NETWise
A Podcast About Neuroendocrine Cancer

Episode 25
Small Bowel NETs:
Transcript

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Welcome to NETWise. This is a podcast for neuroendocrine cancer patients and caregivers that presents expert information and patient perspectives. My name is **Jessica Thomas**, Director of Patient Education at the Neuroendocrine Tumor Research Foundation.

We here at NETRF are committed to always presenting the most current, timely, and credible information about NETs and NET care, and so we've started to go back and refresh older episodes of this series to make sure they are up-to-date. This is a revised version of an episode that originally aired in December of 2020, where we focused on diagnosis and treatment of NETs that start in the most common primary site for neuroendocrine tumors, the small intestine.

Let's start with a little anatomy. When you eat something, it travels down what is essentially a long tube that goes all the way down from your mouth to your rear end, called your "gastro-intestinal tract". Along the way, it passes through several organs that work to digest food and pull the nutrients out for your body to use. Here's Dr. Daniel Halperin of M.D. Anderson Cancer Center at the University of Texas:

> Halperin: *"After the esophagus, it goes into the stomach. And then after the stomach, it moves into the duodenum, the jejunum, and the ilium. And then from the ilium, it moves into the large bowel, right through the ileocecal valve, and then moves into the colon and eventually out of the body."*

The longest portion of this tract is the small intestine, also known as the small bowel, which is made up of three sections: first the duodenum (dew-oh-DEE-num), which attaches to the stomach, then the jejunum (juh-JEW-num), then finally the ilium, which connects to the large intestine at the other end.

The small intestine is called "small" because of its diameter – only about one inch around – but it's actually our longest internal organ, sometimes more than 20 feet long if it were all stretched out. This is the area where the most digestion happens, and it's the most common location for neuroendocrine cancer to originate. Here's Dr. Namrata Vijayvergia (nam-RAH-tuh vee-jay-ver-JEE-ah) from Fox Chase Cancer Center in Philadelphia:

> **Vijayvergia:** *"Small bowel neuroendocrine tumors are actually one of the most common neuroendocrine neoplasms, and actually one of the most common small bowel cancers. Even though NET never associates itself with common, the most common small bowel neoplasm is actually a small bowel neuroendocrine neoplasm."*

And interestingly, small bowel NETs were the first neuroendocrine tumors to be discovered, back in 1907 in Germany. Here's Dr. Mark Lewis, an Oncologist at Intermountain Healthcare in Utah, who is both a NET specialist and also a NET patient.

> **Lewis:** "There was a pathologist, so a man that was almost exclusively looking at things under the microscope. His name was Dr. Siegfried Oberndorfer. He was brilliant. And around the age of 30, he was the first person to document the discovery of neuroendocrine tumors - very, very tiny tumors in the small intestine."

Dr. Oberndorfer's work also created a lot of the confusing terminology which has unfortunately stuck with NETs.

> **Lewis:** "*The root of all the confusion dates back to his description of these tumors, in German, he described them as "karzinoid", which of course is a sort of quick cognate in English to carcinoid. And, and what he was trying to say was when he looked down the lens of the microscope, the cells he was looking at did not look entirely benign, they didn't look clearly malignant either. They sort of fit in*

this new category and hence he develops a new word in that word karzinoid or carcinoid has been with us ever since."

And while that term – Carcinoid – has largely been rejected by NET specialists these days, the unusual qualities that Dr. Oberndorfer saw more than 100 years ago are very important to the way small bowel NETs are treated.

As we've often heard in this series, the treatment strategy for low-grade NETs is very different from the strategy for most other kinds of cancer, and small bowel NETs are almost always low-grade.

Vijayvergia: *"So, high-grade neuroendocrine cancers are very, very rare in the small intestine. I have to say, I have yet to see a patient who would have that."*

Lewis: *"Not all treatment in cancer is chemotherapy. And in fact, when it comes to neuroendocrine tumors, it's the exception, not the rule that I would be giving one of my patients chemotherapy.*

So sometimes when doctors are referring patients to me, they will describe me, sort of like a colloquial shorthand. They'll say, 'you're going to go see the chemo doctor,' and that's okay. But it means I have a little bit of work to do sort of reframing the conversation when I meet the patient. And I, I often get to kind of talk them off the ledge immediately and I say, 'Hey, listen, if you're here

thinking I'm going to recommend chemotherapy, let me just clear the air and tell you. That's actually quite unlikely, at least at the beginning.'

Like many low-grade NETs, the treatment for NETs with a small intestine primary can often look more like the treatment of a chronic condition, such as diabetes.

Lewis: *"One of the ways I conceive of most neuroendocrine tumors, including my own, is I think of it like a chronic illness. So as we're recording this, I actually cannot envision that I'm going to be cured of my disease. I'm going to be living this, living with this, I should say, with the rest for the rest of my life. and it takes some sort of careful recalibration of expectations to say, '\Hey, listen. You could actually live with this and not die of this, but we are gonna have to manage this.' Oftentimes, that means coming in for a monthly treatment and it is cumbersome in a way that a lot of other diseases aren't.On the other hand, it also doesn't require chemo the way many cancers do. So there's a, it's kind of a weird trade-off."*

There are some particular difficulties in treating small bowel NETs, though. To start with, they can be especially tricky to correctly diagnose. One reason is the size, shape, and location of the small intestine itself. Because it's a very long, very thin tube, all twisted around in the middle of your belly, it can be very hard to actually see what's going on inside. The

normal tools you would use to look for tumors – things a standard endoscope – just won't reach all the way through.

> **Vijayvergia:** *"When you do an endoscopy, like an upper GI endoscopy, people can look in the stomach, you can look in the duodenum, but really doesn't go further up than that. If you do a colonoscopy, it looks at your entire colon, maybe the end of your small intestine, called the terminal ilium, but not much. Small bowels are, like, really long, right? They're extremely long and they're difficult to maneuver, so it's not very easily evaluable."*

> **Lewis:** *"It's a very tricky part of the bowel to get to. As my colleagues have described, there's almost a no-man's land in the middle, third of the gut, essentially, most of the small intestine. That can be very, very challenging to get to, if not impossible to get to using a scope."*

But that hunt is important, because unlike with more aggressive forms of cancer, it's important to accurately find and diagnose the primary tumor even after it has metastasized.

> **Lewis:** *"Most of the time as an oncologist, if I encounter a patient who is stage four, meaning that their, their, their tumor has already metastasized, uh, at the time of diagnosis. We seldom actually think about, okay, well where did it start? But actually with neuroendocrine tumors, it matters a great deal that you figure out where it started."*

This is also complicated by the fact that small bowel NETs can also have what are called "multifocal primaries", where several tumors develop at the same time in the same organ, and these tumors can be very, very tiny – too small to see with diagnostic imaging. They can be so small, in fact, that some of them are only discovered when a surgeon feels the entire length of the intestine with their fingers – a process called "running the bowel". This unfortunately makes surgery an important diagnostic tool for small bowel NETs that are especially stubborn and hard to pinpoint.

Because these tumors can be so good at hiding, they unfortunately often remain undiagnosed until they metastasize to someplace like the liver, where the tumors are more likely to be spotted.

And even though they can be small and slow-moving, small bowel NETs often do metastasize.

> **Vijayvergia:** *"It's a very interesting disease that, in a way that it doesn't… um, the size… you know, we always worry about what was the size of the tumor that they took out, right? We always worry about that. We always think that if it's a tinier tumor, it's probably not going anywhere. But there's not much correlation between that. Even tumors that are about one centimeter or smaller have about a 15% chance of the cancer spreading to other places. And if you're greater than two centimeters, there's a 50% chance that cancer is spreading to somewhere else. And*

that's why, even though it's a small tumor, if we find something in the small intestine, you tend to do a bigger surgery to take the lymph nodes out, no matter what the size of the tumor is."

Local lymph nodes and the liver are the most common areas for metastasis, but other areas are possible.

Vijayvergia: *"Another area is your abdominal cavity in general. So, you know, all the organs in your abdomen are covered with a lining called the peritoneum - that's just the lining of it. And tumors can just direct spread, or through the bloodstream can just gain access to this lining. And I always tell patients, it's akin to how moss can grow over surfaces. So, because it's a lining that covers all or most of the organs in your abdomen, the tumor cells can sort of form a film on this lining, so as to cover the organs. So, you may not see big masses there, but it's like, there is a lot of disease on the inside, like small, small specs, which are spread in the abdominal cavity. That is called 'carcinomatosis'.*

Rarely, bone disease is seen too with this disease. I actually have more than a few patients who tend to develop bone metastases from the neuroendocrine neoplasms of small intestine, too. And then there's rare… I have a breast, I have a patient with a skin… but like, there's, you know, everything is heard of, but the most common ones are the liver, the lymph nodes, abdominal cavity, and maybe bone, less likely."

Another way these tumors can be diagnosed is when they cause some kind of a symptom. Some symptoms appear in the form of some kind of bowel obstruction or blockage, where a cancerous growth in the intestine makes it harder for partially digested food to pass through the system the way it's supposed to. This can sometimes be caused by the primary tumor itself.

> **Vijayvergia:** *"Even small tumors can cause uh… they can become blocked or, you know, just like a plumbing problem, because the narrow is the lumen is further narrowed or they cause something called intussusception where basically, because of that small tumor in your intestine, that part of the intestine is not moving in synchrony with the rest of your intestines. One part is telescoped into the other part of the intestine because there's a tumor in there, and what it leads to is a blockage."*

Another classic cause of bowel obstruction from NETs happens when they locally metastasize out of the small bowel itself and into something called the "mesentery", which is a kind of protective layer that surrounds it.

> **Halperin:** *"The mesentery is just the apron of fat in which the bowel is suspended and there's all the blood vessels, the lymphatics, are running through there. And so it's common, right, for the neuroendocrine tumors to involve the mesenteric lymph nodes as they sort of work their way back from the bowel up towards the blood vessels, towards the liver."*

This can cause something called a "mesenteric mass".

> **Vijayvergia:** *"It is basically that in the center of your abdomen, or somewhere in your abdomen, you have like this rounded structure, like a mass with spokes of wheels on its side - that's how you can imagine it to be. And it's deep in your abdomen, usually around big blood vessels and stuff too."*

This kind of growth can cause digestive problems and other symptoms in a number of ways – first by blocking the flow of material through the bowel, but also by interfering with the flow of blood to the small intestine.

> **Vijayvergia:** *"So when the blood vessels are sort of narrowed, affected, it can affect the blood supply to your intestine, which can produce symptoms of 'bowel ischemia' - that's the fancy word for just lower blood supply to the intestine, typically presenting as abdominal pain after you eat, after you have heavy meals. And then it gets better, and then you lose weight because you don't absorb nutrients as well because of the lack of blood supply, and this leads to swelling of the intestines."*

And third, in a less well-understood phenomenon, it seems that symptoms can be caused by "fibrosis" – the network of scarring that tends to surround a mesenteric mass.

Vijayvergia: *"What it tends to do is, these masses over time, because scar tissue likes to contract – if, you know, if you have a scar anywhere, if you get a surgery, that area gets smaller and smaller with time, like scars contract over time. And as they contract, they tend to pull the small intestines towards each other while doing so, and that can lead to complications down the line."*

In the worst cases, these physical blockages can be quite severe and debilitating.

Halperin: *"The most severe presentation is a frank small bowel obstruction, which is when someone really can't tolerate anything by mouth at all and absolutely nothing is making its way through the GI tract. And those folks will present with severe pain and nausea and vomiting, and really they will frequently find themselves in an operating room very quickly to get the mechanical obstruction relieved as quickly as possible.*

When things can't move through, you know, your GI tract is making liters and liters of fluid a day that can't pass through. And so people will, um, they will start to get nauseated and start to vomit that up. And it's really unpleasant."

Often, though, small bowel NETs cause only partial obstructions, which can produce symptoms that are much more subtle and easy to

misinterpret, causing small bowel NETs to be misdiagnosed as much more common digestive complaints.

> **Halperin:** *"We also tend to see folks who have issues with recurrent intermittent bowel symptoms that may not necessarily be quite as severe as frank obstruction. We certainly see folks who have recurrent issues with pain after they eat, where things will eventually make their way through the GI tract, but just isn't working normally and the bowel is just not healthy."*

> **Vijayvergia:** *"A lot of my patients have been incorrectly diagnosed with irritable bowel syndrome for the longest time before they think of this."*

Another way small bowel NETs can cause symptoms is by producing an excess of a hormone, which in this case is almost always serotonin. This causes the constellation of symptoms called "carcinoid syndrome" – the one situation where the term "carcinoid" is still widely used among NET experts. We've discussed carcinoid syndrome at length in earlier episodes of this series, but it's worth mentioning again here, because it's more strongly associated with small bowel NETs than any other kind of NET.

> **Halperin:** *"The association is strong. We did an epidemiologic study with its own strengths and weaknesses several years ago trying to understand this, patients who have well-differentiated metastatic small bowel*

neuroendocrine tumors being most likely to present with carcinoid syndrome. In that particular manuscript, we estimated about 55% of patients with metastatic small bowel neuroendocrine tumors would have carcinoid syndrome at presentation, based on the particular definition that we used in that particular study. I wouldn't use that number as being absolute, but just to give us a sense that that's more common than other groups."

While small bowel NETs of any stage can produce serotonin, the symptoms of carcinoid syndrome, things like facial flushing and diarrhea, very rarely appear until after the cancer has metastasized outside of the small bowel, especially to the liver.

Vijayvergia: *"Typically, we feel that when the tumors are localized to just your intestine, if you release a hormone it goes into your bloodstream, but as soon as it reaches the liver, the liver sort of degrades them, right? It basically metabolizes them. So, you don't get carcinoid syndrome symptoms in early stage disease. Now that is, you know, never say never in medicine – anybody can have any kind of symptoms and I've seen it all – but typically we see that carcinoid syndrome is seen in patients with advanced disease. So when the cancer is not just in the intestine, once it gets to the liver or any other place where the blood is not pumped into the liver directly and it's actually going into your circulation and the hormones*

are released into your circulation, you get these symptoms of carcinoid syndrome."

"Well, my name is **Quintin**. *I'm calling from Portland, Oregon. I'm 71 years old. I was having some prostate issues about six years ago, and I went in for a CT scan. And when the urologist looked at the scan, he noticed there were some lesions on my liver which I was totally unaware of. The prostate turned out to be fine, but he immediately referred me to an oncologist, and I was diagnosed then with neuroendocrine tumors.*

It was totally out of the blue. It just took myself and my family completely by surprise. We were just totally shocked. In hindsight, I had some symptoms – I had some flushing and I had some diarrhea, but I had no idea that they were symptoms of cancer.

They did a colonoscopy and endoscopy at the same time and couldn't find anything through there. He didn't have any idea, really, where the primary was. He just knew that they could see these tumors on the liver.

What happened then was, first I was told by the oncologist that my tumor was – uh, well, I had numerous tumors – but there was one that was too big for surgery. And he went by the book and looked up and there was these Octreotide treatments, and that's what he suggested, once a month. And my condition, I would get scanned every six months, and the

doctor would tell me that, 'well, you're stable', but there was always a slight bit of growth, just a little bit of percentage growth. And we were like, 'well, um, how much is too much? You know, when is this gonna be a problem?' and I could never get an answer, a really good straight answer on that question. He says, 'Well, you know, the numbers are stable.'

So that went on for about a year or so. My wife and I finally decided to do some research on our own. So, as we did some research, we discovered a NET specialist here in Portland at OHSU, and that's when the journey really began as far as getting these things going on the right track. He said, 'I know right where your tumor is at', and he pointed to my abdomen. He says 'right there, I just know it's there.' So he looked at me. I was, I guess, 66 at the time and said, 'Hey, you're young, you're healthy. You're a perfect candidate for surgery.' And after hearing that it was far too large to operate on initially, it was like, we were just shocked, dumbfounded that somebody thought they could take these tumors out. And so sure enough, when they went in there, it was all wrapped up and balled up so they had to do a small incision to get it out, but he said, 'yep, that's the primary tumor,' and they took it out.

I had two surgeries. The first was in August of 2016. It was a laparoscopic procedure where the doctor explained that he had taken out about a foot and a half of intestine, the lower and the upper, some lymph nodes, they had done a

little bit of work on the liver as far as taking out some tumors on that. And then, in October, same year, I had the open surgery. They took out about two-thirds of my liver. That one was the one that took out the big… the large tumor, along with a number of small tumors. So anyway, that was in October, 2016. I've been having scans since then, and so far things have been stable. There's a little growth in some tumors, a little shrinkage and others. I've been getting Lanreotide injections monthly since the surgeries. And I'm going about my life."

There are a lot of surgical options for small bowel NETs, both for localized and metastatic disease, and some of these can have really excellent long-term outcomes for patients. But surgery isn't always the right path. It really depends on the nature of your particular NET.

Lewis: *"You essentially have to ask yourself as the clinician, maybe as the patient, two essential questions: Number one, this tumor somewhere deep in the gut, is it going to cause an intestinal blockage? And number two – and these are not mutually exclusive – if that tumor is deep in the gut, is it going to bleed in that location?*

If you don't anticipate blockage and you don't perceive bleeding, you can actually leave the primary tumor where the tumor started. You can leave it alone. So it's only in,

I would say, relatively rare or at least less common circumstances that we absolutely need to find the small intestinal tumor and remove it. But that's absolutely a discussion that patients should have with a multidisciplinary team. That includes, ideally, both a surgeon and a medical oncologist because we all have different tools to bring to the literal and a figurative table."

And it's important that patients keep in mind that small-bowel surgery can also have side effects, especially to your digestion.

Halperin: *"You know, a lot of it depends on the specific anatomy. Many patients in this group will have the tumor arrive somewhere close to the terminal ilium or the end of the ilium, where there's a valve between the ilium and the cecum, which helps to sort of slow down the transit, so you can absorb more out of a food before it moves into the large bowel and on out of the body. And so a lot of folks will lose that ileocecal valve and it can take months or years for them to regain normal transit time through the GI tract, just because they've lost some of the control of the flow and they just have to reequilibrate.*

There's also, to a lesser extent, there can be issues with the gut being shorter and therefore having just not enough opportunity to absorb nutrients, although surgeons are very, very diligent about ensuring that they leave

sufficient bowel to keep its absorptive capacity, so that's usually not much of a problem."

Even when all known tumors have been removed and there has been no visible activity for years, these tumors can reappear at any time.

Vijayvergia: *"In general, these have good outcomes. Having said that, they do carry a risk of coming back, and that risk of coming back never really goes down to zero. So, you know, for example, if you have colon cancer, if you're five years out, your risk of getting cancer coming back is very similar to a normal, you know, unaffected individuals, so you go back to your PCP.*

In this disease, it never happens that, 'okay, if I'm 15 years out, now I'm safe. It's never going to come back.' We cannot say that any time. So, we typically recommend that we follow these patients for a longer period of time, maybe don't follow them very frequently because these are slow growing cancers, but we do like to follow them because if they return we can bring in surgery and other things to improve the outcome sooner."

After surgery, or when surgery isn't an option, there are some very good systemic therapies for low-grade small bowel NETs.

Halperin: *"There's a finite number of therapies that we have available for patients with mid-gut neuroendocrine tumors. The good news is that they tend to be pretty effective in clinical practice. Probably the most commonly employed would be somatostatin analogs like Octreotide or Lanreotide. Both of those have randomized data. They look like they reduce the rate of progression or death by about 65% compared to placebo for patients specifically with small bowel and mid-gut neuroendocrine tumors. There's also Everoliumus, another systemic therapy, FDA approved. It also significantly reduces the rate of progression or death for folks in this group, at least as best we can tell from the randomized data. And then, of course, there's Peptide Receptor Radionuclide Therapy, or PRRT, which for folks who have somatostatin receptors that are visualized on the tumor using somatostatin receptor imaging, this was shown to reduce the rate of progression by about 80% in a randomized trial."*

Luckily, a large majority of small bowel NETs do seem to have somatostatin receptors that make treatment with somatostatin analogues and PRRT possible.

Vijayvergia: *"Most of the small bowel neuroendocrine tumors have somatostatin receptors on them. What mainly determines sometimes is what grade it is. As you get a little more higher grade, sometimes you lose the receptors. So it's a KI67 score. And if it's between 3 and 20, those are intermediate grade. The more you move towards the 20,*

there's a higher chance of you losing the receptors. But in general, the small intestine ones tend to have somatostatin receptors on them.

Halperin: *"Beyond that, there's a group of sort of loco-regional or anatomical therapies that can be deployed specifically in certain situations. The evidence base is not as robust, but certainly in clinical practice using various liver-directed therapies or ablative therapies, or surgical and resective… resection-type therapies to clear disease for specific reasons, these are all things that are certainly done in practice, as well."*

Up until now in this episode, we've been discussing low-grade neuroendocrine tumors that arise in the areas of the small intestine called the ilium, the section at the end closest to the large intestine, and the jejunum (je-JEW-num), the middle section.

Halperin: *"We often refer offhandedly to 'small bowel neuroendocrine tumors', and what we really tend to mean in that situation is really mid-gut. We're really just thinking about ilium and jejunum."*

These represent the vast majority of small bowel neuroendocrine tumors. There are rare exceptions, though. For instance, they are very infrequent, but high-grade small bowel NETs do exist.

Vijayvergia: *"And then the entire treatment paradigm changes. Because we know that they tend to spread a lot, and we found them spread, we tend to use chemotherapy more often in those diseases than anyone else. Again, because a lot of the symptoms are anatomic, like the location of it and everything, the symptoms are not very different except the high grade tumors tend not to produce as many hormones. So the, you know, the diarrhea, the flushing, the carcinoid syndrome symptoms are not very common with that."*

Also – NETs can develop in the duodenum, the section of the small intestine closest to the stomach. These are rare, quite different from the more common NETs of the ilium and jejunum, and much less well understood.

Halperin: *"Duodenal NETs actually have a totally separate biology course and natural history. They're nowhere near as common as ilial or jejunal neuroendocrine tumors, for sure."*

Vijayvergia: *"If it's there, you know, typically the symptoms from that lead to more nausea, vomiting symptoms, not so much so abdominal pain, just because if you have a blockage there, things are not even passing through the stomach, so you tend to throw up more than it leading to pain. And in the pattern of spread to the lymph nodes, the mesenteric mass is not associated with the duodenum, but jejunal and ilial primaries are associated with it."*

Halpering: *"But there's very, very little data. It's just… it's very challenging."*

As promising as the current treatment strategies are for the low-grade, ilial and jejunal tumors that make up the vast majority of small bowel NETs, there's a lot of interesting research currently going on to make them even better.

Halperin: *"Yeah, I think there's a lot of interesting stuff that's being done right now. One area where there are a number of interesting compounds being studied, would be the area of, sort of, other somatostatin receptor targeted agents – things where they're seeking to optimize something about the delivery of treatment based on the somatostatin receptors. So whether that's changing out, say, the radionuclide – we know a number of folks in the NETRF community have been interested in Alpha-emitting Peptide Receptor Radionuclide Therapy, where you change the energy profile of the isotope, and one day we might know whether that offers patients any benefit. There are other studies looking at drugs that will just target the receptor with a different agent, so maybe switching out an agonist for an antagonist, maybe switching out radiation for something else entirely like a toxin, so there's a lot of different studies going on in that space.*

Lewis: *"You know the whole notion of PRRT, you know, peptide receptor radio nuclide therapy, that's an umbrella term. At the moment covers a very few number of approved*

treatments. In fact, the United States as of early 2023, there's only one, but I think we're going to see that particular class of treatments explode. Because PRRT is not specific to neuroendocrine tumors. It's an umbrella term, just like we say, antibiotics, that covers a host of different treatments. So I think PRRT is definitely where we're headed, both inside and outside of neuroendocrine."

Halperin: *"There still is also, I think, substantial interest in whether immunotherapy could be useful. So far, the results have been fairly disappointing. There is a drug and ongoing studies right now, actually, that sort of mixes the last group with this group, and it uses a bi-specific antibody to drag immune cells specifically to cells that express somatostatin receptors, which is just sort of a neat mix of the two ideas.*

And then there are still active investigation in the targeted therapy realm, as well. So, there's a number of targeted kinase inhibitors that are being studied mostly in the VEGF pathway, and sometimes in combination with existing agents like Everolimus or other things."

And because this is a disease that many patients manage for many years or even decades, much work is being done not just on how effectively treatments kill cancer cells, but also how they affect the quality of life of someone taking them over a long period of time, particularly when taken in combination with each other.

> Lewis: "So I think the future of oncology at large is about being more effective and less toxic. Medical oncologists like myself… I think of myself at least in the past and, and partly in present, as a blunt instrument. My most common way of treating someone is to give them a chemical that goes through their whole body and just says, okay, which cells are devi... They're dividing the fastest, and can I kill those cells? And that strategy is extremely unsatisfactory on a host of levels. So where I think the field is going, Is being very thoughtful about not just this treatment, but how does this treatment fit into a larger spectrum? And are you doing things now that are actually limiting your therapeutic options later? So to sum it all up, I think target, Therapy in every respect is where we're headed because I think that way you get more effectiveness and ideally you're more discriminating and you get less sort of off-target toxicity, if you will."

Neuroendocrine cancer is a complex disease that can be difficult to diagnose and treat, but as you heard and learned in this episode, there are many strategies that can offer promising outcomes for patients with small bowel NETs, and with continued research, prognoses will continue to get better and better.

Thanks for listening to NETWise. I'm Jessica Thomas, Director of Patient Education for the NET Research Foundation. Our Production Partner for this series is CitizenRacecar. This episode was produced by David Hoffman, who did the original

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