THE LACNETS PODCAST

With Jun Gong, MD
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Transcription:

Lisa Yen
Welcome to The LACNETS Podcast. I'm your host, Lisa Yen. I'm the LACNETS Director of Programs and Outreach, as well as a caregiver and advocate for my husband who is living with NET. In each podcast episode, we talk to a NET 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. Thank you for joining us for today's episode of The LACNETS Podcast. I'm excited to introduce today's guest, Dr. Jun Gong. Dr. Gong is a GI Medical Oncologist at Cedars-Sinai Medical Center in Los Angeles. He graduated from New York Medical College, completed his internship and residency at Cedars-Sinai, and his fellowship at City of Hope in Duarte, California. Dr. Gong is focused on translational and clinical cancer research with interest in early therapeutic trials, including immunotherapy, targeted therapies, biologics and other systemic therapies, and biomarker development to improve patient outcomes in both GI and GU cancers. We've had the pleasure of having Dr. Gong speak at pre-pandemic monthly educational programs back when we were meeting in person. And he also joined us for our 2019 Annual Conference at Cedars. Several of our NET patients see Dr. Gong for their NET care and they find him to be very personable, caring and knowledgeable. We're so glad to have you join us today. Would you start by telling us a little bit more about yourself, and how you got interested in NETs?

Dr. Jun Gong
Thank you, Lisa. And thank you LACNETS for inviting me to this podcast. That was a very kind intro. I think this is a very informed population of patients that encompasses what we treat as medical oncologists in the GI medical oncology field. Also neuroendocrine tumors are becoming more common in other organ types as well. So it encompasses a lot of different disciplines. And so I think a lot of us in our training, have been trained and will eventually be exposed and working with patients of this disease type. And so we're happy to help patients with neuroendocrine tumors.

Lisa Yen
And we're so glad you're doing it because we need more and more people interested in involved in NET care. And I hear only good things about you, Dr. Gong,

Dr. Jun Gong
Thank you so much.

Lisa Yen
Let's get right into it with these questions. As I mentioned to you, these are questions that came out of our 2022 annual conference that were left unanswered, and they are very common questions. So the first question is, which is better, if the tumor is expressing somatostatin on its receptors by dotatate scan, or biomarker in tissue biopsy? And if you can explain what these two things mean.

Dr. Jun Gong
This is a very, very good question, Lisa. Ultimately, what we try to treat patients with one of the foundational medicines in neuroendocrine tumor treatment is somatostatin analogs or SSAs. And it's thought that in order for these therapies to technically work, you need to have these receptors present on the neuroendocrine tumor cells themselves. So this is kind of a logical question, how do we figure out which patients have tumor types that are positive for these receptors? You can intuitively think, well, maybe we can just look right at the tumor. And this is what it means to look at the tissue biopsies for this to stain for these receptors. But in this day and age, and in many patients in general, if an invasive procedure can be avoided, such as a biopsy, sometimes these patients are very frail, sometimes they have a lot of symptoms, or sometimes they just don't want to do an invasive procedure and they want to have a non invasive means. So this is where imaging techniques come by, where you can just do a scan, and see if you can confidently detect the presence of these receptors so that you can guide therapies in these patients. And I think this is where this question is diving into. In the literature, in my experience, it's largely recognized that both the tumor expression and imaging detection predict benefit to SSAs. Another way to say this is that we don't think that there is a superior method one way or another in predicting response to SSA therapy. It's been shown that imaging detection of somatostatin receptors is more than 80% of the time concordant or similar with tissue detection. And then we largely recognize that tissue detection is not routinely recommended when you have a non invasive means to detect somatostatin receptor positivity.

Lisa Yen
That's really helpful to know. So either way works, and as you said, looking at the whole patient. Sometimes if you can avoid getting stuck, none of us necessarily like getting stuck and being put under anesthesia and under the needle, the imaging that we have now with the dotatate is enough. And that leads into the next question. I know I get this question, so I'd like to ask you this. Since the medicine analogs bind to the somatostatin receptors, as you just mentioned, can NET patients take what's known as statin medications for high cholesterol?

Dr. Jun Gong
So this is a confusion because of the word "statin" that remains in somatostatin and a lot of the cholesterol medications such as simvastatin and rosuvastatin. The short answer to this is yes, patients can take it for high cholesterol. The reasons why, because statins for high cholesterol, although they have a similar root in the name of their medication with somatostatin, they're actually completely unrelated mechanisms where the statins of cholesterol medications bind to a different enzyme involved in lipid cholesterol production, while the somatostatin that we think of completely different receptor involved with hormone production of a complete different set of molecules. So we can comfortably say that if patients need to take statins for high cholesterol, they're safe to do so for neuroendocrine tumor patients.

Lisa Yen
So, it's a word that sounds similar and it's embedded in that somatostatin, but it's not related at all.

Dr. Jun Gong
I try looking at it why the root word perhaps remained the same. I think it's either Latin or Greek. Statin means to stop. So you want to stop a certain kind of hormone release. So I think that's what sometimes as medical providers and pharmaceutical industry, we stick to a common kind of word across different medications.

Lisa Yen
Ah, that's insightful, to stop something. So then with the somatostatin, what are we stopping?

Dr. Jun Gong
Somatostatin is normally a hormone that would stop the secretion of a lot of digestive hormones in the intestinal tract. So that's why we call it somatostatin. For the other statins, you're thinking of rosuvastatin, simvastatin, they're stopping synthesis of certain cholesterol.

Lisa Yen
That's interesting. Thank you for enlightening us with this. This is helpful and reassuring to know that if someone needs to take something for cholesterol, there's no problems with it. Another confusing area is in this area of psychiatric medications. Is there a link between psychiatric medication and NETs? And can someone with NET take selective serotonin receptor inhibitors, like SSRI or SNRI, that might be prescribed for them for depression?

Dr. Jun Gong
When dealing with malignancies and cancers and tumors, I use those terms interchangeably here, there is a lot of anxiety, and you can imagine a lot of psychiatric conditions that can result from that ranging from depression, just with a diagnosis itself. I just wanted to make that point forward, because I think a lot of our patients in oncology will have symptoms such as this. And so this is a very relevant question. A lot of patients will be on some kind of psychiatric medications. And that is not uncommon. But I think the link between psychiatric medications and neuroendocrine tumors, if you look at the literature, in the past, maybe 20-30 years ago, there were some earlier case reports that suggested a link between SSRIs, which is a class of antidepressants that can possibly unmask carcinoid syndrome or even unmask carcinoid tumors. And these findings propagated into subsequent literatures where there were some strong concerns and recommendations for antidepressants and SSRIs in patients with neuroendocrine tumors. But if you look at some more larger and more recent studies, we've actually shown that there's really no adverse outcomes for NET patients treated with SSRIs and SNRIs. And as a result, I think we should always monitor, firstly, patients starting antidepressants with neuroendocrine tumors, I think that's always safe practice whenever you start any new medication on a patient. But I think the statement that antidepressants must be avoided in patients with NETs is a little strong. And I think we're a little bit more comfortable that they can be safely used with patients with neuroendocrine tumors these days.

Lisa Yen
Thank you for acknowledging that there's a lot of anxiety and depression, and taking medications is common. The common concern is that, of course, with these medications, these antidepressants, there's a blocking of the serotonin receptors, and so that might elevate the serotonin, and would that

trigger carcinoid crisis or carcinoid symptoms like you mentioned. Would that happen if they're on these medications?

Dr. Jun Gong
So it makes intuitive sense when you think about it that way, but the way we've evaluated and studied this across larger patients, aside from the smaller case studies that were before, we really haven't seen it can consistently enough for us to say, please avoid these, sometimes, very important medications that help with patients' mood and mental well being while being treated for these disorders.

Lisa Yen
Thank you for clarifying that and just reiterating that it's okay to take these, and that studies show that it's fairly safe. The next question is, what's the difference between genetic and genomic testing? And we know this is something you're interested in. When would you do genetic screening or testing? And when would you do genomic testing or tumor sequencing?

Dr. Jun Gong
Yeah, again, I think this is a very confusing, similar-sounding terminology that we use often. When I like to think of genetic testing, I think that generally refers to testing for hereditary causes of cancer. And genomic testing refers to testing of tumor tissues for mutations that can be used for prognosis or used for targeted therapies. So we like to think of genetic testing in those who present with a strong family history of cancers, a strong family history of neuroendocrine tumors. There are some neuroendocrine genetic predisposition syndromes as well. So those are cases when genetic or germline testing would be indicated. While we would try to send genomic testing in search for additional therapies, targeted therapies, or precision based therapies that we can use to complement our treatment paradigm for patients with neuroendocrine tumors. And here at our institution, we like to do that first off the bat in those with advanced or metastatic neuroendocrine tumors. So we try to get genomic testing often through next generation sequencing, or NGS, as soon as possible in our care of these patients.

Lisa Yen
Thank you for that. What does it involve to do the genetic versus genomic?

Dr. Jun Gong
Genetic testing, we are fortunate enough to have colleagues known as genetic counselors that helped us with this evaluation. When we meet a patient that we suspect may have a strong family history, or they may just have some features of their case that are concerning for a hereditary condition, we refer them to our genetic counselor who are trained professionals. And the genetic counselors themselves will construct usually a family tree, try to detail the family history of cancers, and then they'll send off a test. Sometimes it can be a saliva test or sometimes it can be a blood test, looking for hereditary causes of cancer. While genomic testing, this often classically involves using a tumor tissue. So sometimes biopsy, or in those who have undergone surgery, we can use those. Our colleagues and pathology are very kind to store these and archive these for years on end. So even if you had a biopsy some several years ago, sometimes if we're able to find that specimen, connect with the pathology department of that institution, we can request that tumor specimen to be sent off for NGS, or next generation sequencing through use of various commercial companies. And oftentimes, in several weeks, we're able to get a report telling us if there are any targetable mutations that were identified.

Lisa Yen
Thanks for that explanation. That's really helpful. So with genetic testing, you would refer to a genetic counselor and they would do a lot of talking and workup, and then blood tests as indicated, and then the genomic testing would be of tissue, so you would have to have a biopsy or some surgical specimen.

Dr. Jun Gong
Yes, that's right.

Lisa Yen
So that goes really nicely into the next question. Is it possible to find NET markers on serum or blood by using mass spectrum without biopsies? And is there a promising liquid biopsy?

Dr. Jun Gong
I think that would be a very important technological development, if we could have a blood based test that can tell you that you have a neuroendocrine tumor. A lot of companies these days are looking for cancer screening through blood based biopsy. So I think that this is active and ongoing research. But as of our current juncture here, tissue biopsies remain the gold standard. And unfortunately, there hasn't yet to be a liquid biopsy that can reliably confirm neuroendocrine tumors, just like tissue biopsies. Here, we often get it's important to clarify that some of the tumor markers that we're familiar with, such as urine or plasma 5HIAA or chromogranin A, these are used as guides to see if your cancer may be responding to therapy or your neuroendocrine tumor me responding to therapy. But they're not diagnostic of neuroendocrine tumor themselves. So as we try to find something that's equivalent to a tissue biopsy in the liquid, tissue biopsies remain the best way to diagnose neuroendocrine tumors.

Lisa Yen
Thank you for that. And I think we're all familiar with other kinds of cancers. Maybe we have a friend or family member with other cancers and you certainly see other types of cancers, and with those other cancers, people might periodically get full body scans to see if there's metastasis and other places, or make sure there's other places not missed, and maybe other places that haven't been missed, and maybe periodically get these full body scans. So with NET, how often should full body scans be done to discover metastasis and other parts?

Dr. Jun Gong
Right. I think for patients diagnosed with NET, we should always get a full body scan at the initial diagnosis just to make sure that there isn't spread of the neuroendocrine tumor elsewhere in the body. But after that, I think it really depends on the type or the stage of your neuroendocrine tumor. If this whole body scan showed that your NET is usually confined to an organ and you undergo surgery or watchful waiting, then we would only recommend a neuroendocrine tumor whole body scan as clinically indicated. While in those patients who are diagnosed with metastatic neuroendocrine tumors, they're more likely to undergo more routine therapy, and you need more regular scans to see if the therapy is working in this population. So here, we often get more frequent scans, usually around every 3-6 months, depending on the institutional practice for these patients.

Lisa Yen
And what would you use for whole body scan?

Dr. Jun Gong
We like to always start off with a CT scan or an MRI, those are what we think of the conventional scans. But now with the PET Gallium-68, we like to use those at initial diagnosis as well. We have used Gallium-68 routinely over time as well, but usually not more frequently than six months at a time. So usually, we think of these scans if something changes along the clinical course that we need more information, we often get another Gallium scan. But these are not to the frequency as CT or MRI is what we're doing more frequently.

Lisa Yen
And do those pick up brain mets, just out of curiosity?

Dr. Jun Gong
The conventional CT and MRI, unless you designate an MRI or CT head to be included in there, they do not. And we generally don't look for brain metastases, unless there's certain clinical signs that we obviously are worried about, then we definitely would include those in our whole body scans as well.

Lisa Yen
Thank you. With NETs, a lot of times we're told, especially with well-differentiated, they're slow growing, which is a comfort. Of course, the question comes up, can well differentiated tumors become poorly-differentiated tumors?

Dr. Jun Gong
This phenomenon has actually been described in the literature. There have been cases that have been described of patients who were diagnosed with well-differentiated tumors, and then on subsequent biopsies, they were found to have poorly-differentiated tumors. Our understanding of this phenomenon is still not clear of how this develops, or how this evolves. But I think the reassuring thing to know is that overall, the incidence of this phenomenon appears to be very, very rare. And the majority of the time, this phenomenon doesn't happen. In the rare cases that have been documented in the literature, they've had to been treated with more different kinds of systemic therapies for these patients tailored to their histologic features, as you described.

Lisa Yen
So, it's rare, and if it does happen, then oncologists and the treating team is prepared to treat it.

Dr. Jun Gong
Oh, yes. The key word here is that we don't see it often, it's extremely rare. But in the rare cases that it's happened, we are here to help you guys.

Lisa Yen
Thank you for that. That's reassuring. So as we all know, NETs can produce hormones, and that's a concern. So can NETs produce multiple hormones, and should one try to control any production of any hormones for general prevention in general? And should we control serotonin production generally?

Dr. Jun Gong
This is a this is a good question, too. I would say the majority of neuroendocrine tumors produce one specific hormone, mainly serotonin. This is the main hormone associated with carcinoid syndrome. However, there are other rare neuroendocrine tumors that may produce one specific hormone different

from serotonin. This includes gastrin, which is another hormone produced by gastrinomas. There may be insulin secreting neuroendocrine tumor, or insulinomas. There can be glucagon secreting tumors from glucagonomas. But majority of the time, there is one specific hormone that's produced, and the most common one, again, being serotonin. With that being said, there's no conclusive evidence that we're aware of that control all these hormones has firstly been shown to prevent neuroendocrine tumors. In fact, we often recommend that the best practice is to attempt to minimize certain diets tailored to the individual after a specific neuroendocrine tumor condition is diagnosed. So for example, in those who may be diagnosed with the rare case of an insulinoma, here we're really watching how their intake of certain foods that may contain sugars are washed. And then there's a whole list of foods for serotonin as well. But instead of having a preventative strategy because a lot of these are found in a lot of healthy foods as well, it's better to have it tailored with your clinician and dietitian after diagnosis of your condition.

Lisa Yen
We all like to think about prevention, prevention is key, but it's tough in neuroendocrine tumor unless you've had a diagnosis and know what to tailor the diet for.

Dr. Jun Gong
That's right. And in general, a healthy balance of diet and exercise is often the best way to prevent a lot of malignancies in addition to neuroendocrine tumors.

Lisa Yen
Good point. We really have to think about prevention of other cancers as well, and a healthy balance is important. So, many of us are told, of course, that when the disease is stable, that we don't have to make a change. But there are some patients who might have side effects, and they are concerned about their side effects. And they might want to get rid of tumors even when things are stable. So how aggressive should a patient be to seek out new treatments when the tumor burden is stable?

Dr. Jun Gong
That's a really good question, as well. We often forget that stable disease is what we as oncologists classify as a good result too, in addition to shrinking disease. We lump them together. This means that your disease is being controlled on the therapy that you have. It's true, I think a lot of us, myself included, if we had the opportunity to get rid of a tumor, we would definitely want to explore that option. And here, I think it's very important that we acknowledge that a lot of these cases should be, as much as possible, discussed in a multidisciplinary setting where we have oncologists, surgical oncologists, radiation oncologists, interventional radiologists, so that they are actually gathering together. They review the imaging, the diagnostic workup for a patient. And we can comfortably say, we actually think we can try to get rid of as much tumor as we can in this patient through surgery or a combination of local therapies, liver directed therapies as well. But unfortunately, some cases, some patients have either some disease that's too widespread, or they're in some tough anatomical locations, or it's often difficult for them to try to get rid of all the tumors. And so I think in those cases, systemic therapies remain the best option. And we recommend what we call standard of care. Systemic therapies, these are the best we currently have as FDA approved. But that's not to exclude patients from always searching for other options. There are clinical trials undergoing all the time and we're really hoping to find that new breakthrough where even patients who are not candidates for surgeries or local therapies, maybe there will hopefully be that breakthrough systemic therapy that can get rid of all the tumors. So I

think it's always helpful for patients to be informed and aware that there is ongoing developments, that if not develop now, maybe in a year, two years from now, it's possible.

Lisa Yen
That's really helpful. That reminder that everything needs to be tailored to the patient and encouragement to stay informed and empowered. So we are always a step ahead and know what's out there, both the standard of care and also clinical trials and what's on the horizon. And a plug for clinical trials so that we can be part of shaping the future. As you know, many NET patients also have tumors in the liver, and that becomes an issue of concern in terms of liver function and then many medications in general might affect the liver. This question comes up quite frequently, how common is having issues with liver functionality? And if it happens, what are the signs of liver failure due to tumor burden?

Dr. Jun Gong
I'll start off with the second question. Signs of liver failure due to tumor burden usually manifests with symptoms such as buildup of fluid in the abdomen. Other times, it can be in the lower extremities and we call this edema, and it can look like abdominal bloating. But you could get other signs such as jaundice, which is characterized by yellowing of the eyes. You can even have itchy skin. You can sometimes have confusion as well. And sometimes you can have dark colored urine, almost described as Coca-Cola. Fortunately, despite these scary signs that can sometimes happen, we don't see a lot of patients with liver failure with neuroendocrine tumor. The concern for affecting liver function can not only come from liver metastases from NETs, but you know, certain drugs can also cause liver dysfunction as well. So that's also important to take into consideration of causes of liver impaired liver dysfunction in patients with neuroendocrine tumors. Now the incidence of those to develop liver metastases is very dependent. Every patient is different, where there's a lot of factors that play in such as the size of the tumor. If the tumor is very small, for example, on diagnosis, there's a very low chance that you'll develop liver metastases compared to other types of neuroendocrine tumors, where the chance of metastases can be as high as 50%. So every patient is a little different, and it's dependent on the type of neuroendocrine tumor and other features. But as I hinted before, we actually have really good therapies too to target liver metastases. You can have local therapies, liver directed therapies, surgery remains an option in certain cases, and systemic therapies, again, are available with clinical trials for patients with liver metastases.

Lisa Yen
So with those type of targeted treatments, liver directed therapies or surgery, where you remove the liver tumors, does that permanently affect the liver function? Because you're cutting out the tumors, but does it permanently damage the liver in any way?

Dr. Jun Gong
So the nice thing about the liver is that it's a very regenerative organ. So we've seen throughout our experience that even resecting portions of the liver will be fine. And our interventional radiologists throughout the country and the world are generally very skilled in choosing out portions of the liver for which they're going to embolize or direct their liver directed therapies. Our goal is to never compromise liver function. It's always to minimize risk and maximize reward.

Lisa Yen
Yeah, always weighing the pros and the cons and the potential risks and benefits. And then of course, doing what's best for the patient.

Dr. Jun Gong
Absolutely.

Lisa Yen
So in closing, I just invite you to share any last thoughts, any words of encouragement or advice or hope that you might have for the audience?

Dr. Jun Gong
I think this is a really good set of questions. I applaud LACNETS for having such educational conferences. Empowering the patient, as you said, is always a good trait to have. I just wanted to end though, that there's sometimes a lot of scary things on the internet too. So be careful of that. And some of these findings, it's often better interpreted with the help of your clinical team, whether it's a dietary question, or a treatment question, or even a hereditary family history question. This is why we have a multidisciplinary team. So that we are there to give you the most accurate up to date information, and hopefully also help distill and clarify some of the confusing aspects that are out there as we are in the social media age, the internet age, where access to information is readily available.

Lisa Yen
Thank you for that reminder. And it can be overwhelming when patients Google search it, as they commonly do, and they see all sorts of information out there, and not understanding how the information relates to them. So talking to you, talking to your team, you can help put that in a proper context and give good tailored information, as we've been talking about the whole time, tailoring it to the patient.

Dr. Jun Gong
That's right.

Lisa Yen
Thank you so much for your insights and for this information for meeting with us today and for sharing what you know about NETs and these words of encouragement and hope. We really appreciate you and all your hard work in research, in the clinical field, and seeing patients. We really appreciate all you do and we hope to see you again in person soon.

Dr. Jun Gong
Thank you so much for having me. It's been a pleasure.

Lisa Yen
Thanks for listening to The LACNETS Podcast. We want to thank our podcast supporters Advance Accelerator Applications, TerSera Therapeutics, and Ipsen Pharmaceutical. For more information about neuroendocrine cancer, go to www.LACNETS.org.