



EPISODE 55: Neuroendocrine Cancer Treatment Sequencing & Strategy
Dr. Chandrikha Chandrasekharan

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 today, we're joined by Dr Chandrika Chandrasekharan, a gastrointestinal medical oncologist at the MD Anderson Cancer Center in Houston, where she focuses on neuroendocrine tumors and pancreatic cancer. She is board certified in both medical oncology and palliative medicine, and she has advanced training in GI cancers, with a particular expertise in neuroendocrine cancers. Dr Chandrasekharan is also a national leader in the neuroendocrine cancer field through NANETS, where she chairs the Continuing Education Committee and Women in Neuroendocrine Tumors Special Interest Group. She has been a longtime friend of the Neuroendocrine Cancer Foundation, formerly known as LACNETS, and a frequent speaker in our community, including her in depth 2024 conference presentation "Understanding NET diagnosis." And if you haven't listened to that before, I encourage you to check it out. We're grateful to have her with us today to help break down treatment sequencing and strategies, how clinicians think about choosing and timing therapies and what patients should know as they navigate their options. I know this is a big topic, and we will do the best we can to try to break it down in broad principles and in a way that helps people

understand this topic. So one fun fact before we dive in is Dr Chandrasekharan, her dream would be to retire and open a dog boarding facility. So welcome Dr Chandrasekharan. If you don't mind sharing a bit about how you got involved in this field of neuroendocrine cancer.

Dr. Chandrikha Chandrasekharan 02:00

Thank you, Lisa. It's always great to be part of any activity that Neuroendocrine Cancer Foundation does, and always welcome the opportunity to help the neuroendocrine larger community as much as possible. So yeah, I've been in MD Anderson about a year previously I was about seven, eight years on faculty at the University of Iowa and other large neuroendocrine center. And I had no idea about neuroendocrine tumors, honestly, not pretty much throughout even that medical oncology training. And then when I went to Mayo Clinic for my advanced GI fellowship, I definitely saw a lot more patients of this rare tumor. And it was very intriguing, and got me really fascinated about this, and that's kind of where it started. And it's a field that keeps giving a lot of satisfaction to me.

Lisa Yen 02:38

And you've given back a lot to this field already, and we really appreciate all you've done in your publications and your leadership, in your clinical work, and all of your thought in this field. So, as you know, and as we've discussed, treatment sequencing is one of the most common topics we hear about in our community. Patients and caregivers, they often tell us that they feel unsure about the order of treatments, how decisions are made, and also what it means to save options for the future. In our weekly support groups and through the emails we receive, people consistently ask, "What should come first, what comes next, and how do I know if I'm on the right path?" So that's why we're going to take the time today to break this down in a clear and practical way. So, if you're ready to get started, I'll start with the first question.

Dr. Chandrikha Chandrasekharan 03:23

Yes. So definitely a hard topic to tackle, and without any clear data and guidelines, something that's still based on practice, patient preference and kind of the what's ongoing at that time. So happy to see how we can slice and dice and get down to more practical approach as possible.

Lisa Yen 03:40

Thank you for that. One general concept that I think would be helpful to tackle first: Is neuroendocrine cancer ever benign, and what does that mean in the context of neuroendocrine tumors?

Dr. Chandrikha Chandrasekharan 03:51

This is one thing I try to explain with every visit with a patient that it IS a cancer. Unfortunately, there are still medical codes that use the word "benign carcinoid," which we are trying to actively discourage. We also trying to go away from the term carcinoid. The word carcinoid actually comes from the word "carcinoma like." Going back to 100 plus years ago, one of the pathologists looked at this under the microscope in autopsies and was like, "kind of looks like a cancer, but not like a cancer, because it's kind of indolent." And so, the term "carcinoma-like" started then, but it kind of stuck. In fact, even as late as the 70s and 80s, as we didn't know a lot about this cancer, there was the classification based on if it's

localized, it's not a cancer, but if it is more spread or advanced or another organ, it is a cancer. But then slowly the realization clearly was there that what is localized is what actually become a spread. So ultimately, any cancer, neuroendocrine tumor, has a potential for a spread, potential for getting to another organ, even if at this moment it is localized. What's different from other cancers is that, if it is a slow growing type or the low-grade type, it may take a long time or it may never. But it is a cancer. So there is nothing benign about this, and we should shy away from explaining to the patient, "Don't worry about it. It's a benign thing." It is not. It's just different from other cancers.

Lisa Yen 05:09

Clearly different from other cancers. The other term that comes up often is that word “**cure**”. So can neuroendocrine cancer ever be cured?

Dr. Chandrikha Chandrasekharan 05:17

Yeah, if it's localized to the organ where it starts. So, for example, if it's a small bowel origin neuroendocrine tumor, which may present oftentimes with a lymph node, what we refer to technically the medical word is **mesenteric lymph node**. This is referring to some lymph nodes that are inside your abdomen cavity, and it's kind of like the first step it may spread to, and that's still within what we expect those cancer to do in a localized stage. So if that's all that person has, and they're able to have this found in this stage, early stage. Then a surgery is indeed with an intention to cure and get rid of it, for it to never come back. Now, just like any other cancer, when we talk about cure, the cure rates are different, and it can be very different between person to person. But technically, if this cancer is localized to the organ of origin and to the regional areas, and if a surgery or something is definitive, meaning it's done to cure. Similar example with pancreas, if it is found only confined to the pancreas, and maybe it can be removed by surgery because it's a good size, not involving blood vessels, and resectable, that person is undergoing that surgery with an intention of this cancer hopefully never coming back. But with the word hopefully, because there's, unfortunately, there's a chance that for any of the cancer that there's a recurrence risk or spread risk.

Lisa Yen 06:34

So if I'm hearing you correctly, if the cancer is localized, it can be cured and benign, is not appropriate term to use, because it does have a chance of spreading, so it should be considered cancer.

Dr. Chandrikha Chandrasekharan 06:47

Yeah. So even in those patients who had what we consider as a **curative resection**, like a removal by surgery with an intention for cure, they also need **surveillance**. In fact, patients with neuroendocrine tumor need long term surveillance. A person with a colon cancer, for example, we normally follow them after surgery for up to five years, and because the risk of recurrence is the highest in the first three years, then it goes down. Kind of opposite with the neuroendocrine tumor is because they're slow growing, the risk of it coming back is not right away, typically, especially for a small bowel. And so even if they undergo surgery, it is a cancer, not a benign thing. It needs surveillance, just like any other cancer and in fact, **longer term surveillance**.

Lisa Yen 07:26

Yeah, and that leads into my next question. I mean, many people are told that their tumors are **slow growing** or maybe even **indolent**. So how should patients understand tumor behavior, and what does that even mean, if they've been told that theirs is slow growing or indolent?

Dr. Chandrikha Chandrasekharan 07:41

That's a great question, because I use the word sometimes also, "oh it's slow growing." And then there are some people who ask and like, what does that mean? Like, what does slow mean? Because slow and fast is relative terms. Slow can be sometimes monthly, weekly, yearly. What are we talking about? So it's kind of hard to describe that or quantify that. I think the slow word comes maybe because we compare neuroendocrine tumors, again, to other cancers like pancreas cancer or colon cancer. But an individual person is the tumor growing slow or fast or slower or faster than we expect is going to really depend on many factors.

One of the first clues we get is the **grade** or the biopsy specimen from the tissue that we get. So at this moment, if you just had one single factor to predict what the cancer may do or how it may grow, I think we rely a lot on the grade. But there are definitely caveats to understanding what does grade mean. So grade, for people who don't know what grade is, it is **different from stage of a cancer. Grade is the term we use for the description of how the cells are dividing or proliferating under the microscope**. So pathologist, when they get a specimen from your liver or some other tissue, they look under the microscope, they spot the cancer areas, and then they zoom in basically on the ugly areas, let's say, of the cancer specifically and then they use various dyes. We, specifically, one we use called **Ki-67** and this is a marker. Wherever the ki-67 goes, those cells are actively dividing or proliferating, so they can quantify that. And based on that ki-67 so there are 100 cells that are there and only say two or three cells are dividing or taking up this dye, we call it 3% or lesser. So that's a very slow growing indolent grade one. Anything that's in the three to 20%, so let's say about 100 cells, but 17 of them are dividing or 10 of them are dividing. That's a grade two, technically, it's a grade 2 neuroendocrine tumor. So this is one of the first clues we have to predict the behavior of the cancer and get a sense of how it may grow. But that's not the only thing, and it's also not an absolute number. So, what if the ki 67 is 21% that's literally on the spectrum of this grading, grade three tumor. But how different is it from a 19%? So we got to understand there's always limitations to this. But this is one of the good tools we have. There is, in fact, some data that 10% and lesser are the better kind with better survival. And 10 to and above, a bit faster. This is not an absolute, just so we know. So that's one of the things.

The other things we have sometimes is, I'm sure people who are listening in have had, oh, I had a scan like five years ago. Somebody said something was vaguely seen there, but never really followed up. So if you have that kind of a history, and we have those images, yeah, the fact that it took four or five years before it grew to what it is today, that also tells us how it's growing.

And then the clinical symptoms. So these are all put together to assess what we call the grade or the medical word, sometimes we say **biology** of the tumor.

So when it's grade one, and we have some data points that it is slow growing based on the symptoms, or sometimes based on some other scans we have, it's reassuring. Going to tell the patient, listen, maybe you've had this for four years, because look, there's a scan. I can look back and tell you it was maybe there, maybe it's more today, but it was there, and that's taken four plus years. So that's one way to tell them it's slow growing. But sometimes, when you just have one scan, one point of information today, then we look at the ki-67 or the grade of the tumor, to say, "Listen, it's grade one, which is supposed to be extremely slow growing," which, again, if it's a small bowel neuroendocrine sometimes it can be growth over years. Now, if it's a pancreatic neuroendocrine tumor that is a little bit faster growing, then yes, growth may happen a little bit sooner than a small bowel origin. So again, the site of origin of the tissue, the grade, the history, the clinical symptoms, all this help us predict. If this was a pancreas cancer, meaning an adenocarcinoma, the other kind, not the neuroendocrine, when we say it's slow, we're comparing maybe to something like a pancreas cancer, where, if it is an advanced cancer or pancreas, we're talking about growth, weekly, monthly, kind of deal. So, it's a relative term in an individual person. It's something we learn with the tumor, we learn with the person, we learn with the scan eventually.

Lisa Yen 11:49

Thank you for putting that into context. How slow is relative, and then also defining what the big picture is. That's other term we hear, right, big picture. So you're saying grade, scans over tests of time, clinical symptoms, the whole big picture. And how grade is different from stage, right? You mentioned localized and spread, but the grade is how the tumor is behaving.

Dr. Chandrikha Chandrasekharan 12:10

We have to put everything in the context, yes. Having said that, there are people who present with a lot more at the time of diagnosis in terms of the volume of cancer. So unfortunately, in that person, I'm going to be a little bit more worried about that person, just because they have a lot now, no matter when it started. So it's probably is still slow growing, but now that they do have so much organ involvement, let's say of the liver or something, we got to be watching them a little bit more often.

Lisa Yen 12:37

Thanks for adding that. It's not just about the tumor behavior, but it's also tumor volume, how much tumor they have that matters. I'm also going to refer the listeners back to your wonderful presentation from the 2024 Annual Conference, "Understanding NET diagnosis." So if people want to look at Dr Chandrasekharan's slides and pictures of what ki 67 looks like under the microscope and how you break that down, that you do such a wonderful job explaining all this and going into much detail. So thank you for that reference, and we'll have that on the podcast landing page as well.

So now that we defined all these basic terms, I think going into a little bit more of the meat of sequencing questions. What is the real goal of treatment?

Dr. Chandrikha Chandrasekharan 13:18

I think this is the question we have to first ask. What is the goal for the patient starts first? What is the goal for the clinician? What is the goal for that time? And just to be clear, the goal of therapy can change, where when you start with the diagnosis versus when you have had the diagnosis over the years. And that's totally normal. I want the people hearing to know that it's okay to shift your goal post in the journey. If the cancer is advanced, meaning at the time of presentation, has spread to another organ, like the liver, the lung or the bone, no matter where it started, unfortunately, by definition, it's not curable. Now, are there people who have low volume of cancer, and we can do such a good job with whatever we have to kind of render them visibly without cancer on a scan for some time? Yes. A lot of people ask can they go into remission? I kind of answer that question a bit more philosophically, if at this time, the least is equal to remission. You can call whatever you want to call yourself at that time, right? There is no absolute definition for these terms, in my opinion.

So, the goal depends on what the patient desires in the context of the cancer and how it affects them. It depends also on what's going on clinically with the person. For example, if it is, say, a person presenting with very symptomatic weight loss and a liver full of tumor that is significant, even if the grade of the tumor shows this to be a grade two or a grade one slow growing tumor, which means they've got here to this situation over time. In that person, the goal for me as clinician first is to make them feel better. The person's goal may be to get rid of it, which, unfortunately, I have to explain that it's not feasible. But my goal for them is to make them feel better. So, I would reach in the treatment sequencing toolbox for a tool that has a higher chance of response or shrinkage, not just control. So, in that situation, to get an example of pancreatic neuroendocrine tumor, there are many treatment options. All of them are technically correct. You have data to say yes to all of them. But what are the two tools I may reach in that situation for that person is probably either the **chemotherapy called capecitabine temozolomide**, which in a pancreatic neuroendocrine tumor can have very good shrinkage, it to 30 to 40% of the patients. Again, to clarify 30 to 40% mean 100 people I give it to, 30 or 40 will have shrinkage. It's not 30-40% of the tumor. The number of people. So that's a good treatment option in that person. Or **PRRT**. Usually, though, yes, we say, "Oh, we can do it later, our upfront." Right now, we have FDA approval, so we can use it as we see fit. So, in that person, that could also be a very good choice, because if they have their octreotide receptors to target, they can have very good shrinkage with PRRT. If that person is so symptomatic, I may not reach out in the sequence to the lanreotide or octreotide as the only option first, because it's good for controlling the cancer, but that is not going to relieve this person of the discomfort that they are having. So definitely, symptoms is one of the factors to decide on this treatment sequence, and what the patient wants is obviously very important.

Lisa Yen 16:21

Thank you for speaking to that, that it's a shared decision that takes a conversation and planning and collaboration between the two people involved. I think that it's really difficult when someone's newly diagnosed. And I can say this personally, because I remember when my husband was diagnosed, and people come to us all the time, whether you have one localized tumor, just in one organ, or it's spread, I think that there's this feeling like there's a ticking time bomb in you, and you want it all out. I just want to get rid of it all. So, can you speak to that fear, and how can people wrap their heads around this? You're talking about shrinkage, but then it sounds like it might not all go away. So how do you weigh in

all of this? The feeling of, "Oh, there's a sticking time bomb. I want to get rid of it," and how treatment goals are set.

Dr. Chandrikha Chandrasekharan 17:06

I can't speak for what goes through the patient or the caregiver's mind. So all I can say is, I think we need to hear, as clinicians, what's going on in their mind. And that's the first fear. Like anybody hears the word cancer, it doesn't matter, actually, which type of cancer. First of all, we don't want it in your body, number one. So we want to get rid of it and that's the first instinct. I don't think there's any easy way to get out of the thought process to come from there to "what do we do." As a clinician, my job there is a **gatekeeper**, I would say, because sometimes the fear can drive to bad decisions or what turns out to be bad decisions. I'll put it that way, right in the moment, it feels like the best idea to do this and that. And the data we have suggest in, not just in this cancer, actually many cancers that **more is always not necessarily better**. This is a general statement, but I'm not saying specific neuroendocrine cancer. More is definitely more toxicity, and toxicity has consequences, both physical, financial, all kinds of stuff. So I think that moment of diagnosis comes with the fear and that has to be navigated. I think we do a poor job as clinicians, maybe sometimes may be dismissive, which is not correct. And I think everybody is including myself. I'm sure I'm guilty of that in the clinic, but I think the intention should be, at that moment for me as a clinician, to stop somebody from doing what could be harmful, because when you talk about treatment sequencing, that's important.

So for example, this is, you know, a very common thing I get to hear in clinic. You know, everybody probably here knows about histotripsy, which is one of the liver-directed treatments that is available now in many places. So a lot of questions come for newly diagnosed patients with extensive liver disease, like, oh, I want histotripsy. I have heard that's the magic thing. Or I want this. I want that. And I think we have to explain the context of what's going on. It's a good tool. It's a good tool to have in the armamentarium of treatments. But in the context of what's going on today for you may not be the best thing. We don't have data. We don't have data that it will help all the other tumors you cannot target with this treatment. Histotripsy's very liver-directed at this time, and it's going with some ultrasound waves of specific kind to shake up the tumor, to kind of cause tumor death in the liver. Now, it's great technique, for sure, if you can reach and see the tumor in a good space, but if you have 80% of your liver full of tumor, that's definitely not the best option. And somebody going for it, I would probably try my best not to go for it at that plan, because there could be better options than that person that would actually help them in that time.

So, I think that there's no good shortcut for the fear. I think we the clinicians have to help the patients navigate. And I think the patient, once the fear is there, pause, take a moment and look at what this means, not just today, but for years from now, hopefully when we're talking about this. And listen and ask questions to the doctor about the treatment options. Ask clearly what the treatment could leave in terms of the tumor, like, what does it mean for the tumor and what does it mean for toxicity? So if an option is proposed, I think it's very reasonable to ask, what are the other options? So that's one thing I encourage the patients to ask, okay, is this my only option, what about the other options? If another option is presented, it's also good to ask, from the physicians perspective, the pros and the cons of one

approach or the other. So, what if I go with this option, what are my side effects? How would life look like? What can I expect the tumor to do? And when you talk about side effects, ask what's temporary versus permanent, potentially. So those are all the questions to ask the physician to make these decisions. First few visits can be very long for both the patient and the clinician, but it's very crucial to help set a path.

Lisa Yen 20:41

Thank you for acknowledging that. Part of it is wrapping our heads around what's going on inside of us and fears and just acknowledging what's going on and then also understanding this disease and how it's different from other cancers. So thankfully, at least with neuroendocrine tumors, there is time to take that pause that you mentioned, to slow down and hopefully to make a wise decision that does no harm. I think that that's the goal. Or at least, do as least harm as possible.

I love the questions that you added too: What are the other options and what are side effects? And we'll dive into that. You were starting to get into this in terms of talking about what percentage this treatments like CAPTEM or Lutathera would work, and that's really a key question for patients, which treatment works the best, quote, unquote, the best. And how do we even define best when it comes to neuroendocrine cancer?

Dr. Chandrikha Chandrasekharan 21:32

Yeah, no. I think these are all very common questions that are asked in clinic, and I'm glad to give my take. I think you could do math. What does best mean to you? To the patient? Most patients, the answer will be like, I wish it to be gone, right? That's the best answer. Unfortunately, that's not possible. And then look at the limitations of the drugs versus the success of the drugs we have, or drugs versus treatment options. Let's put it that way. So again, the best is very much defined in the context of the patient, the cancer, the grade, the site and how it affects them. The best in many situations, I tell the patient is, maybe it's low volume, let's do nothing. And that's sometimes hard. The best is when the cancer will say, incidentally found, and you have two spots on the liver. Yes, it's cancer, but sometimes we don't even tell those people to be on **octreotide therapies**, because it is an option still for you in the future, even if we don't do anything to this tumor. I mean, it will grow, but it's going to likely grow at such a small volume or slow rate that you could get by for some more time without treatment and the side effects from the treatments. Yes, octreotide is well tolerated, but all the people that have been on it know it definitely a pain in the you know where you get the shot, and also the side effects of high blood sugars and things that you have to navigate and then the back and forth of going to a cancer center to get this monthly. So, in that context, maybe it is okay to wait, and that is the best treatment for that person. And it may take a little time to understand or accept that. But like I said, the other example of a person, the best treatment, when someone is coming in symptomatic, is not observation, is not an injection that is just going to keep things steady.

So, if you look at the response rate of all the drugs we have, remember the cancer itself, again, majority of the times, it's a slow growing type of cancer. And so the drugs we have at this time, unlike the traditional chemotherapy in other cancers, which chemotherapy typically attacks the growing cells of

the dividing cells in many different ways. And then in a neuroendocrine tumor, that's not necessarily the primary pool of cancer cells. There are only few cells that are actually dividing at a time. There are other complex signals that trigger the growth that we attack. So for example, everolimus a drug that to attack for signaling pathway called **mTOR**. So it's not really attacking directly the dividing cells that the chemo does, but it's attacking a signal that feeds the cancer growth in a different way, and the same thing with **cabozantinib or sunitinib**, some other drug. The result of these treatment, if you look at, is oftentimes stability. It makes the tumor grow slower and stable for much longer. And very few of these treatments, the **targeted treatment**, as we call them, actually produce shrinkage to a great degree. But it's a great goal and still, in the cancer situation, if it's growing, putting a brake on the cancer that's growing is a very important tool. And so it doesn't have to always shrink, and that's what I have to tell patients. And in fact, even when **PRRT** happens, all the cartoons of PRRT show this gigantic tumor just kind of melting away, or something, which actually doesn't always happen. In fact, the slower the tumor is growing, like a small bowel grade one tumor, the response rate, meaning the shrinkage, is actually lesser. What you get as a success in that person is actually stability for much longer. So it's an effective treatment--puts a pause, but a protracted pause on the growth, which is very valuable. Best is not always shrinking as the emphasis, the best is really what's best in that clinical need of the hour in the context of the volume of the cancer and how it affects you, and what we want from a drug to happen.

Lisa Yen 24:58

That's a perfect way to summarize it. Best is not always shrinkage. It can be stability. It's slowing it down, and it also depends on the person. Thank you.

So, you also were talking about side effects, and that's one question to ask your provider. So, what treatments tend to have the fewest side effects, and how should patients think about balancing effectiveness with quality of life?

Dr. Chandrikha Chandrasekharan 25:19

The fewest side effect is no treatment, but it's not possible that then we have to think about, what are the side effects that worry the person and what worries the clinician? And I think we are, again, when we look at the data, a lot of. Sometimes we don't collect the patient reported outcome. Oftentimes you hear all of us giving presentation. "Oh, the drug was well tolerated by the patient." So, say if the doctor was not taking the drug, right? So, I'm sure all the people who actually take the drug do have some impact. But again, every person is going to tolerate the same drug very differently.

So, it is important to learn and get familiar with those. It's important to get familiar with these options, not exactly when you have to make a decision sometimes. So, I do encourage patients, even if it's not time to talk about it. I kind of, over the course of time, gently introduce some names and drugs and side effects, just so you're familiar with it. Thankfully, this cancer typically does not have a rush where you're having a scan today and it shows growth, and tomorrow you've got to decide tomorrow what you want to do. That's typically not the case, but the more familiar you are with the drugs and treatment options and their side effects, I think when the moment comes when you have to make the decisions, you will one, have better questions to ask and have a better discussion with the clinician about next option. So

that's something I do encourage our people hearing to educate themselves if they are willing to. Some people don't do it consciously because it makes them more anxious. But if you are like, okay, that education helps me, that knowledge helps me, please do that.

So, side effects again, every individual drug I try my best to explain in clinic before I decide. If you look at the general data that's out there, one of the reasons PRRT is done more common, more often earlier on, is one, it's convenient, because it's like a course of four treatments. You're not doing something all the time. And then there are side effects, the worst one being the possibility of having like a **bone marrow leukemia** in the future. But that's a small number of people, 2 to 3% but it's still relevant. And then otherwise, you have some fatigue and nausea, and then you go about and do your treatments once every two months. Have some restrictions for a week after for the radioactivity exposure, and then you're hopefully good for some time. So, it makes it attractive that way, but it doesn't mean that is the best. So, in a person who has got, let's say, very small volume of cancer, or let's say just confined to the liver alone, we could think about a procedure-based option just as one time and that can be effective and also avoid drug therapies and long-term side effects for later.

So again, I think when you make this decision with your clinician trying to understand what the treatment will do for the tumor and do for you is important, and to balance that. Sometimes when you have to have a decision made because there's a need for a treatment and you have all of the options available to you, if the clinician can make a recommendation as "I think this is a better option," I think sometimes the best way to go about it.

Lisa Yen 28:10

And that's probably the perfect lead into the next question is, really, how can someone know—there's all these tools in the toolbox, there's the pills, there's PRRT, there's liver directed therapies, there's surgery. How can someone know what is the right treatment for their type of neuroendocrine cancer in their current situation and all these factors, which one would matter the most? But there's all these tools, and how would they know? Perhaps it's through education, as you mentioned, clinician recommendation. What would you say?

Dr. Chandrikha Chandrasekharan 28:37

I think sometimes the issue is that patients may not be actually offered all the options. So that's kind of where it starts. A lot of the NET centers, which are more multidisciplinary, meaning, I have a surgeon, I have an interventional radiologist, I have a nuclear medicine, not just on the wings, but actually actively involved in the treatments and planning. So that's a bit different from hey, I can use them if I want them, versus I always have them for a part of my discussion. So, I think the whole plethora of treatment tools are sometimes not offered or made available to some patients, maybe because of that.

So, ensuring that your team comprises of no matter who the front man or front woman is, but making sure there's a team behind is important so that the patients are being considered for all the treatments, or they can feel reassured that they're being considered for all the treatments. I think the input from the clinical team is probably the best in that situation for the person. I think there are situations where we

clearly can tell the patient that this is *not* an option for you. Sometimes use this **elimination mode** that's easier. Okay, well, the liver directed surgery may not be a good option for this person because they have extensive bone involvement, maybe not going to help this person by doing a surgery. So that's one tool that may never be a good option for that person. Sometimes it's easy, like I said, to start with an elimination in that context, but it also is important when we talk about neuroendocrine tumor, the toolbox that's not open today doesn't mean it's shut down forever. So, for example, with liver directed treatments, somebody may not be offered a liver directed treatment today, but in the future, they, out of the 10 spots in the liver, one spot is growing, that liver directed therapy may come back in the bucket to be offered.

So, this toolbox is open. It's open at all times, depending on the circumstance. So that's important for the patient. Now, typically, though, a drug, if we have tried it and the person couldn't tolerate it just because of the side effects or it didn't really work, we don't go back to the same drug that's usually an easier elimination. So I think of this treatment argumentarium as, what is there never there? And among the options that are there, what makes sense in that situation?

Lisa Yen 30:43

So what you're saying is making sure, number one, that you have all the tools available to you, a robust toolbox, all the tools available. Number two, that "the elimination, the not for you," bucket, and then also the "not now or not today, but maybe later," bucket. And then a discussion, because there's a lot of things going on. So those are ways to strategize a little bit.

And perhaps another follow up question that is relevant is, is there a best way to sequence? How do patients and clinicians prioritize options in a way that doesn't burn bridges for future options.

Dr. Chandrikha Chandrasekharan 31:15

I think the short answer is **shared decision making**. That's literally the key word. Again, some easy elimination options are when you know the side effect from a drug is just not for you. So, for example, if, let's say the tumor does not have any octreotide receptors, that person is likely not a candidate for PRRT. So, their bucket is down to just a certain option. And then in that bucket that's available to them, the question of, do we need to treat comes? And then, then the context of how much is there and where things are, and how do we treat it comes next. And then a logical way to go about is, truly, if I have to, then I have to present to them all options to the patient. And say, this can cause this, and that can cause that. This can produce this much shrinkage, and that drug, or that treatment can produce that much shrinkage. And I think that's where the person should ask. It's almost like going down a road, the path. I would like to think about it and imagine, okay, well, let's say I did everolimus first in this patient, and it worked for some time. But what bad things can happen to them? So well, you have to maybe have diarrhea, but when you stop the drug, the diarrhea will get better. It may take time. Or if you have anemia, yes, that may happen, but it may also recover once you stop the drug. Okay, well, is the person willing to take that risk in the context of where they are? Yeah, maybe that's a good option for that person. Or, let's say I have a person who just had a major heart surgery and a stroke or a heart attack leading up to this diagnosis around the time of this diagnosis. Yeah, Cabozantinib or sunitinib, these are

drugs we call them VEG-F TKI, which is basically playing on the blood vessel. Now maybe that's not the best option for that person, because these drugs technically increase the risk of blood clots and bleeding. Sometimes we do use it in the context of these events, medical events, but maybe that's not the right time if they just had a heart attack, like I said three months ago, and that's not the best choice for them. So, I have to tell the patient, listen, it's an option for you later, but not today. I don't think you should risk it now. And then, maybe I have a patient who has a kidney problem and their kidney function is not bad. Bad enough for dialysis, but bad enough to be worried. So in that person, then it's a very different discussion to have, because anything you give them, may not have a direct impact on the kidney, but there's always an indirect impact on the kidney function. PRRT, for example, could have a direct impact on the kidney function. It may not be the best option if they don't want to risk their kidney function right then, which could compromise their life. Some will say, "You know what, I am prepared for, what may happen to kidney I would rather get the PRRT treatment, because, the way, I'm done with four treatments, if it works for me, or two treatments, because my kidney function is not good." And that's where I'll have a discussion with the nuclear medicine doctors and say, "How do we do this PRRT in this person safely?" So I think truly, the best way, when I say shared decision making, is to walk down the path of the option in that individual person's situation, and then think of what I tell the patients to ask the question, "What's the worst that can happen and what's the best that can happen?" And that's a good way to think about this exercise.

Lisa Yen 34:24

Yeah, a real deep dive, also considering what else is going on with the person, other medical issues and their preferences. How do age, gender, race, ethnicity, those things influence treatment decisions, if at all?

Dr. Chandrikha Chandrasekharan 34:39

I think it's actually very understudied. We don't know, because we don't study this, is the answer. I think if I draw inspiration, like literature, from other cancers, you can talk about these factors affecting many aspects of treatment. There is some data that carcinoid syndrome is maybe a little bit more in women with the flushing, whether it's clouded by the menopausal symptoms that may be parallelly experienced like so that's one way the gender can affect how the burden of a neuroendocrine tumor is perceived or experienced, I should say, between a male and a female. So then, in terms of a treatment options, though, I don't think there's any data that says gender-based differences, but then we do know what we call **pharmacogenomics**, which is basically the enzymes in your body and your liver that are important for metabolizing some of these drugs that we take. They're not the same between a person to person, gender, race, a lot of things. So that could explain some of the differences in toxicity. So, the same drug, as we know, can have such difference in different people. Same dose, the same five milligram, can be different for one person to the other. So, there are certainly differences I think these are underexplored And I think part of the reason is majority of the clinical trial, the drug data that we have is very dominant the Caucasian population. And that's not just neuroendocrine tumor. There's the same with many other cancers. So, we don't always have representative sampling in a lot of these studies that we do to generalize this into the population of different backgrounds, different sex and age. And now age is a little bit easier, maybe, I think in terms of decision, because not necessarily easier, but different context.

For example, an older person may be more likely to have kidney dysfunction problems. There is data for if you look at the PRRT related leukemia, slight trend towards older women. You can generalize it, but that just tells you that age may have a role in the toxicity, which, in turn, can have an impact on your treatment decision. On the other hand, when you look at a young person, you have to think about maybe fertility. You have to think about, how does this affect your livelihood in a slightly different way than an older person, or you think about PRRT or radioactive treatment in a younger person versus an older person. Again, the risk you take may be very different. So, age, I think, a little bit easier to define, but the race and ethnicity question is very underexplored. It's a problem.

Lisa Yen 37:03

Perhaps a call out to both for researchers to really include that and to delve into that, and for those of us who can participate in clinical trials as well, so that there's diversity. So another common question that comes up is, if a treatment worked well for me before, is it possible to use it again. And then, on the flip side, if it does not work, well, what does that mean?

Dr. Chandrikha Chandrasekharan 37:25

The best example where we actually have some data in this question, saying, for these questions, answer is PRRT. So, we clearly have data now for what we call **repeat PRRT**. When I say clear data, I think it's already been in practice. We have to generate more data. PRRT, whether you're referring to the lutetium PRRT, which is FDA approved, followed by the clinical trials with alpha PRRT that are ongoing, or the lutetium, you had a great stability of the cancer for two, three years, and then another bout of Lutetium. So yeah, the answer is yes. It can be repeated certain treatments. Same thing with liver directed treatments. If you had one spot of the liver that was growing and you had it will be called embolized, which is a procedure to shrink the tumor in that one area, and let's say another spot goes in another place or something sometime later, that embolization is still an option. So, there are some treatment options, even surgery. The young and healthy person, basically we have a subset of patients who've had surgical cytoreduction, meaning reducing the volume of the cancer more than once. The key is how well it worked the first time, how well the person tolerated the first time, and what's the interval between the treatment and the growth of the tumor. Now, for example, the PRRT context, let's say somebody had PRRT. We like to wait at least one to one and a half years after the last cycle of PRRT. Again, where you count may vary, but let's say you had four treatments, and you had a scan after the four treatments, and from that point to at least another year or year and a half, you had stable disease. That's somebody we could definitely consider the repeat PRRT. But if another person had PRRT four cycle, they got a scan after that, it looks okay, and then the very next scan within six months or so on the next scan in six months already shows clearly growth, not a small amount or questionable amount, but enough growth, I think that would not make sense go back to the same option. So it's possible to repeat depending on how it work and how the patient tolerated it, and what other options are available to them, because that's also important. Well, sometimes it doesn't need to be the same option.

Lisa Yen 39:29

What about the other treatments? I think some people think that you can only have surgery once, or liver directed therapy once. Can you repeat those kind of treatments? Surgery, liver directed therapies.

Dr. Chandrikha Chandrasekharan 39:39

So it's a different undertaking when you talk about surgery. And it's not for everybody, maybe just because of the recovery and other things involved, but certainly, again, the strength of a multidisciplinary team comes here. I've worked with wonderful surgeons, Dr Howe, I work with Dr Maxwell here at MD Anderson, and we always have this discussion. Hey, listen, this person is healthy. What they have is primarily in the abdomen, and it's, you know, reassuring. It grew over so many years. Yeah. I mean, we did the first cleanup very well. Maybe we can go ahead and do a second cleanup. I tell patients who walk into the clinic with a treatment as a goal. Let's say they come in, and I want this as a goal. I kind of try to rephrase and say, you know, the goal is not that treatment. *The goal is you and what we need to do for this cancer.* So that's just something to put it in context. So, there are some patients who come in and say, "I just want another surgery." I'm like, "Sure, let's talk about it, if it makes sense. We can definitely do it." But sometimes it's not. And then the same thing with liver directed treatment. Again, the practice can be a little bit variable between institution to institution on who they think is a good candidate for certain liver directed treatments and what time. So, for example, some centers may be a little bit more experienced in doing liver directed treatments with more volume in the liver versus some may say this is something that's better dealt with PRRT or a pill or something else. So there can be some variation, and it's not uncommon. If a person gets one opinion in one place and a different opinion than the other places, I always tell it's probably both are correct, and that's really where the patients have a struggle deciding what's best, and it's hard to define the best in that situation.

Lisa Yen 41:30

It also is hard to decide sometimes, and this is again, discussion with clinicians like you, whether or not to take something to shrink a tumor before surgery. Or to have surgery and then take something, these questions come up as well.

Dr. Chandrikha Chandrasekharan 41:30

Yeah, I think to shrink something before surgery. I think the first thing before that is, I always have the surgeon first day. Do you think it's doable? And this is, again, assuming a person is healthy enough, because there are also some people who are not strong enough, they have other health problems. So, is it doable? And if it's not doable, what's the hindrance? And I ask the surgeon. Do you think it's possible or better surgery, if we do something to shrink it? Now, as we talked about in the earlier segment, there are not many things that shrink tumors, and so this could be a good discussion to have in the context of a pancreatic neuroendocrine tumor, we've certainly had some individual as well as institutional experience with large tumor in the pancreas or maybe some large volume tumors in the liver, but where we could do some chemotherapy with capecitabine temozolomide before, shrink it and then convert them to surgery. Again, not with an intention to cure if it's spread, but it's possible. Or there are some reports, or even clinical trials with PRRT being in that context used, only in a clinical trial at this time. So, it's doable, if it makes sense is always the answer. But that's not how we should start a treatment. Like, oh, this is what I want. It's usually not how we want to start it. This may make sense, and we can try it, but if the surgeon says, "No matter how good it looks, this is just not something I can ever do a good job of doing a surgery." For example, there are people who have liver only involvement, but they just have

these tiny spots in the liver scattered like little seeds scattered in the liver. And then surgical oncologist may say, "You know I probably won't find the majority of them in the operating room, and I won't be able to do a good job of cleaning up and removing these." In that person, I would not see, if otherwise they're doing well, a reason to put them on a drug to quote shrink it. I may just opt to say, "Okay, let's just put you on the injections to keep it steady and hope for other options when you need them."

Lisa Yen 43:18

And then I'm going to go back to the other question. Sadly, some people don't have a quote, unquote, good response or treatment. It doesn't work well for me. So what if a treatment does not work well for me? What does that mean? It's sad, right? It's hard. It's discouraging. Does it then predict how I might respond to another therapy? Does it imply anything overall about my condition?

Dr. Chandrikha Chandrasekharan 43:40

Yeah, I think I would always ask the person, what is lack of response? How is it defined, right? So, a person may be disappointed because the tumor did not shrink with a drug. So, if somebody says the everolimus did not work for me because the everolimus did not shrink my tumors, I probably will say, "Well, probably never going to shrink in the majority, right?" It's only shrinks in two or three out of the 100 people. So, it still worked. It kept it stable. So, I've always defined what is response and how it was defined first. So truly, if the person has a cancer, we put them on a drug or a treatment, and it grew. Clearly, this is something we did not expect, or we hoped it would work. Then it doesn't mean other treatments won't work for the person. So, I tell people, we attack one signal, and that signal doesn't seem to be the key. So, the hope would be to then if we need to do something again because the tumor is growing, or we are again needing to do a treatment, there could be another signal it may work very well, and unfortunately, we don't have good tests to predict this upfront. Talking about the context of pills, that one doesn't work doesn't mean the other won't work at all. Certainly, there are people in a situation where many treatments have been tried and worked, did not work, eventually. So, let's say somebody has gone through PRRT more than once, or the drug treatments, and let's say quote "their toolbox is running low." I mean, that is certainly a situation where we say, "Okay, well, we're always, hopefully expanding and exploring the toolbox." There are always in those patients, if it makes sense to revisit all the old tools, but there could be a time, yes, when the toolbox is empty for the cancer, but there are always toolbox continuing for symptom control and quality of life as much as possible in that person.

Lisa Yen 45:27

Thank you for that thoughtful answer. So, I've heard some patients and clinicians say, "Hey, that's a big gun. Let's not do that yet. Or we can only do this once. Let's save it in our back pocket for when we really need it." So, could you speak to that? What are the big guns with neuroendocrine cancer care, and when should they be used? And is there such a thing as wasting a treatment?

Dr. Chandrikha Chandrasekharan 45:52

I'm assuming that as often this is used in the context of PRRT, just the way it's described, you know, like the big gun, PRRT or something, and potentially limitations, because there's some data that you get four

treatments, then you can get four more, and that's it. And again, a lot of this is still being explored. So, I think a lot of times this big gun is used in the context of PRRT, I think in some ways what it could mean is, to me, I cannot talk about it as a cruise control drug or not cruise control. I explain to people like, "Okay, listen, your cancer is growing at some speed where we need to act. We can maybe at this point, sit tight. Let's do something. But what we need to do does not have to be dramatic." Meaning like it doesn't have to produce a shrinkage. We just want some good response or good stability. In that context, a pill-based therapy like Everolimus, Cabo may be good options, and so is PRRT. Now technically, in that maybe in the context of what you call a big gun there. The big gun could be PRRT compared to the small guns of the pills. And that person, how do we tell them to save it for later? I don't think we have data to necessarily say one comes later or one comes first. I think if that person says, "I do like the idea of PRRT now, because it's the least disruption, and I could have potentially no lingering side effects, and kind of be done with it." It would still be fine to do it.

The only time I would be cautious about doing PRRT is in some situations, let's say you truly have low volume. You're not affected by the cancer. You could carry on with your business, if not for the six-monthly scan you get your oncologist office. Otherwise, you're just thankfully, hopefully, living as you normally would. And then the scan, let's say, shows a growth of one or two centimeters or something in one spot, and somebody talks about PRRT or something that I'm like, "Well, maybe to put a big gun at this time for you." So, in that context, yeah, maybe I would tell people, listen, we can do this technically, but we haven't shown benefit by doing it so early versus late. You know, there's a discussion about early versus late PRRT, but no overall survival benefit yet. So, in that person, yeah, I mean, just say, Listen, we could explore other options if you want to try not to burn bridges. But if the person says, you know, I don't like the idea of being on a drug that gives me so many side effects, I'm like, Well, fine, then it's okay. You know, we can do it now or later. We can flip and flop. I think that's the best way to approach. I don't think there's a schema.

Lisa Yen 48:19

Thank you for answering that and clarifying that. I think that's reassuring. What about clinical trials? When should someone consider clinical trials, and should they only be considered after standard treatments, or earlier?

Dr. Chandrikha Chandrasekharan 48:31

So, a misconception about clinical trials in general is that it's available all the time. So, all clinical trials have a rigorous set of framework, or what we call **eligibility criteria** and **exclusion criteria**, which means, depending on the trial, they have criteria of who can enroll and who may not be able to enroll. This is kind of where you have to start. Is there actually a clinical trial? And many times, a clinical trial at this point, majority are designed after one type of treatment is not working well. I mean when I say one, more than one also, but typically, when a treatment is not working. There are a few trials also right now, available for what we call **upfront**, meaning as soon as you're diagnosed. So, first is to clarify, when you talk about a trial, what is the trial we're talking about and what context? And then, I think another misconception about clinical trials is I will not get any treatment. I can assure you that if a cancer needs the treatment, you will not be or ethically, morally not be on a trial that needs you to be on a placebo or

not. Now, having said that, there are some clinical trials that do have the placebo arm in neuroendocrine tumor, because the tumor is different again. So, in some patients that we wait and watch and we can offer treatment. So that's why in some neuroendocrine tumors, there may still be a placebo arm for that reason.

And also, **randomization**, so you could get one treatment which is being investigated versus another treatment, and patients all want to be on that treatment that is quote, shiny and new, but we don't know if it's better, is why it's being studied against another comparator. So, these are just basic things to learn about the clinical trial for the patient before. When is a good time is, you know, anytime there's a good trial is a good time. So that's the answer: if there's a good trial. But before we enter onto the trial again, just like a treatment option, I think it's very important, because I am very thankful to all the people who participate in any trials or consider it, because it is a big, big undertaking, you know, in terms of the commitment you make to a trial, to go to the clinical trial center to get your treatments, the follow up, which is a little bit more sometimes than the usual standard of care. It may not be right in the moment for you, whatever is going on in life, that may not be the best option, right? So some, it is a practical decision, a financial decision, as much as it is a scientific decision for a clinician.

So, if there's a good trial, then the next question to ask is always about the side effects that we know don't know. So again, you know, what do we know about this trial, and how do you feel about it? So, we encourage clinical trial participation, because that's how we move the science forward, and can discover new drugs, new treatments, and answer all these questions. But again, it is a big commitment from the patients and their families and the caregivers.

Lisa Yen 51:21

Yeah. Yeah, thank you for speaking on that. So, we touched on earlier how sometimes to be sure that people have all the tools in the toolbox, all these options available to them, they may need to seek additional opinions. What about people who then receive differing opinions? What advice do you have for people who now may be weighing different opinions from various providers?

Dr. Chandrikha Chandrasekharan 51:45

It's perfectly normal and okay to get second or third opinions, because in this cancer, you don't have a great algorithm. And in the context of that, I will encourage the patient, though, that, you know, it's hard to have 10 drivers driving a single bus. I mean, the driver is always the patient, I tell them, but there can only be one co-driver, and that co-driver is somebody you have to like and trust. So, start there. I think many people will say, you know, when they've seen doctors, then like, oh, this is, this is a good fit. And that's not a good fit. They're all medically competent. But then sometimes the trust factor and the resource factor, it comes in. So that's one way to decide.

I think, a practical way to decide for the person, just to make sure you're comfortable and able to communicate well and discuss everything you want to. And outside of that, if you're talking about different neuroendocrine tumor experts and different neuroendocrine tumor centers, when you have some potentially varying opinions, I always also tell the patients to ask as to why that recommendation

is being made. So, understand what the recommendation comes from. So, if somebody is just making a recommendation without giving the context of why they recommend that, that is a little bit hard for me to digest as a person. Okay, why are you saying that? And so, if you can get a good rationale, and that rationale, it makes sense to you in your disease context, that's also really the opinion that fits best your situation, and that's a good opinion to go with. That's probably the two things I can think of that I've seen that helps patients decide.

Lisa Yen 53:18

It is a challenge right to navigate that. And sometimes, I know I've heard you say, sometimes there's not a wrong answer. They're just different answers. So, I think we'll end with this, you've mentioned quite a bit how the patient's values and preferences really shape this discussion. Some people may feel like, okay, well, I'm really stuck on this fear. Maybe it's irrational. Should I be more open and perhaps maybe speak to that in terms of that person as they're communicating these values and preferences. And also, there's other people who are like, I want my doctor to tell me what to do. I think there's a range. What advice would you give to people in how they communicate values and preferences and enter these discussions with their providers?

Dr. Chandrikha Chandrasekharan 54:01

It's a two-way street. It doesn't have to be initiated necessarily by the clinician or the patient, but you know, just it's important. Ultimately, the center of the journey is the person, the patient. Sometimes the caregiver is part and parcel of it because they become the spokesperson for the patient, sometimes in the right context. So, I think it's very helpful for the clinician to hear as well. Because I do have definitely patients who come and tell me, "I don't know, doctor, just tell me what's the best for me." I mean sincerely in those words with that much elaboration. Then I asked them a little bit more just to learn about your personality. It's a long-term relationship that you develop with your clinician. So, over the years, we know a little bit more about the person. We know what is their family made of? What is that they enjoy? Do they love golfing? Do they love going on cruises? You know what is important the person, the value. I think even if it is not explicitly stated in the context of a cancer, everybody has their preferences and values. So when we're talking about preference and value, if you're not necessarily talking about in only the setting of cancer, we're talking about it in the setting of life, because that has an impact on the decision you make in a cancer and treatment, and it also has an impact on how the clinician may recommend a particular treatment. So, I feel like this whole values and preferences discussion is not in the pigeonhole of a cancer. It's really broad what's important to you in life kind of question. It's a very big question. Then you could rephrase it and "what's important to you in life in the context of the cancer?" Or "what gives you strength as you navigate this journey?" Or "what is your biggest fear as you navigate this journey?" Or "what is always on your mind when you think about neuroendocrine?" And "what is on your mind when you don't think about this neuroendocrine tumor?" So, these open-ended questions sometimes do help to learn more about the person, and at least to me, it gives me some idea to tailor my recommendation if the person truly says, "Just tell me what to do." "Hey, I heard this from you. Sounds like this is important to you, and in that context, maybe this is a better treatment that you can tolerate at this time. And so, here's the recommendation based on that." I don't think there is any person who does not have a value or preference in life, right? That's not life.

Lisa Yen 56:14

Yep, that's right. What matters most to you and having that conversation around what matters most. I guess, as we close, what if anything, would you like to say in terms of closing comments about this topic?

Dr. Chandrikha Chandrasekharan 56:26

I think this is going to be a topic, there are many discussions are going to happen on this with maybe still not a lot of clarity, even in the future. I think that's my sense about the treatment sequencing. I think the good thing is, I'm hoping that we actually have more treatments to make it more complicated in the future. That'll be a good thing, because as we add treatments like the new PRRTs, if they get approved, or new drugs if they get approved, they do complicate sequencing. They do complicate both the patients and clinicians' life. A little bit more complicated, but in a good way. And hopefully in the future, we can identify better ways to actually tailor the treatments. I'm sure there will be some day, some way. Until then, the discussion will keep happening.

Lisa Yen 57:05

More to follow. I know when my husband was diagnosed with advanced neuroendocrine tumor 11 years ago, there were very few options. Lanreotide had just been FDA approved. PRRT was not yet. The trial had closed. So, there were a few options. This wasn't quite the issue it is now in terms of understanding sequencing and strategy. And even more so, we have several people in our community who are far into the double digits, who've been around 15, 20, 20 plus years where there really weren't any options. So, as treatments evolves and as there's more and more options, this becomes more of a challenge, which, of course, comes with its own anxieties and that feeling of overwhelm. So, thank you so much for sharing your insight. Thank you for bringing some clarity to this topic that can feel overwhelming for many. And we hope today's discussion gives patients and caregivers the tools to ask informed questions and to partner more confidently with their care teams, with their clinicians. And as always, the Neuroendocrine Cancer Foundation is here for you.

Thank you, Dr. Chandrasekharan, for all that you do. We're so grateful for you all your dedication and hard work, and we look forward to seeing you again.

Dr. Chandrikha Chandrasekharan 58:13

Thank you. Thanks so much for this opportunity.

Lisa Yen 58:16

Thanks for listening to the Neuroendocrine Cancer Foundation podcast. We want to thank our podcast supporters Novartis, Exelixis, Lantheus, ITM, Crinetics, and Boehringer Ingelheim.

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