, the same receptor targeted by GLP-1 medications. New studies of human tumor samples suggest that GLP-1 receptor expression varies considerably by tumor type. It appears uncommon in many neuroendocrine tumors but may be more frequent in certain types, particularly duodenal and pancreatic NETs. At the same time, GLP-1s can provide significant health benefits. And for people with cancer who take them, there's another consideration: how weight loss, decreased appetite and potential muscle loss could affect nutrition, strength, and treatment. I'm Jessica Thomas, Director of Patient Education at NETRF, and you're listening to *NETWise*, the podcast designed to inform, empower and guide patients and caregivers through the world of neuroendocrine cancer. In this episode of *NETWise*, we're taking a closer look at GLP-1-based medications, including drugs used for diabetes and weight loss, and what their growing use may mean for people with neuroendocrine cancer. Could these medications affect some neuroendocrine tumors? What does the research tell us so far, and where are the important unknowns? And how should patients think about the potential benefits of these medications alongside considerations such as nutrition, weight loss, and their cancer treatment? We'll hear from endocrinologist Dr. Amr Wahba, neuroendocrine cancer specialist, Dr. Udhayvir Grewal, researcher Dr. Po Hien Ear, and oncology dietitian Meghan Laslow. Let's start with the basics: what exactly is a GLP-1? GLP-1—and another hormone you may hear about, GIP—are hormones our bodies naturally produce. Here's Dr. Wahba.

Dr. Amr Wahba, Clinical Assistant Professor of Internal Medicine and Endocrinologist at University of Iowa Health Care
GLP-1s and GIPs are essentially two types of hormones. So that's a natural substance that our own body produces. In a normal sense, it happens when someone eats, and that can be a stimulus for these hormones to be produced. And think of it as sort of messengers or a signal that your body is telling you we've got food coming, and so we need something to help regulate our insulin production, help regulate our blood sugars, sort of slow down how the food leaves the stomach for it to be processed. And so a couple of those hormones that help in those metabolic regulations are the GLP ones and the GIPs. And so, GLP-1s and GIPs are natural substances. But over the past several years, there has been a rise in what we hear as GLP-1 agonists and GIP agonists, which are basically medications that mimic those kind of hormones in our own body, to hopefully give the benefit of of these hormones, whether it comes to blood pressure regulation or weight management, etc.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
And it's important to understand that these medications aren't simply about losing weight. They can provide substantial benefits for people living with conditions including diabetes, cardiovascular disease and kidney disease. It's the importance of those benefits alongside

emerging questions specifically involving neuroendocrine tumors, that makes this conversation complicated.

Dr. Amr Wahba, Clinical Assistant Professor of Internal Medicine and Endocrinologist at University of Iowa Health Care
For the past several years, these medications have been very commonly and increasingly prescribed for a ton of medical conditions, a ton of medical benefits. They–they help people primarily with type two diabetes get better sugar control. They help people lose weight, feel–they get this sense of full stomach after a smaller-sized meal, and they help the body cope better from an insulin response. And for–for many years, this has transitioned to even better benefits for people with heart disease and kidney disease, and so there is a lot of benefits that come from these medications. But recently, there has been a question that came out from lab studies–so looking into sort of samples in a petri dish or sort of mouse models– into whether these medications can have an effect on the growth or progression of neuroendocrine cells or neuroendocrine tumors, and this is how that question came into our clinical practice. Whether there is any concern of using these particular medications in patients with neuroendocrine cancers.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
That concern centers on something called the GLP-1 receptor. A receptor can be thought of as a docking site on a cell. A hormone—or a medication mimicking that hormone—binds to the receptor and sends a signal. And researchers have known for some time that at least some neuroendocrine tumors can express GLP-1 receptors. Dr. Po Hien Ear, an Associate Professor at Emory University and Winship Cancer Institute, is an expert in neuroendocrine tumor biology and has conducted extensive research on GLP-1 receptors in human neuroendocrine tumors.

Po Hien Ear, PhD Associate Professor, Hematology & Medical Oncology | Emory University School of Medicine Winship Cancer Institute
Why they are often in the news now is because the new GLP-1 drugs. These are fantastic molecules that are very effective at helping people to control their diabetes and their obesity, and overall has improved the lives of many many people, so that's why it's really a very hot topic at the moment. So for us working in the cancer field now, GLP-1 and especially the neuroendocrine tumor field, we've been overall very curious and and all and a little bit cautious, just because the link to GLP-1 was that the the so the GLP one is a hormone that binds to a receptor, so so that then it transmits the signal in the cells. Now, the reason why we are a little bit cautious for the neuroendocrine tumor field is that some neuroendocrine tumor actually express a lot of these GLP-1 receptor, and in fact the the receptor was originally cloned from the cDNA samples of an insulinoma, which is a form of pancreatic neuroendocrine tumors.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
That led to a basic but important question: How common are these receptors across different types of neuroendocrine tumors? To investigate that, Dr. Po Hien Ear and her colleagues analyzed hundreds of human tumor samples. And, in some ways, what they found was reassuring.

Po Hien Ear, PhD, Associate Professor, Hematology & Medical Oncology | Emory University School of Medicine Winship Cancer Institute
In our field, it's been a big mystery because we we know that some of these tumor express the GLP-1 receptor, but we don't know like how often. Do–is it every tumor that will express this? Or and there are so many neuroendocrine tumor types as well, so we don't really know yet, like, which category actually expressed it. So, so it is a very important question because, as you can imagine, like the way that the drug work is that it has to bind to the receptor. So, if the tumor cells don't have the receptor, therefore it can't really actually activate the the survival signaling of the tumor cells that is downstream. So that's why we think it's important to look at this question.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
So, the presence of that receptor may be an important piece of the puzzle. If a tumor doesn't express the GLP-1 receptor, the drug would not be expected to act directly on those tumor cells through that receptor. The next question, then, is how often do neuroendocrine tumors actually have these receptors? That's what Dr. Po Hien Ear and her colleagues set out to investigate.

Po Hien Ear, PhD Associate Professor, Hematology & Medical Oncology | Emory University School of Medicine Winship Cancer Institute
In our latest study, we profile 576 tumors from patients to see, and these are actually from 13 different neuroendocrine tumor types and different neuroendocrine carcinoma types as well. So there are 13 in category in total, and there are 576 tumor in this study. And then so our pathologist, Dr. Andrew Belizi, had optimized clinical-grade assay that he uses in the clinical lab, so that it's really high quality. And then he used this method to to determine how many or which one of the 576 tumor actually expressed the receptor or not. And then so that so that we reported these data in in the last manuscript, and overall it was kind of surprising, but it was opti– it's kind of optimistic at the same time because we tested seven well 576 tumors, and only 7% of them actually has the receptor. So basically, it's telling us that we have to be careful about like these 7% But the other 93% don't have the receptor. Meaning that the patient who has the tumor, they could potentially benefit a lot from the GLP-1 drugs for controlling their diabetes and their obesity.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
That 7% overall number is encouraging… but it doesn't tell the whole story. Because GLP-1 receptor expression wasn't evenly distributed across NET types. Some were much more likely to express the receptor than others.

Po Hien Ear, PhD Associate Professor, Hematology & Medical Oncology | Emory University School of Medicine Winship Cancer Institute
We only found five types of the 13 types that we tested that actually express the receptors, and we reported them in, in our, our last study. So they are actually what came up the most often positive in four like the tumor types that has expressed the receptor often is the duodenal NET, so 45% of the duodenal NETS actually express the receptor. Afterward, I think it was the gastric NET, and it's only 17% of the gastric NETS that we tested actually score positive, and then

afterward it's the pancreatic NETS which comes out to 13% and so this is an important group because usually in terms of incident pancreatic neuroendocrine tumor covers probably 20… 30% of our patient population and, so, knowing that only 13% or out of this big population that we have to be careful is actually good news to us. We are encouraged. These are like the three– There's the other the two, other category that we found was the pheochromocytoma, which is only 9% positive, and then the lung NET is 2% positive, but all the others are negative.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
Across 576 tumors, only seven percent expressed the GLP-1 receptor. But that seven percent wasn't evenly distributed. In this study, receptor expression was found most often in duodenal NETs, followed by gastric and pancreatic NETs, with much lower percentages in pheochromocytoma and lung NETs. That begins to move the conversation away from a broad question like **"**Are GLP-1s safe for NET patients?" toward more specific questions, including: What type of neuroendocrine tumor does this patient have, and what do we know about GLP-1 receptor expression in that tumor type? But there's an important limitation here. Right now, testing a patient's tumor for the GLP-1 receptor is not a part of standard clinical care, and we don't yet have evidence telling doctors how to use such a result to make medication decisions.

Po Hien Ear, PhD Associate Professor, Hematology & Medical Oncology | Emory University School of Medicine Winship Cancer Institute
So that's why we, we think it's actually overall good news. And then we'll focus on subsets that do express the receptor to better understand their biology. Our biggest hurdle at the moment is to try to get other clinical labs to set up this assay so that clinicians can order the tests. That said, so at least we our study basically flagged these five types so that at least you know I feel like my clinician colleagues are a little bit more comfortable with like when they see other types of tumor, and then they know like oh well this is probably not a big concern or at least it's most likely it's negative for the receptor. So I think it and patients too. So if they unfortunately have like– I know these tumors are really a lot to deal with already. So thinking about GLP one expression on top of that is another layer of complexity and all that. But at least now we are beginning to have data to support and to actually just help guide or help provide these annotations so that patients can look it up. Their healthcare provider can look it up and then move forward with their decision making.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
And here's an important distinction: Finding a GLP-1 receptor on a tumor is not the same thing as proving that taking a GLP-1 medication will cause that tumor to grow. Dr. Wahba says the evidence simply isn't there yet to make that leap.

Dr. Amr Wahba, Clinical Assistant Professor of Internal Medicine and Endocrinologist at University of Iowa Health Care
The information that we have right now is very much in the research stage, but recent few studies have shown that some human cells in certain organs, like the pancreas or the small bowels, like the duodenum, can have receptors or docking sites where these medications can act on, and potentially cause these tumors to progress. We currently don't have evidence to

suggest that there is harm for using these medications in patients with neuroendocrine cancers. However, because of the biology of of those cancers expressing those docking sites, it is something that we are taking into consideration–whether the type of neuroendocrine cancer that a patient may have could potentially be affected. Do they have a genetic problem which would raise the risks of being starting or continuing those medications, and whether they are at a stage where the harms from using such a medicine may be overweighting the benefits that they get from a blood sugar control or a weight loss standpoint.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
So tumor type matters. Disease status matters. Medical history matters. And the reason the medication is being prescribed matters. Dr. Wahba says those are the kinds of factors he weighs in clinical practice.

Dr. Amr Wahba, Clinical Assistant Professor of Internal Medicine and Endocrinologist at University of Iowa Health Care
Based on the data we have right now, tumor type does make a difference. So, for example, some areas in the small bowel, like the ileum, which is the sort of the distal or the further part of the small bowels, didn't seem to express as much docking sites for these medications to act upon, as compared to people with neuroendocrine tumors or cancers in the pancreas or the duodenum, and so these patients with such tumors would be at a higher risk, and so would require closer monitoring. I think someone with a very low burden of tumors is generally at less risk than someone who's got spread tumors throughout their body, or a type that is progressively going at a faster rate than we would hope for. So these are things that I would think of when making a decision or recommendation as to continuing such medications. These medicines are used to, or have been used and still for treatment of diabetes or high blood sugar. So, one of the types of neuroendocrine cancers, namely insulinomas, which produce a lot of insulin, can lead to low blood sugars. In that case, using a GLP-1 agent may not be in the best interests of the patient because it may increase the risks of further or life-threatening low blood sugar levels, and so these would be things that I would take into consideration or discuss with my patient if they bring up that topic.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
And that's why a single headline, or even a single study, can’t answer this question for every patient.

Dr. Amr Wahba, Clinical Assistant Professor of Internal Medicine and Endocrinologist at University of Iowa Health Care
I think a big misconception is a sort of a one-size-fits-all. Medications do have side effects, and we are aware of that, and we make sure that patients are aware of that as well before we start one. But then they also have much more benefits that we know of, and so headlines are catchy, but they're–they're not the big picture–and that by itself is a misconception. I think patients should be aware that a–a discussion with their provider or physician is really the best way going forwards, as opposed to making a decision based on a single paper or news outlet that speaks about a possible connection or association between one medicine and one type of cancer.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
So far we've focused primarily on whether GLP-1 medications could interact with a tumor. But cancer patients have another consideration: The very effects that make these drugs useful for weight loss—reduced appetite, early fullness and lower calorie intake—can become more complicated when someone's body is also dealing with cancer and cancer treatment. Meghan Laslow is a registered dietitian and board-certified specialist in oncology nutrition at Cedars-Sinai Cancer. She says she's seeing more patients remain on GLP-1 medications after a cancer diagnosis.

Meghan Laszlo, MS, RD, CSO, Clinical Nutrition Coordinator | Cedars-Sinai
Initially, when I was seeing patients come in on a GLP-1 that then had a cancer diagnosis after starting it, most of them were taken off the GLP-1 right away, and that was–became the practice. And I worked mostly in gastrointestinal oncology, but what I've seen now is that a lot of folks are staying on them. That there might actually be secondary benefits to being on them during treatment, but there's a lot of variation in the dose that somebody's on and how much it's affecting their body and their eating habits, and so maybe their dose is lowered after cancer diagnosis. I'm seeing that too, but there's–there's a lot of variability. But we are seeing–I'm seeing– a lot more of it than I've ever seen. There's emerging evidence that they may help with cancer treatment outcomes, and so that's something we want to keep looking at and seeing if they are being prescribed at the same time or for recurrence risk reduction. I think we may see some of that in the future, but this is very much emerging with the GLP-1s, so I think it's something we need to better understand. Just like so many factors with GLP-1s, we need to better understand and have criteria and rubrics for using them. I think that's very much needed, especially in the nutrition side of things when it comes to patient monitoring. But we are seeing much more of them, and I'm not seeing patients being taken off them right after a cancer diagnosis.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
From a nutrition standpoint, one of the first effects is obvious: people often eat less.

Meghan Laszlo, MS, RD, CSO, Clinical Nutrition Coordinator | Cedars-Sinai
Well, there's a lot of changes that occur. Typically folks feel less hungry. They get full very quickly. They feel full for longer. Sometimes there's some acid reflux that occurs–some of those types of symptoms. Sometimes it can lead to constipation or diarrhea, fatigue. You know, it's a lot of–It can cause a lot of difficulty with eating, and it really just depends on how much someone is–is on, and you know whether they're started on a low dose and titrated up, and what their situation is. But those are the most common anticipated side effects with the GLP-1s.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
For someone taking a GLP-1 specifically to lose weight, that's part of the desired effect. But in oncology, weight loss can mean something very different—particularly when some of that lost weight is muscle.

Meghan Laszlo, MS, RD, CSO, Clinical Nutrition Coordinator | Cedars-Sinai
One of my primary roles in patient care is to prevent weight loss, and has been. And the assumption has been, if someone's losing weight, that has a cancer diagnosis, particularly if there's disease in the liver or–or it's advanced disease, and someone's considered to be catabolic–they're losing muscle–then we really try to prevent weight loss as one of our primary strategies to protect the muscle. We don't want folks losing muscle because it's associated with poor treatment outcomes, and we don't want folks losing strength and endurance as well. And so, when folks are on the GLP-1s, that's that's the concern. You know–if we know that it's going to cause weight loss, and we also know that some of that weight loss is going to be muscle loss as well, and we don't have clear thresholds for how much weight is okay, specifically for the GLP-1s. You know, as a dietitian, we have tools that we use as part of our assessment and diagnosis of malnutrition, but something like our American Academy of Nutrition and Dietetics malnutrition diagnostic tool hasn't been validated for GLP-1, so it can be tricky to say this much weight is too much weight.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
And that's an important distinction. For someone with cancer, the goal isn't simply to track pounds lost. It's also to understand what is being lost—particularly muscle—and what that could mean for treatment and recovery.

Meghan Laszlo, MS, RD, CSO, Clinical Nutrition Coordinator | Cedars-Sinai
One of my top concerns is loss of muscle, because we know that muscle loss is an independent predictor of poor treatment outcomes. If someone is losing muscle, they're going to have potentially less response to treatment. They may not be able to withstand more treatments. They're at higher risk for complications after surgery or other sensitive situations, so we want to make sure that someone is getting enough protein to protect their muscles and–and fuel their muscles, and that they're also getting enough calories so that they don't have muscle loss because of inadequate calorie intake. And then at the same time, we want to make sure that someone is exercising and doing resistance exercise as much as possible during treatment to also build and maintain muscle mass and physical strength. We usually assess weight loss based on percentages because every– everybody's different, right? And so five pounds could be a lot for somebody, and for somebody else, it's not that much. So we really look at weight loss in terms of percentages.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
So how do you know when weight loss becomes concerning? Meghan says it's less about the number of pounds and more about how much is being lost, how quickly—and what that weight loss actually consists of.

Meghan Laszlo, MS, RD, CSO, Clinical Nutrition Coordinator | Cedars-Sinai
Typically, 5% weight loss in a month is considered clinically significant in the oncology setting, and so we want to assess, you know, how much weight is being lost over what time period,

and– and base it on–on that. We're, you know, we use BMI; is just–is–is only so helpful because it doesn't consider someone's body composition, right? It doesn't take into consideration muscle mass or muscle function or fat mass, so it can be helpful, but it's kind of just part of the picture. I think it's a much better tool to use body composition, which can come in different forms. I think the most easy way that we've seen it is with bioelectrical impedance or like these Inbody machines, or other special scales that can assess for body composition. But I think there is value, and–and monitoring someone to see how much muscle they're losing versus how much fat, and to establish thresholds and goals and expectations around that as best as possible.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
There's another challenge: Early fullness, loss of appetite, fatigue and other symptoms associated with GLP-1s can also come from cancer or its treatment. So how do you know what's causing what? Meghan says that from a nutrition standpoint, the response may be similar either way.

Meghan Laszlo, MS, RD, CSO, Clinical Nutrition Coordinator | Cedars-Sinai
You'd probably just start with whatever they were on first and what their experience was like, and kind of suss it out that way. But does it matter, I think is a good question, and I think we'd still treat it the same way. Someone's having early satiety, loss of appetite, loss of interest in eating–those are very common in cancer treatment, and so we're familiar with helping to support individuals that are experiencing those side effects. But we'd still try to support them as best as possible because we still, even though you're trying to cut back calories and calorie intake from the GLP-1s, we still want to prioritize protein and we still want to prioritize diet quality as much as possible, especially when intake can be so limited, and that's the same philosophy that we follow for individuals that just have anorexia from their cancer diagnosis or from cancer treatment.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
So if a patient and their medical team decide that a GLP-1 is appropriate, nutrition needs to become a part of the plan. Meghan says that means paying particular attention to protein, hydration, and how much someone is actually able to eat.

Meghan Laszlo, MS, RD, CSO, Clinical Nutrition Coordinator | Cedars-Sinai
I think most folks do know that muscle loss is part of the weight loss with the GL with the most commonly used GLP-1s right now. There might be better ones soon that don't cause as much muscle loss, we'll see. But with– you know the–with the current prescriptions, I think it's important to know that a lot of the weight loss can be muscle loss. That individuals really need to prioritize their protein intake, and that means that's the first thing you eat off your plate is whatever the protein is. If it's tofu, if it's chicken, if it's meat, you should eat that thing first, and then eat the other foods because you still want to protect the muscle and get enough protein as possible. Knowing that the other foods are hard to eat, I think hydration is really important–an important thing to think about in advance–and just knowing that foods might need to be modified. It might be difficult to eat solid food. You might need to have smoothies and soups and liquid foods if eating is very difficult or things aren't digesting fast enough.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
GLP-1 medications can also be prescribed outside a patient's cancer team—from primary care and endocrinology to tele-health and other providers. So for someone living with neuroendocrine cancer, another important part of this conversation is simply making sure everyone involved in your care plan knows you're taking one.

Dr. Amr Wahba, Clinical Assistant Professor of Internal Medicine and Endocrinologist at University of Iowa Health Care
I think that patients asking questions in clinic is always a good thing. I think that patients should bring up that question to their primary care or endocrinologist or oncologist, whoever they are following with, because a lot of the challenge that we see right now is that these medications are so widespread that sometimes they don't need a physician to be prescribing them. You can get them at medical spas. There is insurance issues, and so it is not uncommon for me to find out that a patient has been on that medicine not through a prescription, but rather, you know, an online pharmacy or someone that is outside the healthcare team. And so I think keeping that open line of communication between the patient and their physician, letting them know that they are on this kind of treatment, whether a good assessment of the benefits that they are getting out of it versus the potential knowledge and risks that we know at the current stage, and whether there is any medical history background that would make us sort of shy away from continuing such medications. Or I'll give an example of people with a genetic mutation that leads to a syndrome or a set of tumors, in which we would typically try to avoid these medications because of the heightened risk of the potential for neuroendocrine cancers, as opposed for someone without a genetic mutation.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
And even as clinicians work through those practical questions, the medications themselves continue to evolve. Newer drugs can target more than one receptor—which means researchers are already confronting a new set of questions.

Po Hien Ear, PhD Associate Professor, Hematology & Medical Oncology | Emory University School of Medicine Winship Cancer Institute
So I think we know a lot about the GLP-1–specific-like agonist that targets the GLP-1 receptor, like semaglutide. But we know even less–Actually, we know little– about the dual agonists, such as Tirzepatide or the triple agonists, the new drugs that are coming out. So, so I think that's one area of caution: is that we we need to those those drugs needs to study to be studied more because we don't even know the expression of those other receptors in in the tumor types.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
It's an intriguing possibility, but also a reminder of just how much remains to be learned. Dr. Wahba says the next step is larger studies that can begin answering some of these questions in patients.

Dr. Amr Wahba, Clinical Assistant Professor of Internal Medicine and Endocrinologist at University of Iowa Health Care
Neuroendocrine cancers are relatively rare, and so the–the studies need to include more numbers of patients to– for us to really have a good, generalizable results to everyone. I very much appreciate our patients who come to clinic and express their interest in being part of the research study that may just include–just sort of following them over time and seeing if there are any changes with their health. But I think yes– we do need larger studies, And hopefully, these studies can give us information about the different types of the medications, the GLP-1s, the combined GLP, GIP agents, whether they come with any true risk to the patients, whether the dosing matters, and whether there are certain particular types of tumors that would be affected by the use of those agents. That is what I hope the research is going to uncover in the upcoming years.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
But patients are making decisions about these medications now. And while researchers work toward clearer answers, clinicians still need to help patients decide what to do with the information we have today. As we were finishing this episode, a group of neuroendocrine cancer specialists published a new expert consensus statement addressing exactly that question: how to approach the use of GLP-1s and other incretin-based medications in people with neuroendocrine neoplasms. Incretin-based medications are a broader group of drugs that act on hormones involved in blood sugar regulation, appetite, and digestion, and include GLP-1 medications as well as newer drugs that target more than one hormone pathway. We'll link to the full expert consensus statement on the NETRF webpage for this episode, along with the transcript, for anyone who would like to learn more or use it as a resource when talking with their care team. We spoke with one of its lead authors, Dr. Udhayvir Grewal, a GI and neuroendocrine medical oncologist at Winship Cancer Institute of Emory University.

Udhayvir Singh Grewal, MD, GI/Neuroendocrine Oncologist, Winship Cancer Institute at Emory University
A lot of our patients have increasingly turned to us for advice: whether these agents are safe, what could they do to determine the risk associated with these agents—and a lot of us don't know the answers. I think there's a lot of research that's ongoing, but as of today, the answers aren't quite there. We do have some data to guide us, but largely robust prospective clinical data are lacking… So we wanted to come together as a group of neuroendocrine specialists and put together a piece of advice for our colleagues, for our patients, for our caregivers…and we wanted to largely just share what's out there in terms of data, how we are approaching this in our own practices, and what kind of data we look forward to having in terms of being able to give more definitive advice to our patients and caregivers.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
So the consensus statement doesn't offer a simple yes-or-no answer about whether someone with neuroendocrine cancer should use a GLP-1 medication. Instead, it offers a framework for thinking through that decision based on the individual patient.

Udhayvir Singh Grewal, MD, GI/Neuroendocrine Oncologist, Winship Cancer Institute at Emory University
The two important questions to ask… are: What is the reason for you to be on a GLP-1 receptor agonist? Someone might be on it for diabetes. Someone might be on it for obesity. Multiple reasons, right? So it's really important to understand what the reason is. Once we have determined that there is a strong reason for someone to be on that drug, the other important question to ask is: Is there a hereditary syndrome at hand that we're looking at? If there is a strong indication, and there is no hereditary cancer risk, then it is important to consider: how is the neuroendocrine tumor doing? Are we dealing with a very large burden of disease? Are we dealing with progressive disease? Are we dealing with disease that has been associated with a lot of symptoms? I think if there's no hereditary cancer syndrome at play, and there's a strong indication for patients to be on these agents, and we're not dealing with worsening metastatic disease or progressive disease, and we're not dealing with a lot of symptom burden from your neuroendocrine tumor, neuroendocrine cancer, I think it's fair game to be on these agents, but we just need to make sure we check all of our boxes before we do that.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
And if a patient and their care team decide that a GLP-1 medication is appropriate, Dr. Grewal says careful dosing and monitoring become important parts of the plan.

Udhayvir Singh Grewal, MD, GI/Neuroendocrine Oncologist, Winship Cancer Institute at Emory University
Another piece of advice that I've given to my patients is, if we ultimately decide to start this—a GLP-1 receptor agonist or GIP receptor agonist… we can always keep a close eye. We usually do scans at three months or so, or four months or so, depending upon the biology of the disease. But we can always stick to a more frequent cadence of scans. We could start with like every two months or so and keep a close clinical follow-up on the symptoms and how patients are doing overall. So we can always stop the drug if there is concern that the disease is progressing sort of more quickly than expected. And the other thing that I always highlight is it's always beneficial to start with the lowest possible dose, and not to escalate the dose for weight loss alone. You know, higher doses will lead to greater weight loss, but also greater toxicity. And we don't know if that will also lead to greater oncologic harm, but will definitely worsen some of the adverse effects associated with these agents, like GI toxicities, etc.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
And because these medications may be prescribed by someone outside your cancer care team, Dr. Grewal emphasized one more point: make sure your oncologist knows you're taking a GLP-1—or even that you're considering one.

Udhayvir Singh Grewal, MD, GI/Neuroendocrine Oncologist, Winship Cancer Institute at Emory University
I think this is true for any medication that my patient is on. I want to know about it because the patient may not think that that's important information for me, but there are more chances that

you know that is relevant to your overall care. I think this is a rule of thumb. Don't hide anything from your doctors, and definitely not your oncologist– coming from an oncologist.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
So where does all of this leave us? Dr. Grewal says the evidence is still evolving, but that doesn't mean these medications should be viewed as either inherently dangerous—or completely without risk.

Udhayvir Singh Grewal, MD, GI/Neuroendocrine Oncologist, Winship Cancer Institute at Emory University
Ultimately, I would say this is an ongoing effort, and this question sort of remains open. The benefit of these agents is undeniable, but we should not present these agents as risk neutral to our patients. There is potential risk of oncologic harm. It's best for you to discuss this with your oncologist, with your physician who's prescribing the GLP-1 receptor agonist or another incretin mimetic… ask all the questions, check all the boxes, make sure you've done everything within your reach or your oncologist's reach to make sure that we're making a well-informed decision before you get onto these agents and once you're on it, just make sure we keep a close eye on the disease, on how you're doing overall, and then start low and go slow.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
And maybe that's the most useful place to leave this conversation. For someone living with neuroendocrine cancer, the question isn't simply, “Are GLP-1s good or bad?” It's more personal than that. What kind of Neuroendocrine cancer do you have? What is your disease status? Why are you taking the medication, and what benefit are you getting from it? How is it affecting your appetite, weight, strength and muscle? And does your oncologist—and the rest of your healthcare team—know you're taking it? The science around GLP-1s and neuroendocrine cancer is still evolving. But we know considerably more than we did just a few years ago, and researchers are actively working to answer the questions that remain. So rather than starting, stopping or changing a GLP-1 medication based on fear or a headline, bring these questions to the healthcare professionals who understand both your cancer and the reason you're taking the medication. Thank you for listening to *NETWise*. I'm Jessica Thomas, Director of Patient Education at NETRF, and you're listening to *NETWise*, the podcast designed to inform, empower, and guide patients and caregivers through the world of neuroendocrine cancer. This episode was brought to you in part by the generous support of Lantheus, Novartis, Boehringer Ingelheim, Exelixis, and ITM. Special thanks to everyone we interviewed for this episode. For more information, visit our website at NETRF.org. You can find a whole library of *NETWise* episodes on different topics at NETRF.org/podcast, where you'll also find infographics and videos that expand on this material. And if you would like to join NETRF in our mission to fund research for neuroendocrine cancer or help support educational programs like this *NETWise* podcast, please go to NETRF.org/donate. If you have a story to tell about your own neuroendocrine cancer journey, please email us and let us know: podcast@NETRF.org. *NETWise* is a production of NETRF. We are committed to improving the lives of patients, families, and caregivers affected by neuroendocrine cancer. We fund research to discover cures

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