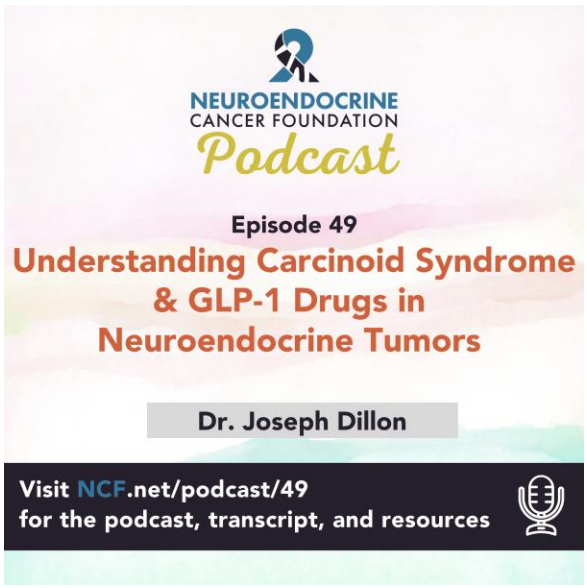

EPISODE 49: Understanding Carcinoid Syndrome & GLP-1 Drugs in Neuroendocrine Tumors with Dr. Joseph Dillon

Lisa Yen 00:00

Welcome to the Neuroendocrine Cancer Foundation podcast. I'm your host Lisa Yen. I'm the Director of Programs & Outreach, as well as a caregiver and advocate for my husband who is living with neuroendocrine cancer. In each podcast episode, we talk to an expert who answers your top 10 questions. This podcast is for educational purposes only and does not constitute medical advice. Please discuss your questions and concerns with your physician.

Lisa Yen 00:30

Welcome to the Neuroendocrine Cancer Foundation Podcast. I'm really pleased to introduce our guest for today, Dr Joseph Dillon. Dr Dillon is a Professor of Medicine in the Division of Endocrinology at the University of Iowa Hospitals and Clinic, and he directs the University of Iowa Neuroendocrine Multidisciplinary Tumor Clinic. This was the first and only US NET clinic to be recognized as the Center of Excellence by the European Neuroendocrine Tumor Society. He is also the director of the PheoPara Alliance Center of Excellence at the University of Iowa, and his clinical practice is entirely focused on the care of people with neuroendocrine tumors, both with carcinoid type or neuroendocrine and paraganglioma. He has participated in clinical trials and publications related to the diagnostic and the therapeutic nuclear agents and drug therapies in this population.

Prior to focusing on neuroendocrine tumors, he has made important discoveries in the field of GLP-1 which are now becoming of importance to NET patients taking these popular weight loss drugs, and I know we'll get into that a little bit.

So, we invited Dr Dillon to join us today to discuss carcinoid syndrome, a very common and hot topic in our community. And we will also take the opportunity to hear about his work on the GLP-1 drugs and the recent discoveries and how it might apply to NET patients. So, one fun fact about Dr Dillon is that he's been diligently

working to master the challenging art of playing classical guitar for about 50 years. Dr Dillon, we're really excited to welcome you today and thank you for joining us. And if you could also share a little bit about how you got into this field.

Dr. Joseph Dillon 02:13
Thanks, Lisa. It's an honor and privilege, and it's fun to be with you today. How I got into the field of taking care of people with neuroendocrine tumors way back in my time looking at GLP. GLP is a hormone from the gut, and it acts through particular receptors in the body, and so I've always been interested in gut hormones. And one of the main gut hormones of the gut is one of the biggest endocrine or hormonal-producing organs in the body, and it produces a lot of serotonin, for example. And people with neuroendocrine tumors frequently make a lot of extra hormones such as serotonin.
And then I was lucky enough, about 15 years ago, to be able to have as my mentor one of the sort of godfathers of neuroendocrine tumor in the United States, and that was Dr Tom O'Dorisio. So, for a long time, I was just able to sit as an apprentice at God's table and learn all about neuroendocrine tumors from Dr. Tom O'Dorisio. And between one thing and another, here I am today.

Lisa Yen 03:20
Yeah. May he rest in peace. He really has built and left a legacy.

Dr. Joseph Dillon 03:57
Yep.

Lisa Yen 03:25
What a table that must have been with you, Dr. O'Dorisio, Dr. Howe. I mean, amazing minds at the table talking about neuroendocrine tumors.

Dr. Joseph Dillon
Right.

Lisa Yen 03:35
Well, we're really grateful that you got into this field, that you have an interest and this whole topic, things that affect the gut. I mean, that speaks directly to our community. And actually, it relates to the topic that we're gonna talk about today, carcinoid syndrome. So if you're ready, we'll just get right into it.

Dr. Joseph Dillon
Yep.

Lisa Yen 03:52
So, the first question is a really just a basic foundational one. What is carcinoid syndrome?

Dr. Joseph Dillon 03:57

An important basic, foundational question. So, for the physician's side, the caregiver side, a **syndrome** is a collection of symptoms or physical features that usually relate to some specific disorder. So, our audience will have heard of many syndromes. There's Down syndrome, irritable bowel syndrome, carpal tunnel syndrome. In Down syndrome, it was a set of physical features. This was described in the mid 19th century, so they didn't know any of the blood work or work or the genetics. They just had a person with particular physical features. Irritable Bowel Syndrome is a particular set of symptoms. You know, we've ruled out Crohn's disease, and we've ruled out ten other things, and it's called irritable bowel syndrome. Carpal tunnel syndrome—there's no blood test for carpal tunnel syndrome—it's a pinching of a particular nerve in the hand, and it gives rise to a particular type of tingling and numbness in a particular place.

So, a syndrome, then, is just symptoms and are physical signs, and it's usually associated with a known disease process. So, to take that to carcinoid syndrome, then, **carcinoid syndrome is a group of symptoms and sometimes physical features that are related to neuroendocrine tumors**. Which of course, when carcinoid syndrome was described, neuroendocrine tumors were called carcinoid tumors. So, the carcinoid syndrome is the symptoms that are associated with a particular type of tumor. And now we know that the tumor causes these symptoms by virtue of its production of hormones and chemicals that it produces into the body that are actually the things that cause the characteristic symptoms of carcinoid syndrome.

Lisa Yen 05:53
Yeah, that's really helpful, breaking down the words and what they mean. And thank you for explaining in such a clear, easy to understand way.

Dr. Joseph Dillon 06:01
Yeah, and I think we'll talk about it a little more as time goes on. Carcinoid syndrome is not a particular blood test positive or negative. Carcinoid syndrome is a particular set of symptoms that are associated with a tumor. There may or may not be a blood test.

And I should point out that carcinoid syndrome is just the most frequent of the syndromes, the group of symptoms that are associated with neuroendocrine tumors. To some extent, the type of syndrome a person has, the type of symptoms that they develop are dependent on where that tumor starts. The majority of neuroendocrine tumors start in the small bowel, and they produce the classical carcinoid syndrome. Whereas neuroendocrine tumors that start in the pancreas, they can rarely produce the classic carcinoid syndrome. They can produce many other hormonal syndromes, the insulinoma syndrome, the ectopic ACTH Cushing's Syndrome, the glucagonoma syndrome. And tumors in the lungs can produce carcinoid syndrome, but they can also produce Cushing's Syndrome. So, carcinoid syndrome is just the most frequent set of symptoms associated with various neuroendocrine tumors.

Lisa Yen 07:17
Thank you for clarifying. So that was actually my next question. So, if carcinoid syndrome is a set of symptoms associated with neuroendocrine tumors, who's affected by it? Do all people with neuroendocrine tumors experience carcinoid syndrome?

Dr. Joseph Dillon 07:30
Great question. The quick answer is that a relative minority of people with neuroendocrine tumors have any hormonally-mediated syndrome. So, who is affected by carcinoid syndrome? Well, people who have neuroendocrine tumors. That's part of the definition a group of symptoms that are associated with neuroendocrine tumors. So, you'd have to have neuroendocrine tumor first of all. But it's most frequently the people with the small bowel tumors that arise in the small bowel, also called the ileum, sometimes the jejunum. But small bowel neuroendocrine tumors, the small intestine neuroendocrine tumors. And a lesser proportion of people with lung neuroendocrine tumors or pancreas neuroendocrine tumors would have some of the classical symptoms that we'll talk about that constitute carcinoid syndrome.

As I mentioned, it is a minority of people, so **about 20% of people at the time of diagnosis** have carcinoid syndrome. Less than 10% of people with lung neuroendocrine tumors, or less than 5% of people with pancreas neuroendocrine tumors have carcinoid syndrome. As I mentioned, the people with pancreas or lung can have other hormonal syndromes, but it's still a small minority. Probably less than 20% have any type of syndrome whatsoever.

Now, as time goes on and as tumors grow, that number of people who are afflicted with the symptoms of carcinoid syndrome can grow as well. There was a very nice study by Dr Halperin when he was at MD Anderson, looking at the percentage of people who had carcinoid syndrome over their lifetime. And basically, although about 20% of people had syndrome at the start of their diagnosis, **50 to 60% of people develop carcinoid syndrome if they had small bowel neuroendocrine tumor, develop carcinoid syndrome over time**. So, it really does vary with time.

Lisa Yen 09:28
Okay, so it can change with time. So, you said, roughly 20% of those with small bowel have carcinoid syndrome at the time of diagnosis. So even if someone doesn't have it at the time of diagnosis, they may develop it with time?

Dr. Joseph Dillon 09:41
Yes, and that's a very important part of following people over time, because as a physician and sort of on the caregiver side, I'm looking to hear from people whether they're developing symptoms related to their tumor, such as the symptoms of carcinoid syndrome, diarrhea and flushing, particularly. Perhaps we'll have a question about what specific symptoms I'm talking about, but most people, diarrhea and flushing. But I am looking to hear whether those are debulking over time because that tells me something about what's going on with the tumor. We have only a few things to figure out what's going on with the tumor. We have scans. We have blood tests for tumor markers, and we have what a person feels themselves. And the easiest thing to figure out is what a person feels themselves.

Lisa Yen 10:32
So, what exactly are you looking for in terms of symptoms or testing? How do you know someone has carcinoid syndrome?

Dr. Joseph Dillon 10:39
The classical symptoms of carcinoid syndrome are **diarrhea and flushing**. So, in about **80%** of people who have carcinoid syndrome, they have one or both of those symptoms. Other symptoms can be components of the carcinoid syndrome. Some people get palpitations, either very rapid or irregular heartbeat. They can get wheezing, almost an attack that feels almost like an asthma attack. But I think it's important to understand that when physicians and scientists and publications talk about the symptoms of carcinoid syndrome as diarrhea and flushing. Diarrhea and flushing are relatively easy to quantify: number of times a person goes to the bathroom. There are a lot more subtle things that people notice that are probably being driven by hormones and chemicals, and therefore carcinoid syndrome. But you can't easily lump them into just diarrhea and flushing. For example, people may notice a lot of abdominal gurgling and noisy bowel. And there are a number of reasons for noisy bowel, but that may be something that's related to one of the hormones called **serotonin**, which causes the bowel to contract regularly. It may not give rise to diarrhea. It may just only give rise to gas and gurgling and pain, but that may be a component of carcinoid syndrome. And I think there are other subtle feelings that individuals have that may well be part of hormonally driven symptoms associated with carcinoid tumors, which I classify as part of carcinoid syndrome. But what you will see, in terms of carcinoid syndrome written down, is mainly flushing and diarrhea.

Lisa Yen 12:31
I'm glad you mentioned that, because someone could be listening to this and never have had anyone else name that, "Oh, that gurgling sensation. That's me. I've been experiencing that, but nobody has ever asked me about that, or I didn't have words for it." So maybe that could speak to someone in the audience.

Dr. Joseph Dillon 12:46
And I urge people to try and clarify some of those feelings for their physicians. Again, physicians and caregivers may just focus on the top line, most obvious things. But when it comes to treating people or carcinoid syndrome, some of those symptoms can be very uncomfortable. Though they don't rise to the level of diarrhea x times day, and it would be unfortunate not to try and help people with uncomfortable symptoms, just because they don't fall into the big buckets of diarrhea, flushing.

Lisa Yen 13:24
Yeah, they can be subtle. Thanks for naming that and just widening the language around what could be in that classification of carcinoid syndrome, so maybe people can have more awareness and body awareness as well. So, what test would you use for carcinoid syndrome?

Dr. Joseph Dillon 13:40
Going back to the **definition of carcinoid syndrome is specific group of symptoms associated with a neuroendocrine tumor**. And before we classify people as having carcinoid syndrome, we've diagnosed a neuroendocrine tumor. And you've had other great podcasts about diagnosis of neuroendocrine tumor, so I won't go into CT scans and PET scans and MRI scans and biopsy. So let us say that there is a diagnosis of a neuroendocrine tumor and a person is having the symptoms.

Now, in my book, that person already has carcinoid syndrome. They are feeling specific symptoms. And I think the important caveat to just looking at symptoms in a person with neuroendocrine tumor is *specific symptoms for which we do not have another good reason in a person with neuroendocrine tumor.* So, the question as to, what are the tests are there for carcinoid syndrome? Well, the carcinoid syndrome is caused by chemicals that are produced by the tumor that cause flushing and diarrhea. I think it's important for folks to understand that while we have a lot of sophisticated technology that seeks to diagnose people with neuroendocrine tumor and PET scans and other scans and and there are a lot of blood tests, and we do have some knowledge about these hormones and chemicals, our knowledge is not complete.

So probably the single most important chemical in terms of causation of diarrhea is **serotonin**. And so, a blood test for serotonin, or a blood test for the chemical that serotonin gets broken down into, which is a chemical called 5-HIAA. Or a 24-hour urine test for that same chemical, 5-HIAA. Those tests, **blood serotonin, blood or plasma 5-HIAA or urine 5-HIAA** have been performed to look over the characteristic hormone that causes carcinoid syndrome.

However, it's important to understand that serotonin probably only causes **50%** of the diarrhea that's associated with neuroendocrine tumors. Serotonin causes even much less component of the flushing that's caused by carcinoid syndrome. So, there are things that are unknown still and reasons to continue research in terms of what causes the other 50% of diarrhea with carcinoid syndrome? What causes the flushing in carcinoid syndrome? Those things are as yet poorly understood. However, serotonin and its breakdown product, 5-HIAA are the best we have in terms of the carcinoid syndrome, because that's the most frequently produced chemical. But there are people with carcinoid syndrome who do not have elevated serotonin. There are people with elevated serotonin who do not have carcinoid syndrome. So again, **carcinoid syndrome is a set of symptoms that we don't have other causes for in a person who has a neuroendocrine tumor**. The tests, as in blood tests, they're helpful for certain reasons that we can go into. But I wouldn't say that a person who has normal serotonin and who has flushing and diarrhea, they don't have the carcinoid syndrome. No, that is not correct, because there are other things that cause some of these symptoms.

Lisa Yen 17:05
So, you could have normal serotonin 5-HIAA and still have carcinoid syndrome.

Dr. Joseph Dillon 17:11
Yes, you can have this, and it's complicated. I certainly wish we understood more about the actual molecules that cause symptoms, because there are probably more than 20 different hormones and chemical substances that have been isolated in research labs that have been isolated from neuroendocrine tumors. The focus has always been on serotonin because it's been worked on since the 1950s and was realized back in the 1950s that, yes, this serotonin can cause diarrhea. But there really is a relatively poor understanding of other substances that can cause some of the symptoms of carcinoid syndrome.

Lisa Yen 17:56
Wow. It is complicated, and if serotonin only causes about 50% of the carcinoid syndrome, then how do you know if someone has carcinoid syndrome for sure?

Dr. Joseph Dillon 18:07
It can be complicated, because, again, the principal symptoms of carcinoid syndrome—diarrhea, flushing—both have multiple other potential causes. So loose stools, well, it could be irritable bowel syndrome. It could be decreased pancreas function. It could be decreased gallbladder function, celiac disease, Crohn's disease, drug-induced diarrhea. And indeed, flushing, there are multiple drugs that can cause flushing: menopause, rosacea, multiple things can cause either of these things. So, I spend a lot of time, at least initially, to clarify some aspects of the symptoms to really understand whether this is carcinoid syndrome that I'm dealing with, or whether it's another cause of these symptoms for which the treatment is entirely different.

For example, I told you that 20% of people have carcinoid syndrome at the time of diagnosis, meaning that 80% of people don't have carcinoid syndrome at the time of diagnosis. They get diagnosed because they happen to have a CT scan for something else, or they get diagnosed because they have a bowel obstruction.

Now, those people who do not have diarrhea or flushing before diagnosis, if they then have a surgical procedure to remove the blockage and remove the carcinoid tumor, and then have diarrhea after the surgery, that is not carcinoid syndrome. The surgeon has already taken out, you know, 60, 70, 80, 90, 100% of the tumor, and now they have diarrhea. That is not carcinoid syndrome. That is a post-operative complication. That is either **short bowel** or the surgeon may have also taken out their gallbladder, which is common. Up to 10% of people having a gallbladder removed for any cause can get diarrhea. Or we may have them on drugs that cause loose stools, such as the monthly agents, lanreotide and sandostatin. Or after a surgical procedure, anybody can get a condition called **bacterial overgrowth**.

So, all of these conditions occurring after surgery, not one of them was carcinoid syndrome. And it's important not to treat them as such, because we're both aware of people and situations where a person has symptoms such as diarrhea that's poorly controlled after a diagnosis of carcinoid cancer, and they get treated with PRRT, for example. Or they get treated with some additional therapy because it was assumed that they had uncontrolled carcinoid syndrome. They don't have uncontrolled carcinoid syndrome. They happen to have a complication of their lanreotide. Or they happen to have one of these other issues. So it's important that the care provider and the person who has these symptoms clarify what is the cause of these symptoms and not call it carcinoid syndrome, if it's short bowel syndrome or **bile acid induced diarrhea** or **low pancreas level [exocrine pancreatic insufficiency or EPI**], because it that leads you down to treatment of carcinoid tumor that is not needed at that time.

Lisa Yen 21:19
Yeah, so looking at the whole picture and clarifying and going through all the other possible causes. So how would carcinoid syndrome then be distinguished from the other possible causes of the symptoms?

Dr. Joseph Dillon 21:31
I think it's very individual. The symptoms have to be thought about. So, a person who comes and tells me that for a year before their diagnosis of neuroendocrine tumor, they were noticing more frequent diarrhea, and they were flushing. And the particular flushing was the characteristic flushing of carcinoid tumor, rather than, say, the

characteristic flushing of menopause, which can be commonly difficult to tease out. So, if a person has come to me with those two characteristic features occurring together, that's much more likely to be carcinoid syndrome. If I see such, as my example, with the post-operative onset of diarrhea, if I see a definite other cause for them, I'm going to treat that definite other cause. So, there's a treatment for removal of gallbladder induced diarrhea. There's a treatment for low pancreas function diarrhea. There are treatments for bowel resection induced diarrhea, and there's a treatment for bacterial overgrowth. So, if a person has bacterial overgrowth, and I am treating them with more and more and more octreotide, or I'm sending them to PRRT, that's a failure on my part to recognize what the true nature of the symptoms were. So, I think it's important to assess the history and be as sure as possible that they're not other clear causes of diarrhea or flushing and even treat some of those before making a big decision on some of the big therapy changes in relationship to neuroendocrine tumor.

Another example would be a person is diagnosed with neuroendocrine tumor has a surgical procedure which looks to have cleared everything out. There's nothing left on the dotatate PET scan, their tumor markers are back to normal, that person may well have remaining carcinoid tumor that's just too small to see on the PET scan, etc, etc. So, it's possible that they have carcinoid syndrome. But if they have symptoms in that situation, it's somewhat more likely that the symptoms are related to something else, and that one should not be drawn into overtreatment of the neuroendocrine tumor. We have to be very careful in putting these treatments out, such as PRRT, that you can only have a certain number of times in your life. You don't want to be treating a symptom that is not neuroendocrine tumor related with your heavy guns for neuroendocrine tumor.

Lisa Yen 24:00
I'm glad you brought up that situation, because I was going to ask, as I'm sure you've been asked by patients before or other providers, "Can someone have no evidence of disease on any scan, but have carcinoid syndrome?" I know you started defining carcinoid syndrome as someone who has a set of symptoms with those diagnosed with neuroendocrine tumors. But I guess there's two situations. One, what if they were never diagnosed and can't find evidence of tumors? Can they have carcinoid syndrome? And number two, the one that you just mentioned, if they had a diagnosis and the tumors were resected?

Dr. Joseph Dillon 24:32
Thank you, Lisa for bringing that up, because that issue of never been diagnosed with carcinoid syndrome and you have the symptoms that's I think that's super important. And many in your audience have the same story of, "I was going to the doctor for, you know, five years with diarrhea and then flushing, and they did CT scans, and they did an endoscopy, and nothing was found, and nobody said anything about this until I was diagnosed." So, let's just take a minute on the person who does not have a diagnosis of neuroendocrine tumor, but has the symptoms. So again, the symptoms are mainly diarrhea, flushing. For some people, palpitations. For some people, wheeziness. Those are some of the cardinal symptoms of early carcinoid syndrome and the unfortunate thing is that all of them are what I would call **non-specific**. Again, multiple causes of diarrhea, multiple causes of flushing, multiple causes of wheezing, etc. So, the added complexity in individuals with those symptoms and no diagnosis is that there are other things that can cause diarrhea or can cause flushing. There are some conditions which can cause both and that look exactly like a carcinoid syndrome. And one of those unusual conditions is a condition called **mast cell disorder**, where some of the white blood cells, which contain serotonin, start producing excessive serotonin and histamine.

So, I think the important aspect of people with symptoms and not a diagnosis of neuroendocrine tumor, and in trying to educate colleagues and primary care providers about neuroendocrine tumor, it is to get people to just ask the question, "Could this be a neuroendocrine tumor?" Okay, I've got a patient with diarrhea. I know there are 15 other causes of diarrhea, but could this be a neuroendocrine tumor? Because I've ruled out 13 of those other causes with various tests.

And in a person who is symptomatic with carcinoid syndrome, most often a carcinoid tumor that is still localized within the bowel—if we just talk about carcinoid tumor starting in the bowel, most often, the carcinoid tumor that is fully localized in the bowel will not be associated with carcinoid syndrome. Because the blood that leaves the bowel tumor, which contains serotonin, goes directly into the liver where the serotonin gets degraded. So, it never goes through the heart. It never gets out into the bloodstream in general. It goes straight to the liver and gets degraded. So, people who have carcinoid syndrome more often are people who already have tumor in their liver, and once the tumor gets in the liver, then there's much more production of serotonin and other chemicals that come straight out into the body and cause the symptoms.

So, I think in terms of symptoms prior to diagnosis, if primary care doctors would ask themselves, "Could this be carcinoid tumor?" They could, beyond doing endoscopies, which generally will not find carcinoid tumor with the majority of people with carcinoid tumor, at least a CT scan that has, on the clinical information, "**rule out carcinoid tumor or neuroendocrine tumor**" so that the radiologists then do the appropriate imaging, at least to the level of the CT scan. Not everybody can get a dotatate PET scan up front, but at least an appropriately done CT scan, where the question is raised on the clinical information as to whether this could be a neuroendocrine tumor.

Lisa Yen 28:19
Yeah. I think the concern is, "Well, what if I've already had a CT, MRI, dotatate colonoscopy, and could there be a hidden tumor somewhere?"

Dr. Joseph Dillon 28:30
So, I think another thing that I learn more and more as I go on and on is that any test that we do just makes it a little more or a little less likely that a person has a disease, rather than telling us that a person has a disease or doesn't have a disease. By which I mean, if you do a CT scan in a person who has all of the classical symptoms of neuroendocrine tumor, and the CT scan of the abdomen and pelvis and say the chest and abdomen and pelvis does not show any tumor. It makes it less likely that that is a neuroendocrine tumor. It certainly doesn't rule out a neuroendocrine tumor.

If you can get your insurance to cover perhaps the best, most sensitive test for a neuroendocrine tumor, at least a neuroendocrine tumor in the bowel, the dotatate PET scan. A **dotatate PET** scan will show **90 to 95%** perhaps of the neuroendocrine tumors that start in the small bowel, a somewhat lesser percentage of tumors that start in the pancreas, and a somewhat lesser percentage of tumors that start in the lung. But focusing just on the small bowel, for a while, there still are **5% or more of people whose tumor may not light up or be seen on a dotatate PET scan**, and that may be because they don't have the binding sites or the radioactive substance,

which is essentially radioactive octreotide, or an equivalent of radioactive octreotide. But some people don't have binding sites, don't have receptors for octreotide or somatostatin. So, if a person doesn't have those binding sites, that tumor will not show up on a PET scan. If a person has very small tumors, it won't show up on any scans. So most frequently, when people have tumors in the liver. Those tumors, certainly, once they're diagnosed, they're more than one centimeter. Some of them are, you know, two centimeters. One inch, two inches or bigger. So oftentimes they're not very subtle. But sometimes they are half a centimeter, so a couple of tenths of an inch, and just won't be seen on a PET scan.

So, it is possible to have carcinoid syndrome, but not to have visible carcinoid tumor, because there are multiple very small tumors. I think that's incredibly rare, but I've certainly had people who have had tumor that's not visible on scans, even a PET scan, but their serotonin is elevated. So, where's their serotonin coming from? Well, it turns out that it's coming from the multiple small, half centimeter or less peritoneal tumors that they may have developed. By **peritoneal**, I mean studded on the inside of their abdominal wall. Or even very small tumors in the liver, which are producing hormones and chemicals causing symptoms and yet not visible on scans.

Now, I have many patients like that. I have many patients who have come to me and I've inherited from Dr. O'Dorisio over the years who have symptoms exactly like carcinoid syndrome, but our scans do not show those tumors. Some of them have elevated serotonin. Some of them don't. And in those people, I continue to follow them, because one thing I do know is that if they have a tumor, it will grow and become more evident. So, it's important to go back over any new symptoms. It's important to try and tease out, apart from carcinoid syndrome, what other syndromes can there be? Again, many physicians get tunnel vision that excludes carcinoid syndrome. But it is possible for a person to get tunnel vision that excludes multiple other causes of the same set of symptoms.

So, I think it is important, each time you visit your physician, to really consider whether we're clear on the diagnosis and these specific individuals who have a lot of symptoms, but we don't have a unifying diagnosis yet. It's important to have a broad view of what can be going on here, including carcinoid tumor, but also including mast cell disorder, neurological disorders, autonomic disorders. It can be quite complicated in those people.

Lisa Yen 32:54
To really have this thoughtful discussion, because it's not a slam dunk just because someone has flushing and diarrhea, even with the diagnosis of neuroendocrine tumors, that it's for sure carcinoid syndrome. So, making sure that other things aren't missed.

Dr. Joseph Dillon
Yes.

Lisa Yen 33:09
So, for those who have carcinoid syndrome, you know they have carcinoid syndrome, what additional tests should they have?

Dr. Joseph Dillon 33:16

So, this would be, there's carcinoid syndrome, there's a carcinoid tumor, and the major focus will be on the growth of the tumor and scans that are done for that. And I'm not going to go into that. With carcinoid syndrome, I mentioned already the difficulty in attributing some of the symptoms to particular chemicals, that serotonin is not the whole answer to the cause of diarrhea, and certainly not the answer to the cause of flushing. However, it's thought to be a major player in the development of heart valve disease associated with carcinoid syndrome. So, people who are dealing with neuroendocrine tumor and they have carcinoid syndrome, they are at a higher risk of developing heart valve abnormalities, particularly tricuspid valve abnormalities. So having an **echocardiogram**, a baseline echocardiogram. In people who truly have the syndrome, I may end up repeating the echocardiogram on an annual basis. Certainly, in people who have high serotonin levels, I repeat an echocardiogram on an annual basis. Along with some other physicians, we monitor the level of a chemical from the heart called BNP. **BNP** is a chemical that, as a non-cardiologist, what it tells me is about heart efficiency. And if the heart becomes inefficient because of hardening of certain heart valves related to carcinoid syndrome, then the BNP level will go up, and then people really do need an echocardiogram to clarify what's going on there. That would be the additional tests that may not be considered.

I guess other tests that should also be considered really relate to just how bad that diarrhea is, because things are going through so quickly that it's hard to absorb much of the goodness. So that vitamin deficiencies: **vitamin B 12 deficiency, vitamin D deficiencies, niacin deficiency, and other vitamin deficiency in carcinoid syndrome**. So, I think it's important to consider the nutritional deficiency aspects that relate to persistent diarrhea. If a person has a very high serotonin level, that can give a deficiency of a vitamin called **niacin**, and that can cause an itchy skin rash on sun exposed areas, and it can give you a fuzzy brain, and it can make you feel poorly in other ways. So again, a person with carcinoid syndrome, nutritional status needs to be considered more thoroughly than usual.

Lisa Yen 35:52
I'm glad you mentioned carcinoid heart disease, and for our listeners, I'm going to refer you to the podcast episode we recorded with Dr Jerome Zacks covering carcinoid heart disease, which is really important topic and often missed. I'm also glad you mentioned the nutritional deficiencies. Again, really important to check those vitamin B12, niacin and vitamin D levels.

I think that these are really important topics to think about. What else could be causing the symptoms? What else should be looked at. Let's also look at, why should carcinoid syndrome be treated? I mean, other than being uncomfortable, but what are possible issues if it's not treated?

Dr. Joseph Dillon 36:28
Some papers from colleagues at MD Anderson, I recall they put out a paper just looking at how having carcinoid syndrome affects your wellbeing, and it negatively affects your wellbeing. People are more depressed, more socially isolated. They feel worse with carcinoid syndrome. And if you're looking for a bathroom every 10 minutes, you can certainly imagine that that's going to crimp your social life, seriously. But also getting super flushed while you know you're in conversation with people; it is very impactful. So, I think comfort is an important issue. Indeed, people with carcinoid syndrome actually have worse outcomes in terms of mortality than people who don't have carcinoid syndrome, and whether that's because the more tumor a person has, the

more likely they are to have carcinoid syndrome, as I mentioned earlier, that may be one thing. But it could also be related to the impacts of chronic diarrhea on nutrition and things like that. So, carcinoid syndrome, it's a sign. It's one of the ways a person knows whether their tumors are somewhat controlled or not controlled. Tumors that are active in terms of producing hormones and chemicals that cause symptoms, they are tumors that are alive and they are tumors that are growing. So many of our treatments for the symptoms of carcinoid syndrome also have an impact in terms of treating the tumor and slowing down its tumor growth. Also, carcinoid syndrome, it's frequently a sign of high serotonin levels. And again, high serotonin has the issue of heart valve disorder. So, there are many reasons to treat the syndrome, both comfort, to stop further damage to structures like the heart, and to stop the continued growth of tumor.

Lisa Yen 38:24
It's like your indicator light, right?

Dr. Joseph Dillon
Yeah.

Lisa Yen 38:27
And wellbeing cannot be overestimated. As you said, it's all about the quality of life.

Dr. Joseph Dillon
Yeah.

Lisa Yen 38:32
So, we know, of course, why it should be treated. How is it treated? How is it currently treated? And what would you do for it?

Dr. Joseph Dillon 38:41
For some people, their carcinoid syndrome, their symptoms of flushing, or their symptoms of diarrhea, have events that precipitate them. So, people can realize that, oh, if I eat this, this or this, I get a flushing episode, or I need to run to the bathroom. Or if I start exercise, I get a flushing episode and need to run to the bathroom. So, I think it's important in terms of what a person themselves can do, just understanding how their body reacts to things is to really try and identify any of the precipitants that they may have for symptoms of carcinoid syndrome. My old mentor, Dr. O'Dorisio, used to always talk about the **five E's**, and those were **eating and exercise and ethanol or alcohol and emotion**. And there's always, whenever I give a list of five something or others, I always get forget one of them.

So, breaking that down, then eating. Some people notice it's a large meal. Some people notice that it's particular foods. For some people, it's foods containing **amines**, and those foods would be aged foods, fermented foods, pickled foods. So aged cheeses and meats and pickling and fermented. So different people, it's different precipitants, and many people don't have any precipitants whatsoever. For others, as I mentioned, exercise, medications. Epinephrine, I usually tell people to tell their dentist not to use epinephrine along with the Novocaine in their local anesthetic in their mouth, because epinephrine or medications like epinephrine, and

that includes pseudoephedrine, which is in many antihistamines and can precipitate a carcinoid symptom. Alcohol, for many people, can precipitate carcinoid syndrome.

Perhaps the majority of people don't have a precipitant, but if you have a precipitant, you can do some workarounds. You can *not* eat those things, or you can take some short acting octreotide 30 minutes before engaging in any of these activities, and that will frequently get rid of the carcinoid symptom for you. So, just trying to identify things in your own body and how your own body works and what it is that precipitates the event, because we may be able to pretreat with that event.

Lisa Yen 41:07
I'm glad you brought up the five E's, because those for a while, they're floating around, and some people almost see it as biblical, like those are the precipitants for all people. But you're saying it can be but not necessarily.

Dr. Joseph Dillon 41:21
Thank you. Lisa. Yeah, it's only for, I would say, a relative minority. So, when people ask me, “Well, you know, I've heard about these dietary restrictions, should I be doing these dietary restrictions?” And I say, “If you don't have symptoms, I don't see why you would do dietary restrictions. If you don't have symptoms, I don't see a problem with exercise or alcohol in moderation.” They're only for people for whom this is a precipitant, and that is a relative minority of people. So, you probably had much more expertise on the show in the past with dietary expertise than I have, but I don't legislate a diet or these dietary interventions in a person who doesn't have the symptoms.

Lisa Yen 42:03
Thank you for clarifying. So, avoiding known precipitants.

Dr. Joseph Dillon
Yeah.

Lisa Yen 42:06
And then what else?

Dr. Joseph Dillon 42:07
So again, carcinoid syndrome is symptoms associated with a tumor. So many times, treatments of the tumor will alleviate symptoms. Some of the things that can alleviate symptoms, sometimes quite rapidly, would be removal or killing off of large components of tumor, such as surgery. So, a person can have bad carcinoid syndrome going into surgery, and the day after surgery, they're dealing with how painful it is postoperatively, but they're not having carcinoid syndrome.

Similarly, another treatment for people who have large tumors in their liver producing a lot of chemicals which produce the carcinoid syndrome, sometimes by treating the bulk of the tumor with embolization treatments or ablation treatments, including **histotripsy**, that some people may have heard of treating the bulk of the tumor

may significantly improve symptoms. And **PRRT** can also, by killing off a proportion of tumor can also have a significant impact on the symptoms.

And then there are medications that are given to people to treat carcinoid syndrome. And the medication group that many in the audience may be well aware of is a group of medications which are sometimes called **somatostatin analo**gs because they are artificial forms of a hormone called **somatostatin**. Somatostatin is a hormone that's in your body from day one, but most people's neuroendocrine tumors have specific docking sites that somatostatin will stick onto. So, if we use artificial somatostatin, which is what your octreotide or your lanreotide. **Octreotide** is also called **sandostatin**. **Lanreotide** is called **somatuline**. Those are generally monthly injections, and they are there to do two things, really. Specifically for the carcinoid syndrome, they decrease the hormone output, they decrease the serotonin output, and by doing that, they decrease the symptoms associated with it. They also inhibit tumor growth, although there are other chemicals that inhibit tumor growth and don't specifically inhibit the symptoms. These medications both inhibit tumor growth and inhibit the symptoms.

And those are monthly medications, but there are **daily or short acting forms of octreotide**. That's one of the ones that I mentioned that can be self-administered by injection prior to an event that might precipitate some symptoms. So that is probably the biggest group of medications that's given for neuroendocrine tumors.

There's some newer medications, particularly because serotonin is such an important component of the diarrhea. We have a medication that is given to people who still have diarrhea because of carcinoid syndrome, despite being on monthly lanreotide or octreotide. And that's the medication called **telotrostat or Xermelo**, which is a tablet given three times a day, which is there specifically to block the production of serotonin. It doesn't block the production of other hormones and chemicals, so it only blocks the production of serotonin, whereas the octreotide and lanreotide block the production of multiple hormones and chemicals from these tumors.

Lisa Yen 45:30
It sounds like there's two main buckets. One is to treat the tumors with surgery, liver-directed therapies, potentially systemic therapies. And then the other one to treat the symptoms with somatostatin analogs, telotrostat or Xermelo. So, two main ways. It's like a multifaceted approach to treat the carcinoid syndrome.

Dr. Joseph Dillon 45:49
That's exactly right. There are people then who still have symptoms despite being on the monthly medications and Xermelo. That can be a reason for us to say perhaps we should do PRRT now, or perhaps we should do some other treatment now, because we can't inhibit the symptoms just with shots or the Xermelo alone.

Lisa Yen 46:11
Yeah, so really a thoughtful approach, I mean, really attacking it in all different ways and adding different things to try to help control all the symptoms.

Dr. Joseph Dillon 46:20

And I think that's a good call out for if a person can have access to a multidisciplinary group of physicians and providers that bring different aspects, because at different times in a person's journey with the neuroendocrine tumor, they need expertise from different people. It's important to, if it's possible, for a person to find a group of providers who have some sort of complementary views on the treatment of the conditions.

Lisa Yen 46:53
A multidisciplinary approach. It's helpful to know there's not just one treatment, one thing to be relied on. Now, if someone's tried all of those treatments already and they still have carcinoid syndrome, what else might be on the horizon?

Dr. Joseph Dillon 47:08
Yes, so people who still have the syndrome. One thing I would say is that it's really important for the provider to clarify the nature of the symptoms with people. Some of our neuroendocrine tumors produce histamine, particularly the ones that are lung or sometimes stomach, sometimes even pancreas, and they may benefit from **antihistamines**. Indeed, before octreotide came on the market, we had a very old antihistamine, **Cyproheptadine**, which blocked some of the effects of serotonin, and it also blocked histamine. So sometimes I have people on medications such as **ondansetron**, which is an anti-nausea medication, but it blocks serotonin. Cyproheptadine, Zyrtec and Pepcid. Those medications for very specific symptoms, I sometimes talk to people about that. And then in the presence of symptoms that cannot be blocked by those medications, I'm thinking about how we can get rid of some of the tumor, either by surgery or PRRT or other approaches.

There are some newer medications that are being trialed for neuroendocrine tumor symptoms particularly, and these are tablet forms of the somatostatin analogs the octreotide and lanreotide. So there are tablet forms of octreotide and a tablet form of an agent which also acts like octreotide and binds to tumor. And those trials are ongoing, and they're very exciting. And full disclosure, I'm involved in one of those clinical trials, but I think this will hopefully allow people to not have to show up on a monthly basis for an injection. And also be able to administer additional short-acting medication to take care of events that precipitate symptoms.

Lisa Yen 49:01
I believe you're talking about the **Paltusotine trial with Crinetics**.

Dr. Joseph Dillon
That's right.

Lisa Yen 49:06
We'll list that trial on the podcast landing page for those who are interested in learning more about that. So, what about people whose tumors were completely removed? Can carcinoid syndrome be prevented? Can it be detected early?

Dr. Joseph Dillon 49:19
So, if a neuroendocrine tumor has been completely removed, i.e., the person is cured, then there shouldn't be a carcinoid syndrome, because the syndrome is symptoms related to a tumor. Of course, the question after a

seemingly successful surgery with a person with neuroendocrine tumor is that these are very slow growing tumors. They can be very small for a very long time. You know, could we have a situation where a person still has symptoms and nothing visible on the scans? And we've discussed that already, that can occur, but it's an unusual thing, but it can occur.

So, if a person still has symptoms. So a person had symptoms before the surgery, has the surgery, and the symptoms say, go away for six months or 12 months or two years, and then start creeping back again but there's nothing visible on scans, that may very well be carcinoid syndrome, but it is a manifestation of a recurrence of tumor, as long as we've ruled out other causes. And in that situation, we might see an increase in serotonin or the 5-HIAA, even if we don't see anything on a scan. Because, again, scans are limited by how big the tumor is. ***A scan will not see a tumor if it's less than five millimeters***. It won't be seen. But if a person has 20 tumors that are four millimeters, nothing will be seen. But that's 80 millimeters of tumor of which all can produce serotonin, so that blood serotonin level may be up and the symptoms may be present. In that situation, I would be talking to people about considering getting on to one of these somatostatin analogs, the octreotide or lanreotide, or perhaps entering a clinical trial for one of the newer agents in that general category.

So, if a person is having symptoms, it gives me concern that they still have a tumor, we just hadn't seen it. Or it gets me to look again at the other causes of the same symptoms, because, again, the symptoms are nonspecific. So, if a person develops diarrhea two years after a surgery, well, anybody who's had a surgery can get bacterial overgrowth, which causes pretty severe diarrhea, and the treatment for it is not octreotide or PRRT. The treatment for it is antibiotics. When I don't see a tumor on the scan, but they have the symptoms, I need to clarify. Have we ruled out the other causes of this symptom? And then have a discussion with people about whether we should treat with the injectable medication or not.

Lisa Yen 52:00
So high suspicion for carcinoid syndrome and also making sure you don't miss other causes. So, is there anything people can do to prevent or lessen carcinoid syndrome symptoms? And I guess oftentimes people wonder if there's factors that worsen their syndrome, like, I don't know, weight, other diseases, age, any other factors.

Dr. Joseph Dillon 52:21
In terms of factors, worsening carcinoid syndrome, again, because of the non-specific nature of the symptoms, many times, other factors, other drugs that people get put on over time, can cause the same symptom. For example, as we get older, we tend to produce less insulin, we tend to have more and more risk of developing diabetes. One of the first drugs for diabetes is a drug called **Metformin**. The classical side effect of metformin is diarrhea. So as with age, with weight, we get put on other medications. Many of the symptoms can get worse with other conditions and other treatments. Those treatments, Metformin, for example, for diabetes, does not worsen neuroendocrine tumor, to my knowledge. It doesn't actually worsen carcinoid syndrome, to my knowledge, but it makes diarrhea worse so it can be difficult to tease out there.

If a person has a neuroendocrine tumor with age, with passing time, those tumors only get bigger and more active, so there will be the potential for worsening of carcinoid syndrome over time, along with the increasing tumor. Again, I think it's important in terms of lessening symptoms, it's important to make sure you're treating

the right thing with the right approach. Or symptoms that are truly carcinoid tumor-related symptoms, increasing doses of the somatostatin analog injections, the lanreotide or octreotide, possibly newer medications in the future, avoiding things which precipitate symptoms, as we discussed already. And then if symptoms get worse, even despite that, then consideration of dealing more forcefully with the remaining tumor, with procedures that kill tumor, such as surgery, ablation, embolization, PRRT, certain forms of chemotherapy for certain neuroendocrine tumors.

Lisa Yen 54:20
So whole person, multifactorial, multidisciplinary approach with the goal of lessening symptoms so you have a better quality of life.

You know, I think we can end with this last question and this opportunity to discuss your work that you've been doing for quite some time. I know that you've recently published a study discussing the possible risks of using certain weight loss drugs, and you've been working on this, the **GLP-1 drugs**. Could you tell us a little bit more about your work and about the study?

Dr. Joseph Dillon 54:48
So, these agents, most famously, I suppose, **Ozempic, Mounjaro**. They go by various names, but I'm going to just focus on Ozempic and Mounjaro since those are pretty well-known names. Agents such as that have been in the market now for 20 years. I think their first FDA approved in 2003, 2004, something like that. And they are remarkable agents in terms of helping diabetes, and they're remarkable agents in terms of weight loss, particularly the most recent ones, the Ozempic and Mounjaro. And they are agents which decrease overall cancer rates because they decrease cancers that occur related to obesity. And then there are many cancers that have a higher rate related to obesity. Breast cancer comes to mind. Prostate cancer comes to mind. I believe colon cancer is another one. So, they have reduced the risk of many cancers.

Back when these agents were initially authorized by the FDA, the FDA noted that the agents could cause growth of a neuroendocrine tumor in the thyroid of mice and rats. So, it was a particularly unusual neuroendocrine tumor of the thyroid, a tumor called **medullary thyroid carcinoma**. And medullary thyroid carcinoma occurs in a group of patients who have genetic condition called **MEN2, multiple endocrine neoplasm two**. So right from the start, we had what we call a "**black box warning**," which is the highest warning level that the FDA have on these medications. Do not use these medications in people who have medullary thyroid carcinoma or a family history of MEN type two. So, we've known for a long time, then that some neuroendocrine tumors could grow with these agents. Now I should say that there's always been a lot of controversy about that finding and whether a finding in mice and rats is important for humans or not important for humans, and there's a lot of literature coming and going with questions on that. But it was a question that my patients have been asking me for a couple of years now, as we've used more and more of these agents: "Any problem with these agents while I've got neuroendocrine tumor?" And for the longest time, I told them that there is no evidence that these agents cause a problem with your neuroendocrine tumor. There is this weird neuroendocrine tumor in the thyroid that maybe you should stay away from them, but no direct evidence.

But we realized that the data from last year is that 12% of the population the United States are taking these agents, and 6% were continuing to take these agents. And so, I look at our numbers in our clinic, and exactly the same percentage are taking these agents. 6% of our population in our neuroendocrine tumor clinic were taking these agents.

The other aspect to this is that we've known for a long time that the receptor or the docking site for ozempic or for Mounjaro is present on neuroendocrine tumors. Many of your audience will have heard of somatostatin receptors. That's the docking site for somatostatin or the docking site for octreotide on neuroendocrine tumors. And it's the basis for why their monthly octreotide and lanreotide work. It's the basis for why the PRRT works. It's the basis for why the PET scans work. Because there's a docking site for that particular substance. Well, there are also docking sites for, for the substances that are in Ozempic and Mounjaro. So based on that concern, I asked Dr Ear in our research group to do an experiment where she took pieces of neuroendocrine tumor that Dr Howe had removed from patients and grew them in test tubes or in petri dishes or grew them in mice and administer Ozempic. And what we showed was that in some neuroendocrine tumors, they actually grew when they were exposed to Ozempic. And we also have the same data now for Mounjaro. So that's concerning. Now it's only concerning if a person's tumor has the docking site for ozempic or if the person's tumor has the docking site for Mounjaro.

So, the concern is, "Do all neuroendocrine tumors have the docking site for Munjaro? Do all neuroendocrine tumors have the docking site for Ozempic?" Because, if that's the case, at least in mice and in test tubes, that would cause these tumors to grow. So, then Dr Ear has been looking at, well, what proportion of neuroendocrine tumors, or what type of neuroendocrine tumors have docking sites for Ozempic? What proportion of neuroendocrine tumors have docking sites for Monjaro? So, it turns out that in round numbers, **40 to 50% of pancreatic neuroendocrine tumors and 40 to 50% of duodenal neuroendocrine tumors have docking sites for Ozempic and Mounjaro**.

Lisa Yen 1:00:06
You're saying that nearly half of duodenal and pancreatic NET, 40 to 50% have those receptors.

Dr. Joseph Dillon 1:00:14
That is correct. But almost no individuals with ileal neuroendocrine tumor have the receptor for Ozempic in our studies. So, it's complicated to do this research, because on the one side, you don't want to scare people with preliminary research, which is done in mice and test tubes. And on the other side, it's really important for us to understand *these are new drugs*. *We haven't seen the true impact of the Ozempic, and certainly not Mounjaro because it's more recently FDA approved, in the development or the growth of tumors.*

So, it looks like Ozempic, there's approximately a half of the people with duodenum NET and pancreas NET have the possibility that that can cause further growth in their tumor. There appears to be almost no one who has a somewhat more common small bowel neuroendocrine tumor who has the receptor or the docking site for Ozempic.

So, what I'm telling people now is that in people with small bowel neuroendocrine tumors, I'm explaining to them that there doesn't appear to be a way that Ozempic would affect their small bowel neuroendocrine tumors. In people with pancreatic and duodenal neuroendocrine tumors, that's a long discussion. That's a discussion of the pros and cons, and I am looking at people very carefully from six months to six months, and if I'm seeing any change in their tumor while they're on Ozempic, if they want to continue on that medication, we're really having a very long discussion about whether they should continue that or not.

There's a lot of complexity here. One of the complexities is that most of our patients who are already diagnosed, they are on somatostatin analogs. So they are on octreotide, or they are on lanreotide. Well, octreotide and lanreotide may directly negate the effect of Ozempic on the tumor. So, there may be no growth on the tumor, but it may be that the Ozempic is negating, is blocking the effect of sandostatin on the tumor. Those are things that we're trying to work out in the research lab as quickly as we can.

I must say that I have even more of a concern about Mounjaro. I think Mounjaro is also Zepbound, or I can't remember all of the trade names for it. But Mounjaro, the receptor, the docking site for Mounjaro is much more widely distributed. It's present in ileal neuroendocrine tumor so small bowel neuroendocrine tumors and pancreas neuroendocrine tumors, so I have somewhat more concern about that medication.

So, these explanations take a while because it's difficult, but my preference for people who have a small bowel neuroendocrine tumor, who want to go on an agent like this is for them to stay with the Ozempic-related agent rather than the Mounjaro-related agent. And that's a tough sell as well, because Mounjaro is a better agent for weight loss than Ozempic is.

So those are some of the things that we're working on, and I'm sure other people are now working on because of that concern. It's one thing about people who are already got a tumor that we're looking at and we're keeping a close eye on, and they're on a octreotide that might be negating some of the effect of the Mounjaro but what about the people who have small neuroendocrine tumors that haven't been diagnosed yet and therefore are not on octreotide or lanreotide. Those are the people that I'm particularly worried about, because they potentially have an unopposed effect of Ozempic or Mounjaro on tumors that they don't know they have.

Lisa Yen 1:04:10
And can people be tested for these docking sites?

Dr. Joseph Dillon 1:04:14
So that's one of the things that we're trying to set up, because it would be nice to be able to take a sample of tumor and do a test for the GLP receptor. The **GLP receptor is the docking site for Ozempic**, and if your tumor did not have a GLP receptor, we would say, "Yep, go ahead. No problem." Whereas if it did have a GLP receptor, we'd say, "You should be cautious with this." So, we're trying to develop such a test now. Dr Belizzi, who I think has been on your program, has developed such tests for our research in this area. And of course, Dr Bellizi has also developed tests for serotonin receptors, which we do routinely on our patients' tumors. So, we're hopeful that we can get a GLP receptor and a GIP receptor. **GIP being the receptor for the Mounjaro**. We're hopeful that we can get those up and available for patients, so that once a patient and their doctor has decided that, "Yes,

this would be the best medication for their obesity or diabetes," that they can then have a specific test for their neuroendocrine tumor to clarify "Am I at risk for anything related to my neuroendocrine tumor?" And if not, then continue with the treatment.

Lisa Yen 1:05:35
Yeah. So, you continue to be at the cutting edge of work being done in neuroendocrine tumors, including potentially developing this test for a receptor.

So, as we close, what do you want the NET patient community to take away from your work here with these GLP drugs and also carcinoid syndromes?

Dr. Joseph Dillon 1:05:55
Well, I think that there are new medications and new treatments for neuroendocrine tumors. For a person who has a neuroendocrine tumor, research cannot happen fast enough. It can never happen fast enough. There are some new things on the horizon in terms of therapies, and you've probably spoken to people about newer forms of PRRT and some other exciting new medications that can attack these tumors. And we've already mentioned for the carcinoid syndrome some new ways to use drugs now as tablet forms, rather than as injections, that will make it easier for patients to deal with and to have ability to self-manage their syndrome.

As with all new drugs, and I'm talking about now the new drugs such as Ozempic and Mounjaro that have proved so incredibly successful for major public health problems such as obesity and diabetes and even the obesity-related cancers, it's always important to be cognizant of the possibility of unforeseen complications with those medications, and to be open to clarifying any new trends in development of neuroendocrine tumor that might relate to them, and try to figure out which of our patients with neuroendocrine tumors can safely take these versus where there's a question.

Lisa Yen 1:07:18
There's a lot of research being done. You're on the forefront of a lot of it, so we can be hopeful. And a lot of questions yet still be answered.

Dr. Joseph Dillon
Some things to still be answered.

Lisa Yen 1:07:28
And we're continuing to understand and learn more, and you're behind a lot of that. So, we really appreciate all that you've done. All the work you've done in the past and continue to do now and moving towards the future.

So, thank you so much. Thanks for this really thoughtful discussion, for answering so many questions and bringing awareness also about these new drugs and how it might interact with neuroendocrine tumor so we're aware and can make a more informed decisions about our care. Thank you for all you do.

Dr. Joseph Dillon 1:07:55

Thank you, Lisa. Thanks for having me on and it will be remiss of me if I didn't say that the research that I talk about is done by all the great people at the University of Iowa and colleagues elsewhere that we collaborate with all the time. So, I'm just a bit player in a great group, and I'm so happy to be able to do that.

Lisa Yen 1:08:16
It's a team approach, and we appreciate the whole team. Really, it's amazing work that you all do. Thank you so much.

Dr. Joseph Dillon
Thanks, Lisa.

Lisa Yen 1:08:25

Thanks for listening to the Neuroendocrine Cancer Foundation podcast. We want to thank our podcast supporters Novartis, Ipsen, Exelixis, Crinetics, Tersera, Curium, ITM, Rezolute, Interscience Institute, and Boehringer Ingelheim.

For more information about neuroendocrine cancer, go to NCF.net. We depend on donations to bring you programs such as this podcast. Please consider making a donation at NCF.net/donate.