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Diagnosing NSCLC: A Look at the Complete Picture

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Chapter 1: Diagnosing NSCLC: A Look at the Complete Picture

Dr Johnson:
Hi, I'm Bruce Johnson. I'm going to be speaking on the evolving landscape of non-small cell lung cancer. I'm the co-director of the Center for Cancer Genomics at the Dana-Farber Cancer Institute and a professor of medicine at Harvard Medical School.

One of the things we're happy about is that lung cancer incidence is decreasing due in part to reduced smoking rates. But in addition, new trends are emerging as things change. Smoking rates have decreased over the past decade, and most lung cancers are now diagnosed in people who have quit smoking.

In 2019, 14% of U.S. adults ages 18 or older years currently smoke. However, non-smoking-related lung cancer cases are increasing and are disproportionately affecting women, Hispanic, and Asian individuals. And today, more young women than young men are being diagnosed with lung cancer, so the incidence rate per 100,000 for patients 15 to 39 in the U.S. is 0.95 for men and a higher 1.12 for women. We are also seeing the impact of screening on detecting early-stage lung cancer. It's recommended for annual screening with low-dose CT because it's beneficial for the early detection of lung cancer.

The impact of annual screening with low-dose CT is a 20% decrease in lung cancer mortality and a 7% decrease in all-cause mortality. However, only 6.5% of the U.S. eligible population received their annual screening in 2020. In addition, there's an increasing number of key biomarkers that guide treatment decisions for patients with non-small cell lung cancer. There's more than 25 biomarker-driven targeted therapies and immunotherapies that are now FDA approved for non-small cell lung cancer. The pace at which these are being discovered are increasing, with five key biomarkers identified since 2019 that are associated with these targeted therapies.

This graphic on the right side of the panel shows the proportion of biomarkers with a high of EGFR mutation positive at 21% and a low of NTRK rearrangements at 1%. Up to 69% of patients with advanced non-small cell lung cancer have at least one actionable alteration that can affect the impact of the treatment. In addition, patients with non-small cell lung cancer who have the oncogenic driver or the biomarker present and are treated with targeted therapy live longer. So the two year relative survival rates increases from 2001 to 2014, going from 26%, surviving two years in men to 35% in 2014. And for women, it goes from 35 to 44% from 2001 to 2014, showing survival improvements and are likely driven by targeted therapies. The panel shows the outcome of patients who have a targetable lesion identified and are treated with a targeted therapy. Here are the patients who have a target and get treated with targeted therapy have a median survival of 31.8 months. The non-targeted cytotoxic therapy, it's 12.7 months, with those who have observation only it's 5.1 months.

Despite these advancements, some challenges remain to be solved; there’s challenges in diagnosis of people being aware of the symptoms. The evolving patient profile with more never smokers and more former smokers. The adherence to the screening guidelines of patients getting annual low-dose CT scans and the screening guidelines do not include people without a history of smoking, for instance, people with family histories, and a risk assessment. The challenges in the biomarker testing are long turnaround times, where

people don't feel they have time to wait for the results. The obtaining adequate tissue quality and quantity to be able to do a next generation sequencing panel or broad molecular testing.

The lack of standardized testing processes, i.e. an efficient and timely sample collection, ordering the tests, and testing, and getting the results. The next generation sequencing testing rates and the ability of next generation results interpretation that allows one to choose the appropriate treatments. The challenges of both diagnosis and biomarker testing are that health disparities in vulnerable populations make it less likely. The lack of support resources to carry out the testing and get the diagnosis, and the potential financial burden involved in the diagnosis and biomarker testing.

The key points from this are the majority of lung cancers are diagnosed in people who have quit smoking. The cases of lung cancer are increasing in young women and individuals without a smoking history. An inadequate number of patients who meet the criteria for CT screening are getting chest CT scans. Comprehensive biomarker testing, including next generation sequencing, is the most effective method for identifying biomarkers in non-small cell lung cancer and matching the patients with appropriate targeted therapies. And despite good progress, challenges and disparities in screening, diagnosis and biomarker testing exist, which are impacting vulnerable populations and women with non-small cell lung cancer. Thank you.

Dr Johnson:
Thank you. I want to call on some of my colleagues to make some comments about the evolving landscape of non-small cell lung cancer. First, I'd like to call on Dr. Feller-Kopman and address some issues around screening. So I'm going to ask you a couple of questions about this. The first is that you want to talk about the updated screening guidelines and how they offer the opportunity to get an early diagnosis on more of our patients.

Dr Feller Kopman:
All right, so as we all know, the guidelines have been recently updated to expand the age group. We now have the ability to screen patients from 50 to 80, who smoked a pack a day for 20 pack years, and that’s certainly going to increase the number of patients at risk of lung cancer who get screened. One of the big issues is that, as we've discussed, unlike breast cancer, cervical cancer or colon cancer, where about 70 to 80% of eligible patients are getting screened for those cancers, only about 6% of patients with lung cancer getting screened. And that's a huge issue, and there are a lot of barriers to that. Some of it has to do with physicians and the amount of time that we have to make these conversations, which take a lot of time and insight, and it's really a shared decision-making process.

Others are barriers to those who are at risk. There's a nice study by George [inaudible] Group suggesting that patients who are at the highest risk of lung cancer tend to have less access to primary care. They can't identify primary care physicians. They tend to be more nihilistic about it. So there's a lot of work to do, both in terms of education of our patients, education of our colleagues and expanding access to lung cancer screening in general.

Dr Johnson:
One of the things that comes up and especially if the screenings being done in the primary care setting, you want to talk about your personal experience with how you manage the incidental pulmonary nodules and some clues that can get to other members of our audience about how you handle this once it's detected?

Dr Feller Kopman:
Yeah, so that's a great question. So in addition to screen-detected nodules, this is really almost an epidemic of these incidental detected lung nodules. Patient falls off a ladder, goes to the emergency room, get a CAT scan and they get a lung nodule. Even though they may not be in that screened high quote unquote “high-risk” population, there are a percentage of those that will turn into cancer, and it's really important to make sure that those aren't just written off as lung cancer and a female non-smoker. We're seeing increased incidence of cancer in female non-smokers, as well as traditionally underserved populations such as African Americans, especially women, Hispanic, Asian patients. So those nodules need to be followed and should be followed as per current guidelines. You can't just assume those are non-malignant nodules.

Dr Johnson:
On to Dr. Duma, and one of the things that happened this year in the CA Cancer Journal population and cancer statistics in 2022, it went so that there's more women being diagnosed with lung cancer now than men, which is quite a change from when I first got into business, number one. And then number two is that we're seeing a greater number of women than men, particularly those who are relatively young. So do you want to comment on the evolving patient demographics and talk about the diagnostic steps that one takes?

Dr Duma:
Thank you, Dr. Johnson, what you, you know, what you said is something that has been described and continues to be seen not only in the United States but all across the globe. Our colleagues from Europe or Asia, have been seeing that younger women are now the

number one patient in that the incidence continues to go up despite other groups going down. And what these means is we need to change and eliminate the perception that lung cancer is a disease of elderly white men because these stereotypes and sets up delays in diagnosis of patients. So one recent study shows that young women actually are facing twice to three times delays in diagnosis. And if you're a woman of color, that can be longer because they are not seen as a traditional patient with lung cancer.

So let's eliminate all those stereotypes and realize there are more women dying of lung cancer than breast, colorectal, uterine, and ovarian combined. And see our patient with a blank sheet right? Instead of how we have been taught to associate diseases to certain groups. And what is important about this is that younger women live longer. So now lung cancer survivorship is shifting to a different face. And I'm glad to be with these great experts to see how we continue to improve the care of all patients with lung cancer.

Dr Johnson:
Well, let's turn to Doctor Wistuba, and you want to talk about, especially over the last I guess it's 18 years now, about the rate at which they're discovering biomarkers in non-small cell lung cancer that are determining treatment and how best to identify them and how it is impacting our patients.

Dr Wistuba:
Thank you, Bruce. I think that when we look at metastatic non-small cell lung cancer, particularly the non-squamous histology, most of them being adenocarcinoma, this varies in different parts of the world. But in western countries, we can say safely that about 60% of these patients go through biomarker testing could potentially benefit from actionable findings. (It) even is higher in some other part of the world, like Eastern Asia. But these are required, of course, to have a comprehensive panel of molecular testing, because you know, all the mutations, translocation, increased copy number that have been discovered. Thank you.

Dr Johnson:
OK. And Dr. Kurzrock, do you want to talk about the impact that targeted therapies and immunotherapies are having in our patients with lung cancer?

Dr Kurzrock:
Yes, thank you. I think lung cancer a decade ago was the poster child for a lethal malignancy where we had very poor therapy. And now it's becoming the poster child for still a lethal malignancy, but a malignancy in which targeted therapy, often driven by genomics, as well as immunotherapy, really can make a difference to the outcome of these patients. So I think what we've seen is literally a transformation in lung cancer, and we are just getting a glimpse of the road here. I think this will continue to accelerate. And this is important for lung cancer patients. But in addition, I believe that the lessons learned in lung cancer are applicable to many other solid tumors going from a cancer that we literally felt we had very few ways to treat to now a cancer in which we have an abundance of genomic markers and which we can address in the clinic.

Chapter 2: Reducing Diagnostic Barriers

Dr Duma:
Hello, everyone, my name is Dr. Narjust Duma, I'm the Associate Director of Cancer Care Equity at Dana-Farber and a thoracic medical oncologist. We're going to be talking about reducing diagnostic barriers to have inclusive testing for all patients with lung cancer. Disparities in diagnosis exist and they are particularly for certain groups of patients. And these are vulnerable populations. Black patients, Hispanic, Asian, Native American, members of the LGTBQ+ community and women. Black individuals in the United States are 16% less likely to be diagnosed with early-stage lung cancer. This also applies to woman; women can experience delays at diagnosis compared to their male counterparts. In addition, patients without a smoking history often face barriers to diagnosis, as they're not seen as patients at risk for lung cancer.

I have an example, a patient, a 45-year-old Hispanic female, with very limited smoking history. She presented to the E.R., with chest pain and diarrhoea, but she experienced significant weeks of delay for her diagnosis, a mammogram, several COVID-19 tests and other causes before she was able to be diagnosed. Unfortunately, at the time of diagnosis, she already have metastatic disease. And you can see that in the CT scan with multiple pulmonary nodules. Unfortunately, her story is way too common in my clinic. Many women with limited or no smoking history experience delays in diagnosis, or other diagnoses are attributed to them like anxiety, asthma, or sarcoidosis.

Including the complex and lengthy diagnostic process, many patients may require several biopsies, several visits to the doctor. Resources change depending on the setting, academic versus community settings. 85% of patients in the United States are diagnosed and the community centers, which they have limited resources compared to centers like mine. And additionally unconscious bias for providers, physicians, nurse practitioners, physician assistants and which they may don't see lung cancer as a disease of women or other populations. Access to an annual screening is important but is not equal in the United States. We have two large studies that have

shown that annual screening for lung cancer saves lives. Unfortunately, certain groups like Black, Asian, Hispanic, women are less likely to receive a screening education, or screening period. We need to make sure that patients receive education and appropriate screening on time. There's also a low perception of risk among patients that are never smokers or women. Often healthcare providers don't see lung cancer as a disease for these patients, delaying diagnosis. Only 6% of U.S. adults are aware that lung cancer is the primary cause of cancer death in women in the United States.

The disease is associated with stigma, so that delays diagnosis. Health care providers like myself sometimes contribute to the stigma, and patients may feel ashamed if they have a smoking history to seek care. Our complex healthcare system is a major reason for delays in diagnosis for lung cancer, and this is associated with social determinants of health. Access to your cancer center can be 200 miles away. You may not feel comfortable talking about medical issues if English is not your first language. All of that contributes to delays in the diagnosis of lung cancer, and they should be addressed at the time of diagnosis, and they should be addressed as the patients continue their journey.

Effective communication is vital for addressing diagnostic disparities. We need to get away from all of these complex words that we all learn in medical school. Yes, we know that you are smart, but let's use language that our patients understand. Also, let's break down information. Don't provide all the information at once, it can produce information overload. Work as a team with advanced practice professionals and navigators. And it's important that we see lung cancer as a disease that affects everyone. The only requirement for having lung cancer is having a pair of lungs, regardless of sex, race, and regardless of smoking exposure. These are key points. Health disparities in non-small cell lung cancer are present, affects our patients' quality of life, and our patients' survival.

There are significant delays and diagnosis of lung cancer for women, patients who never smoke, and other vulnerable populations. Access to screening, access to social and economic factors should be essential when providing diagnostics workup and when following up with patients. Effective communication is also vital.–

Dr Duma:
Thank you, everyone, for being with us as we continue to discuss barriers for diagnostic making, the diagnosis of lung cancer as well as biomarkers barriers, barriers go from the moment of screening all the way until the patient receives treatment. We're going to continue this very fruitful discussion. We have few questions to our panelists. So Dr. Wistuba, in your opinion, what are the top three barriers for diagnostic testing in non-small cell lung cancer today?

Dr Wistuba:
Thank you for the question. As I will discuss briefly in the presentation, there are several barriers to have a broad, comprehensive molecular testing in non-small cell lung cancer. But the top three, in my opinion, are lack of a universal algorithm for biomarker testing in this disease. That's number one. The second, I think that is the variable insurance coverage, which includes the requirement of preauthorization in many instances. And the third one is the challenge of having enough material for molecular testing. Diagnostic biopsies, some of them in form of cytology specimens fine needle aspirations, are very limited, and many times, they are sometimes completely used in the diagnostic workup of the case, and there's not enough material left for molecular testing. So, keeping molecular testing in mind from the beginning in the diagnostic process, I think that's very important to at least improve on this barrier. Thank you.

Dr Duma:
Thank you. And as appears, the issue is still the issue. Dr. Johnson, do you want to add something?

Dr Johnson:
The comment I would have and one of the things we polled our providers here and the issue the doctor Wistuba brought up is about the concern about insurance coverage. In most of our cases, there's more of a concern than there is in reality about the companies covering it. Indeed, most of them cover it, and certainly it's increasingly so the one thing that is a bit of a challenge is that the coverage will vary from one insurer to another. Most of them cover it, but if you don't, and you don't necessarily know that ahead of time.

Dr Duma:
And that's true, and that's a concern not only to not only to the providers, but also to patients, you know, out-of-pocket expenses continue to grow and now with testing happened to all phases of lung cancer, you never know which way you're going to go. Many studies have shown that multidisciplinary care in lung cancer has many benefits, included for patients to get adequate care, to get unbiased care. So, Dr. Feller-Kopman, how can we improve multidisciplinary communication to ensure timely diagnosis for lung cancer? Over time, we have more ways to communicate, but in my personal opinion, has become more challenging as the email, text, page, phone call. What are your recommendations?

Dr Feller-Kopman:
Yeah, that's a great question. I sort of liken that question to how we encourage our patients to quit smoking or do anything. There's the

pre-contemplated phase, that contemplated phase, that determination phase, and the action phase. So the first thing is understanding that you want to increase your multidisciplinary communication for this and then you got to look at your specific practice pattern. How are you going to do this? Are you going to do a virtual tumor board where you get the pulmonologist, thoracic surgeons, interventional radiologists, medical and radiation oncology, pathology, and radiology all in a room or on a webinar together? Are you going to come up with pathways that say if a patient has a peripheral lung nodule but it's actually a sizable peripheral lung nodule, maybe they should go for bronchoscopy with EBUS staging first as opposed to a transthoracic needle biopsy?

So I think you've got to really be a little introspective and see what your practice pattern is like, what your local expertise is like. Do you have an outstanding interventional radiologist or interventional pulmonologist or both? And then take the action of making sure that you work together to communicate.

Dr Duma:
I'm a big proponent of phone calls. I may be a little bit on the negative, but training at Mayo Clinic, I really like the phone call as quick, instead of just messages back and forth, but you need to find the style that works for your team. For sure.

Data has shown that unfortunately disparities in diagnosis of lung cancer not only by race but also by gender, location to the patient, or rural area, for example. Dr. Johnson, can you share your views on how we can reduce these disparities in the diagnosis of lung cancer?

Dr Johnson:
Well, number one is, you know, access to a health care system and that can take many different venues. So, for instance, you know, people who are insured are more likely to be able to access the medical care system. The second is that we vary a lot geographically by the support for people who are poor, underserved, both in terms of ethnic group as well as income disparities. One of the things that's a bit different about lung cancer than some of the other commonly screened cancers is that, you know, for instance, with breast cancer and with colon cancer, both those track with higher socioeconomic status. And one of the things for lung cancer, that it's higher in people with less education, and it's also higher in people who have lower incomes. So it becomes a group that it can be a challenge to be able to access and effectively utilize the medical system. Some of the things that have helped is making certain that diagnostic procedures are available beyond typical work hours; number one. Number two, is that the other part that's been helping for people getting screened is having navigators to make certain that people are able to show up and get their screens on a regular basis.

Dr Duma:
Thank you, Dr. Johnson. And navigation needs to be tailored to the needs of each patient as the navigation needs in all of US are quite different for us here in Boston. We continue to talk about systemic change, but I'm a big proponent of individual work and individual responsibility. So Dr. Kurzrock what can health care providers do at the individual level to reduce these disparities in lung cancer?

Dr Kurzrock:
So I think there's a couple, there's a few things that physicians can do. And one you alluded to earlier is to recognize that lung cancer is not a stereotype of an older white person that has smoked for a long time, but increasingly is occurring in younger people, including women and that with appropriate symptoms, the patient needs to be fully worked up. I also think that there are some systemic things that can be done once lung cancer is diagnosed.

For instance, since almost 70% of lung cancers now have a targetable alteration, it might be time to think about reflex next-generation sequencing, just as part of just like we would look at the pathology under the microscope and do certain stains, perhaps we should at this point be doing next generation sequencing as a reflex.

Dr Duma:
Thank you, doctor. And as we learn from another, from our colleagues, I think we need to see lung cancer like we see breast cancer. It is hard to report a breast cancer just as it is without hormonal status. So we should adopt the same culture in lung cancer, in which when a fellow presents a patient with lung adenocarcinoma, it still feels incomplete. Give me more and we need to get more. So thank you all for your input.

Chapter 3: Test to See the Complete Treatment Picture

Dr Wistuba:
Hello, everyone. I'm Ignacio Wistuba, Head ad interim of Division of Pathology and Laboratory Medicine and Chair of the Department of Translational Molecular Pathology at MD Anderson Cancer Center. I will discuss briefly the challenges and opportunities for broad molecular profiling in lung cancer.

The lung cancer pathology community has developed an algorithm for the rational use of tissue and cytology specimen for the pathology diagnostics of the disease and to preserve samples for biomarker testing. This algorithm includes a limited use of immunochemistry to

properly identify the subtype of non-small cell lung cancer. The key biomarkers in this disease recommended for testing are least here, including the assessment of key mutations and gene fusions affecting several genes, in addition to the immunohistochemical assessment of expression of PD-L1. Broad molecular profiling, including next generation of sequencing, or NGS, is the most effective method for identifying key biomarkers in non-small cell lung cancer, offering substantial benefits over single gene testing. Importantly, broad molecular profiling with NGS can identify all four types of genomic alterations in lung cancer: point mutations; small insertions and deletions; amplifications; and gene rearrangements. Also, NGS provides most effective use of tissue and can be performed in routine small, Formalin-Fixed Paraffin-Embedded tissue, and cytology specimens, and blood samples in the form of biopsy. NGS offers more options for patient treatment and the use of upfront NGS testing in patients with metastatic non-small cell lung cancer has been associated with substantial cost saving and shorter time to test results for both CMS and commercial payers.

How are we doing with regard to NGS testing in the United States? Testing with NGS is at an all-time high and has increased dramatically over the last few years. However, still 40% of metastatic non-small cell lung cancer patients are still not being tested with NGS in this country.

Despite the benefit of NGS testing that I mentioned before, barriers to its use exist, some are logistic and some are technical. On the logistic barriers, we should consider the infrastructural differences between academic and community setting, which can also pose challenges with regard to molecular testing in this disease. Academic centers tend to perform molecular testing in-house with better communication between health care providers. For community settings are more likely to utilize commercial laboratories and send out the test, the material. There is variable insurance coverage and need for pre-authorization among insurance companies and also the system of some companion diagnostic labels can deter health care providers from ordering NGS panels. On the technical barriers, we need to consider the turnaround time, since the usual ten business days to get results on a comprehensive NGS panel may represent an issue for certain patients. There are challenges in tumour sample acquisition, since for pathologists limited tissue availability from small biopsy and cytology specimen is the main barrier to conducting broad molecular profiling. And there are challenges associated to interpretation of the results for healthcare providers, since the report can be difficult to interpret.

Unfortunately, there are still significant disparities in NGS testing, with vulnerable and socioeconomically disadvantaged patients less likely to receive testing. It has been shown that Black individuals are significantly less likely to be tested than White individuals.

As key points already explained, there is consensus that NGS is the most effective method for identification of key biomarkers and enable treatment decisions for decision making and the standard of care in clinical trials. Also, NGS testing rates are rising. Some challenges and barriers to adoption remain. So what is needed to increase adoption and utilization of NGS? Here we have five points to consider. We need to increase the familiarity and adherence to guidelines that endorse testing methodologies and algorithms, improve infrastructure and availability of expanded NGS testing, address reimbursement barriers develop metrics to assess turnaround time and utilization of biomarkers testing, and increase the adoption of reflex testing for NGS testing. And thank you for your attention.

Dr Wistuba:
Welcome back to our panel discussion, and now we're going to have a brief conversation about how we can actually overcome the barriers for biomarker testing in lung cancer. So to start the conversation, I would like to ask Dr. Johnson to share his view on how we further increase the adoption and utilization of NGS in the United States.

Dr Johnson:
But one of the things that you know, as a practicing oncologist and it's happened this week is that, you know, I see a lot of people that have been diagnosed a few days, sometimes a couple of weeks before I see them and it's extremely rare that they would have next generation sequencing panels ordered before I see them. And the typical amount of time that we wait to get the results is about two weeks. And that's kind of the limit about how long oncologists want to wait before they choose their treatments. It's right at the border. Actually, Dr. Wistuba and I are on something called the National Lung Cancer Roundtable, and that which is organized by the American Cancer Society, and that's taking it upon itself to work with primary care physicians, interventional radiologists, interventional pulmonary physicians, and surgeons to try to make certain that once a person has a diagnosis of lung cancer is that the next generation sequencing panels are ordered earlier on in the course and hopefully before they end up getting seen by the oncologists because that's such an important piece, as Dr. Duma mentioned, in our managing the patients.

Dr Wistuba:
Thank you. Thank you, Dr. Johnson. It takes a village, right, because it has to be a multidisciplinary approach and talking about, you know, the approach that is needed to overcome some of the barriers, one of the issues is actually the complexity of the reporting on some of these next generation of sequencing panel. So I'd like to ask Dr Kurzrock to share her views and perhaps outline some available resources on how we can make it easier for our colleagues to interpret NGS test results.

Dr Kurzrock:

I think you're asking a very important question, and I think we have room for improvement here. So the first thing is that many commercially available panels do have a pretty good interpretation guide and similarly for many lab-based panels. But I think it's still confusing, and one can go to OncoKB™ and see the relevance of certain alterations. But as I mentioned, I strongly believe that there's room for improvement. And one thought might be to have some sort of online tool that is basically universally available on the internet and is continuously updated, where physicians and other health care personnel and patients can go and just click in to what they see on the panel and get information that is easily readable even by the layperson.

Dr Wistuba:
Thank you. And many institutions have these tumor boards right, or genomics tumor boards that but they're not accessible to everyone, right? If you work in a community setting, sometimes it's hard to access to those, so that's a very good suggestion. Thank you very much. So then to talk about the processes that are required to facilitate routine use of a broader molecular profiling including NGS, I would like to ask Dr. Feller-Kopman to share his views about how we can actually improve on these processes.

Dr Feller-Kopman:
Yes, thank you, it's a great question. I think as with a lot of this, it really depends on communication. So as Dr. Johnson pointed out, he can't really make a treatment decision until all this information is back. And if you can think about it from the patient's perspective, if they're coming in, they're seeing their primary care doctor, then they eventually go to see a pulmonologist. A pulmonologist decides to do a bronchoscopy, the bronchoscopy is done several days later, the pathology results come back several days later showing cancer and prompting oncology consultation, it is still going to take several more weeks, if that is when you're ordering your markers. So what we've done at the several institutions that I've worked with is talk with pathology inside of pathology, such that once the biopsy is obtained and it shows a lung cancer that's reflex testing for broad molecular sequencing, including NGS. And even at the time of this high suspicion, if you have onsite site of pathology, for example, you could certainly make sure that that is ordered at the time of the biopsy, but also perhaps the liquid biopsy at that same time.

Dr Wistuba:
Thank you very much. We have heard over and over reflex testing, right? So one potential good solution to some of these barriers. And then a very important topic and we have discussed this already, but I would like to get from Dr. Duma her opinion on, given the disparities in biomarker testing, how we increase the adoption and utilization of NGS in these vulnerable populations?

Dr Duma:
I think there are still things we can do. One is accountability. We need to make people accountable for doing an incomplete job. Not have biomarker testing with patients with non-squamous, non-small cell lung cancer is an incomplete job. I told my patients that sometimes it can be a slightly provoking to wait for results for weeks; I use a wedding dress analogy, the majority of my patients are women, and which is say will you pick your wedding dress right away? We need to find out what fits for you and how we're going to do that is by doing biomarker testing. And I can tell you that even this morning in clinic, one of my patients mentioned the wedding dress analogy just like, OK, we're waiting for the wedding dresses. Yes, we're waiting for the biomarker testing, so accountability is important. We need you to understand that community providers have many limitations. They're seeing many patients on many diseases. So making accountable not only the provider, but the institution.

And finally, reimbursement. You remember when we started doing the DVT prophylaxis in the hospital? Now, most hospitals would not get reimbursement, we get limitations of reimbursement if that person doesn't have a DVT prophylaxis in the note. So what can we do that for lung cancer and which reimbursement will be affected if the patient doesn't have biomarker testing, right? And where money is, action follows, as we've seen in our healthcare system. So that's my two recommendations: accountability and reimbursement.

Dr Wistuba:
Thank you very much Dr Duma, great insight and I'll remember the wedding dress analogy.

Chapter 4: Q&A

Dr Wistuba:
So now we are going to move to a question-and-answer section. I'm going to turn this over to Dr. Kurzrock who is going to lead the conversation. Thank you very much!

Dr Kurzrock:
Thank you and for the very nice discussion. So one of the first questions I want to ask is or what question that I just see has come in. What can we do at the community level to increase screening rates to ensure that all patients are considered? And perhaps Dr. Duma could help us with that answer.

Dr Duma:

So during my time in the mid-West before the pandemic, I had the opportunity to visit several private practices. In order to have an intervention, you need to understand how these practices work, so we can now try to, we continue to try to find the solutions that work for academic medicine, to apply to community practice, and that is not true. So it would be is good to sit down and listen to our community providers who see 80% of the patients with the limitations they have. Something that really helps is having that extra person to help this provider. It can be a designated molecular person, a designated pathology person and that kind off-lift their responsibility, not fully, or their processing. Where it is the tissue, let's get a tissue test and all of that's logistics because community providers are seeing 20 patients a day, right? So are we adding more responsibilities, so that help and mostly listening to our community providers and what works for them.

Dr Kurzrock:
And so I want to expand a little bit on that because I personally find this an important question. Young people are getting cancer more often, and they have delayed diagnosis, especially young women. But how do you balance not working everybody up unnecessarily versus not missing the relevant cancers? Do you want to try and address that Dr. Duma?

Dr Duma:
So working everybody up, like all patients with lung cancer or young patients?

Dr Kurzrock:
Young patients that come in with symptoms, how do you balance that, not doing excessive numbers of work-ups versus not missing patients? Do you have some suggestions there?

Dr Duma:
I think is when we try to when we get out of the algorithms, it becomes too creative, we start doing things that are unnecessary. Right? And we forget to listen to patients. I think a lot of my patients, younger patients, their main complaint is that they complain about a cough and then their the provider just listen or their complain and focus on that complaint. So that delays diagnosis. And another thing I have to add is that COVID had brought this you extra layer because I have a patient that got COVID test 8 times for a cough. So that's an extra thing. So I think following algorithms listen to our patients concerned and removing the stereotype that all woman with shortness of breath have anxiety; like let's just let's work this out. This is an issue that's affecting your quality of life would be my recommendation.

Dr Kurzrock:
Thank you. Dr. Wistuba, I was hoping that you could address another question that we haven't touched on too much: liquid biopsy. What do you think about liquid biopsy and especially at diagnosis and by liquid biopsy, obviously mean blood tests for next-generation sequencing?

Dr Wistuba:
Thank you for the question. I mean, cell-free DNA testing for lung cancer, molecular normality is an alternative, or is an additional option, and it brings an opportunity for testing, particularly when the diagnostic tissue or cells inform a cytology specimen is not enough for a comprehensive molecular testing because similar platform with kind of almost equivalent level of sensitivity can identify the same molecular normalities in the blood that in the tissue. However, sensitivity is not as good as tissue, so tissue's preferred by this tissue is not available or is too risky to get another biopsy from the patient, I think that cell-free DNA is a great alternative and in many places, and it has some issues with reimbursement. Actually, they run them in parallel. Biopsy and tissue, because the liquid biopsy results come faster than the tissue.

Dr Kurzrock:
Thank you. I agree with you and I personally run the blood and the tissues simultaneously in order to try and ensure that a patient gets an answer that is relatively expeditious. Dr. Johnson, what are your thoughts about repeat tissue biopsy at relapse?

Dr Johnson:
There are times when it's very helpful. You know, one of the things that we have we typically do is you know biopsy people at the time of progression, and it's how we end up defining mechanisms of resistance. Some of them are important scientifically, you know, for instance, defining the mechanism of resistance. Other ones are clinically actionable. So, you know, in our own field of lung cancer, one of the things that can change how you manage this is find out if they have MET amplifications, one of the first resistance than what the second resistance mechanism discovered with the class of EGFR TKIs and the MET inhibitors combined with the EGFR inhibitors extend the person, the length of time a person could be treated with targeted treatments. It's a bit more challenging to get it covered by the third-party payers. for this. My own, I think in terms of the relative importance, I think getting the initial next generation sequencing panel is very critically important and would focus the efforts there. The number of times you can apply and make treatment decisions based on a repeat biopsy is relatively small. So I think here and we spent most of our time focusing on getting the initial next generation sequencing panel, I think that's appropriate.

Dr Kurzrock:
Well, thank you for that nice answer. There is a question how will targeted therapies impact patients? And I'm just going to very quickly try to address that important question. Targeted therapies, I think, are transforming lung cancer. But the critical issue is that you have to know which patient gets the targeted therapy and that requires having a comprehensive next-generation sequencing panel.

Dr Feller-Kopman:
Well, thanks everybody for participating in this webinar.

Announcer:
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