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Precision Medicine Podcast, Season 5 Episode 58

Dr. Pranil Chandra and Dr. Luis Raez: Enabling Comprehensive Genomic Profiling—The Standard of Care in Lung Cancer *Sponsored by Janssen Biotech*

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Karan Cushman, Host

Welcome to Season Five 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.

Welcome back to the Precision Medicine Podcast. I'm Karan Cushman, your host, along with co-host Clynt Taylor, and today we have two guests. First, we are excited to welcome back Dr. Luis Raez, Medical Director and Chief Scientific Officer at Memorial Cancer Institute. There he leads the thoracic oncology program and specializes in treating patients with lung cancer. We also have with us Dr. Pranil Chandra, Chief Genomic Officer of Genomic and Molecular Pathology at PathGroup. Gentlemen, thank you, and welcome to the Precision Medicine Podcast.

Dr. Pranil Chandra:

Thank you.

Dr. Luis Raez:

Thank you very much.

Karan Cushman:

Before we get started, we want to thank our title sponsor, Janssen Biotech, for supporting this educational episode focused on enabling comprehensive genomic testing in non-small cell lung cancer. This episode is not certified for continuing medical education. Our guests are not paid speakers for Janssen Biotech Inc., but are presenting on behalf of Janssen and must present information in compliance with FDA requirements applicable to Janssen. Some areas of the audio have been edited slightly to remove sensitive information.

So, with that, let's dive in. Dr. Raez, it is hard to believe that it's been two years since you joined us on the podcast. It was November of 2020, and we were in the thick of COVID back then, but for our listeners out there, as a companion to this episode, I want to invite you to check out episode 41 with Dr. Raez for more on the impact of precision medicine in lung cancer. And of course, there is some bonus content there around how Memorial Cancer Institute approached getting patients back in the clinic during COVID, so I think you'll find it very interesting.

So, we know that delivering the right treatment for cancer begins with the appropriate testing. Yet in diseases like non-small cell lung cancer, where we've seen remarkable advances in the

identification of driver mutations and related targeted immunotherapies, appropriate biomarker testing still lags significantly behind guideline recommendations. Of course, there have been a number of studies and articles published on this, but today we're going to focus on the MYLUNG retrospective observational study published in April of '22. This study investigated metastatic, non-small cell lung cancer patients receiving first-line systemic therapy within a large community oncology network from April of 2018 through March of 2020. The study found that while most patients were tested for one biomarker, only 46% were tested for all five of the guideline recommended markers. These include PD-L1, EGFR, ALK, ROS1 and BRAF, and this includes the use of next-generation sequencing.

This growth in complexity translates into an enormous gap between available life-extending, targeted therapies on the market today and the lung cancer patients who need them. So, in this episode of the Precision Medicine Podcast, thanks to our expert guests, Dr. Luis Raez and Dr. Pranil Chandra, we will address the root causes of biomarker testing adoption, the barriers associated with guideline adherence, and how pathologists and oncologists can work better together to create stronger collaborations that enable a comprehensive and routine approach to precision oncology.

So, Clynt, thank you for joining me today as co-host, I will turn it over to you to kick off our discussion.

Clynt Taylor, episode co-host:

Great, thanks Karan. Gentlemen, again, great to have you on the podcast. As Karan mentioned, we've been talking on this podcast for some time now about the lag in biomarker adoption and related appropriate testing, especially in lung cancer, where we've made tremendous progress and perhaps the greatest known therapy developments exist. Dr. Raez and Dr. Chandra, we're hoping you can help us better understand why it's taking so long to achieve a higher adoption rate. Let's talk with you Dr. Raez. What do you feel are some of the key barriers for oncologists in performing comprehensive genomic profiling in non-small cell lung cancer patients?

Dr. Luis Raez:

I think we have several different factors. I think technology and science are moving very fast and it's very hard to catch up, especially because oncology is very broad now. Some of us, for example, spend all of our time fighting lung cancer, and for me, today, it's very easy to believe that every new lung cancer patient metastatic needs to be screened for 10 biomarkers that are well documented. But I think even for a general oncologist, that's not something easy to keep in mind with so many cancers treatments and biomarkers that exist for all the old tumors, so that's why I think education of the providers is a very important factor.

The other thing is regulatory. Sometimes, for example, the data we publish that the EGFR therapies standard of care post-surgery for adjuvant therapy, I'm not sure how many biomarker companies have the approval for that indication. So, in other words, the indication for approval for the use of the drug came while I think most of the biomarkers were approved only for metastatic disease. So that's why it's not only the doctors or the providers, it's also something at the level of the regulatory that needs to move, I think, a little bit faster.

Then you have the insurance companies, also, that they are a little bit, sometimes, slow to adopt these issues. And then you have disparities, the adoption of the biomarkers in communities is not the same. I'm not only talking about race of ethnicity, that is very obvious, but rural communities don't keep the pace with major cities, academic centers don't have the same pace as community

oncology, et cetera, et cetera. I know that's why this is a very exciting topic because I guess we can discuss a lot about these issues.

Clynt Taylor:

Yeah, thanks, I appreciate that. And some of these points you're bringing up, they're familiar. Dr. Chandra, anything to add to that?

Dr. Pranil Chandra:

Yeah, I think you hit the nail right on the head by saying that these factors are familiar. So, first of all, I agree there is an enormous amount of complexity, and the pace of innovation in precision diagnostics is increasing very rapidly, and so that poses a very significant challenge to not only oncologists but pathologists as well. And this requires an immense amount of engagement and education to make the appropriate stakeholders be aware of the criticality of making sure that you're ordering the right test for the right patient at the right time. A few years ago, it was standard of care to perform EGFR and ALK testing in lung cancer. And as Dr. Raez mentioned, today the standard of care in patients with advanced non-small cell lung cancer is comprehensive genomic profiling. And not everyone understands that, and there is now published data that supports what I'm saying and underscores the significant gaps that exist today in the delivery of precision oncology and precision diagnostics.

There are a few other factors that come to mind, and so I'll just review them one by one. So, the next factor that comes to mind is quality, quantity, and access to tissue. Now that we need to be performing comprehensive genomic profiling, it is extremely important that there is enough tissue, both quality and quantity, and I'll get into that, there is enough high-quality and high-quantity tissue to not only make the diagnosis, but also to perform ancillary molecular testing. By high quality of tissue, what I mean is that you have an ample amount of tissue that lacks areas of necrosis or fibrosis, and so there is a good and high quality of tumor content that's present, and that's what I mean by quantity. Usually for molecular studies, you need at least two to four millimeters of tissue with at least 20% tumor.

The next challenge that comes to mind is the report readability and interpretation. Oftentimes, our oncology colleagues get reports, next-generation sequencing reports, comprehensive genomic profiling reports, that are 15 pages long. And you get all this information, and I'll get calls from my oncologist, "Hey, Pranil, what do I do with all this information? I've got 15 pages, and do I go after this target or do I go after this target?" because there might be 10, sometimes 15 genomic aberrations that are listed in the report. So, I think there is an opportunity to improve the report readability and the interpretation.

So, in our practice, a little bit about our practice at PathGroup, we offer pathology and molecular diagnostic services to greater than 100 hospitals that are part of integrated regional healthcare systems, as well as to hundreds of physicians and outpatient practices, and we designed a report that was simple, lucid, where everything is summarized on the first page, and all of the biomarkers are ranked based on the strength of medical and scientific evidence. So, this is an example of what the pathology lab or what a molecular vendor can do to make sure that the reports are more easily readable and interpretable to the busy, practicing oncologist.

I think the other challenge is improved coordination and collaborative communication between pathologists and oncologists, because sometimes the test just doesn't get ordered. And the oncologist may be waiting for the pathologist to order the test, or by the time the oncologist sees the patient, it's too late, in the sense that the patient already has advanced disease and results

are needed yesterday. And oftentimes, the pathologist might be reluctant to order an expensive, comprehensive genomic profiling test because they may not be comfortable with the test ordering, and so the test never gets ordered. And so, as I mentioned earlier, there's data that shows that there is a very significant under-utilization of molecular oncology and precision diagnostic testing.

And finally, the last thing that comes to mind is reimbursement and regulation. While the reimbursement for next-generation sequencing is improving and involving, it has gotten better, but it can still be a barrier, because there are, believe it or not, some insurance carriers that will not reimburse for comprehensive genomic profiling in patients with advanced lung cancer. It just blows my mind. I'd love to get your thoughts, Dr. Raez, on this, but we have multiple payers that just do not pay for the testing, and that's unfortunate because the cost of NGS can be much less than performing multiple single-gene tests at a time. So, I think there are a number of factors that I've summarized. Reimbursement, we can also talk about the 14-day rule - I'll get into that in a little bit - but I've said a lot, so I'm going to take a pause there, and I would love to get the reaction from my other colleagues here.

Karan Cushman:

Dr. Raez, would you like to add some color?

Dr. Luis Raez:

Yes. I think, as I said, this topic is very broad, so and ...

Karan Cushman:

It is.

Dr. Luis Raez:

And really, we can complement some aspects of that. For example, the pathologists, for example, I always wonder why, for example, they don't do what we call reflex testing. If you see, the best example is breast cancer. You get the report says adenocarcinoma of the breast, and then the report carries the ER+, PR+, the HER2+/-, everything is there. So, when the patient comes to you, you already have all the information that you need. In the specific case of lung cancer, we are, the medical oncologist, is the ones that we need to order this test, and that takes, we have lost probably two or three weeks since the patient had the biopsy, and that's a big problem. So, that's why maybe one day we can find ways to collaborate with the pathologists and try to advocate for more reflex testing, because I don't think there is any doubt that we need these 10 markers anyway, and so that's one thing.

The other thing is for tissue, maybe the solution is the liquid biopsy. I am in a couple of international committees that we advocate liquid biopsies worldwide, and the liquid biopsies have proved to be as good as tissue biopsies, and the benefit is the turnaround time. As an average, for example, here in Florida, we get in nine days the result of the liquid biopsy, while the tissue takes two or three weeks, and the NGS is the same. The problem is that in a lot of major centers like mine, we get patients from different and small hospitals, and we don't have any authority to be sure that if I order the tissue biopsy today, that that small hospital submits to one of the vendors the same day. Sometimes they submit three days later, one week later, ten days later, and that is why we have so many delays with the tissue NGS.

That's why we advocate that liquid biopsy in the frontline. We have a publication this month in Clinical Lung Cancer you'll want to review. We have 170 patients that we did at the same time, liquid and tissue, and we show that in 70% of the patients, nine days later, we can make a treatment decision based on the liquid biopsy only, without the need to wait for the tissue biopsy. At least in this group of patients, I think we can have a more accurate, faster approach to what we do today. So, that's why there are many caveats in these issues about our lack of biomarker testing, but certainly we cannot have a standard of care for lung cancer that is proper without the biomarker testing.

And the other thing is very compelling is that, honestly, I don't understand why they don't pay for that. As you can imagine, the-

Dr. Pranil Chandra:

Chemo cost.

Dr. Luis Raez:

Yeah, the cost of immunotherapy and chemo is staggering, it's extremely expensive. If I will be the medical director of any insurance company, I will require biomarker testing, because the cost of the oral therapies is much cheaper than the cost to be bringing the patient to a chemo unit, administering chemo, charging for the administration, the nursing and all the hours sitting there, plus the cost of the medication. So that's why, I don't know, something is wrong with the way that they approach medicine. If they want to do a cost-effective medicine, I should be requiring mandatory testing before to approve any immunotherapy these days, you know?

Dr. Pranil Chandra:

Absolutely. And that's the one thing that really gets to me, is that we've seen, in some of our practices, where immunotherapy has been administered to the patient, and then you do the molecular testing and you come back with an EGFR mutation. And obviously hindsight is 20/20, but I couldn't agree more. You've got to get the molecular testing, whether it's through tissue biopsy or liquid biopsy testing. You need those biomarker results before making therapeutic treatment decisions, because I think, correct me if I'm wrong, once you start immunotherapy and a patient has an EGFR mutation, it's not like you can switch them to a targeted therapy right away.

Karan Cushman:

Right. That's-

Dr. Luis Raez:

Yeah, that's correct. And something that is becoming very common in United States is honestly nobody's following the guidelines, because what happens is because you know that the tissue takes three or four weeks, and the poor patient and their family are so impatient to start therapy as soon as possible, what we do is we start chemo along empirically, until we get the NGS results three or four weeks later, because we don't want to use immunotherapy and then to discover that the patient needs an EGFR or ALT fusion. And that can be detrimental, because it increases the risk of pneumonitis, so that's why it's surprising that, in this country, we are starting chemo only in a stage four lung cancer patients, because all of these logistic issues with biomarker testing.

Dr. Pranil Chandra:

Yeah. Now, I think the other thing, Dr. Raez, that I think might help ameliorate these challenges, is something that you mentioned earlier, which is reflex testing. And that's music to my ears, because I happen to be a huge proponent of reflex testing that is coordinated between the oncologist and the pathologist. And so, in some of our institutions, we have actually implemented standing orders that have been signed off by, let's say, the head of thoracic medical oncology and basically allowing the pathologist to act as a surrogate for the oncologist in driving the right test for the right patient at the right time. And there are now studies that show that such coordinated, multidisciplinary, institutional efforts can lead to shorter time to treatment, can lead to a better identification of targetable alterations, and just a better sense of what's going on at a molecular level with the patient.

And then liquid biopsy is a tremendous asset, and I hope that we move to a paradigm where both liquid biopsy and tissue biopsy are used together, and they do complement each other. And of course, when liquid biopsy is negative, you can't exclude a genomic aberration, but when it's positive, as you mentioned Dr. Raez, you've got yourself a treatment target that you can act upon ASAP.

But I did want to share an anecdotal example of a liquid biopsy based on a recent conversation that I had with one of my oncologists. We had actually performed tissue biopsy testing, and we found an EGFR exon 19 deletion on tissue biopsy. And I got a call from one of my oncologists and he said, "Pranil, your test results are wrong." I'm like, "Okay. Well, thank you, and help me understand why you feel my test results are wrong." And he said, "Well, you're telling me that there's an EGFR exon 19 deletion, but I did liquid biopsy, and I found a KRAS," I think it was a G12-something mutation, "and those are supposed to be mutually exclusive."

So, we had a really good conversation about that, and I asked him, "Does the patient have metastatic disease in multiple areas of metastases?" And he said, "Well, yes, multiple metastatic sites." So long story short, the patient did have an EGFR exon 19 deletion, but the patient also had a KRAS mutation, and the full scope of information for the patient was available through the complementary information that was rendered from tissue biopsy sequencing and liquid biopsy.

Karan Cushman:

So, Dr. Chandra, that's really insightful. And Dr. Raez, obviously this is a really broad topic, and there's so many different avenues we could go down right away. Can we, let's spend a few minutes looking at a more specific example, and talk through liquid biopsy and some of the other technologies that we're touching upon here. And so, if we were to use a rare-case example of EGFR, or epidermal growth factor receptor exon 20 insertion mutation, let's use that as a real-world example. Let's talk about, can you both explain why it is so important to do comprehensive genomic testing upfront? We've touched on that a little bit, but if you both could kind of articulate that. And I think, Dr. Chandra, from your pathologist's perspective, let's start with you.

Dr. Pranil Chandra:

Yeah, I'm happy to kick things off on that topic. So first of all, EGFR exon 20 insertion mutations are very, very important. They are not very common, and single-gene testing like PCR-based testing, they might be able to pick up one or two types of EGFR exon 20 insertion mutations, but the rest of them are going to be missed. And the reason is because the type of exon 20 insertion mutation can be very diverse, and picking all of them up is not conducive by PCR-based testing. You need a comprehensive genomic profiling test to be able to pick up that mutation.

Karan Cushman:

And Dr. Raez, why do you think so many oncologists are still treating exon 20 the same way, using PCR, and not moving towards the adoption of new technologies?

Dr. Luis Raez:

But at the end of the day, how you discover the exon 20 is you discover it because you are looking for the 10 genes, so it's not like you are only looking for exon 20.

Karan Cushman:

Right.

Dr. Luis Raez:

The problem is very complex because, for example, in EGFR, the most common are exon 19 and 21, but this is only 80% of the EGFR mutation. So, if you want to find the other 20%, and you're talking about hundreds of patients, if not thousands, you need to do NGS because you cannot have, I don't know how many, the percent thereof varies, how many PCR probes you can have. The last time I checked, there is like 60 different types of EGFR mutations, including exon 20, and the only way that you can catch them all is to doing NGS, and not even NGS hotspot, NGS on the whole exon. That's why I don't see a way to get out of this. It has to be NGS, and I don't think the PCR can replace it.

Dr. Pranil Chandra:

First of all, I completely agree with the PCR's lack of ability to capture all the different alterations. PCR is really no good. And I am now today, my answer 10 years ago was very different to what it is today. Today, I am of the mindset that you go all the way, comprehensive genomic profiling, or you don't do anything at all, unless you have very, very little tissue and you can only do one, two, or three tests. But if you have a patient with lung cancer, what my team and I, and when I say my team, we have a team of molecular pathologists and scientific directors across our enterprise network, we have collectively championed and articulated that it is in the best interest of patient care to do comprehensive genomic profiling in patients with lung cancer, period.

Speaker 5:

The precision medicine podcast will continue right after this.

Karan Cushman:

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Clynt Taylor:

When tissue is inadequate, liquid biopsy is becoming the standard, especially critical for lung cancer patients in detecting these rare cases like EGFR exon 20 insertion mutations. Some feel liquid biopsy may even transform early screening for lung cancer patients. Now, you guys are dialed into the benefits of liquid biopsy. Why aren't more oncologists adopting this? Is it just too early? What's slowing down its adoption?

Dr. Pranil Chandra:

There are a couple of things there, Clynt. One is, in medicine, when there is a major breakthrough, it always takes time for it to get adopted. And, so, what happens is you'll have some breakthrough publications that will come out, and then you'll have more publications that come out, and then somewhere down the road there is a change to medical practice guidelines, for example, NCCM guidelines, and, so, all of that takes time. The other is reimbursement. I will tell you that payers are generally excruciatingly slow in adopting reimbursement to keep up with the rapid pace of scientific advancement. I would say that tissue biopsy testing reimbursement is getting better, but there are still a lot of barriers there. Liquid biopsy testing is still relatively new, and there are only some assays that get reimbursed, but reimbursement is generally pretty decent in non-small cell lung cancer, but all of this is just going to take time.

Karan Cushman:

Dr. Raez, Dr. Chandra touched on the issues with reports, right? I mean, an oncologist receives a report back that's pages and pages long, and so that's one of the known barriers in adopting and following new guidelines. Can you offer your perspective on whether you feel that the major oncology testing labs are making enough of a dramatic improvement in the reformatting of the reports so that that key information is more upfront? What's your feeling on the current reports from labs?

Dr. Luis Raez:

No, that's totally true, because especially I am a lung cancer doctor, and it's not unusual for me to have trouble sometimes recognizing some variant or some new mutation or something I've never seen before in the report. And I'm lucky that I have a molecular tumor board, where that we have two or three precision medicine experts that explain to me what is that. But even that happens once a month, so I cannot imagine being in any community where 80% of the patients are taking care, trying for the doctor to learn by himself. And of course, the vendors always tell, "Oh, don't worry. You can contact us," but these doctors are very busy also, so that's why it's very complex.

And also, the oncologists also are worried about liability. They don't want to see things there that they don't know what to do, because they don't want these things to come back one day and say, "Hey, you didn't do anything," and the doctor say, "I didn't know anything about this." That's what I have heard of several panels that we had done in the community. I think that in one way it's good that they report a lot, because for me the value is in the clinical trials. Even if I don't find one of the ten genetic aberrations for what there are FDA-approved agents, I still get excited when I found three, four, five other genes, because that gives the patient a chance to be enrolled in a clinical trial, but that is not the case everywhere, yeah. You may have a practice that don't have any clinical trials, so that information for you, it doesn't have any use.

I think the reports should be more black and white, they can tell you exactly if the patient benefits or not, and really put a disclaimer that the other genes may be used for clinical trials or maybe for future discoveries.

Dr. Pranil Chandra:

I totally agree, and that's one of the reasons why we spent almost two years designing our reports, because of the feedback that we got from oncologists. And personally, I do not agree with the way that most of these other reports are rendered. What you get from some of these other companies is a 15-page report, here are the alterations, Dr. Oncologist, and you figure out what to do with the patient with these 15 different genomic aberrations, right? And I don't think that's right, first of all, because oncologists are really busy, number one, and number two, there needs to be a way that you go through all of the alterations and you digest it down for the oncologist, and you present it to the oncologist to make their lives easier.

And the way we did that was by designing a one-page report where a biomarker is only going to make it to the front page of the report if there is enough strength of medical evidence, and there is at least compelling scientific evidence of therapeutic efficacy of a targeted therapy. So, that highlights the importance of grading your strengths of evidence, whether it's A, B, C, D or tier one, tier two, tier three, where the strongest level of evidence is FDA approval, and then you may have clinical trials and published data that show efficacy of other targeted therapies. And so, you need to be really, really clear on here's the biomarker, here's the strength of evidence, and here are the therapies, number one.

The other thing that I think is really important is to be able to take all of the different technologies that have been utilized to test a patient and to provide an integrative paragraph summary. In our reports, we termed that the clinical genomic pathology consultation that's written by a molecular pathologist. And so, for example, if you've got an EGFR exon 19 deletion and 30 mutations per megabase, a high tumor mutational burden, well, there needs to be a reconciliation of, hey, which therapy do you go after? And, so, in our reports, we would actually spell out that NCCN guidelines recommends going after driver mutations, because patients with EGFR mutations do not have as high of a response rate to checkpoint inhibitor therapies. And these are things that need to be in every report, and today they're not.

The second thing, Dr. Raez, that you mentioned is Molecular Tumor Board Series, and I am a huge proponent of Molecular Tumor Board Series and having them in a multidisciplinary format where you have PhD-level scientists, molecular pathologists, general pathologists, medical oncologists, genetic counselors. You really need to have a diverse constituency of attendees to these tumor boards, and those make for just wonderful, outstanding and very educational discussions, where you might discuss something as simple as, okay, this is HER-2 alteration. Is it a mutation, is it an amplification, is it a protein expression? What does it mean for the patient? Or you might need to dig right down into the science about the variant allelic frequency. So again, it's hard to implement molecular tumor boards at scale. Sometimes it can happen once a month, but I am a full supporter of these efforts, because you have to supplement what's in the written report with live discussions with the various stakeholders.

Clynt Taylor:

Dr. Chandra, just to draft off of what you were just talking about, I mean, pathologists are the first to receive results. You guys are obviously doing some exciting things to improve on the way the reports are being viewed and understood. Those are exciting things. So, how does this expand to include and engage oncologists, where you have pathologists and oncologists, working better together really from the beginning of patient diagnosis, to improve best practices in patient care and really ensure that more patients get access to precision oncology treatments?

Dr. Pranil Chandra:

Yeah, as I mentioned earlier, I am a strong believer in implementing institutional reflex-testing protocols. And those protocols need to be individualized and customized based on local multidisciplinary discussions between the pathology team, the oncology team. But you also need to involve the hospital administration team, because if you're going to be doing testing for patients within the 14 days, which sometimes is medically necessary, then it's important to know what the clinical aspect of doing that is, but also what is the economic aspect of doing that, and come to a win-win that balances cost and quality, but really at the end of the day, places the patient at the center of care.

I think it's important to support the use of right technology and working collaboratively with oncologists to discuss cases, either during existing tumor board sessions or carving out a separate molecular tumor board. I think we have seen the implementation of these molecular tumor boards, but we need to do a better job at scaling that. We need to do a better job at making sure that you have the right people at the molecular tumor boards, because there are some molecular tumor boards that only have oncologists, and you may not have pathologists who can really guide on the interpretation of results and what actually the results mean, and what the difference is between results within various technologies. So, it's really important to really be inclusive in the molecular tumor boards.

And then, again, communication, communication, communication. I think it's really important that if there's a highly actionable finding, myself or someone on my team, we will make a call out to the oncologist and be like, "Hey, listen, you're going to receive this report and here's what it means, and if you have any questions, let me know." Or sometimes we'll have a signature that actually refines a diagnosis, something that's a carcinoma of unknown primary. Based on the molecular profiling results, you're able to actually tell the oncologist that actually this is a cholangiocarcinoma, because you have an IDH-1 mutation, and therefore you now have an FDA-approved category, a tier-one biomarker to target. So, those are the types of things that I think pathologists and oncologists can do better to communicate better with each other, but also to stress the importance of biomarker testing and utilize tools like molecular tumor boards.

Clynt Taylor:

That's good. Dr. Raez, anything to add to that?

Dr. Luis Raez:

Yeah, maybe that I want to mention the same thing. I want to mention briefly, because we're running out of time, is the economics. For me, it's clear that there is no one vendor or company that does the absolutely accurate testing. So, I think all of them are 99.9 or something, but there is not one test that is the test only. That's why, for example, between liquid and tissue biopsies, even in the example of that, that I gave you, that we make decisions based on liquid biopsies 30% of the time, we still need the result of the tissue, meaning that we need to order both. So, from now on, we still need to order both, and that creates a lot of concern. I know a lot of doctors that don't like to order both, because they're worried about the insurance coverage of the test, especially if you order both.

And that's a major disadvantage for the patient, because I think the reality is, as today, we need both, until the day that one liquid biopsy company does the perfect test, or one tissue biopsy company does the perfect test. That is unlikely, because there is always an issue with the tissue among, and there'll always be an issue in the liquid biopsy that the amount of tumor, no? And, so, you have a very small tumor burden, there is no way that the liquid biopsy can be totally accurate. So that is why I think economics has an important issue here, and that is another barrier for

ordering both at the same time, reimbursement for both at the same time. And we need a solution for that, otherwise you don't even have the doctor's ordering because they're worried.

And that creates the fact that, "Oh, let's do one first and let's see what happens." For example, we order the tissue first, and then only if the tissue is not, then, "Oh, we'll order the liquid." That's what a lot of doctors have been doing because tissue came first. The problem is you are not thinking about the patient. If you remember, this patient started with a cough 90 days ago, as an average, 90 days later they come to you with a terrible diagnosis that is a life-threatening diagnosis, and now you're telling, "Hey, you need to wait three or four weeks until we can figure it out what's the best treatment for you." So, it's hard to do the sequencing testing. It's very difficult for the patients. That's why they need to find a way to fund the economic issue.

And the other way is also difficult, because if I do the liquid biopsy, I don't find anything, okay, it was only nine days, but now you have to wait three weeks for the tissue. And in the meantime, all of us are doing empirical therapy with only chemo – that's the only solution that we can have until we get the proper testing. That's why I think a lot of things that Dr. Chandra has said, like doing the reflex testing or doing both tests at the same time, getting the insurances to cover for this is going to help.

The other thing with economics, also, is I'm sure that the cost of the test is going to go down. These tests were extremely expensive five years ago and are getting cheaper. And since the fact that also there is competition are getting cheaper, they're getting faster. So, I'm confident that hopefully that will be, that's something that can be solved, so it's not something that we cannot address.

Finally, one way to make also cost-effective, that has to do a lot of disparities, because that's not necessarily a reality in the United States. But if you find a place or a population that one gene, like EGFR, is extremely prevalent, for example, Asians or Latin people - of course, I am Peruvian. In my country, EGFR is 40% - so maybe you can screen for EGFR first and do a PCR, and then for the 60% that are negative, you can do NGS. And that's another way to approach and do a more cost-effective medicine, because this cost-effective, even if you are doctors, I really have learned that if we don't fix this cost-effective issues, we have a lot of administrators, we have a lot of insurance, and we have even doctors that are afraid to make the patients upset with a lot of bills, not helping to solve these issues and not helping to fix these problems.

Karan Cushman:

Dr. Luis Raez, Medical Director and Chief Scientific Officer at Memorial Cancer Institute, and Dr. Pranil Chandra, Chief Genomics Officer at PathGroup, thank you both for being guests with us today on the Precision Medicine Podcast. And before we let you go, Dr. Raez, I know you are super-active out there in the oncology community, you're currently VP of FLASCO. How can some of our listeners get in touch or follow you on social media or otherwise?

Dr. Luis Raez:

I have a Twitter handle, it's @LRaez1, and I always try to tweet medical information. My passion is to be tweeting about that and trying to spread knowledge basically in social media. I also, they can find me at LinkedIn. I try to publish a lot of medical information there, and hopefully that can be of value for patients or for other doctors. Thank you very much.

Karan Cushman:

Absolutely. And Dr. Chandra?

Dr. Pranil Chandra:

Yeah. First of all, thank you for having me. It's been a pleasure to be here. I'm also on LinkedIn, and I love posting informative articles, but also reading them. I'm trying to do a better job at posting more informative articles on there. So, LinkedIn is definitely one way to get in touch with me, and the other is just simply email pchandra@pathgroup.com, and I'll be happy to answer any questions that you guys may have.

Karan Cushman:

Perfect. Thank you both. Dr. Raez and Dr. Chandra, that was quite a robust discussion. I imagine it won't be the last. I would love to have you both back, and thank you for your time today.

Clynt Taylor:

Yeah, that was great. Thank you, gentlemen, that was awesome.

Dr. Pranil Chandra:

Thank you.

Dr. Luis Raez:

Thank you for inviting us.

Karan Cushman:

And one last shout to our episode sponsor, Janssen Biotech, for making this episode on Enabling Comprehensive Genomic Profiling in Lung Cancer possible. If you are interested in sponsoring the Precision Medicine Podcast, simply contact me Karan Cushman your host and producer at kcushman@trapelohealth.com. You can also find me and message me on LinkedIn @karancushman. Thanks everyone for tuning in to and your support of the Podcast.

Karan Cushman:

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