THE LACNETS PODCAST

With Andrew Hendifar, MD
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Transcription:

Lisa Yen:
Welcome, everyone. It's great to have you on our LACNETS podcast and welcome Dr. Hendifar. So before we get started, I thought I'd introduce our guest today. Dr. Hendifar from Cedar-Sinai Medical Center. He's someone very special to us here at LACNETS because he's been with us since the very beginning of LACNETS. He's been a close partner and colleague and involved in many of our in-person meetings and annual conferences. Dr. Hendifar is the Director of the Neuroendocrine Tumor Program at Cedars-Sinai Medical Center, and an Associate Professor of Medicine. He's very dedicated to clinical research and patient care. We're really excited to have you here with us today, Dr. Hendifar, and if you might introduce yourself a little bit and tell us how you got interested in the care of neuroendocrine tumor patients.

Dr. Andrew Hendifar:
Good afternoon, Lisa. Thanks so much for having me. Of course, LACNETS is very special to me as well. And is always a pleasure to join you and talk about neuroendocrine tumors. So my interest in neuroendocrine tumors began when I worked with Dr. Edward Wolin. He was a senior physician when I was just starting out in medical oncology at Cedars, and he was something else. For those who are lucky enough to still work with him, I know he's in New York right now, continuing his legacy, but when he was here, these were a rare disease that I hadn't seen much up in fellowship. Even though I trained at the county hospital where we saw thousands and thousands and thousands of patients, this was still a very rare disease. And really not that much formal training was available. We didn't really get more than a couple of questions on our boards. And there was no neuroendocrine tumor specialists were I trained. And so it was a whole new world in a way. And Dr. Wolin was kind enough to teach me and show me. I attended his tumor boards, where I learned things that I never knew. I started to attend the North American Neuroendocrine Tumor Society conferences, and network with other physicians who are interested in neuroendocrine tumors, and slowly gained the knowledge necessary to care for patients with this disease. And after a while, I myself have become somebody who, just through the learning about the disease, and through sheer numbers of seeing patients, fortunate enough to be able to care for them and to help them out and really contribute in a meaningful way. So it's been great. That's something I never could have predicted. I don't think anyone could ever grow up as a child and say, I'm going to be a neuroendocrine tumor specialist, right? But it's just interesting the way life works out, and very fortunate to have met Giovanni Imbesi, who introduced me to this group, and then, of course, to Lisa and Lindsey, and the whole team.

Lisa Yen:
Wow, thank you for your kind words. It's so wonderful you had such a wonderful mentor and Dr. Wolin. And it's what amazing journey, right? Going from not seeing any neuroendocrine patients to seeing many, many patients, and we're so grateful that you do. Thank you. So, Dr. Hendifar, our first questions this: I've just been diagnosed with neuroendocrine tumor, what do I need to know?

Dr. Andrew Hendifar:
So this is a very good question. It's something that for the ones a patient hears that they have a neuroendocrine tumor for the first time, I think it's quite overwhelming. It might be overwhelming for the provider, because many of the providers don't even know what to tell the patients. So I think the first thing to do is to get a pathology report that says, what the diagnosis that you have. Usually you're going to be told you have a neuroendocrine tumor based on some kind of biopsy. So that would be essential, what you need. You need that piece of paper and if it does, in fact, say that you have a neuroendocrine tumor, you should find a neuroendocrine tumor specialist somewhere in your area who can be able to understand what that report means, and help guide you in the right direction. So I think that's the most essential. You just got to get that pathology report in your hand. And that's the key to taking those first steps.

Lisa Yen:
Okay. As you know, it's very overwhelming getting that diagnosis, trying to know these things. And then, what do I need to do next?

Dr. Andrew Hendifar:
What's really important is take a deep breath. Having a neuroendocrine tumor doesn't necessarily mean you have a cancer like other cancers, it might not mean that you need chemo, it might not mean that you need other treatments. So I would try to like not jump ahead and come to too many conclusions. Just find the right team. Once you do that, you'll be able to get the appropriate staging. Staging is when you get the right pictures that shows where the cancer is. Hopefully it's just localized or if not, you know exactly what you're dealing with, you'll have that pathology report reviewed, meaning the pathologist at a center who sees neuroendocrine tumors more frequently, will request the path to be sent over which is the tissue, and they will review that tissue to make sure that you do in fact, have a neuroendocrine tumor and not another cancer, that's actually what's more likely. Something that you should always look out for too, is pathology code. Pathologists have their own language. So they'll sometimes say neuroendocrine features, or they'll say neuroendocrine tumor, or they'll say neuroendocrine carcinoma. And those three things, they're completely different meanings. And I wouldn't expect the patients to be able to read that and understand that. These are important distinctions that your provider will read through. And if they have the appropriate experience, they would understand exactly what's being suggested path report. So again, you need a path report, a neuroendocrine tumor team. Path report gets sent, pathology gets reviewed. And you go from there and get your staging. You get your opinions. Eventually, if you're in the center, you'll have a multidisciplinary discussion. Because neuroendocrine tumors there are many ways that you can approach this problem. And it's only fair that if you have a consensus opinion from many different specialists about how to proceed, and that's what you do.

Lisa Yen:
That's very insightful, Dr. Hendifar. And as you said, there's almost a whole language to it. So as patients and as allies in the community, we're trying to learn to speak NET. And it's good to know we're not alone. And it's not just one expert like you, also it's a whole multidisciplinary team. Well, one question that often comes up is what really causes NET? Particularly, did I do

anything to cause it? I as a patient? Or did stress cause it? What also makes NET tumors grow or spread? And I guess there's a lot of anxiety around "Is there something I should or shouldn't do to keep it from spreading?"

Dr. Andrew Hendifar:
These are great questions. Neuroendocrine tumors do come from so many different parts of the body. The only one that has an association with a risk factor, are those who have small cell lung cancer, and that's associated with smoking. Outside of that, most neuroendocrine tumors do not have a modifiable behavioral risk factor that you could change. Furthermore, it's hard to recommend any dietary changes, or any lifestyle changes to most of our patients, because those don't really contribute to the disease. And if you go even deeper, a lot of what we understand about most tumors, the genomic underpinnings of tumor suppressors, etc, being mutated, we don't really have that as much neuroendocrine tumors. So there's a lot of a deeper understanding that needs to be put together before we communicate exactly what a patient can do or not do. But I'd say in general, it's very clear that you don't have to necessarily change your diet. You don't necessarily have to do anything different. I do recommend that you exercise. Everybody should be exercising 150 minutes per week, especially patients who have a malignancy because that'll help give you the strength and vitality and optimal health to continue to do well. And also, it's important that you eat well. Take the opportunity, even though you might not have caused the tumor. But if you have a tumor, it's a good time to take stock of your diet. Eat whole foods as much as possible, avoid red meat, avoid tobacco, entirely limit alcohol. All those things that you always talk about doing. Maybe this is a good opportunity to to try to incorporate as much as them as you can. And also it's because of the disease, and because the treatments can really modify the way you utilize nutrients. A dietitian consult is usually very helpful. And I know dieticians come to LACNETS a lot, so you can probably click to another podcast episode about nutrition, probably more interesting than mine too about nutrition.

Lisa Yen:
Thank you so much for that reassurance. It's helpful to hear from you, as a NET expert, that there's nothing that we as patients do to cause neuroendocrine tumor. And I also really liked your holistic approach to things. Diet, exercise. And we know that you practice what you preach as an avid cyclist and someone who exercises.

Dr. Andrew Hendifar:
Yeah, I love exercising. I got into it because one of our patients who was a neuroendocrine tumor patient, is a very accomplished, open water swimmer. We live near the Pacific Ocean. So she goes and swims pretty regularly outside. And I've known her for many years. And she would tell me, I have to start swimming and I don't swim. I know how to swim, but I've never been in a high school team. So she would come and I'd see her every few months. She'd say, have you started swimming yet? I said, No, I haven't started swimming yet. And she's like, well, go here, you can start. This is where you need to be. And after months and months and months of her persistence, I did. I'm a not a good swimmer. She put me in a master swimming class, which I learned on my first day was full of people who have been swimming their whole life. So they couldn't even put me in the slow lane. They had to put me in the "you have to learn how to swim lane." My own private, little pool away from everybody else. But because of her, I found I loved swimming. So I still swim to this day. I think for two to three years now I'm swimming regularly. And I convinced some of my friends to do it. And we do triathlons together. None of us are as good of a swimmer as she is, I gotta admit, but it's definitely been fun.

Lisa Yen:
I love that story. I love to hear how you've been inspired by patients.

Dr. Andrew Hendifar:
Well, I don't know if it's inspired or told what to do. But it's something like that. But she's great. She's a great swimmer. She's always ranking really high. It's great.

Lisa Yen:
And it just goes to show that we can be thriving despite living with the disease. And that you are learning from your patients as well. So wonderful. I guess another follow up question to what causes it that often comes up is, is if this is genetic? Should I be having genetic testing? And should my family members, especially if I have kids, should they get screened or tested for NETs?

Dr. Andrew Hendifar:
That's a great question. Genetic syndromes that contribute to neuroendocrine tumors are very rare. So does that mean you should get tested or not get tested? I think it would require a conversation with your provider. I think neuroendocrine tumor specialists would know when it would be appropriate to test. If there's a constellation of findings that would be suspicious. If there was a young age. If you're told that you have a paraganglioma or you were told you have a pheochromocytoma. These are neuroendocrine tumors of different organs that are a lot more associated with genetic syndromes. So there are certain clues and certain types that you might be more concerned. If you have a thymic carcinoid. If you've had a pancreatic neuroendocrine tumor at a very young age. There's certain things that could, Zollinger Ellison syndrome, which is a gastrinoma. So there's a few things out there that could make you more suspicious for genetic syndrome. If you're suspicious, if you think or know that something's not right here, I have a family member with a neuroendocrine tumor and I keep telling my provider that thinks I don't need genetic testing, but if you're really concerned about it, everyone has a right, I think, to genetic testing. That is very simple. It's almost always covered if the appropriate guidelines are met. And if not, there are affordable ways to have it done. So I don't think it can hurt especially with the rare disease, I would say the vast majority of patients have no genetic syndrome, more than 90%. And we see patients who have syndromes and when they come seek out our care, so I think my patients are probably more enriched for people with MEN, SDH deficiencies etc. So the short answer is that no, you probably don't need it. But if you think you need it, you should get it.

Lisa Yen:
Okay, that's really helpful. And that is also reassuring to know.

Dr. Andrew Hendifar:
Then the other part of it is, do you test family members? Well, anytime you get genetic testing, you always test the person with the tumor. And then if it's negative, you end it. There's no reason to test anybody else. If it's positive, then you proceed, with the help of the genetic counselor. So there's very specific approaches and guidelines, depending on what the underlying syndrome is, these have all been worked out by very smart people. So it's just checking boxes. If you do have a certain issue, then how to take care of the family is all going to be baked in, and they'll know exactly what they need to do.

Lisa Yen:
Thank you for that. That's really helpful and very clear. Thank you for making that clear. Another question that comes up along this line of thinking of family and wanting to be around. But as you know, many people come to your office asking, how long do I have? We want to know in terms of planning and what to expect?

Dr. Andrew Hendifar:
This is a very difficult question to answer. Because it really depends on what type of neuroendocrine tumor. So what's the site of origin? It depends on what's the grade of the tumor. And then it depends on where it's metastasized to. And with those three pieces of information, the prognosis can differ a lot. We're talking about going from months to decades. So these details are really important. For the vast majority of my patients, they're going to do incredibly well compared to any other cancer. And normally I wouldn't even think that we have to discuss about that important question, how long do I have, because it's so long, where they might be just as likely to have another problem, or another cause that would cause them bigger problem. They could have bigger problems in their life, whether it's heart disease, other types of chronic illnesses, etc. There are some patients that it's important to talk to them about it. I think that the physicians would know who needs that kind of a conversation. But it never hurts if you really don't know, and you're really worried about, it never hurts to just directly ask that very question, how long do I have? And you deserve an answer, if you really want to know. They can never give an exact number. But they can say, based on statistical looks on patients and the SEER database, they can say, okay, this is where we would give a guesstimate of what to expect. But in general, I think in this disease, for most of the patients, it's going to be very difficult to get the kind of answer that you want. Because there's gonna be a lot of uncertainty. The best way to figure out the answer to that question is probably going to be a little bit of time. Give your team a little bit of time to see how things are going. And at the same time, just start to think about, what is my team telling me? What is that? And then what are my values? What do I want to accomplish? What other things are important to me? And maybe start communicating that to your team because usually when the question is "how long do I have" it's actually a very general question for something more specific that somebody is thinking about. So when my patients are specific with me, sometimes we understand each other a little bit better. Sometimes someone will say, well my child right now is six or 10 and I want to make sure I see them to high school. And I then can say, "yeah..." These are things that are very specific things, like how long do I have? They're thinking more specifically. So I think these are great conversations to have with your providers. And just to talk about it. Open up as much as you can to tell them what's really concerning you. What are your goals? What are you trying to accomplish? What do you worried about? I think that might be just as important as talking about what your scans show and everything else. Because, although you are new to this scenario, the physician, whether they like it or not, they've had the opportunity to meet thousands of people in a similar scenario. And you can maybe draw on lessons learned from that collective experience, so to speak. So I think just go ahead and get right to it and ask the direct questions that you really want to have answered. I think it's great.

Lisa Yen:
That's really insightful, Dr. Hendifar. Really opening up that conversation and it really involves the level of trust that you're building.

Dr. Andrew Hendifar:
Yeah. And sometimes, opening up, you develop the trust, right? Because if you make yourself a little bit more vulnerable then a doctor will share also. So sometimes someone has to jump in a little bit.

Lisa Yen:
Thanks for that. That's really beautiful. Kind of along that line, to segue from there, how do I know that if my tumors are growing or spreading?

Dr. Andrew Hendifar:
I mean, fortunately for neuroendocrine tumors, you don't really feel them, which is a blessing, thank God. They're not that painful. Sometimes they can be. And so for those who are having pain from them, sorry about that. My heart goes out to you. But for the most part they're painless. And there are not many great markers. Some patients, you can check the urine 5HIAA. And everyone else will be checking things like chromogranin, which isn't such a great marker. So, it's really hard to tell from the blood tests if it's growing or spreading. So what we frequently do are scans. Unfortunately, for the most part, most of the patients grow pretty slowly, so we do scan six months apart, and we compare them to the scan that was done previously, and then compare them within the context of all the scans. That's sometimes hard to do. It requires a little bit of diligence, not just comparing two scans, but a set of three, a set of four. And the radiologists who have come to know this disease, they do make a note to go back a year or two or three, four, just to kind of get an idea of what's going on and to convey that in the reports. So that's how we usually know. If pictures like MRIs and CTs shows that tumors are growing or something's changed, we typically order what we call functional testing. And for our disease, that's somatostatin scintography. And normally, it's a Gallium-68. There are variations of that. You'll hear different name brands. You hear copper scans. You can do those as well. But basically, they all show the uptake of the somatostatin receptor. And there are what we call PET scans. And these PET scans, specific for neuroendocrine tumors, show us a lot. Is this tumor spreading in just one or two places? Is it moving from one organ to another? What exactly is happening? How many? What is the extent of the involvement? So those are the things that we use; those are our tools that we have to get an idea if the tumors are really changing in a significant way. For the most part, and I explain this to my patients, all neuroendocrine tumors grow. And no matter what we do, they're going to grow. We just want them to grow incredibly slowly, right? Because there's no way to get the tumor if it's not growing from something. So the expectation that they'll never grow and just freeze completely, is not what we expect. Not only they grow slowly, but with the therapies that we have, what can make them to grow even more slowly, to the point where there's no they won't cause a problem. So that's one thing that's hard to explain. So somebody might say, well my tumor has grown one millimeter in a year. I'm like ready to do high five and jump up and down the clinic. I'm really excited and happy. And the patient looks at me, like what is wrong with you? It's grown a millimeter. I'm like one millimeter, it's nothing! And then we have this camera, and then I say, well, one millimeter a year, we'll take that right? Because in 10 years, that's one centimeter and that's not that big. And so, this is something that yet we have to incorporate. And what is stable mean, right? When you say does my tumor grow, your doctor will say it's stable, and you'll say well it's growing and the doctor says it's stable, and you're not talking the same language. So, again, all tumors typically grow. But when they grow a certain extent, then we say it's changed. And I wouldn't say it's very important for neuroendocrine tumors, but your provider might not be a neuroendocrine tumor person, might be a specialist. So they might use this language called response, stable, partial response. This is a language that oncologists use, where growth means very specifically 30% increase in unidimensional size of a number of lesions. So there's a very specific criteria. What basically means 30% growth. So what does that mean for you, when you tell your physician it grows? And he says that it's stable? Well, you could grow but still be stable, so you could still grow a little bit but still not reached the threshold to be considered progression or growth. So sometimes the language barrier you have to get over and talk to your doctor a little bit and say, okay, what does this mean? I think the most important thing to ask, do you need to change your treatment? I think that's the main question. So that's your litmus test for okay, things are significantly different. If your doctors saying, well, there's a little bit of change and everything is great. That means that's great. That's what you want. If the doctor says there's some change, but we need to change your treatment, then that's your cue for this is something significant. If the doctor says, well, I want to present your case at the tumor board. I'm going to order imaging. That probably is a sign that there's enough growth here to warrant some further investigation. So I think those are the

levels. But if your doctor is telling you, yes, there is growth, but everything is good. That usually means that you know, everything is okay, and a little bit of growth to be expected.

Lisa Yen:
That's really helpful how be clarified all of that. And also, you started going into what I was gonna ask next about follow up labs and imaging or scans. To clarify, because we talked about tumor markers and Chromogranin A, what labs do I need to get and how often?

Dr. Andrew Hendifar:
That's great question. I think a lot about this because we often order a lot of tests, and everybody gets kind of upset and sometimes thrown off. So let's talk about this. So this is the thing with tumor markers, they're very specific to the type of cancer that you have in neuroendocrine tumors. So some markers work for some patients, some markers don't work for other patients. So let's talk about midgut neuroendocrine tumors. I think a 24-hour urine for 5HIAA is really the gold standard tumor marker. Not everybody is going to have it, it's not going to be high for everybody. But if it is, it's very useful, reproducible, and gives your physician some kind of information they can use to understand not only what's going on today, but what might need to be done in the future. Chromogranin is a general marker for neuroendocrine tumors that's nonspecific, which means that it can go up for many number of reasons. For example, when you check the chromogranin, in regards to when you eat, can make a big change in it. So it should always be done when you're fasting. So don't forget chromogranin should be done fasting. And if you're on a proton pump inhibitor or other medications, you can also significantly change your results. So that's another issue. And then the other thing is like, what does a changing chromogranin really mean? Again, a little bit of a slow increase in your chromogranin wouldn't be concerning to me. Big changes in your chromogranin that are unexplainable might warrant additional testing like scans. I think for the most part, I would make sure that the conditions that you used, meaning you were fasting both times, meaning that you're on the same medications both times or off the PPIs, and off those medications that can alter it. And also labs. Sometimes you check a chromogranin, lab A, lab B's using a different assay. You're going to be getting two completely different results and it's the same result. It's the same number, right? It's just two different labs have different ways of computing it so you have to be a little bit careful about that, too.

Lisa Yen:
That's helpful. I'm sure you get this question very often. What does it mean that my Chromogranin A is all of a sudden very high?

Dr. Andrew Hendifar:
Right? Happens all the time.

Lisa Yen:
And it doesn't seem like it would necessarily worry you.

Dr. Andrew Hendifar:
I think it warrants a discussion. It warrants an exploration. It happens to us at least once a week where we have a conversation about an elevated chromogranin and what it means. So it definitely happens, it's definitely important to our patients to understand it, and just gotta go through the steps of understanding what are the limitations of the test? What can the test really tell us? How can it help us? At the same time, we don't want it to derail us either or make us make decisions that aren't helpful. So put it within the context of what it means. It's important.

Lisa Yen:
Right. Look at the whole person. And you were also talking about scans and thank you for talking about CT and MRI and then also the functional imaging with DOTATATE somatostatin receptor imaging scans. So to follow up on that, what scans do I need to get and how often? And another point of clarification, should I be getting a CT or MRI scan? And what's the difference?

Dr. Andrew Hendifar:
Let's just talk about basic principles. If you have a low grade tumor, you need pictures less often than if you have a high grade tumor. CT and MRI are we call cross sectional imaging. Usually they're in interchangeable, although MRIs have a very good fidelity for liver, and oftentimes are used for patients with liver disease that are being monitored, because it's very reproducible. CT scans and the way they show the liver lesions are very dependent on the timing of the contrast provided. So to try to explain this to you, when you get a CT scan, they inject IV contrast in you. And then based on the timing of how many seconds it takes after the injection, to when you go through the scan, is when the contrast will be in your liver. So there's certain ways to time it. But that timing is very variable from scan to scan. And it can really dramatically change the way your neuroendocrine tumors appear to the radiologist versus a real change in the tumors themselves. MRIs, because of the technology used, is not based on these types of issues. So it's a much more reproducible test. So if you're using liver lesions as your index, or using liver tumors as your index lesions, a lot of times we use MRIs just because they're very reproducible, very easy to compare, every six months or so. And neuroendocrine tumors because of their vascularity, they just really stick out nicely in an MRI. You can see even the smallest little lesions, which is kind of reassuring to surgeons who are thinking about surgery. To your cancer doctors, it feels very comforting to have that much clarity into the organ itself. It's really great. And then so how often? More often if you have a high grade tumor, and less often, if you have a low grade tumor. And then what kind of scans? So you always need a Gallium-68 or what's called functional imaging PET scan. These are all terms that are synonymous with each other. Somatostatin receptor scan. You need that definitely at diagnosis, and you need it whenever there's a change in your scans. Now often otherwise, you need it in other circumstances, it's very hard to give anyone some kind of definite answer. It really would depend on what the scenario is. Generally speaking, you can't get them more than once a year. But you can if you need to do these for PRRT or peptide receptor radiotherapy. So again, you definitely should get one a diagnosis. Definitely should get one when your tumors have changed. Definitely before a major surgery. Those are key points in the journey when you want the high power test.

Lisa Yen:
That's very helpful. I really liked the way that you explained things in a way that's easy to understand. Talking about all these terms and everything, I know that you talked about how important it is to know things like the primary site and the grade and where it's metastasized. Another term that comes up a lot is if the tumors are functional or non functional. How do I know if the tumors are functional or non functional?

Dr. Andrew Hendifar:
That's a great question. And you know what's so funny is that functional versus non functional can actually mean different things to different people. I think it's good to define different types of functional. So when I'm saying functional, it means that you have a syndrome attached to your tumor. Syndromes that are attached to tumors occur based on the site. So if you have a midgut tumor, the most common functional syndrome is carcinoid syndrome, and it doesn't occur in all patients. And not all patients whose tumors secrete serotonin will have symptoms. So it's a very nuanced and complex situation. So how do you tell? Basically, you need to see if you have a midgut tumor, you want to know if you're flushing or have diarrhea. And you want to

check the urine 24-hour test. And between those tests, you'll probably get a good idea whether or not your tumor is making serotonin, and what needs to be done about it. In any of our patients that have carcinoid syndrome, we are much more likely to use somatostatin analog therapy, much more likely to do surveillance of the cardiac heart valves. It's definitely important to determine and to treat accordingly. Same goes for pancreatic neuroendocrine tumors which also have a number of syndromes. Now, a lot of times if you have just a tumor in the pancreas and nowhere else, and you're going to go get surgery, it might not be crucial, but I still recommend it. Every pancreatic neuroendocrine tumor should be tested for all the functional tests just to make sure. Because sometimes you can have a functional tumor, but you just don't notice the symptoms. And it could become important down the road. And so there are a number of syndromes and things that we test for. I'll try to go in order of most likely. So serum gastrin is important to check to make sure you don't have a gastrinoma. The hormone gastrin the tumors can produce can cause diarrhea, interestingly. It doesn't really cause flushing and it doesn't cause stomach ulcers. It's very important to check it and the treatments a little bit different for gastrinomas because we use proton pump inhibitors a lot in the treatment of those tumors. Others serum hormones to check include insulin and proinsulin. So a lot of times these tumors can secrete these hormones that cause your blood sugar to go down. But sometimes, the blood sugar doesn't go down, but they're secreting it. So it's important to know about it and to keep in the back of your mind in case you need it for later, especially for post surgical surveillance. And then there's tumors called glucagonomas that secrete the tumor glucagon. Those are important to also consider. There's some tumors that secrete a hormone called VIP, which is really rare. But it's also important to consider. And then there are other somatostatin producing tumors. We're getting even rarer. There's ghrelin producing tumors, even rarer. You can go down the rabbit hole of really rare ones but I don't think we need to do that. But the point being that these are the things that we need to know about at diagnosis. If you do have a functional tumor, usually, it means that we do have a good hormone that we can use to also determine how you're doing with your treatment. We have a measure of your disease. And it's also important to know that if you have functional tumor, the biology of your disease is somewhat different and the approach that we would take is somewhat different than if you don't have a syndrome. So when a patient has a functional tumor that's causing a syndrome, we take that into account. We use the syndrome as our scan. So we sometimes say to you, okay, how many times did you flush today? How many bowel movements are you having over the last few days, over the last few weeks? If someone has an insulinoma, they'll always keep a glucose diary and they'll be able to say, okay, for the last month, this is what your blood sugar's have been. So you can get real world, real time feedback on what's happening with the disease instead of waiting for scans every so often. And so it's important. And also these syndromes, most neuroendocrine tumors are silent. And if you have a syndrome, they actually can be quite pesky. They can cause issues that you have to deal with. Not the worst in the world but definitely something that would decrease your quality of life. Maybe limit your ability to enjoy activities with your family and friends, to leave the house, to work and be productive. These are things that are really important to address, and actually different than non functional tumors. So it's actually quite different, although they have a lot in common. They're really significant differences between them. So I would say for patients whose disease is localized, however, the differences is quite small. But for patients who have metastatic disease, identifying these syndromes and treating them appropriately are really important.

Lisa Yen:
That's really helpful. And before we get to the last question, if you don't mind going back and clarifying another term. When we're talking about how long do I have you said, primary site matters, the grade and where it metastasized. So would you go back and clarify grade, and also the primary site? Especially after someone has the primary site removed, do you still go by that site where it originated? Or do you call it now, for example, if it's only in the liver, would you just call it liver NETs?

Dr. Andrew Hendifar:
So the name of your NET always goes by the site where it started, especially when you're talking prognosis because it gives you a better idea of what's going to happen. So what does grade mean? Grade is a way that pathologists are communicating to us how aggressive or what the growth rate of the tumor is going to be. So do we use grade 1, 2, and 3? The easiest way to remember this is just based on the Ki-67. People are grouped into these three grades. Grade 1 is low grade, grade 2 is intermediate grade, and grade 3 is considered high grade. But the Ki-67 goes from 0 to 100. Now that's one way to categorize tumors. Another way is by differentiation, which is well differentiated and poor differentiated. Well differentiated is usually low grade and poorly differentiated is usually high grade. Now, what does that all mean as far as your prognosis? Well, we understand a lot more about the disease and what to expect based on the site of origin and those different features. Once we have those pieces of information, we really know a lot. For example, if I know that you have a rectal neuroendocrine tumor arising out of a polyp that's low grade and small in size that was removed by a polypectomy on an endoscopy, I'll know a lot about your prognosis, which is actually going to be quite excellent, and your ability for these things to metastasize is quite low. And we know that not only from personal experience, but based on looking at huge databases, such as the SEER database. And similar conclusions can be made based on whether or not what type of lung carcinoid you have, or pancreatic, etc. Based on the size, the grade, we can give you prognostic information that can be helpful.

Lisa Yen:
This is all very helpful and helps us to understand what we as patients or loved ones/allies need to know going into an appointment with you, or another NET expert. The last question I have for you is how can we as patients or caregivers / loved ones help you, as our NET oncologist, make the appointment go better, or help you do your job better?

Dr. Andrew Hendifar:
I think the NET community has been very supportive and helpful, and patient with all the providers. They're going through a difficult and rare diagnosis and dealing with a lot of people who don't know that much on how to help them. I do think one way to really help this process along is to connect with LACNETS. It's a lot easier when the time of the appointment can be supported by a lot of background information. So you can be caught up to speed on all the different questions you might have. If you have a certain amount of knowledge about your disease, then your appointments with your doctors can be done much more efficiently. And LACNETS has funded a number of resources to really help you be prepared and knowledgeable so that when you go into your appointments and go into meet with your providers, you know exactly what you need to get out of those appointments and information that you need back. And I think that would be something that would be helpful for the patients themselves. Sometimes I feel bad for them. I feel like they really want to ask a, b and c but they're confused about some other things. And so they can never get all the things they want to talk about that are really important to them. Or sometimes they'll get confused and be sidetracked. I find my most knowledgeable patients are the ones who are happiest with the business because they really pin me down and say, okay, I know this and that, and I want you to tell me this. This is what I really need to know about. I think the more educated you are as a patient, the more satisfied you're going to be with the care that you receive. Go to the LACNETS website (www.LACNETS.org). Download and fill out NET Vitals (www.LACNETS.org/netvitals).

Lisa Yen:
How does the NET Vitals help you? Some patients will say, hey, I filled it out and my doctor didn't look at it. So how does it help you if a patient fills it out?

Dr. Andrew Hendifar:
It helps make sure that we have all the information needed. This is like the information that's like passport info that's necessary to travel around. And to communicate your case to anyone at any time. So I think this type of information is crucial. NET Providers all speak a similar language. So that's the language that we need to really understand how to triage patients with the best care plans possible. So always fill that out. Don't worry if you're one provider might not [look at it], the other one might. But there's support staff for sure using it, your intake staff. People are putting together these charts and know information need to be communicated [and] are definitely taken into account.

Lisa Yen:
That's all very helpful. Thank you so much, Dr. Hendifar. You're very, very insightful. We also really appreciate your dedication and hard work for the whole community. Thank you so much. It's been a fun conversation, and we hope to talk to you again.

Dr. Andrew Hendifar:
Thanks for having me, Lisa. Always a pleasure to talk to you.

Lisa Yen:
Thank you so much. Take care.