**SEASON THREE: Episode 41**

Dr. Luis Raez Discusses the Impact of Precision Medicine on Lung Cancer Treatment

Nov 25, 2020

Karan Cushman: Welcome to season three of the Precision Medicine Podcast sponsored by Trapelo. This is the podcast where experts come to discuss the problems oncologists, reference labs, and payers face as precision medicine grows and consider solutions for advancing the quality of patient-centered cancer care. Be sure to subscribe at precisionmedicinepodcast.com to get the latest episodes delivered straight to your inbox.

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Jerome Madison: Welcome to another episode of the Precision Medicine Podcast. I'm Jerome Madison and today we have Dr. Luis Raez, medical director and chief of hematology oncology at Memorial Cancer Institute in South Florida, and current president of FLASCO, Florida Society of Clinical Oncology. Dr. Raez, thank you for being a guest on the podcast.

Dr. Luis Raez: Thank you very much for the invitation, Jerome. It's a pleasure to share with you and with the audience about this important topic.

Jerome Madison: Absolutely. Now I understand that you were born and raised in Peru. Give us a little bit about your upbringing and what attracted you to medicine, and why specifically did you choose oncology?

Dr. Luis Raez: Yeah, I was born in Peru. My father was a doctor. My father has live before in the United States, he went back to Peru. He brought me when I was small, and I thought that this was an amazing country. When I decided to study medicine, I studied medicine originally in Peru. I liked the idea to practice in the best medicine in the world, that's why I came to America to learn as much as I can and to use all of these resources that we have to practice medicine. And I became oncologist because it's very challenging.

Dr. Luis Raez: As we discussed before, things change all the time. We have new medications and the fight is a very difficult fight. So intellectually, is your whole life dedicated to a course that is worth to live for, and that's why I choose oncology. I'm involved in the field of lung cancer mainly and have decided to dedicate the rest of my life to fight lung cancer and save as many patients as we can through research, clinical trials, education, advocacy, everybody seen that we can do for our patients.

Jerome Madison: Yeah. 10 years ago, treating lung cancer in your honorarium of what you had to treat patients with was very different than it is today. How has the emergence of next-generation sequencing testing changed your approach to lung cancer treatment?

Dr. Luis Raez: Is amazing because we used to use empirical chemotherapy when I started. I started practicing lung cancer in 2001. And that was very frustrating because as you know the response rates are low, 30% maybe of the patients, and the survival is like a year. And we didn't have anything better, so the first 10 years were very difficult. We were only able to discover Bevacizumab, the monoclonal antibody anti-VEGF, and that really didn't make a lot of difference either, but at least now our patients were able to maybe live, some of them, more than a year. And that is why next-generation sequencing is a revolution, because now we are able to customize the treatment and do a personalized medicine, because we know what is the driver for the tumor. So now we're going to find the treatment, the inhibitor for that driver. And that is why is becoming fascinating because now we really feel more useful, and I now really feel that we can impact the natural history of the disease of the patient. And that is why next-generation sequencing has been so fascinating for us.

Jerome Madison: Lung cancer has become the envy of other diseases because of the number of targets that they're finding, druggable targets that they're able to find for lung cancer patient. There is an NCCN Biomarker Compendia, but we still hear a lot about the lack of testing. What do you think the adoption rate for physicians has been for the recommended markers as precision medicine has grown?

Dr. Luis Raez: Well, if you see the statistics they are not very good because depends how you do it. For example, everybody agrees that any new lung cancer patient needs to be tested. But these are the bait if, how many times you're going to test it. To give you an example, we start doing testing by tissue. We do NGS in tissue and you know that probably in America or any part of the world, 20% of the times the tissue is not enough. The sample is insufficient. Then you took away 20% of the candidates to get precision medicine. So as a doctor then you have to make a decision. You say, "Oh, I'm sorry. You have bad luck. You are in the 20% that you will never have a molecular marker." Or you can do the extra mile and say, "No, I have now liquid biopsy. I can do NGS in liquid biopsy. So I will test this all the 20% with NGS."

Dr. Luis Raez: But there is a major difference in both situations because if you are only going to test 80%, you are leaving without testing more than 40,000 lung cancer patients in America, because we have a lot of lung cancer patients, 225,000 a year. So that is why, for example, a lot of doctors don't do the extra mile. They say, "Okay, I checked the box. I did NGS, and I don't want to be sending a liquid biopsy when I can do chemo-immuno tomorrow." And the patient say, "Oh yes," because the poor patient [inaudible 00:06:21] sometimes patients spend 90 days from the day that they notice that the cough that they have is important, to the day that they come to the medical oncology office. This is when you tell patient, "Oh, don't worry, your NGS is negative. I want to send a liquid biopsy, come back in two more weeks." And the patient is already ready to start treatment the same day.

Dr. Luis Raez: That is why NGS by liquid biopsy is a very, very good option, because even waiting for the tissue is a four week waiting. And that is why the success of chemo-immuno is not helping us. Because since we have chemo-immuno available, some patients say, "But why need to wait four weeks? And how about if in four weeks you tell me, oh, I'm sorry that there was not enough tissue." We only wasted four weeks. I need to do another biopsy and wait another four weeks. So I need to do a liquid biopsy and wait two more weeks. So that is why I think there is a need to be more aggressive in doing NGS for new patients, especially lung cancer. Maybe one solution is to do liquid biopsy in everybody and tissue in the ones that you can.

Dr. Luis Raez: The other problem with tissue also is that, of course, 80% of the time you can get a diagnosis, but a lot of times for example, at tertiary center, meaning that a lot of the patients come from all the facilities. And then I have to order a tissue NGS in a facility that is not mine. So the pathology technician in the other facility gets an order from me to submit tissue to one of the vendors and the technician may say, "I don't know who is Raez, maybe I will do tomorrow, I'm busy today. I'll do in three days from today, or I'm overwhelmed, I'll do next week." And I don't have any power to obligate the technician to do this because it's not my hospital is not my healthcare system. So that's another disadvantage of tissue. If you practice in a big center, a lot of these samples will be coming from other centers that are not yours, so that's why the delay may be more than four or five weeks.

Jerome Madison: Yeah. Understood. You mentioned a lot of challenges, but despite those challenges, it seems that every week there are significant findings or reports from studies that show patient improvement, new drug indications or combos or new discoveries. So we asked Dr. Raez to come on and share with us what he feels were some of the most significant developments in precision medicine for lung cancer patients over the last year. So what are the highlights over the last year that you think are significant for patients and providers to know about?

Dr. Luis Raez: Oh, they're not that a lot. Let me see. For example, we can talk about the RET inhibitors. RET is a fusion. RET, R-E-T, is a genetic aberration that we didn't have a drug until this year. And is agnostic because you can have RET fusions in lung cancer, you can have RET fusions in medullary thyroid cancer, but also there are RET fusions in pancreas cancer, colon cancer and other cancers. So for the last four or five years, we have been working with developing two drugs for these RET fusions. And we were very happy that this year, both drugs got FDA approval. The LOXO-292, selpercatinib got approved for lung and medullary thyroid cancer and the other company BLU had the drug approved, pralsetinib, for lung cancer, and hopefully soon for medullary thyroid cancer too.

Dr. Luis Raez: So this is a very important topic because RET is present in maybe... Some people say, "Oh, it's only 1% or 2% of the lung cancers." Yes. But we go back to the same thing. We have 225,000 new lung cancers a year. So these drug maybe important for some several thousand patients. Plus if you add the thyroid, and I'm still having the trial open for the cohorts that are GI. So we're still trying to find if it works for pancreas and colon. So that's why this is a very exciting moment that we have been able to add another genetic aberration to the list that we are targeting.

Dr. Luis Raez: I know that interesting development for me is the fact that we have been attempting to target KRAS for many, many years. Because KRAS is a very common mutation in lung cancer, and we weren't successful, and we didn't understand why we weren't successful, we had tried several times in the last 10 years to target KRAS. But then we realized that KRAS is not only one genetic aberration. We realized that there are many subtypes of KRAS genetic abnormalities and not all of them behave the same. So that is why in the last years we started to do research for a specific subtypes of KRAS and for example, for the KRAS(G12C) we have a drug developed by Amgen that now is very promissory. I don't know if it will ever get approval now, because we're only talking about the phase one and two.

Dr. Luis Raez: But the fact that at least now we have a drug that will give a response rate by at least 30% to 40% as it was presented in the last ESMO, for example last month, is becoming very exciting because as I said, these genetic aberration is very common. And we need to discover also inhibitors for common genetic aberrations, because most of the inhibitors that we have now for RET, NTRK, ROS are very uncommon, all of the money in the 1%. So we need to really make a home run and discover the role for genetic aberrations that are more common. That's why I say I'm very excited that maybe we have now the potential to have a new agent, even if either response rate is low, you can say maybe 30%, 40%, but is better than zero, is better than put all of these patients on chemo. And you can still put them on chemo once that they failed it and become resistant, they can still have the current benefit today that is having chemo-immuno. So that is why we are adding another option for the patients.

Dr. Luis Raez: And then another important development this year in precision medicine, maybe it's the fact that in lung cancer that we can use now a combo, Ipi/Nivo, ipilimumab and nivolumab without a chemo. Is the first time that in lung cancer we can use in frontline a combination for lung cancer that doesn't need chemo. Because if you remember, we are using checkpoint inhibitors. We have three checkpoint inhibitors approved by FDA for second line, third line, fourth line, but we incorporated all of the checkpoint inhibitors in the frontline with the help of chemo. But this year, finally, we have enough data that the patients have PD-L1 more than 1% as biomarker, they can be allegeable for Ipi/Nivo. So that is very exciting too, because it's an option, maybe, for patients that don't have a large tumor burden, maybe they are senior.

Dr. Luis Raez: I work in Florida. I am treating with Ipi/Nivo an 86 year old and maybe for them it's not easy to take chemo, even if it's a short chemo, because most of the combos that use chemo with immuno are only four cycles of chemo. But that's why this Ipi/Nivo is a very interesting development that we were waiting and now that's another option for us.

Dr. Luis Raez: The other exciting topic is ALK. First of all, there was a publication in the Journal of Thoracic Oncology from the group of Denver, Colorado. They have been developing inhibitors and doing research for ALK for a long time. And they published the first 100 patients that they treated with ALK inhibitors, it's only a retrospective publication. You can say, "Oh, that's not very important." But it's amazing to me to discover that the median survival for these ALK patients is 82 months, seven years. It's a stage IV lung cancer patients that are living now seven years.

Jerome Madison: Wow.

Dr. Luis Raez: Remember I begun this conversation saying all my patients live one year or less. That's why going back to what you were mentioning before, is imperative that if somebody is ALK you need to discover that, because that patient can be alive seven years. And if you don't do the effort with the proper NGS, you are going to deny this patient that survival, because you don't find the ALK aberration. So that is why it's very important that we find the proper genetic aberration.

Dr. Luis Raez: So in the same field of ALK in ESMO, finally, we have data that lorlatinib, the last ALK inhibitor, now can be used in frontline because is superior than crizotinib, that is like the standard of care for many years. It was a standard of care because it was the first algabrew. Lorlatinib, we have very good data in the last three years. With lorlatinib you pretty much can rescue any patient that has failed another ALK inhibitor, but we didn't have data in frontline and now we're waiting for FDA approval, because we don't have approval.

Dr. Luis Raez: Also in this year, we have another ALK inhibitor called ensartinib that also in the data presented in the Presidential Symposium show how he beats crizotinib with a much better progression-free survival. So we have another option with ensartinib for these patients, also, we're waiting for the approval. But it's exciting because these two agents are adding to their armamentarium that we have for ALK. So now we have six agents approved and there are still more coming. But these are four major things that I think are very important in the lung cancer in precision medicine that I remember this year.

Jerome Madison: 2020 has been an incredible year in so many facets. I mentioned in the intro that you are the current president of the Florida Society of Clinical Oncology. The challenge is with late diagnosis of lung cancer, Dr. Raez, how has this whole COVID shut down quarantine affected the practice of cancer care, specifically for lung cancer patients.

Dr. Luis Raez: This has been terrible because this morning I was telling you I was doing some interviews. I had eight interviews with TV stations because, I don't know if you're aware, but in August six, there was a JAMA Oncology article that shows that there has been a decrease, 46%, in the number of diagnosis of six more common cancers in the United States. And nobody's happy because we're not curing cancer, normally this will be great news. Is because we know that we are not going to cure all the cancers yet. So we are diagnosing this year 46% less patients that we expected.

Dr. Luis Raez: There is also a report of the COVID oncology network that they say the number maybe as high as 70%. The National Cancer Institute director was interviewed about this and he said that, "If we are delaying cancer diagnosis, for example, in the case of breast and colon, that can mean 10,000 more people dying in the next 10 years, because we are going to diagnose more people in the late stage instead of earlier stage. So instead of going for cure, they're going for palliative treatment." So that is why this is very important.

Dr. Luis Raez: The same is happening in England, in UK. In specific case of lung cancer in UK, they say that probably they are going to have 1,300 more lung cancer deaths due to the delays of the COVID. So that is why we're very worried about this. We are doing a campaign at the national level with ASCO and all the patient advocate large groups and at the local level, with FLASCO. That's what we're doing this campaigning, all the TV, radio stations to tell the patients, please come for your checkups, mammogram, lung cancer screening, colonoscopy, PSA. Also the survivors. When the COVID came, the first group that is not essential to be in the cancer center are the survivors, because they are cured and probably all of them are cured. So we told all the survivors, "Don't worry, don't come for your checkups because this is going to be full of patients that are on chemo, and we don't need more people in the room. If somebody gets COVID is going to be terrible."

Dr. Luis Raez: So a lot of the survivors are postponing his follow-up PET scan, his follow-up colonoscopy, his follow-up x-rays, his follow-up blood test. So that's why somehow then the cancerous make return and we don't find it early, maybe too late when we find it. That's why my cancer center, Memorial Healthcare System, and all the local centers in South Florida, like University of Miami, Jackson Memorial, all of us are doing commercials in TV, asking the patients to please come back, is safe here. Is interesting. Now that we are fully open, the patients believe that if they come to the office, they can get COVID here. But they don't mind to go for a restaurant. The once I study, I love restaurants.

Dr. Luis Raez: Believe me, I'm going to restaurants now because in Florida, everything is open. But the chances to get infected in a restaurant is probably higher than the chances to get in the office, because here in the office, we use shields, face mask, hand sanitizer, social... We're very strict for social distancing. We don't allow relatives of the patients in the office. We don't allow relative of the the patient in the hospital. So this is the safest place to come now, that's why we cannot keep delaying the diagnosis of cancer.

Jerome Madison: Yeah. Thank you for that intimate look behind the curtain as to what the physicians are having to do to drive care for patients. You're obviously very passionate about mentoring and educating physicians, as well as patients. And you do a significant amount of work in Latin American or Latin countries across the world in Central and South America. Can you tell us about some of your efforts in your conferences that you help lead to improve lung care in those countries?

Dr. Luis Raez: Yes. The problem that we have in Latin America is that we have what we call middle income countries or low income countries. And that, of course, puts them on great disadvantage because all the new developments that we have been discussing, for example, for precision medicine, they take an extra one, two or three years to arrive. And even if they arrive there, you can understand the cost of all of these treatments, make it really, really difficult to practice the same level of medicine over there than here. But at the same time there's great education and advocacy. So that is why we cannot fix the economic situation of these countries, but we can influence in the education of the doctors and the patients and the advocacy.

Dr. Luis Raez: So that is why I'm very proud that we have a lot of oncologists in Latin America that are very well-trained. And one of the reasons is because we interact with them constantly. We publish with them constantly. We're trying to be sure that they know as much as we know here, and they learn what are the latest developments here in the United States and Europe. That's what we do, a lot of educational events. I worked for example, with ASCO, we have international group and we do seminars in Latin America, the same as we do in Africa, or in India, or in Asia to try to elevate the level of oncologists with the IASLC, International Association of Lung Cancer.

Dr. Luis Raez: Same thing, we even have annual or bi-annual Latin American meeting, where we present the latest in lung cancer occurring in the world for Latin America, and is well attended. Sometimes we also work with ESMO trying to improve the training for new researchers and young people in Latin America. We do seminars over there. So that's why we are trying to do as many initiatives to try to help our oncologists in Latin America be well trained and be able to one day, hopefully, practice the best medicine as we practice here. But still a big limitation is the fact that, as I said, the economic situation makes it difficult sometimes the access to NGS, for example, or the access to new drugs.

Jerome Madison: Yeah. I listened to your conversation with Dr. Jack West on the West Wind podcast. And you spoke about your wife is an infectious disease doctor who runs the age program, I believe at the University of Miami?

Dr. Luis Raez: Yes. Pediatrics only.

Jerome Madison: Yeah. But over that time, since she's been running the program, AIDS has become a chronic disease. And she's losing patients, which is fantastic. Do you see a future for lung cancer, with the number of targets and the way that liquid biopsy extends the benefits of precision medicine, do you see a possibility for lung cancers to become a chronic disease of some sort?

Dr. Luis Raez: Yes. I give you the example of the ALK. These ALK patients, according to this publication from Colorado, I quote, "They live seven years now and that's there medium." So meaning that patients may leave longer than that. I have my own ALK and ROS1 patients that are alive, now 10 years. That's why since precision medicine, we really need to transform or combat lung cancer to a chronic disease. For example, with immunotherapy, if you see the presentation of Dr. Julie Brahmer before in ASCO, you see the presentations from UCLA with atezolizumab and the presentations also for pembrolizumab, we have now five years survivors. And these five years survivors are with no treatment. So I personally have in my cancer center around 12 people that we give immunotherapy for two years, is pretty much all standard. And then we put them under observation, waiting for them to relapse to start another modality, and they have not relapsed yet. So that's why it's amazing.

Dr. Luis Raez: We were using targeted therapy or immunotherapy, but we didn't saw that we may cure people. So at least we're making this disease a chronic condition because if my patients, when they relapse, they are being already enjoying two or three years without any treatment so if they even relapse, we can start again. Three years without any treatment we start clean now. Or maybe we're curing them. These patients for example, if you get them pembrolizumab because their PD-L1 is more than 50% is amazing that half of the patients are alive five years. Maybe these half of the patients are cured.

Dr. Luis Raez: So that's why I'm very, very optimistic now that at least we're making this a chronic condition not for everybody unfortunately yet, because we need to find drugs for the targets that we already have identified. We have identified targets for 70% probably of the lung cancers, but we don't have the drugs for 70% as you understand. And we also need to improve the use of immuno. We're using immunotherapy as much amazing as it is empirically. Really we're giving immunotherapy to pretty much everybody, and then we saw the patients. The ones that respond they continue immunotherapy, the ones that don't respond we take them out. With the help of the PD-L1, we are trying to figure it out, which ones are going to respond. That's why now we are dividing the patients in PD-L1 positive or not so they can get treatment.

Dr. Luis Raez: But if you are giving immunotherapy with chemo, pretty much doesn't matter what is your PD-L1, everybody gets a chemo-immuno combo. So that's why we need really to find a better biomarker for immunotherapy to really do a better precision medicine. For the last three, four years, we have a lot of expectations in the TMB, in the tumor mutational burden. But as you know, there is no harmonization yet. Everybody does their own TMB the way that they want and doesn't seem that they are compatible with each other, even the definitions of high or low TMB are very different from many different vendors. So that's why this harmonization project that is ongoing it has to give us an answer so hopefully we can agree what's TMB, how to measure and what is high what's low. We'll be able to divide the patients better and use a more accurate way, because we know therapy is very expensive too, and why to put people on side effects if they are not going to benefit from the drug.

Dr. Luis Raez: So that's why this is very important. And talking about discoveries, I don't know if you heard, but the last two years, we have a lot of publications about STK11 and KEAP, and maybe it's time for us to discover genes that can indicate us the immunotherapy is not going to work. They are very valuable because at least we know which case immunotherapy is going to work and which case is not going to work so we accurate research immunotherapy in the cases to work.

Dr. Luis Raez: I know that the data with STK11 is still controversial, but at least it gave us an idea that discovering something like the PD-L1 or TMB that tell us if it's going to work is so important as discovering something that can tell me that immunotherapy is not going to work, because in that way we can be more accurate. We can do a better precision medicine with the patients.

Jerome Madison: Dr. Luis Raez, medical director, chief of hematology and oncology at the Memorial Cancer Institute in South Florida, and the current president of FLASCO, Florida Society of Clinical Oncology. Dr. Raez, if anybody wants to get in touch with you on Twitter or social media, do you have a platform where they can reach out to you?

Dr. Luis Raez: Yeah. My, my Twitter handling is luisraez1. I am a lingering. Is very easy to get in contact with me. Memorial Healthcare System, I am the medical director here. Is a third largest healthcare system in America that is public. So that's why I'm very easy to find.

Jerome Madison: And you can always go to precisionmedicinepodcast.com and you can find his social media handles and a way to connect with him there. Now, before we let you go, one very important question since you being from Peru. What's better? American football or soccer which is played around the world.

Dr. Luis Raez: Okay. So the Superbowl is watched by 150 million?

Jerome Madison: Right.

Dr. Luis Raez: Yeah. The final of the soccer world cup is watched by 1.5 billion. It's not that it's better, but it's only more people watch soccer.

Jerome Madison: Yeah. Well, once you get out of the United States, I guess there's really is no contest.

Dr. Luis Raez: Yeah. And there's no reason for other countries not to learn about football. I guess it's a younger sport than soccer.

Jerome Madison: Well being an ex football athlete, my body says I should have chosen soccer.

Dr. Luis Raez: Yeah. That's true. That's important.

Jerome Madison: Dr. Raez, we really appreciate you giving us updates on the fast moving world of precision medicine and lung cancers. And thank you for being a great guest on the Precision Medicine Podcast.

Dr. Luis Raez: No, thank you very much for what you're doing, Jerome. This is extremely important for the doctors, for the patients. I think education is the key to move forward the need in the fight against cancer.

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**About Our Guest**

**Luis E. Raez, MD, FACP, FCCP**

​Medical Director of Memorial Cancer Institute (MCI)

Dr. Luis Raez is also the Oncology Research Director of Memorial Health Care System (MHS) and Director of the Thoracic Oncology Program. As well as the Clinical Associate Professor of Medicine at Florida International University (FIU) and Visiting Professor of Medicine at Cayetano Heredia University in Peru. Currently, Dr. Raez designs phase I-III clinical trials with new chemotherapeutic agents and combinations. Dr. Raez does translational research in the areas of cancer vaccines and has been funded by NCI and the pharma industry.  Dr. Raez has given oral presentations and lectures in national and international meetings in the US, Europe, Latinamerica and Asia.  He is American Board Certified in: Internal Medicine, Medical Oncology and Geriatric Medicine. He is board elegible in Hematology.  Dr. Raez is a member of AACR, ESMO, ASCO, IASLC, ALLIANCE, NCCTG, ACCP, ACP, ACSG, FLASCO among other institutions.