THE LACNETS PODCAST

With Josh Mailman, MBA
Released on June 15, 2022

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. Welcome, everyone! I'm really excited to have you join our third episode of The LACNETS Podcast on the topic of PRRT. And our special guest for today is Josh Mailman, who is a friend, a fellow advocate and a NET patient. Josh is involved on multiple levels, not only personally with the NET community. He serves on multiple boards and organizations and he's the president of NorCal CarciNET Community. Josh, welcome! I'll let you introduce yourself, as I know, there's multiple ways that you're involved.

Josh Mailman
Well, thank you, Lisa. It's always great to see you and hear you. You probably only are hearing me on this podcast. And yeah, this is the third in the series, but it's also dovetailing really nicely with Dr. Mittra's webinar that you guys did several weeks back, as well. So I'll really call this fourth in the series. It's interesting, when I was diagnosed I had no idea of what nuclear medicine was or what it entailed and molecular therapy, and now I feel like I'm almost, I don't want to say overexposed, but in addition the President of NorCal CarciNET, I've worked with LACNETS since its inception at times. I was the initial patient advocate or the inaugural patient chair, the patient advocacy and advisory board for the side of Nuclear Medicine and Molecular Imaging. I do sit on the NETRF board. I do actually sit on a board that actually supports education for young investigators in nuclear medicine called the ERF. And lastly, most recently, I was appointed as the sole patient advocate to the Nuclear Regulatory Commission Advisory Committee for the medical use of isotopes. So I went from probably not knowing what nuclear medicine is to, on top of that also been on the Scientific Committee for the Theranostics World Congress for all six of them. So I'm well acquainted with nuclear medicine at this point.

Lisa Yen
You are, and it's clear that you're an internationally recognized advocate, you're invited around the world to speak on this topic, and the idea came up to invite you to this podcast because Linda Gardner, who spoke on our first podcast on this topic mentioned you and how you're published in this area.

Josh Mailman
Actually, Lindy and I are even on something that most people in the US don't know anything about, which is the ICPO Foundation, which is actually providing education for medical professionals in nuclear medicine around the world. She is the leader of the nurses. It's called the nursing segment, and I help her in that area, as well. So yeah, it goes far and deep.

Lisa Yen
Well, you are truly dedicated to this field and to this community. And we're really grateful for that. So Josh, you and I know why you're involved in this, but just so those who may not have heard from you before, what got you into this field? And why do you do all this amazing work that you do?

Josh Mailman
Well, I mean, for most of us, right, we're patients first. I was diagnosed in 2007 and there were not that many options available. And much like many of the listeners here, I joined a support group. At that time, it was the Northern California CarciNET Support Group, which was having its first meeting in 2007 and really stressed education. And that's how I ended up finding about PRRT, because I actually went to a conference that was hosted in Toronto. So that's really how I started my journey because I needed it. I didn't have any other options, and I found it there. So that's really how I started. One thing led to another and I ended up having my first Gallium-68 scan way back in 2008, after going to a conference and I didn't need therapy at the time, but when I did need therapy, there was nothing available here at that point. So I ended up in Europe and having three treatments and one thing led to another and I was researching this topic, and honestly, trying to debug information was that that was on websites and on different patient forums about trying to understand why we didn't have PRRT in the US at that time. And that's what really led me to get more involved, was to better understand what really was going on, and I learned a lot. If we go to our first question of why did it take so long to get PRRT here? Interestingly enough, many of the early trials, PRRT was first looked at right around the turn of the century in Europe first, but very shortly thereafter, there was a worldwide clinical trial and it involved the US in 2001 and 2002. The story of PRRT, just in registration, or getting an approved agent, it took a long time. It took over 20 years from the first time in humans until we actually had a product. And a lot of people get confused about that and think that PRRT was approved or something was approved in Europe, and that's why we were all going there. But it really never was. It was really available for something called the practice of medicine or compassionate care in Europe, as opposed to really having a registered trial and a registered product that could be widely available. And that really wasn't until 2018, after there was a pharma company willing to do the clinical trial and the work to actually get registration. Early on, I would read things like the FDA is holding this up, or it's because of the FDA. And it turns out, there was no company that was actually interested in bringing the product to market and the FDA doesn't approve things that it doesn't have an application for. It can't figure out in thin air what should be approved. That was kind of the start of my journey of reading all these posts online that didn't seem to make sense to me, but it was like, let's go talk to our congress people about why we don't have PRRT here. And your congress person wasn't going to help there. And so I learned a lot about the process of what it takes to make nuclear medicine or nuclear therapies or even nuclear imaging to bring them to market and what that process was. And every time I'd peel back the onion one more time, I learned more, and someone

would ask me on a committee or something else. It's funny, we were talking a little bit before about this meeting, I was in New York and sitting next to me at this meeting was Dr. Henry VanBrocklin from UCSF. He's a radiochemist, which is why you haven't heard him on a podcast yet. But in 2011, I was invited to the first Theranostics World Congress. One or two patients that was at this 400 person congress to discuss radioisotopes. And at the dinner sitting next to me, and unbeknownst to me, was this other American. There were only six of us there, including Dr. Eric Liu, Dr. O'Dorisio. And sitting right next to me was Dr. Henry VanBrocklin, who I'd never met, and we introduced each other and he actually lives seven miles from me. And if you want to talk about how random acts really can help you here, it turns out he was the Chair of Outreach for the SNMMI and also the radiochemist of UCSF, and I help introduce him to Dr. Bergsland here at UCSF so that we could start a nuclear medicine neuroendocrine program at UCSF. I have traveled to Germany to have that happen. And he invited me to join the SNMMI Advocacy Board, which I became the inaugural chair for. So without having been in Germany, I'm not sure we would be having this conversation together about this. So random acts of things that happen are just hard to believe.

Lisa Yen
And they definitely don't seem random. But thank you for taking your personal experience and that really has fueled your passion and your drive to learn more and to advocate on behalf of not just those in the NET community. I know you've gone beyond that as well. And I know you've already tackled the first question about why it took so long to get PRRT in the US. Our next question is, how does PRRT, the treatment itself, the doses, etc., how does all of that differ in the US versus in Europe and other parts of the world?

Josh Mailman
So the US and other parts of the world and Europe are all really big places. Europe is a really big place. So there's not one specific thing that differs but let's go through this a little bit. And I started talking about this in the answer before with registered products. We have Lutathera, which is Lu-177 Dotatate. And we have AZEDRA, which is I-131 for para/pheo, although there are some clinical trials using in NETs as well at the moment. So really, we only have two registered products in the world. That's it. Everything else is the practice of medicine or clinical trial or compassionate care. So places which only use registered products, the practice is the same, regardless of where you are in the world. And honestly, in most places this isn't available. This is the challenge. We're really talking places that have strong nuclear medicine backgrounds where this is available or have a market size that's big enough to do this. But that being said, different pockets in different places will do things differently. So Germany, you can do things under the practice of medicine a lot easier than you can do an else place in the world. You have the science clinical trials that are going on that you can see on clinicaltrials.gov. You will see things with different peptides, with different isotopes, with different delivery methods, and not necessarily the adherence to having for standard 200 millicurie doses, which are what we see with the registered product in the United States. Do we know if that's any better or not? Honestly, we don't. We don't have these head to head studies, we have theories. We have things that we think we understand about it, but we don't. And so for the majority of the world, even in Germany, or the UK, where you could do the practice of medicine, or South Africa, really the standard of care is three or four doses of Lu-177 Dotatate or DOTATOC. But we do have places where you'll see different isotopes or different peptides. I know Dr. Mittra certainly talked about the antagonist a little bit, different combinations, some that are done in trials and some that aren't. But the majority of the world uses exactly what we're using because we have a phase three clinical trials study on NETTER-1 which really is the gold standard of understanding how treatment works.

Lisa Yen
That's helpful to clarify what is established now as a standard of care and other things that are used as a practice of medicine so it might differ. So thanks for that. Our next question, Josh, is why is PRRT so much more expensive in the USA, as compared to other parts of the world? And is it covered by insurance, especially for lung NETs?

Josh Mailman
So, we're gonna get back to registration again, right? Or registered products. Lutathera is a registered product for AAA Novartis, and AZEDRA is a registered product for Progenics. It takes a lot of money to do clinical trials, it takes a lot of money to build a distribution network to get things out, and to have salespeople to go talk and do other things. When you're just radiolabeling a product for yourself, for your own center, you don't have any R&D, you're just taking the peptide like DOTATOC or DOTATATE and a readily available isotope, you can do that in your radiochemistry lab. You have to have a radiochemistry lab that knows how to do this, but the costs aren't the same. You don't have all those different things. You didn't have to go through the tens to hundreds of millions dollars worth of clinical trials, all those things that need to go on, and you can do that in places in Europe and other places. So one, you can use a nonregistered product. And that's still PRRT, that's no different. It's Lu-77 DOTA-something, but it isn't Lutathera. So that's one. There is a slightly different pricing for even the registered product. It is still probably a third more expensive for the registered product in the US than in Europe. And that seems to be common across other registered products as well. But we also have a more expensive delivery system here in the US. So, the cost of the drug is one aspect, right? There's that. And then there's the day in the hospital. A day in the hospital for an outpatient treatment might be a couple $1,000 or $5,000 elsewhere in the world. Here, we see a billing that's in the 10s or almost six figures for a day in a hospital that has nothing to do with the drug costs. So, yes, the registered product is more expensive and a registered product in the US is even more expensive than elsewhere. But we also have all these ancillary charges that are much more expensive in the US and probably even contribute a greater deal to the cost of this therapy in the US and elsewhere. And I wish I knew how to tackle that but I don't. As far as their insurance coverage though, that is the one thing. We can talk about how expensive it is, but in the US right now out of pocket maximum is $8,000 a year. And so if you're having all your therapy in one year, if you're covered by insurance, the most you're gonna pay as $8,000. Now, Medicare is slightly different, if you have gap coverage or the other coverage, you're probably not going to pay anything. But if you have private insurance or employee insurance, it's gonna probably be about $8,000 a year for the entire treatment. So ultimately, it's hard for me to tell which is better, or how much this really is going to cost you. I will say, for a long time it was really hard to get lung NETs covered, and I'm thinking we're getting more people who are getting coverage, but you know, the label and we talked about a registered product, and certainly when products come out, the insurance tends to pay for what's on the label. And the label was just GEP-NETs. It didn't include bronchial NETs. And some people were able to get that in saying it's NET of unknown origin and it's DOTA positive. But this is where we have clinical trials that will help us give better guidance and will end up in either than the NANETS guidelines or the National Cancer Comprehensive Network Guidelines, and that will lead to coverage decisions and that will help. But right now, in the NANETS guidelines, lung NETs that are in there as far as for PRRT or as a chance. But we know there's a clinical trial that hopefully will start opening up in more places and neighborhoods around you that will help give us better data so that it will be better level evidence that will make insurance cover that.

Lisa Yen
Really good points, Josh. We're hoping to have definitely more trials. Now you brought up the registered product versus, as I might think of it a homebrew product, is there a difference in quality with the two? So if the institution's making its own non-registered product?

Josh Mailman
Well, in the US, we don't really have anyone who's, I like to call it "rolling your own," but that's a whole different topic. But at the end of the day, people will QC the product and make it as equivalent to what was in the study as they can, but it's Lu-177 DOTATATE, most of those in Europe use Lu-177 DOTATOC. Some of them are using Lu-177 DOTA-JR11, or DOTA-LM3 or LM4. That being said, I think, one, places that you go will QC it to make sure what you're getting and how much are getting in and that the peptide is going to the tumor. So in general, it's pretty much nuclear medicine. Radiochemists actually do make sure that they're quality controlled and know what they're giving you. So they're gonna give you what they say they're giving you. And I know that was kind of like, does it matter where you go? If you're getting a standard dose of Lu-177 DOTATATE, honestly, I don't want to say it's a pretty easy thing to administer because no nuclear medicine is exactly simplistic to administer, but there's no nuclear medicine facility that is actually doing things with patients and nuclear medicine. This is a pretty known entity and how to do and during the pandemic, we had people who were staying in quarantine to go in certain places, and worried about flying across the country from one side or the other. Have it near where you are so you can be near family. 200 millicuries of Lu-177 DOTATATE is 200 millicuries of Lu-177 DOTATATE wherever you go.

Lisa Yen
Yeah, good point. That was a nice segue to that next question of does it matter where to go to get the treatment. Does it matter if it's local versus NET center? And does it have to be a NET center of excellence or by a NET expert?

Josh Mailman
I think one of the really great things that AAA did was to bring this closer to patients. It didn't have to be at centers that you had to travel all over. They were able to get nearly 200 places on board so that traveling to get therapy administered is not the limiting factor. Is a great to consult with a NET expert? Absolutely. You've had how many episodes about that? Does it matter who delivers you 200 millicuries? Probably not. Now, certainly if you have some unusual case or dealing with some type of challenging symptoms that you're unsure and want to go to high volume center, absolutely. But for 85-90% of the people, I think it's going to be much better that you get to stay near your home. You don't have to travel, you don't add all those extra things to it. So if the center is able to do it for you nearby where you are, I don't think any NET expert would say my Lu-177 DOTATATE that I'm buying from Millburn, New Jersey is better than the other centers' Lu-177 DOTATATE that they're buying from Millburn, New Jersey. They're buying it both from Millburn, New Jersey, although that's not where the Lu-177 comes from. I don't think patients completely understand the dance of what it takes to get their therapy to them, but the dance is pretty interesting. Lu-177 comes off a reactor in Columbia, Missouri and gets overnighted to New Jersey where it gets off the plane, picks up its bags at the gate and goes to Millburn, New Jersey, where it gets radiolabeled with DOTATATE and has its return tickets to wherever you're going to have therapy the next day, and that dance has to happen in 48 hours to get it in your arm. But it's the same dance wherever you are that you're getting it, it's the same.

Lisa Yen
And now hopefully available closer to home so people don't have to travel as far.

Josh Mailman
Yep.

Lisa Yen
Thanks. So Josh, you and I know that some people are told they can only receive four doses of PRRT in a lifetime. We hear that by patients all the time. What are your thoughts on this? Do we always need four treatments?

Josh Mailman
One, I'm not even sure we always need four treatments. And I'm not always sure that four treatments are going to be the end of the story. This is back to clinical trials, which is NETTER-1, and also the model that makes this kind of more universal, which is we study clinical trials. Setting variabilities in clinical trials is hard. And so NETTER-1 was designed for four 200 millicurie doses. If you couldn't tolerate it, you dropped out after two or three, and four was considered the maximum for, not lifetime, but for a cycle of therapy. There's no where in the FDA label that says there's a maximum for lifetime. Nowhere is this printed anywhere. I used to get this from oncologists, well you can only have four for the FDA label. No, that's not what it says. It says a treatment is four treatments, or a cycle is four treatments, but it doesn't say one cycle in a lifetime. That's you deciding that. And there are other treatments that are X number of cycles. We do CAPTEM which has a regimen. But we do more than one of those. We do them off label. So why are you saying for in a lifetime? Where was that written? So one, that wasn't written anywhere. Now, there are some studies, there's one in Canada that's looking at four 200 millicurie doses, followed by a maintenance dose of 100 millicuries every six months. I'm not sure if we'll ever see data from that, but that's one. And there are some other studies that are looking to try to or coming up that we'll try to see, maybe we can measure actually how much doses go into the tumor. And if we know we've given enough dose to the tumor, we don't have to do treatment three, or when we're doing retreatments, we don't have to do treatment. If we do one retreatment, we might stop after one and wait for a year or two. We may not have to do these two or four treatments as a retreatment. So the answer is we really don't know. But what we clearly do know is that there's no reason that four is the magic number. We probably are not going to see someone doing five in a row or something. But we'll see two, three and four and then a pause. If it does keep the tumor stable or not, for over a year, we can see people getting retreated. Now, is there a maximum? We don't know and it may be dependent on, you know, we're individuals and it may be dependent on how we function, how our liver, how our kidneys, how our platelets are recovering. And this may be more individualized than saying, there's ten in a lifetime or there's six in a lifetime. I think it's going to be really individual. But the simple answer is, we've studied the four we know four is safe for that initial round, and so that probably is back to the 80% or 90%. There's probably 10% of people who were underdosing and probably 10% that were overdosing but we're not really overdosing because they'll show up early and we'll stop. So we really are covering a giant swath of the population by doing it that way.

Lisa Yen
It's helpful to hear that four isn't necessarily the end of the story. And you mentioned clinical trials and all the different clinical trials that are out there. We know that there's stuff in the pipeline and beyond. So how might you decide, as a patient yourself and as an advocate, between repeating PRRT, meaning

Lutathera versus a clinical trial with a different type of PRRT or combination or another treatment altogether?

Josh Mailman
So, I don't think it's any different than the first treatment. You made an assumption, you do this something that kind of sat there and said, here are my options, what are all my options? What are the risks and benefit I'm taking with each one of them? And with every treatment, whether it's repeat PRRT, or just continuing with PRRT, or whatever you're looking at. At anytime you need to take treatment, you should be evaluating the entire scope of treatments that are available to you because things can change. And it isn't that I must continue this, it's like, wow, it's been two years. I mean, look, if it's been six months, it's probably not a conversation you're going to have. But you're going to take a look at what's on the table. What is there? What have you responded well to? How is your liver function? Did your platelets recover? All of these questions, but these are all the questions you should have across all the treatments, and you should be reevaluating everything that's on the table anytime you need treatment. So I don't know that it's any deciding repeat versus that, it's how you decided to have PRRT in the first place. You do the best thing that's available to you at that time. And that may be different for all of us because we all have other things to consider whether it's quality of life or other aspects of what we're looking at versus other treatment. But you need to look at the whole plethora of options that are out there for you. And there are more every time and will change. Now, how do you tell? Some of these things, you won't qualify for clinical trials. But if a clinical trials available to you, and that is interesting, by all means explore it. But the reason we have clinical trials is because we're answering a question, right? There's a fancy term when you're working in the clinical trial world called equipoise. And I can't, as an advocate, when I'm looking at trial and trial designs and trying to say whether I agree with the trial or not, we can't really move forward with this trial unless there's equipoise, which is the idea that each side is equally balanced. That we don't know the answer. If we knew the answer, we didn't really do the clinical trial. And so we don't have the answer. So if you want me to tell you which is better alpha, beta, or one peptide? We don't know. We have these trials so that we can put to bed the question, and if we make a trial that doesn't have equipoise, no one will recruit to it, right? We'll all try to figure out how to get around it. So these are trials that have questions, like the lung NET trial is doing Everolimus versus Lu-177 DOTATATE. But we have other trials, like there will be in PNETS, there's a Lu-177 DOTATATE versus CAPTEM, for instance, to see if you have a PNET and what you should be looking at first. So that's why we have these trials, because we need to answer questions, that are fair questions. If we knew the answer, we wouldn't be trying to ask the question because I can find people equally on each side of that discussion.

Lisa Yen
Thanks for that. And hopefully, as years pass, we can get more and more answers so that we have more information.

Josh Mailman
We won't always get answers. There's only so many of us that can be in trials, especially for NETs at any given time and who can sponsor. There won't be answers to everything, but we'll get some more answers and we'll we'll try to get that stuff out.

Lisa Yen
Thanks, Josh. So switching gears, you mentioned traveling with PRRT, and hopefully less of that now that there's more Lutathera available across the country. But for those who have to travel, what's the

patient experience, regarding traveling after PRRT? I know you've done a paper on this and a lot of talks about this. Do we need to worry about setting off security alarms at the airport? I know that after Lutathera the nurses usually give you a card for going to the airport. What other security alarms such as event venues or courthouses do people have to worry about?

Josh Mailman
Always carry the card but know that people might laugh at you with the card, and certainly Customs and Border Patrol will most always laugh a little bit because anyone can type up a card and put it in their wallet. Let's let's go backwards a little bit. This was always a source of misinformation and challenges, as well. The people who are concerned about radioactivity happen to be Homeland Security and CPB, Customs Border Protection. They're the guys and gals wearing little clip on belts that actually try to monitor this stuff. So traveling inside an airport and going anywhere domestically, CPB doesn't care. You can go on an airplane, do whatever you want. What people care about are borders and sensitive installations. So when you come back into the country, whether you come via planes, trains, or automobiles (it's Steve Martin's movie). Anything that you do where you're crossing a border, there will be someone wearing a little thing on their belt, that will actually sense a therapeutic isotope from almost 50 feet away and will start beeping like crazy. Doesn't matter who you are, what you are, it's going to beep. And so it's any port of entry, whether it's planes, trains, automobiles, or boats, will have someone like that and any sensitive installations. So are movie theaters sensitive installations? No. Some of the tunnels in Manhattan have agents that sit outside. If you're traveling in Washington, DC, you're likely to have other people who have these things on their belts, but in general, it's sensitive installations and borders where you will be active and potentially sensed for ten half lifes of whatever you're on. So Lu-177 has a half life of 6.7 days. That means for about 70 days. So hopefully you go do something relaxing and go to a cruise after your PRRT and hang out. But if you're coming back through Mexico, you're going to be stopped. And people are going to ask you what you've had. They'll take out once a thing, you'll give them the letter, they might be nice to you, they might figure it out. Or they might get misinformed and try to wand you and find out that you have the same signature as plutonium and need a little bit more verification. And so the big thing is, should you worry? No. Will it happen? Yes. Does it take some time? Yes. Build some time into that and understand why they're doing it and why this might happen, and know that will happen for 10 half-lifes.

Lisa Yen
Thanks for that and for the clarity around that. So one of the big advancements is alpha PRRT. There's a lot of buzz around this, everyone wants to know about it. So when it is more readily available with clinical trials, how might patients go about deciding between various PRRT options, like the alpha versus beta? And what do you consider as a patient and as an advocate and tell those in your group?

Josh Mailman
So I'll go back to the question we answered a few questions ago, it's pretty much the same, right? I mean, first of all, some of the trials you're PRRT naive, you haven't ever had therapy yet. Some of them is you've had four rounds of therapy. So, what's available to you, first of all. And then if it's available to you, is it interesting? Do you have something that's different? Because the registered product is really cool. We've got progression free survival for over three years. That's really outstanding. So how much better could it be? And that, it will take a while to tease that out? We don't know. I mean, there's some unknowns that we don't know about, like long term effects. Other issues that might happen, but we just don't know. And that's why that's why we do these things. That's one aspect of it. The other aspect is, look, if you've had Lu-177 and it hasn't lasted as long as you would have liked, do you look at that as

one of your options in therapy? Will it help you in comparison to the basket of other things that you're looking at? And that might be another reason to explore a retreatment trial that uses an alpha agent, and there'll be a few of those coming out as well. But it's back to what I said before where you lay out what all the options are. Yeah, I'm as excited or potentially even more excited because of the availability of peptide stuff than necessarily isotope. They're all interesting, but they're all questions that need to be answered. And so for the majority of people right now as an initial therapy, it's going to be Lu-177 DOTATATE for the majority of us. There might be special or reasons to take a look at. But even in the Alpha Trial that's now for someone who hasn't had PRRT yet, there's 36 slots over the next two years. That's not a lot. So, we're really lucky. I do a lot of reviewing clinical trials. And we talk about moving the needle for overall survival from four months to six months. We're talking a treatment that has progression free survival of three years plus. That's pretty impressive.

Lisa Yen
Yeah, thanks for that. And we're talking about all the different options that are out there. As you know, some people are told by their doctors, let's save PRRT as last resort. Let's go through everything else that's FDA-approved first before PRRT. How would you respond to this?

Josh Mailman
So I've had to respond to these in meetings before. I don't get it. I understand that it's a second-line treatment, because somatostatin analog therapies are really effective and are well tolerated and have a really low risk profile and treatment burden. So I get that that's first line treatment. But, for many, and it's like evaluating everything across PRRT, it doesn't matter which order you take them as far as we know. There's not subtractive or additive. If I'm in pretty good shape, I'd like to stay in pretty good shape for as long as I can be in pretty good shape. And some of the drugs we take, they're not easy drugs to handle that are second line. And so, for me, I would like to have a joyful life and an easy life for as long as I can. And so for me, I want to take easy stuff first. And I don't mean easy. I mean things that don't crash my quality of life. So there's a lot to do, and why is it the last resort? We get freaked out about radiation, and understood. Look, there are risks with any of the second line cytotoxic drugs, and they're kind of known risks at this point. And as long as you're comparing apple to apple, whether you do PRRT first or whether it's last, or whether you do CAPTEM first or last, or Everolimus, they all have risks that you need to line up and take a look at and understand what those are. And honestly, most of the cytotoxic risks that we're talking about that people of why they were always saying save PRRT for last are the same, regardless of what drug you're taking.

Lisa Yen
Thanks for that, Josh. And thanks, again, for all your work in this area. We know that you've done a lot of work not just as the President of NorCal CarciNET, but on many committees, SNMMI, patient advisory boards, and other different organization patient advisory board, and most recently, in the last year, you were appointed a member of the Nuclear Regulatory Commission's Advisory Committee. So that's really exciting and it's a big deal. But please tell us a little bit about your role as a member in this and what does it entail and how does it this also make an impact?

Josh Mailman
Alright, so I get to put you on the spot. Lisa, how many nuclear medicine, either exams or treatments, diagnostics or exams are done in a year?

Lisa Yen
You tell us.

Josh Mailman
No. Go for it come up with a number. Have fun!

Lisa Yen
How many total?

Josh Mailman
Yeah, diagnostics and therapeutics. For all cancers for everything. And not only for cancer, right? We also can spot infections with nuclear medicine.

Lisa Yen
Couple of million?

Josh Mailman
24 million a year!

Lisa Yen
24 million! Wow!

Josh Mailman
So, these are big numbers. And nuclear medicine is actually regulated through the Department of Energy and through the Nuclear Regulatory Commission. In reality, the Nuclear Regulatory Commission usually works on things like nuclear power plants, energy, safety of the nuclear stockpile, etc. They're not exactly all medical experts, although they have great staff that works on that. But they basically have an outside committee of experts that advise them on the use of medical isotopes so that they can make informed decisions at the commission level, because it really does control a lot of things. We all talk about NETSPOT generators and the ability to actually have a NETSPOT generator is determined by, do you have a safety plan for having that generator there? And so the role of a regulator is really interesting. And the role of the advisory committee is to help that regulator understand what they're regulating. And to help things we call rulemaking. Then there's things we call just giving guidance. And things like release criteria, which we could probably spend a whole two or three days on. And safety of getting nuclear medicine in your veins, which we could also spend a little bit of time on. And really, as a member of the advisory committee, we work on those things. We meet as an entire group twice a year, but as in subcommittees in various different areas. We meet monthly and sometimes every other week to discuss various topics that have come up or to rewrite guidance. And one of them that we really work a lot on is radiation safety and release criteria for patients. And that's an area where there's a lot of confusion. And really my work on the advisory committee is to help put the patient perspective in these regulations and to make sure if there's ambiguity or issues that may come up that may confuse patients that these are addressed. And honestly, especially for therapy, a lot of these regulations for release criteria, or the release criteria that were issued by the NRC, were written in a time where there was just thyroid therapy, I-131, for thyroid cancer. And that was probably the predominant therapy for patients having nuclear therapy for the last six years. And it really isn't until sometime in 2020, that probably neuroendocrine tumor patients having Lu-177 surpass the amount of people having radio I-131. But a lot of those regulations were written specifically for thyroid patients.

And so a lot of the sleep separately, or be away from people for a week at a time, or only eat on paper plates, these are all left over from thyroid, which is a completely different isotope. I mean, the isotopes all kind of decayed the same way, but they have different energy and some of them have different gamma characteristics versus beta characteristics. So it became very interesting to work on the rewriting of the release criteria, and one of the things I did as a patient is I said, look, right now, there's an order of 10 examples of things that we need to tell patients. Are they ordered in any particular way? And it was like no, they're randomly ordered. It's like, well can we put the things that are most important first and put them in descending order so patients understand what's most important? And if there's a reason for something, can we explain what that reason is? And if we don't have any idea of why we're doing something, can we take it out? So one of the instances was flushed two or three times. Every time you go, well what is it, two or three? I don't know. Did we ever study this? No. We actually need it? I mean, yes, flush, but probably more important to put flush with the lid down than flush two or three times. Honestly, I'm not sure that the second or third will do anything, but having stuff splash out of toilet is bad, because that will make the area around the toilet radioactive. So that's why we flush the toilet seat down. Flushing twice doesn't take more radioactivity out of the thing. So those are the types of things as an advocate, you can sit there and say, why are we doing this? I saw so many people who were renting separate apartments, it's like, yeah, maybe for I-131 it's more important. Can we put when and how and why, and make it more universal? Because right now, we have Lu-177 with the latest prostate approval will certainly become the dominant for a while, but at some point, we're going to have alpha particles that will be approved. We already really do with radium-223 for bone cancer for prostate, but we need to make these more universal and better done. What I say is rinse and repeat. They take the thyroid thing and just say sure, we'll give this to the neuroendocrine tumor patients or the Lu-177 patients. But it's a little bit more complicated than that. I know one of the last questions is, what's the process and procedure of safety in the US? As a regulator, we give minimum criteria, minimum guidelines. The RSO, or the Radiation Safety Officer, of a particular center is responsible for releasing patience. And while the RSC [Radiation Safety Committe] can give and the different regulatory agencies around the world can give specific minimum requirements, which turn out to be different in different parts of the world, but only slightly. Individual institutions can change those requirements. And actually not go below the minimum, but suggests more things. And that's why I think it confuses patients, because different people who go to different centers will get slightly different instructions. Last year or the year before, Tom Hope and I did a whole thing on, how long do I have to be separated from my loved ones? I had a paper written in 2013 on this topic with Harvey Turner and Phillipe Calais on this entire thing for Lu- 177, to show that it was completely safe to do as an outpatient. But yet, in Germany and Austria, you need to be in the hospital for 48 hours and can't be released. And the isotope is the same. That's the one thing we know universally. But different jurisdictions can decide to put on different requirements. The IAEA, the International Atomic Energy Agency, has a guideline that is pretty close to the NRC's release criteria, but how individual states and countries decide to do that, and then the individual RSO's can completely change that and add more restrictions that you wouldn't think of. But in general, for what we do in Lu-177, as Dr. Mittra showed on his thing, this stuff doesn't go very far. It's not like gamma. And alpha even can't penetrate past the paper. So we've got different things that are going on that that's certainly naked. It's much safer. We hear the word radiation, and we get really freaked out. But honestly, if it was as bad as everyone said, for keeping people away from you, for a long period of time, all your other internal organs would have a hell of a time with this therapy because they're a lot closer than anyone who's in the room.

Lisa Yen
Thanks for that. Thanks for your reassuring words. So in closing, Josh, what can patients do to learn a little bit more about this topic? Feel free to add any other closing remarks that you'd like to share.

Josh Mailman
Almost every patient organization is doing some type of education day. Talk to your oncologist, talk to your nuclear medicine team, if you have more questions. Since 2012, I've been running a patient education day for the Society of Nuclear Medicine and Molecular Imaging always in June, except when we had these virtual pandemic days. This year, it's on June 12. We keep the URL the same every year, it's SNMMI.org/PED. And if it has last year's thing up, it will switch to this year's thing as soon as registrations open. It's in person, this year will be in Vancouver. However, there will be hybrids so that people will be able to view and listen and participate from other parts of the world as well. We usually have two or three speakers and bring you updates on what's going on this year. 2022 is the 6th Theranostics World Congress, which will be in Wiesbaden, Germany a week after the LACNETS conference. And we'll try to put the patient panel online as well. And that's where we really talk about the real far future of nuclear medicine and things that aren't necessarily even tied to DOTATOC and DOTATATE for NET patients. So that will be online from Wiesbaden. And I've been fortunate to be on the Scientific Committee of all six Theranostic World Congresses where I met Dr. Van Brocklin originally. I think the 7th Theranostic World Congress will be in a year or two in Santiago, Chile, if you happen to want to travel to Santiago, Chile. And that's where you can find more information. ClinicalTrials.gov, you can put in PRRT or Lu-177, or alpha and PRRT and see what the clinical trials near you are. Those are all ways. Keeping in contact with NorCal CarciNET Community, the LACNETS community, always good. But always remember, we see a lot of individual stories and a lot of people get really excited and hyped about certain things. We need to see good clinical trials before you get overexcited. So please participate. Please help out. We look forward to talking to you and hearing any questions in the future.

Lisa Yen
Thank you, Josh, thank you for all you do. Thank you for being the voice for the NET community and for all of us and advocating on our behalf, and for taking your own personal experience, your own personal journey, and really let that be the driving force to make this impact in not just in the NorCal area and not just in the US but around the world. Thank you for that. Thanks for listening to The LACNETS Podcast. We want to thank our podcast supporters, Advanced Accelerator Applications, TerSera Therapeutics, and Ipsen Pharmaceutical. For more information about neuroendocrine cancer, go to www.LACNETS.org.