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### NSCLC & Optimizing Molecular Diagnostic Testing : An Exploration of Barriers to Implementation

Announcer:

You're listening to ReachMD, and this episode of Project Oncology is sponsored by Lilly. Here's your host, Dr. Charles Turck.

Dr. Turck:

Although molecular diagnostics provide data that may help inform treatment decisions for patients with non-small cell lung cancer, employing advanced diagnostics isn't always easy. So what are some strategies we can use to not only implement molecular diagnostics and clinical practice but also optimize the data gathered from them?

Welcome to Project Oncology on ReachMD. I'm Dr. Charles Turck. And here with me today to help answer these questions is oncologist Dr. Christine Bestvina, who's an Assistant Professor of Medicine in the Section of Hematology and Oncology at University of Chicago Medicine. Dr. Bestvina, welcome to the program.

Dr. Bestvina:

Thank you so much for having me Dr. Turck.

Dr. Turck:

To start us off Dr. Bestvina, would you give us a brief overview of the utility of molecular diagnostics and the management of non-small cell lung cancer?

Dr. Bestvina:

Molecular testing has really revolutionized how we think about non-small cell lung cancer, particularly patients who have adenocarcinoma. As we gain more experience with targeted therapies, we're finding that more and more mutations are potentially targetable and can change our treatment recommendations. Great examples of this that have happened over the past year and include RET, MET, as well as EGFR Exon 20. And we'll get into those in just a little bit.

Dr. Turck:

And when it comes to employing these advanced diagnostics, what are some challenges you've seen or experienced?

Dr. Bestvina:

Yeah, absolutely. So, unfortunately, getting molecular testing isn't always the seamless process that we hope that it will be and hope it will become. Some of the biggest challenges that we can see are timing. With tissue-based testing, it can take three to four weeks for some of this tissue testing to come back. The other issue that we've experienced is insufficient testing from tissue. So, depending on what test you're employing, and what amount of material is needed, not all patients may have biopsies which have enough tissue for this molecular testing.

Dr. Turck:

And how do you handle the situation where there isn't sufficient tissue for molecular testing? What's your approach?

Dr. Bestvina:

So first, I'll go ahead and send off a cell-free DNA test. Fortunately, the we get the information that we need from this blood-based biopsy test. Every once in a while, we'll have a patient who is either a low or a non-shedder, or who has very small volume of disease, potentially plural-based disease, where cell-free DNA testing just doesn't have enough its own molecular information to be able to give us what we need. In those cases, I do think it's important to go ahead and think about rebiopsy for these patients because again, for a

patient with adenocarcinoma, the presence of a targetable molecular testing has such deep ramifications both as far as treatment and prognosis.

Dr. Turck:

So, what strategies would you recommend for clinicians who are facing some of those barriers to implementing molecular diagnostics in practice?

Dr. Bestvina:

Fortunately, over the past few years, it's become more commonplace for us to use cell-free DNA testing, which is essentially a blood-based biopsy that allows us to look for many of these mutations. There are several commercial vendors that can use this. Personally, in my practice, I have tended to use Guardant quite frequently. But this can solve many of our problems or barriers, including time. Oftentimes, these CT DNA tests can come back within five to seven business days, as well as insufficient tissue for testing. We can simply add a blood draw for a patient as opposed to needing to repeat a biopsy or put them through an additional procedure.

Dr. Turck:

For those just tuning in. You're listening to Project Oncology on ReachMD. I'm Dr. Charles Turck. And today I'm speaking with Dr. Christine Bestvina about how we may use molecular diagnostics to better manage non-small cell lung cancer.

Now, Dr. Bestvina, if we zero in on the data obtained from these diagnostics, what exactly do we learn from it?

Dr. Bestvina:

There is a fantastic paper published in JAMA Oncology looking at concurrent cell-free as well as tissue molecular-based testing. And we did see that when concurrent testing is performed, our ability to capture patients who have what we would term intervenable or targetable mutations increases with concurrent testing. And some of the mutations that we're looking for are ones that we've been familiar with in the lung cancer space, including EGFR, ALK, and ROS1. Fortunately, again, as our ability to target these mutations grows, we found more and more now actually targetable mutations. In the past year, we've seen approval of two drugs for RET point mutations and fusions. We've also found that Exon14 can be targeted with two new drugs, tucatinib, and capmatinib. The data for which both of these drugs looks quite promising. We're also finding that EGFR Exon20, which historically has been quite a tough target as it doesn't respond to osimertinib or other EGFR-based TKIs in the same way. We now have some really exciting therapeutics that are likely to get approved within the year. Both amivantamab and mobocertinib.

And so it's exciting because as we order this molecular testing, you can truly counsel the patients that their odds of having one of these targeted mutations increases by the year as again, we gain better drugs and more information.

Dr. Turck:

And other any other ways we might optimize the data we get from molecular diagnostics and use them to improve clinical decision-making?

Dr. Bestvina:

One of the things that we're all trying to focus on now is how to get some of this information back to local providers. It's certainly incredibly challenging to keep up with all of the new data, all of the new drugs, and how to apply them. Specifically, I think one of the challenging areas will be knowing about EGFR Exon20 insertions and how they are different than some of the traditional EGFR mutations that we've seen. Additionally, how the therapeutic target that we would choose would be different. I know that a lot of the companies that perform molecular testing are trying to figure out how to best convey some of this targetable and intervenable information back to the ordering providers. We're also always happy to help as referring centers sort through some of this data because again, it's becoming more and more complex by the day.

Dr. Turck:

Now, before we close, Dr. Bestvina, what are some opportunities you see and how clinicians might enhance their ability to interpret molecular diagnostics data?

Dr. Bestvina:

One of the areas that I think we can grow in the most is repeat molecular testing at time of progression. And so, what I mean by this is a patient, let's say, has a standard EGFR mutation, Exon19, or L858R, they're on osimertinib for, let's say, 19 months, and then at that time have progression. It's a part of my practice to go ahead and perform repeat molecular testing, whether through CT DNA tissue biopsy with molecules or both, to see if the patient has acquired any resistance mechanisms that could again be targeted. I think this is an area that we really need additional data on is when these tests and repeat biopsies are appropriate, how to use them, and what some of the resistance mechanisms are. So this is information that I think all of us are looking forward to gathering over the next several years.

Dr. Turck:

Well, it's clear that molecular diagnostics are able to provide us with a considerable amount of information. And it's great to know that there are a number of opportunities available to help us interpret those data. And I want to thank you, Dr. Bestvina, for joining us to share your insights. It was great having you on the program.

Dr. Bestvina:

Thank you so much for having me, Dr. Turck.

Announcer:

This program was sponsored by Lilly. To revisit any part of this discussion and to access other episodes in this series, visit [ReachMD.com/ProjectOncology](https://ReachMD.com/ProjectOncology) where you can Be Part of the Knowledge. Thanks for listening.