Transcript Details
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Operational Pathways for Biomarker Testing in NSCLC

Announcer Introduction:
Welcome to ReachMD. This medical industry feature, titled “Operational Pathways for Biomarker Testing in NSCLC,” is sponsored by Amgen.
Here’s your host, Dr. Matt Birnholz.

Dr. Matt Birnholz:
Over the past decade, biomarker testing has become significant in non-small cell lung cancer[1,2] due to the rapidly increasing number of actionable biomarkers.[2,3] However, many challenges remain in its implementation, which is why today, we’re going to review some best practices for incorporating biomarker testing into non-small cell lung cancer care.

Welcome to ReachMD. I’m Dr. Matt Birnholz, and joining me in this discussion is Dr. David Braxton, who’s the Chief of Service for Molecular Pathology at Hoag Hospital. Dr. Braxton is partnering with Amgen to participate in this program. Dr. Braxton, thank you for being here today.

Dr. David Braxton:
Thank you for having me.

Dr. Matt Birnholz:
Let’s start by taking a look at one of the major challenges associated with biomarker testing in non-small cell lung cancer, which is the turnaround time for test results.[4] In your experience, Dr. Braxton, what are some ways we can overcome this challenge?

Dr. David Braxton:
Well, there is a lot of considerations because biomarker testing of cancer patients is complex.[3] So, in my experience, what’s been successful is actually decreasing the complexity by standardization.[5,6] So, it’s important to have standardized patient criteria for who needs biomarker testing, what kinds of biomarkers they need testing for, and how you go about delivering those results to patients.[5,6] So, in our institution, we’ve implemented pathologist initiated reflex testing protocols, where the pathologist has taken over the responsibility for identifying the patients and their specimens that need biomarker testing.[7] We initiate the orders and can oversee the whole testing process from the time of diagnosis and through the completion of genomic test results.[7] It’s also important to keep in mind that providing comprehensive NGS-based testing, especially for non-small cell lung patients, is important.[3]
It helps reduce turnaround time; it helps the comprehensiveness and completeness of the biomarker testing results; and you are also avoiding getting into a situation where serial testing or cascade testing is needed; they wait for them to come back negative; and then, you go to another test, and our experience has just not been very efficient, not been very effective, and actually increases the cost to your patients.[3,8] So, what pathologist-initiated reflex testing really does it decreases your turnaround time; patients don’t necessarily have to see an oncologist before that order is initiated; it also conserves the amount of tissues that’s being used by biomarker testing.[7] And, more importantly, it enables standardization where you’re gonna get a high-quality comprehensive biomarker testing result all in one report, where even some of these laboratories are now providing treatment guidelines, treatment matching, based on those

comprehensive biomarker reports.[7,9] Another important aspect of biomarker testing is your QNS rates, that's quality or quantity insufficient, and that's where you cannot establish a full complement biomarker testing results based on one specimen.[3] So, that's actually very troublesome for patients because they don't get the results, and it really lengthens the turnaround time for care initiation.[3]

Dr. Matt Birnholz:
With that being said, are there any tactics we can use to help reduce QNS rates?

Dr. David Braxton:
Yeah, there is a number of different manners in which you can handle the specimens from a pathology laboratory standpoint to reduce your QNS rates, and from my experience, talking to other best practice sites, we've been able to implement a number of these, and they've been successful on reducing QNS rates.[10] Some of these would include precutting your core needle biopsies or your other small specimens.[10] The IHC slides that were used for, you know, immunohistochemistries, you can precut those out of your tissue blocks, and that preserves tissue for later molecular studies.[10] The pathologist has these precut slides to initiate any immunohistochemical workup that's needed.[10]
That preserves the tissue block for later testing the molecular results.[10]
Another pathology-centric way of handling QNS rates is actually splitting specimens.[11] If you have a number of core needle biopsies, you can utilize two different tissue blocks; you don't have to put all the cores into one FFPE block, and that allows you two different sort of pools of tissue to work on either immunohistochemistry or molecular testing or any other testing that the patient needs.[11] So, another important aspect to reduce QNS rates is actually sending multiple blocks up front to your laboratories.[12] Historical procedures may be needed who often send multiple specimens up front; so, it's important to get all the tissue that you have with cancer in it on that patient to your laboratories, so that they can have enough tissue to provide comprehensive NGS report.[3,10] Also, rapid on-site evaluation can help reduce your QNS rate and establish better turnaround time.[13]
If you're having problems at your institution with QNS rates, establishing a ROSE program with your pathologist and your interventionalist working together to ensure that the specimen obtained from your patient is satisfactory for all testing; that can be important not just for the rapport between your two clinical departments but for also helping that patient get an adequate specimen not just for diagnostics but for additional biomarker testing.[11]

Dr. Matt Birnholz:
Thanks for breaking down those strategies for us, Dr. Braxton. Now if we switch gears for a moment and focus on another common barrier, there isn't always a standardized process for storing biomarker test results. So can you tell us what processes you have in place at your institution to document and integrate this information?[5-14]

Dr. David Braxton:
That's a great question and this has been something that I have put forth a great load of effort and for figuring out, because it is so important to get these results into the EHR and make use out of them for your clinical care.[5] Some of these biomarker testing results can be lengthy reports, often provided in pdf form.[3,5] Single patient's tumor can have hundreds of mutations in them, and the EHRs right now, at least in many community centers, are just not structured to handle this kind of information.[3,5,15,22] So, some of the approaches to take for incorporating molecular testing results into your EHR would be to append that information into your surgical pathology report.[5,16] So, have your transcriptionists transcribe the molecular testing results, at least the summary of those results into your surgical pathology reports, and addend your surgical reports there.[5,16] If you're not going to provide that level of detail, you can also just addend or append your pdf results into the EHR; often times that's useful, you can see the whole report by clicking a link or something like that.[5]
A development that we're seeing more utility for is incorporating structured results into the EHR, and now that can be accomplished through a number of third party softwares.[3,5] What this allows you to do is drive all your search and query on your molecular results; it allows you to do QA on your molecular testing programs, and it's just very useful to have all of the information at your fingertips when you can get it in structured format.[5,17] Some important developments that are going on along those lines is, of course, the use of decision support tools, artificial intelligence, and we're really seeing these kinds of applications of cancer informatics becoming much more valuable for patients.[5,18]

Dr. Matt Birnholz:
And before we close, I'd like to zero in on testing. How has your institution used liquid biopsy when tissue is limited or when a rebiopy isn't feasible?[1]

Dr. David Braxton:
Liquid biopsy is extremely exciting, and we're seeing broad applications in cancer patients among many different cancer types with liquid biopsy.[19] Some of the uses of liquid biopsy would be to avoid testing failures when your somatic tissues do not produce biomarker testing results, and we've seen a number of different paradigms arise to facilitate testing in these situations.[1,3] One of the approaches that is developed, and we've seen applied in some other institutions would be sequential approach, where the tumor tissue may be inadequate, and then a liquid biopsy circulating-free DNA would be gathered to supply that patient with the genotyping result for predictive biomarker testing.[1] Another approach would be complementary, in which you're gaining access to a solid tissue tumor biopsy, as well as a tumor blood for liquid biopsy testing at the same time.[1] So, this concurrent testing of both the tumor and the blood can often yield a liquid biopsy result several days, maybe even a week sooner, then the tissue results would be available.[1,20] Another approach would be the plasma-first approach.[1] So, once you establish a histologic diagnosis of non-small cell lung cancer, you move straight into liquid biopsy testing; you're gonna gain access to the patient's blood biomarkers much sooner than you would having sent out a tumor tissue specimen to a somatic testing laboratory.[1,20] So, that can provide actionable results, sometimes days or weeks sooner than waiting for that tumor testing to come back.[1,3] If you do not get a actionable biomarker out of the blood, you can move into testing the tumor at that point in time.[1]

Dr. Matt Birnholz:
And are there any considerations to keep in mind when utilizing liquid biopsies?

Dr. David Braxton:
Absolutely. We're really just at the tip of the iceberg in terms of liquid biopsies.[1] So, there are a number of different pitfalls that we're observing across that spectrum of testing.[1] Some of it is where there's very low levels of, what appeared to be, actionable mutations, but maybe very uncommon in that particular tumor type, that, you know, the patients has.[1] Another pitfall is clonal hematopoiesis, where you're picking up mutations in the liquid biopsies that don't come from the tumor that you're trying to treat.[1] In this case, it would be the blood-forming stem cells in the bone marrow that have mutations, and on that, can sometimes look like actionable mutations when you're on liquid biopsy.[1,21] So, we're observing a number of different issues with liquid biopsies; and again, outside of very strong clinical guidelines, it can be very difficult to understand what to do for your patients in these situations.[1]

Dr. Matt Birnholz:
Well, this was a really great discussion, Dr. Braxton, and I want to thank you for taking the time to reflect on biomarker testing in non-small cell lung cancer. It was great having you on the program! Thanks so much!

Dr. David Braxton:
Thanks. My pleasure.

Announcer Outro:
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