**SEASON TWO: Episode 33**Dr. Arturo Loaiza-Bonilla: The Impact of Precision Medicine on Gastrointestinal Disease

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Producer, Karan Cushman: Welcome to season two 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.

Host, Jerome Madison: Thank you for joining the Precision Medicine Podcast. I'm Jerome Madison, your host. And today we have Dr. Arturo Loaiza-Bonilla, Chief Medical Officer and Director of Research for the Cancer Treatment Center of America in Philadelphia. And he's here to talk to us about the impact precision medicine is making in gastrointestinal disease. Dr. Bonilla, thank you for joining us on the podcast.

Dr. Arturo Loaiza-Bonilla: Thank you for having me here. It's always good to talk to you.

Jerome Madison: Absolutely. So, can you share a bit of your background and how you came to lead the program at CTCA Philadelphia?

Dr. Arturo Loaiza-Bonilla: Sure. Yeah. It's always good to go back and think about how you actually get to certain places. So, thank you for asking. Well, as you know, I'm originally from Columbia, and I wanted to do research. That was always my passion and wanting to do something better, meaningful for my patients as I have some family history of not being well taken care of because I didn't have access to physicians and whatnot. So, I wanted to be the first doctor in the family. So, I ended up coming to the United States for training. Lucky enough I was able to do some research in epigenetics and in leukemia at the time when I was doing my training in Baltimore and worked with a few folks at Johns Hopkins doing that and also the NIH.

Dr. Arturo Loaiza-Bonilla: Interestingly enough, by the time my brother actually had leukemia, and I decided to move to the Miami area so I can actually fly back and forth to take care of him while he was on that treatment. And, of course, that furthered my interest in precision oncology and whatnot. Completion of my training at university of Miami, I ended up at University of Pennsylvania Abramson Cancer Center, and I started working with Gail Morrison and other folks and Peter O'Dwyer from ECOG on precision medicine approaches. They were working on the NCA match development. And I also worked very heavily on the Center for Personalized Diagnostics at Penn. And I really had a passion about GI oncology.

Dr. Arturo Loaiza-Bonilla: So, that was most of the time there was dedicated to taking care of my patients there, and I decided to do a master's in Medical Education at the same time. So that really boosted my interest in taking a leadership pathway as part of my roles. And then at CTCA as, I don't know how familiar folks may be with CTCA, but Cancer Treatment Centers of America is a cancer-dedicated institution that is located in multiple cities across the United States. And they have a model that has been centralized. Basically, they find hospitals will come together to work in a way to promote research, to promote innovation. They have a very unique precision medicine program for patients. So, make it very personalized and what they call the [Mother Standard® of care](https://www.cancercenter.com/community/about-us/our-story).

Dr. Arturo Loaiza-Bonilla: So, that really caught my attention, and they wanted to make their research program even more robust. And I felt that was a real opportunity for me to actually do it. And it's been three years now, and I'm very happy that actually those results have panned out pretty well. We have increased our pipeline tremendously, and we come from a single... It seemed like they did clinical trial numbers. Now, we have over 79 and more studies opening and many of them are precision medicine oriented. For example, the TAPUR Study. So, that's a little bit of my background, and I know it’s kind of in long spill, but...

Jerome Madison: Yeah, well, that's tremendous growth over that time. You mentioned your practice focuses on gastrointestinal malignancies, and as I understand that's really a family of different histologic malignancies. What types of tumors does that include?

Dr. Arturo Loaiza-Bonilla: Sure, and that's exactly why I wanted to do it because I didn't want to just do one kind of cancer. It's great to become an expert in certain things, but I wanted to have the variety as well and help as many patients as possible. So, that basically mean any cancer from the GI tract. So, it starts with the esophagus down to gastric or stomach. Then there's bowel and then colorectal cancer, also pancreas, also do some neuroendocrine tumors, rectal cancer, anal cancer and liver cancer and bile duct cancer. So, quite a number of clinical options you have there, when you're talking about GI malignancies?

Jerome Madison: Yeah. And some of those are considered to be rare tumors, which has certain limitations, but what are some inherent challenges with treating GI malignancies, and how can precision medicine help solve these issues?

Dr. Arturo Loaiza-Bonilla: Yes, so I think one of the major challenges is, as you mentioned, a few of them may be considered rare diseases. So, for example, let's say gallbladder cancer or even bile duct cancer on its own, like many people think about liver cancer as just hepatocellular carcinoma, which is the most common dominant one. But of course, it's going to be a proportion of patients that have colonial carcinoma or would have gallbladder cancers. And they're rare, and not only are they rare, but they also have a multitude of mutations that can actually drive the cancer growth. And in the past, when we didn't have access to precision medicine techniques such as next-generation sequencing or other biomarkers, we had to treat everyone the same way.

Dr. Arturo Loaiza-Bonilla: With the up and coming of precision medicine, we have really understood that there's different subsets of patients, and we're able to sequence them appropriately. We can actually find treatment options that are actually better for them than otherwise the standard of care. So, and of course opportunity for clinical trials for those patients. So, and also for other cancers for just—for example, colon cancer—not everything is the same. So, now we know it is not only the molecules but also the precision medicine comes from the sidedness of the cancer, so right-sided versus left-sided, BRA- mutated, MSI-stable or high. All those things are playing a significant role in making the best decision makers for these patients.

Jerome Madison: There has been data published very recently on the utility of liquid biopsies and the detection and diagnosis of GI cancers. I know that you've recently spoken at conferences including ASCO GI and others. What do you feel is most noteworthy in that particular area for liquid biopsies and GI malignancies?

Dr. Arturo Loaiza-Bonilla: That's correct. Yeah, as many of you know on the podcast, we use liquid biopsies right now for therapeutic purposes. So, we use it for detection of cell-free DNA and see which pieces of those can we actually use for targeting, for targeted treatments and in others. But over time it came to the question is, "Can we use these technologies as well to detect cancer earlier before it actually shows happening at CAT scan?" So, that's one question, and the other one is like, "Can we use those technologies as well, those tiny pieces of DNA, to determine if the patient requires further treatment or if they have already been treated?" That means not necessarily cure but maybe get the patient into remission.

Dr. Arturo Loaiza-Bonilla: And a number of these technologies have emerged, some of them or they call single epigenomic assessment and fragmenting atomics, which they actually try to clean up all the background noise on mutations that are really non-important. And make sure that you actually see that real, cell-free DNA pieces in the bloodstream are very high or what they call ultra-deep sequencing. So, they really go deep to really capture those tiny pieces with single blood draws. The other assessments that they're doing is doing it with tumor-informed. That means that they take the tumor out, they make an analysis of different variants. The most common one is 16 variants to look for. And then they personalize the liquid biopsy for the patient based on those mutations or those variants and follow the patient over time.

Dr. Arturo Loaiza-Bonilla: What the most recent data have shown based on these approaches is that you can indeed predict the appearance of cell-free DNA and correlate it with a CAT scan showing a metastasis or a recurrence sometimes as far as nine months in advance. So, kind of help you to guide treatment and be a little bit more proactive. And also helps you to figure it out which patient is going to be benefited most from certain treatments. So, let's say in adjunct colon cancer, if the patient has persistent cell-free DNA throughout the course, no matter how good or bad the stage was for the patient, you know this patient's going to recur regardless.

Dr. Arturo Loaiza-Bonilla: But if you actually cleared the cell-free DNA for those patients or they never had cell-free DNA from the tumor and from the beginning, it's almost a guarantee that the patient will get into prolonged sustained remission and sometimes cures, which sometimes we actually didn't think about it, but it makes sense. If there's no cell-free DNA in the bloodstream, likely the cancer has really not gone elsewhere and has been treated with the chemotherapy.

Jerome Madison: There is a difference of opinion about the use of liquid biopsies, whether it should be more prognostic or predictive. But for GI tumors, one of the difficulties is detecting it early because there's no good Ciro diagnostic test for some of these diseases. Where do you think we are with using liquid biopsy to be able to predict a response to therapy versus the ability to go in and biopsy the tumor itself and doing it on tissue? What are your thoughts about the use of that versus solid tissue in the assessment?

Dr. Arturo Loaiza-Bonilla: Right. Well, I think the jury's still out, so I think if you asked today, 2020, tissue is still the issue. We still need the tissue diagnosis for architecture for us to determine the right histology, etcetera. However, efforts by certain companies such as GRAIL, for example, were looking at a very, very deep analysis of DNA in the bloodstream and looking for epigenetic signatures and all that can help us to detect cancer earlier before we actually go and do biopsies. And sometimes even determine that tissue of origin, which is a very interesting way to look at this using machine learning and artificial intelligence to really finding, based on those signatures, where the tumor was coming from.

Dr. Arturo Loaiza-Bonilla: So, I think it's a very promising technology. It's the future of what we want to do for diagnosis. And for maybe detecting earlier in the game, many of these cancers and potentially for monitoring. I think for monitoring currently it has a lot of promise already without having to reinvent the wheel. In terms of early diagnosis of cancer, we still have a way to go, because we haven't really found how to make a cost-effective measure of this. Because, ideally, everyone can get it. But how expensive is it going to be for us in the healthcare system to get everyone getting blood samples frequently just to see there's cancer coming? So, I think more to follow, but there's a lot of good studies coming, and I'm very excited about the opportunities in the future.

Jerome Madison: You mentioned earlier some of the molecular targets that are interesting, but as we sit here today, what molecular targets in which diseases, GI diseases, are most actionable and relevant today and what biomarkers are emerging in the treatment of GI tumors?

Dr. Arturo Loaiza-Bonilla: Right. Well, I think once again, this is an evolving field, and, as you well pointed, there's a few ones that are up and coming and becoming more relevant. So, in GI malignancies, the first thing we need to do is to make sure that everyone gets tested for MSI high or MSI stable. Basically, mismatch repair, deficiency or proficiency in every single tissue, because we have seen in real-world data that even patients that potentially may be eligible for these immune checkpoint inhibitors, they have missed the opportunity for being tested. And such then the opportunity to get a very good response to IO autoimmune therapy. So, that's the first one that I think is pretty standard.

Dr. Arturo Loaiza-Bonilla: Other very common ones, checking HER2 for example, in now colon cancer, and we also check it in gastric cancer as usual. PD-L1 is also something very interesting as we're looking for different scores for responses in terms of gastric cancer, but other ones that are becoming more relevant. And, for example, the BRCA gene mutations in pancreatic cancer. Why? Because we know now that there's a new drug approved, Olaparib for patients who have been treated with a platinum-based treatment as an induction in metastatic setting, pancreatic cancer. And if they have the BRCA mutation, you can start them on maintenance Olaparib and keep it there based on the POLO trial results.

Dr. Arturo Loaiza-Bonilla: So, I think we should learn more about how that pans out in terms of survival. But it's given a few more people…for my patients…options for maintenance. So, they don't have to stick on chemo and still hopefully keep the cancer under control. In colon cancer, we are seeing a plethora of new things happening beyond the extended RAS. But one thing's important is everyone should get extended RAF testing and BRAF, which is only seen for only half of the patients in the communities. So, we should do a little be more exercise into getting those niches sequencing and more panels are very accurate for those patients. And why? Because we know, for example, BRAF mutations, V600 specifically, we can target them with a combination of an EGFR inhibitor and BRAF make an inhibitor and they're actually very good responses based on the BEACON CRC study.

Dr. Arturo Loaiza-Bonilla: So that can also correlate with MSI status sometimes or high tumor mutation burden, which may also predict responses to immunotherapy. We put the patient in a clinical trial. So, a lot of the things that are happening in that space and certainly more we'll learn as we are doing more sequencing and testing all these patients. I'm interested to see how the in track fusion story happens further in colon cancer. Of course, there's a small proportion—less than 1%—but if you have it, the patient's going to respond well, and it also happens in another GI malignancies. So, there's still a lot of things happening, and I'm excited as well to put my fingers on the clinical trials because that's the way to go.

Jerome Madison: Absolutely. You know on the topic of discovery, I recently read some commentary from Dr. Tanios Bekaii-Saab who spoke at the 2020 GI Cancers Symposium about why it's important to change clinical trial design to develop new agents for new targets in a more efficient way for GI malignancies. Specifically, he suggested changing from a basket trial design, which he says is target specific and tumor agnostic, to an umbrella trial design, which enriches for the target in a specific disease. Can you kind of expound on that for our listeners and how can this help accelerate the use of precision medicine in GI cancers?

Dr. Arturo Loaiza-Bonilla: Yeah, absolutely. I think that it's right on the money. We have been using basket studies right now as a way, as you were saying, discovery, right? So, it's studies, for example, TAPUR or NCA match. They're very, very good because you really want to have as many patients as possible tested for different biomarkers and see how they do over time and then you find the signal. So, so far that's been helpful in a number of different malignancies. When you're talking about umbrella trials, you're really focusing on a single disease. So, let's say a prime example for this is colon carcinoma or bowel cancers. Why? Because we know that those cancers have a lot of mutations but always in low frequency.

Dr. Arturo Loaiza-Bonilla: So, it's going to be very hard to put many patients on the same tumor type on a basket study because they're going to be filled by any other kind of cancer, not the one you're looking for. You focus it only on the tumor type that you really want to enrich. Then you can really dedicate those arms for only the mutations when they appear. And if you do it in that corporate, a good fashion or broad collaboration, you can get enough patients. So, in bowel cancer for example, you can do an arm that is against BRAF. The other one, he has a FGFR, the other one is MSI, the other one is TMB and IDH one and two. So, as you can see, there's a multitude of biomarkers that could be placed on and that can accelerate the feel for that specific disease.

Dr. Arturo Loaiza-Bonilla: Ideally, we can do this effort in a more synchronous fashion with multiple tumor types at the same time in all those studies. So, we can get answers, not sequentially, but at the same time.

Jerome Madison: He mentioned in this commentary that every patient should be profiled. Now he didn't put a qualifier on that statement because we know that there's kind of two schools of thought, some believed that you can't find an aberration if you don't look for it. So, they believe an expansive panel, broad molecular profiling should be run as often as possible. But then some belief that you only need maybe 25 genes to manage the life-time of a patient. Where do you sit on when a larger or smaller panel should be run?

Dr. Arturo Loaiza-Bonilla: Right. So, I think it all comes down to cost-effectiveness. So, in my perspective, if you have a broad amount of clinical trials that are focusing on multiple alterations or genomics, and whatnot, I think it makes sense to actually do testing for as many pages as you can, of course in the right setting. So, in the metastatic setting, refractory setting where the patient isn't going to get an extra bill because of that. And also, at the same time you don't do excessive, repetitive testing unless it's really necessary. So, for example, the patient had genotype four years ago and now the patient has lung cancer and now is progressing makes sense to repeat it. So, I am a strong advocate for sequencing at least one time for most of my patients.

Dr. Arturo Loaiza-Bonilla: Why? Because there's a lot of clinical trials right now, even for NCA match. It's open at over 3,000 practices across the United States community base and academic base. So, I think there's a lot of opportunity to really contribute to the field of precision medicine. And I think at least for our perspective at Cancer Treatment Centers of America, we use that testing for at matching our patients to clinical trials. And so far, has been very successful. We have been able to enroll significantly in TAPUR and NCA match and other sponsor clinical trials and showing how we can advance a precision medicine program with the use of the right biomarkers at the right time for every patient. So, I hope that answered the question that I think is relative, but I am a very strong advocate of doing the testing for patients. Yes.

Jerome Madison: For sure. Well, you also mentioned the Mother Standard of care that you've created across the network at CTCA. I do understand that you know the importance of operationalizing and standardizing the application of precision medicine in the clinic in order to identify patients for targeted therapies and clinical trials. How big is that as community practices and other people trying to apply precision medicine? How important is the ability to operationalize?

Dr. Arturo Loaiza-Bonilla: No, I think it's extremely important. You really need to make sure that you have a dedicated team that is actually looking at how to use this information in the most effective fashion. That any testing and any libraries you have of biomarkers for your patients is aligned with the current treatment pathways that you have. The current alternatives you have for clinical trials and align your portfolio in the future as you understand your own population of patients, and also may help you to set up your referral networks. So even we work in a community, we also want to refer patients to different areas, and if you have a study that focuses on end track for example in a place, send the patient there and they come back when they need it or that reciprocated you have the other studies.

Dr. Arturo Loaiza-Bonilla: So, having that operationalization and quick efficiency and getting the right testing of the right patient at the right time. And share that information appropriately when it makes sense is itself the essence.

Jerome Madison: Dr. Arturo Loaiza-Bonilla, Chief of Medical Oncology and Director of Research for Cancer Treatment Centers of America in Philadelphia. If listeners want to reach out to you and connect with you via social media, do you have a Twitter handle or somewhere they can connect with you?

Dr. Arturo Loaiza-Bonilla: Sure, yeah. It's DrBonillaOnc, O-N-C in Twitter, and you can also find me on LinkedIn—use my full name. I'll be there.

Jerome Madison: Well, before I let you go, Dr. Bonilla, I do my research and often find that our guests are just as interesting outside of the clinic or the lab or the board room as they are inside. And I learned that we almost lost you to American Idol, that you are a classically trained singer, and, in fact, you are a part of the world renowned Handbell choir in Baltimore when you were in residency. So, what was harder? Medical school or auditioning for the Handbell choir?

Dr. Arturo Loaiza-Bonilla: Well, I have to ask our conductor, she was pretty rough, I think. Harder than the medical school. It's always good to have the opportunity to do something else outside of medicine. It kind of like makes you happy, and I think singing is one of those things that makes me feel great whenever I get the chance. So, but yeah, I'm glad you did the research, but yeah, we'll do karaoke next time. How about that?

Jerome Madison: I'll take it. I know many of your peers hear you at conferences all over the world talking about GI malignancies, but I bet they haven't heard you sing.

Dr. Arturo Loaiza-Bonilla: Not, not yet. We'll see. Maybe do the national anthem or something like that.

Jerome Madison: There you go. Well, we really appreciate you for bringing your knowledge and expertise to help our audience broaden their knowledge of precision medicine and GI malignancies. Thank you very much Dr. Bonilla for being a guest on The Precision Medicine podcast.

Dr. Arturo Loaiza-Bonilla: It's my pleasure.

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**About Our Guest**

**Dr. Arturo Loaiza-Bonilla is the current Vice Chairman of the Department of Medical Oncology at Cancer Treatment Centers of America (CTCA), Chief of Medical Oncology and Medical Director of Research at CTCA - Philadelphia.**

A dedicated practicing clinician, international speaker, and precision oncology expert with experience at the Abramson Cancer Center of the University of Pennsylvania, University of Miami, Johns Hopkins and the National Institutes of Health, his major interest focuses in the field of innovative approaches to optimize clinical workflows and trial design (adaptive trials, synthetic control arms, basket trials), and matching for oncology patients to phase 1-3 clinical and translational research cancer trials, integrating next-generation personalized molecular diagnostics, immunotherapy, biomarkers, previous therapies, and the patient's overall status in treatment decision making, with special interest in Artificial Intelligence-based / machine and deep learning platforms. Dr. Loaiza-Bonilla is Principal and co-investigator on several Phase I/III clinical trials in several malignancies, with emphasis in new targeted therapies, novel molecules and immunotherapy, tailored to specific tumor type, its genomics and protein expression profiles. He is also a passionate advocate for improved access to medical care, precision oncology, technology, wearables, medical education, blockchain, organized medicine leadership and health policy, having been awarded the 'Top 40 Under 40' award by the Philadelphia Business Journal, the 2019 Influencers of Healthcare Award – Outstanding Healthcare Provider award by the Philadelphia Inquirer, Castle Connolly’s Top Doctor listing, AMA Foundation Leadership Award, Fellowship of the American College of Physicians, and holding a Master in Medical Education (M.S.Ed) degree from the University of Pennsylvania. He has held several leadership positions in state and medical societies, including his tenure as executive board member of the Pennsylvania Society of Oncology and Hematology (ASCO State Affiliate), and his role as President of the Board of Directors of the Global Alliance for Patient Access.