Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/project-oncology/examining-genomic-testing-and-targeted-therapies-in-lung-cancer/12230/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Examining Genomic Testing & Targeted Therapies in Lung Cancer

Dr. Sands:
Genomic testing has become such an important part of lung cancer treatment algorithms, that it's time we take a look into this advancement in detail and explore some of the big questions, like how it's done and what the treatment implications are. Those questions and more is what's coming up today, on today's program. Welcome to Project Oncology on ReachMD. I'm Dr. Jacob Sands and joining me to discuss targeted therapies and testing strategies in lung cancer is Dr. Ben Levy, an Associate Professor of Oncology at the Johns Hopkins University School of Medicine and Clinical Director of Medical Oncology at Johns Hopkins Sidney Kimmel Cancer Center. Dr. Levy, welcome to the program.

Dr. Levy:
Thanks for having me, Dr. Sands. Pleasure to be here.

Dr. Sands:
Now, Dr. Levy, there are multiple technologies for genomic testing available and we hear things like, NGS and PCR, can you describe some of the differences and including the strengths and drawbacks of these different testing platforms?

Dr. Levy:
Yeah, I think mirroring the therapeutic advances we've had in lung cancer, we've also had a shake-up in the diagnostic algorithm for patients with lung cancer. We started out doing something called PCR, which was sort of, an old way of testing for particular genes in lung cancer or solid tumor oncology, in general. This is a way to test a limited amount of genes. You essentially are creating probes that try to identify specific genes within the lung cancer. But you have to know which genes you're going after beforetesting for them. You knowyou weren't able to get a comprehensive, sort of, look, genomically at the tumor and the turnaround time was a little bit longer, as well. So, I think because of all of those challenges with PCR, we've really moved forward with contemporary platforms, which are called Next Generation Sequencing, which is just a fancy way of, of saying that we're really trying to sequence the DNA, A to Zof the lung cancer. And there's a lot of advantages with this platform: 1) You do get a comprehensive picture genomically of the tumor, sort of, interrogating all of the genes, not just a few, but all the genes , within a tumor, 2) is as we've moved in time and developed more sophisticated platforms, the technology has advanced so that we don't need that much tissueand we used to need so many slides to do this and the tissue requirements for contemporary NGS platforms have gone down; we're able to do this with a limited amount of tissue. And third is the turnaround time, while it still can be long, has generally been a little bit better, than what we saw with, at least some PCR platforms. I'm a big proponent of this and that every patient does need comprehensive genomic profiling through Next Generation Sequencing and there are commercially-available platforms that we're all familiar with, that we can use. Many of us use internal platforms within our hospitals, but there are also commercially-available platforms that we use. And I would make a push, again, that every patient who has at least an advanced adenocarcinoma should have comprehensive genomic profiling done on their tumor, so that this can inform, treatment decisions that we can talk about. And my statement has always been "leave no gene behind", and the only way to do that is through this comprehensive testing called "Next Generation Sequencing".

Dr. Sands:
I like that, the "leave no gene behind". I've certainly seen patients where they've come in, they've run out of all options and when I look through things, there's actually a little more that can be done as far as genomic testing. And, lo and behold, we'll sometimes find something that then they actually have a great target of therapy option that wasn't really known prior.

Dr. Levy:
Yeah, and I would just add on the list of genomic alterations that are becoming actionable or targetable are, in a sense, that we can use

to deliver therapy is getting longer and so we do need to make that attempt to make sure that we're capturing genomically everything in the tumor and the best way to do that is through the contemporary Next Generation Sequencing platforms.

Dr. Sands:
Yeah, one of the newer things now is, in this effort to leave no gene behind, I see increasingly testing being done from blood draw, this is easy to get to then obtain. How do you use blood-based testing in your genomic testing strategy?

Dr. Levy:
Yeah, I mean, we've come again, such a long way. What sounds like science fiction, right, being able to just take 10 ccs of blood from a patient and understand the genomic underpinnings of a tumor, of lung cancer is real, now. I mean, this is something, 15 years ago when I started in lung cancer, I never would have dreamed of. You know, just basic concepts of this is DNA that is shed from the tumor that we can now capture with a simple commercially-available platform and, you know, you said it's easy the running joke is that we all have a hard time sometimes identifying a good interventional pulmonologist or interventional radiologist to do a tissue biopsy, but we all know a good phlebotomist and so this is very, very easy to capture. And we now have really good data that if we use a liquid biopsy in conjunction with the tissue, that we're more likely to capture genomic alterations or genes of interest that can inform treatment decisions. So, again, this is relatively new technology but now commercially-available and the way that I leverage this in my clinical practice is that when a patient comes to see me, if they've already had a tissue biopsy, which many of them already have, most of them have, and I, at least have a diagnosis of lung cancer, specifically adenocarcinoma, remember, the turnaround time for tissue Next Generation Sequencing is going to be around, anywhere from 2 to 4 weeks depending on the platform you use. And so, sometimes, we want to get answers a little bit more reliably and little quicker and one of the ways to do that is through a liquid biopsy. So, if a patient comes to my office and has had a tissue biopsy and we're still waying for the next generation sequencing results, I will also, what I call "layer in the liquid" or add a liquid biopsy. What we know about this is that the turnaround time is quicker, so the turnaround time for liquid biopsy is anywhere from 5 to 7 business days, which is pretty remarkable. The other advantage of liquid that, you know, I always try to stress when I talk is that, you know, I tell fellows this, blood is truth. If you find an alteration in plasma, there's no such thing, generally, as a false positive. So, essentially, if you see it in blood, it is truth, and you can act on it with a very few exceptions. The one caveat about blood is, if you don't find the alteration in blood, it still could be in the tissue, so a negative result tells you nothing; a positive results says "go" if there's a target identified, you can act on it without having to wait for the tissue. What we know about blood result is that they are highly concordant with the tissue, it lines up beautifully. If you have it in the blood, there's a fair amount of certainty you're also going to find it in the tissue, it just so happens that you find it earlier in the blood and you can act on it.

Dr. Sands:
Yeah, so this is all in the first line setting then, where you're describing right now, you're saying you're layering the liquid, and now, let's say, at the time of progression then, are you, if someone is who has an EGFR mutation where you're now looking at resistance, targetable alterations, how are you layering in the liquid in those scenarios?

Dr. Levy:
Carefully. I think this is where gets a little bit more nuanced,. I think we currently have a nascent understanding of the mechanisms of resistance of some of these targeted therapies, but that doesn't mean we're not learning each day about particular mechanisms that may allow us or inform subsequent treatment decisions. And so, because of that, if a patient is on targeted therapy and they develop disease progression, I will consider using a liquid biopsy to try to understand what's going on mechanistically in terms of the resistance mechanisms. And that may be able to inform treatment decisions. I tend to also do a tissue biopsy, as well, because often times, you'll miss things in the liquid. Either at treatment, at the time of first therapy or second therapy, but I do think we're learning more and more, and in fact, some of the best data we have for resistance mechanisms, post osimertinib, and EGFR targeted therapy, comes from plasma, comes from ctDNA. So this is a call and a push. I think we all need to be doing this, not only for what can we do for our patient now, but informed treatment decisions in terms of a collective effort in the future, in terms of better understanding what's at playfor patients who are on targeted therapies.

Dr. Sands:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands and I'm speaking with Dr. Ben Levy about targeted therapies and testing strategies in lung cancer. So, I'm gonna transition a little bit now, into the therapeutic side of things. Is there various targetable alterations with FDA approved treatment options. Co in the first line setting, how do you tend to use targeted therapies across all of these different genomic alterations? Are there any that you would hold off and not utilize in the first line setting? Do you utilize all of them in the first line setting? What's your general practice?

Dr. Levy:
Yeah, this, I think is a great question and an area of controversy. In general, if I identify a mutation that I potentially think is targetable or is targetable, I will try to use what I consider to be my best drug first and my best drug first, generally is a targeted therapy. And so, I try

to really leverage in that genotype-directed therapy or precision medicine frontline and not wait. I think there's some nuances here, if you're starting a patient on chemotherapy and you don't know the result, yet, of their gene, and they're doing really well on chemotherapy, one could make the argument to continue chemotherapy and then give them the targeted therapy second line. I tend not to do that, I tend to switch them and try to, again, push up that precision medicine as soon as I know the result. But rule of thumb, for me, is that if I identify a genomic alteration of interest that's potentially targetable, I will do everything I can to give that target a therapy first. Andtry to get the most meaningful response up front, the most durable response up front and salvage them if they need it, later on, with either chemotherapy or chemotherapy IO strategies.

Dr. Sands:
Now, Dr. Levy, you touched on this in your last answer, so, although most patients can wait for genomic testing, sometimes patients come in and they've got a lot of symptoms and we really have to get to treatment. In those scenarios, what do you go to? Do you incorporate immunotherapy? Do you go with just the chemotherapy? If the testing does show an alteration, what's your plan after you've already started treatment? Can you take us through some of that landscape?

Dr. Levy:
Such an important question and a clinically-relevant one that we see every day in our practice. We need to remember that lung cancer is an unforgiving disease; it's historically aggressive. And even these patients with genotypes, they need to start therapy right away. So, what I tell patients is, and this just happened this week in my clinic, a patient in which we suspect an alteration which we can target with a targeted therapy, if they're symptomatic, I'll generally start them on chemotherapy alone. I generally don't start them with chemotherapy or with immunotherapy, nor do I start them with immunotherapy. I generally start them on chemotherapy and then when the result comes back, it's a discussion. If they're doing really well on chemotherapy, one could make the argument to continue them on chemotherapy and then switch them over to targeted therapy when they have disease progression. I tend not to do that. A patient who's starting on chemotherapy, if I discover a genomic alteration of interest, I will go ahead and stop the chemo and give them the targeted therapy and that's I think there's some controversy there on what can be done, but I try to use my best drug first and, in my mind, that's, that's targeted therapy for our patients. Even for our symptomatic patients who've done well with chemo, I switch them.

Dr. Sands:
So, we've covered a lot of ground as far as the diagnostics and now the therapeutics, let's kind of go next level, now, bringing this all together. What's next? hat are we doing as far as the research now, that's gonna impact the field?

Dr. Levy:
I think that where we're going to move, here, is, and we've already seen this with some data, is how to leverage these drugs for cure. And we've got a lot of great data in the stage IV setting, right? We've got a lot of great data with all these targeted therapies eliciting meaningful and durable responses in our Stage IV patients. The question, now, for me, and I think for a lot of us is, "Can we utilize the science and these drugs to cure people?", and where is that? Is this in patients who are potentially surgically resectable, we start out with the targeted therapy and then they move on to surgery? Is it in the adjuvant setting where patients have surgery and then instead of giving them chemo, we give them, you know, 3 years of a targeted therapy like we've already done with osimertinib and the ADAURA data? I think this is where we really have to head, I mean, it's great to have a, treating patients as a chronic disease, but to really move the needle and the bar, we have to start to learn and design, really innovative trialsto use these drugs perioperatively, or pre-chemo-radiation or post-chemo-radiation, this is where I think the field is heading and this is what we'll be talking about, I think, in the next 2 years.

Dr. Sands:
That's a great way to round out the discussion. Dr. Ben Levy, thank you so much for joining ReachMD to discuss targeted therapies and testing strategies in lung cancer. A lot of fun having you on the program.

Dr. Levy:
Thanks, Dr. Sands, it's a pleasure to be here.

Dr. Sands:
I'm Dr. Jacob Sands. To access this and other episodes in our series, visit ReachMD.com/ProjectOncology, where you can be part of the knowledge.